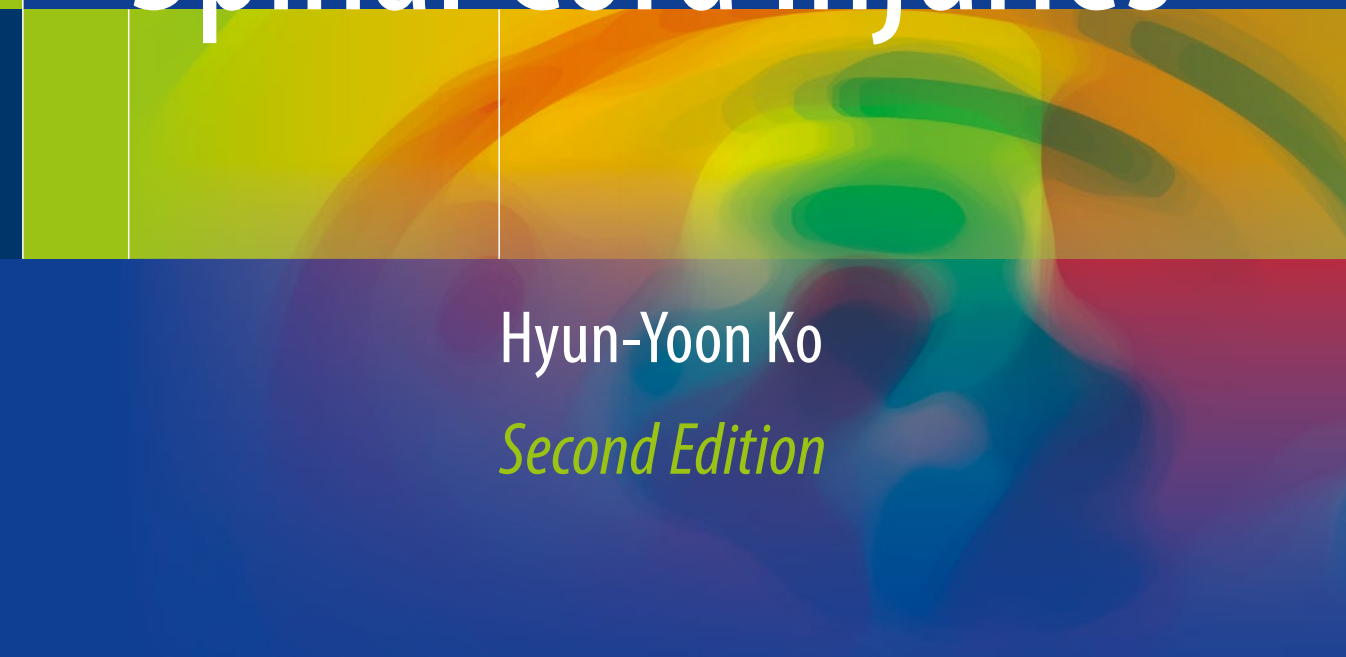
Management and Rehabilitation of Spinal Cord Injuries



Hyun-Yoon Ko

Second Edition

Springer

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Always grateful to my parents
To my beloved wife Insun

Preface to the First Edition

Spinal cord injuries represent a devastating challenge for injured people, their loved ones, and their friends, even for the healthcare and society in general. All healthcare professionals and communities concerned should address these problems through concerted efforts. The science of spinal cord injuries has made remarkable progress over the past 50–60 years, but many medical issues remain unresolved. The medical problems often require careful care for the rest of their lives. From this point of view, we cannot help but be affected by medical limitations as we have been treating patients with spinal cord injuries for a long time. It would be better, therefore, for God to place the segments of the bladder, bowel, and sex in the first or second cervical spinal cord.

I believe that physicians involved in the treatment of spinal cord injuries and those involved in spinal cord medicine should have a responsibility to continue to understand the lives of patients with spinal cord injuries. In order to understand and treat those patients, it is necessary to define the theoretical framework of spinal cord medicine. The purpose of this book is to provide a broad range of knowledge about spinal cord injuries and to better understand spinal cord medicine for a variety of clinicians specializing in spinal cord medicine, including rehabilitation physicians.

Spinal cord medicine has developed amazingly. The development of spinal cord medicine as a science has contributed significantly to extending the life expectancy of patients with spinal cord injuries. Nevertheless, the life expectancy of the patients has not increased in the last two decades. With increasing life expectancy of the general population, the gap between the patients with spinal cord injuries and the general population increases. It is also doubtful if the quality of life has also improved, that is, to live well in relation to a longer life. Even if patients with spinal cord injuries receive appropriate medical intervention and rehabilitation treatment as they wish, it is doubtful that they will function as self-reliant contributors to home and society with equal opportunities for education and employment.

With advances in general medicine, the management and treatment of spinal cord injuries have improved considerably, and advances in technology have contributed significantly to reducing disability in patients with spinal cord injuries, but difficult to satisfy functional aspects, feasibility, and compliance. Scientists around the world have done tremendous research on spinal cord injuries, and many good books have already been published which have already provided enough knowledge. This book is intended to provide concise

and practical information to physicians and medical practitioners who are dealing with spinal cord injury patients. This book presents the functional anatomy of spinal cord injury; evaluation, management, and rehabilitation of somatic and autonomic dysfunctions, including impairment in the bladder, bowel, sexual, cardiovascular, and respiratory functions. In addition, psychological aspects of spinal cord injuries including psychological effects and adaptation processes, intervention in maladaptive emotions, and family dynamics are discussed. It is not intended to fill this book with content that offers a deeper and new knowledge than the great works of the past. I wish the book can provide a good route to learn knowledge and general basics of spinal cord medicine. I hope this book will become a favorite book for physicians involved in treating patients with spinal cord injuries. At the end of each chapter, appropriate references and reference books are available to provide more professional and detailed information. As an author, I would be pleased if this book can help to understand and expose common knowledge of spinal cord medicine for neurosurgery, orthopedics, urology, and neurology, as well as for various medical specialists and rehabilitation physicians.

Professor Ditunno (Philadelphia, USA) is an important teacher to me who has taught the most important lessons in learning and teaching, and his passion and humanity will never be forgotten. I am fortunate to have the opportunity to learn from the leading spinal cord injury consultants, Mr. El Masri (Oswestry, UK), Mr. McClelland (Sheffield, UK), and Mr. Soni (Southport, UK).

Yangsan, Korea (Republic of) Hyun-Yoon Ko
January 2019

Preface to the Second Edition

With the publication of the first edition of this book, it was hoped that it would serve as a practical and reference book for neurologists, neurosurgeons, orthopedic surgeons, urologist, internist, physical therapists, and other rehabilitation professionals, as well as physiatrists, involved in spinal cord medicine. I wanted to update all of the chapters as soon as possible after the publication of the first edition of this book and make the content more fruitful. I have also written eight new chapters, such as Sleep Disorder, Upper Extremity Intervention, Emergency in Chronic Spinal Cord Injuries, and some chapters have been separated or merged to make the content more concise. It is my hope that the second edition of "Management and Rehabilitation of Spinal Cord Injuries" will be a better reference, easy-to-read, and easy-to-access knowledge in spinal cord medicine for all professionals treating people with spinal cord injuries and practicing physicians who are trained in spinal cord medicine.

Yangsan, Korea (Republic of) Hyun-Yoon Ko
December 2021

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1 Introduction of Spinal Cord Injuries

Spinal cord injuries affect most parts of the body as well as the somatic and autonomic nervous systems. Spinal cord injuries result in disruption of normal sensory, motor, or autonomic functions and ultimately affect the physical, psychological, and social well-being of the patient. Damage to the autonomic nervous system causes respiratory and cardiac dysfunction, temperature regulation disorders, insulin secretion, and many associated metabolic disorders. The incidence of secondary complications from immobilization is very high. Immobilization due to voluntary motor dysfunction leads to pressure injuries and coughing impairments (Abrams and Ganguly 2015; Bauman et al. 2012). Spinal cord injuries involve more than just the direct injury to the spinal cord itself. The injury results in a variety of disabilities and obstacles, ranging from physical limitations to social embarrassment.

After World War II, there were tremendous developments in the treatment of spinal cord injuries. The incidence of medical complications after spinal cord injuries has decreased and life expectancy after spinal cord injuries has increased. However, the increase in life expectancy of people with spinal cord injuries has slowed and reached a plateau since the mid-1980s (Middleton et al. 2012; Shavelle et al. 2015), and the life expectancy of the general population has increased relatively, causing the left expectancy gap between people with spinal cord injuries and the general population to widen. As the elderly population with spinal cord injuries increases, the understanding of chronic metabolic diseases in the care of people with spinal cord injuries is emphasized.

Physicians involved in the management of patients with spinal cord injuries should have a basic understanding of the management of medical problems in the acute and subacute phases and should understand the physical changes and complications in the chronic phase, as well as the age-related effects of spinal cord injury. This chapter provides a brief history of spinal cord injuries and describes the characteristics of physiological changes and complications. It also provides a brief review of the changes and pathological conditions in each part of the body due to spinal cord injury.

1.1 Brief Historical Review of Spinal Cord Injuries

In the Balkan War of 1912–1913, some 95% of patients with spinal cord injuries died within a few weeks and in World War II, the mortality rate was still about 80% (Sutton 1973). There has been no hope for spinal cord injury in most of human history until a little gleam in the nineteenth century. With advances in surgery, anesthesia, antibiotics, medical science, and

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technology, we are able to view spinal cord injuries as one of many human disease states that can be categorized and treated.

The spinal cord injury has been known since antiquity. Almost all general discussions of spinal cord injuries commence by quoting from the Edwin Smith Papyrus of the Pyramid Age, about 3000–2500 BC. Physicians in ancient Egyptian have considered spinal cord injuries as "an ailment not to be treated" (Hughes 1988; van Middendorp et al. 2010). The earliest evidence of two cases of spinal injuries around 2500 BC is found in an ancient Egyptian surgical papyrus (*The Edwin Smith Surgical Papyrus*) (Fig. 1.1) attributed to Imhotep (ancient Egyptian chancellor and physician) which was bought by the Egyptologist Edwin Smith from a dealer in Luxor or Thebes in 1862 (Ganz 2014; Hughes 1988; Lifshutz and Colohan 2004). It was first translated from the hieratic by the famous Egyptologist, Dr. J. H. Breasted and published in 1930 under the patronage of the New York Historical Society (Breasted 1930). This included descriptions of 48 cases of war injury that provide insight into Egyptian medicine of about 3000–2500 BC (Lifshutz and Colohan 2004). Six cases of spine injuries and two cases of the spinal cord injuries are included. The cases of spinal cord injury showed devastating injuries with the futile prognosis (Brawanski 2012). The two cases of

Fig. 1.1 (**a**) Egyptian papyrus roll. The papyrus was bought by Edwin Smith from a dealer in Luxor or Thebes in January 1892. Edwin Smith seems swiftly to have recognized the medical nature and importance of the document. After his death in 1906, the papyrus was donated to "the New-York Historical Society" by his daughter. The roll has a height of from 32.5 to 33 cm and is made of 12 sheets. The papyrus is now unrolled and mounted between sheets of glass. It has a length of 4.68 m and, as at least a column of writing is lost from the beginning, it originally measured over 5 m. (**b**) Plate X and XI of the Edwin Smith papyrus, including the five cervical spinal injury cases in hieratic script. From Hughes (1988) and van Middendorp (2010), with permission

the spinal cord injuries were presented in "Case 31. Dislocation of a cervical vertebra" and "Case 33. A crushed cervical vertebra" (Breasted 1930; Howorth and Petrie 1964). The Egyptian surgeons distinguished between patients with open wounds or sprains of the cervical vertebrae that did not involve the spinal cord, and patients with spinal dislocations and fractures that had lost power and sensation in all four limbs. They described that the patient would have priapism and incontinence of urine and semen (Silver 2003).

Homer's Odyssey describes Elpenor, a character whose story is said to represent a serious and fatal spinal cord injury due to falling from the roof. References to spinal cord injury and axial traction can be found in Indian civilization around 1800 BC (Lifshutz and Colohan 2004). After the decline of the Egyptian Empire, the following Greeks left a record of their medical practice, foremost among them, Hippocrates (460–370 BC). Hippocrates from the fourth century BC put a lot of effort to establish the link between spinal fractures and spinal cord injury. He was the first to describe traction in the treatment of these injuries and even attempted to reduce the dislocation by hyperextension. Although he did not manage the spinal cord itself, an extension bench used to reduce spinal deformities is still in use today. According to the Hippocratic records, the spinal cord was always paralyzed on the injured side. In particular, records of pressure ulcers are treated with wine, vinegar, and oil, dried in the air, and replaced every 3 days to prevent infection. In ancient Greek records, there was a chiropractor, and Hippocrates devised vertebral traction and orthopedic equipment.

From the Greek-Roman period, records of spinal cord injuries have been described in detail. Kelso (Aulus Cornelius Celsus), who compiled the medical knowledge of Hippocrates in the first century BC, was the first to report a sudden death from cervical cord injury and left a record of sewing pressure ulcers using hair. Galen (130–200) and Paul of Aegina (625–690) cannot be overlooked for the history of Greek-Roman medicine. Galen, the main physician of the Aurelius emperor, was famous enough to be called the second Hippocrates. Galen described the protective coverings of the spinal cord: the bone, posterior longitudinal ligament, dura mater, and pia mater (Naderi et al. 2004). In a study on the effect of the experimental incision of the spinal cord, the spinal cord was safe with longitudinal incision, but when the transverse incision was made, there was loss of motor and sensory function below the incision level. In addition, he introduced the terms scoliosis, lordosis, and kyphosis in relation to the deformation of the spine (Lifshutz and Colohan 2004). Paul of Aegina further improved the Hippocratic method of traction but also developed the concept of surgical decompression for treatment and removal of spinous process for pain. Paul of Aegina employed a windlass for traction of the spine. Paul concluded that vertebral fracture should be suspected if the damaged spinal cord is not touched, and that the vertebral bone should be surgically removed and sutured. Data and records related to subsequent spinal cord injury are also found in many records in Greece and India. There is a record of immobilization after lumbar vertebral fracture in Indian records of the second and third centuries AD, and there is a record in Hindu records of axial traction to treat spinal deformity. This is a record that is a thousand years ahead of Hippocrates (Guttman 1976b).

In Europe, prior to the Renaissance, medical schools associated with the universities were gradually established, the first at Salerno, where Roland of Parma studied. He used manual extension to treat fractured spines and was the first to emphasize one of the keystones of modern practice (Silver 2003). The Renaissance was the beginning of modern medicine. Throughout the Middle Ages, Leonardo da Vinci (1452–1519) introduced the physiological curvature of the vertebrae and noted that the cervical muscles were important for keeping the cervical spine stable. In the Renaissance period, Andreas Vesalius (1514–1564), a Flemish anatomist and physician, correctly sketched the nervous system in his book De Humani Corporis Fabrica. This was a milestone because the anatomical knowledge made

by Galenoth until now was an anatomical knowledge for monkeys, not the human body (Knoeller and Seifried 2000).

In the sixteenth century, Ambroise Paré wrote a textbook of surgery and recommended a laminectomy for compression of the spinal cord. Unlike Paul of Aegina, he recommended that the fractured spinous process should not be removed if it was still attached to the periosteum. He was the first modern neurosurgeon. In Germany, Fabricius Ab Aquapendente suggested open reduction of fracture dislocation of the spine. In the eighteenth and nineteenth centuries, there was an important debate about management. In the eighteenth century, James and Heister promoted surgery for spinal injuries. Geraud and Louis reported that neurological outcome was improved by decompression of bullet injuries to the lumbar spine.

The early nineteenth century was a period of intense debate about surgery after many failed attempts to improve neurological outcomes. Cooper (Sir Astley Paston Cooper, 1768–1841) described the symptoms and signs of paraplegia at various levels, emphasized the incontinence of urine and feces, and made interesting observations on the preservation of circulation and inflammatory responses in the paralyzed limbs (Silver 2003). A record of typical spinal cord injuries in the modern history of the nineteenth century is that Admiral Nelson was shot in the thorax and paralyzed in his lower body in 1805 at the Battle of Trafalgar, where he soon died. Dr. Surrey, a surgeon who boarded the Nelson ship at the time. According to Beatty's records, Admiral Nelson was shot, and motor and sensory functions below the chest were lost. James Abram Garfield, the twentieth president of the US who served as a combatant in the Civil War, died 2 months after complications of spinal cord injuries in an assassination attempt in 1881 in Washington, DC. The English neurologist Charles Bell (1774–1842) built on the contributions of the ancients with descriptions of spinal cord injury syndromes regard to spinal shock, flaccidity, spasticity, and bowel and bladder dysfunction (Knoeller and Seifried 2000). He pointed out that the damage to the spinal cord occurred at the moment of injury, and that it was not continuing pressure that damaged the cord. Marshall Hall (1790–1857) worked on the reflex function of the nervous system and his delineation of spinal shock made important contributions to the study of spinal injuries (Silver 2003).

During the Napoleonic Wars (1803–1815), Lord Admiral Horatio Nelson was told by his ship's surgeon "Nothing can be done for you," after a sniper's bullet to his spine (Wang et al. 2005). A contemporary surgeon in the US, Dr. Alban Gilpin Smith, performed the first successful laminectomy in Kentucky in 1829. The beneficiary of this operation was a young man with progressive paraparesis who had fallen from his horse 2 years earlier. After the procedure, the patient had improved sensation in his legs. In an assassination attempt, the US President James Garfield sustained a bullet wound on the conus medullaris. He died 80 days later without surgery for "a disease that should not to be treated" (Eltoral 2004). Fortunately, initial attempts at studying spinal cord injury at the end of the nineteenth century and the beginning of the twentieth century began with a truly modern scientific approach. The first quantitative correlation between injury and applied force was determined in 1911 by the Pennsylvanian neurologist Alfred Reginald Allen. Allen used a weight-drop technique for reproducible injury.

An American military surgeon, Harvey Cushing, reported that 80% of spinal cord injuries died within 2 weeks of injury during World War I. He found that only those cases survived in which the lesion was "partial" (Silver 2005; Guttman 1976a). In the note, those soldiers with injured spinal cord did not die from the immediate injury but from later complications such as in the urinary tract, kidney, and cardiopulmonary system. Although complete spinal cord lesions are among the most devastating life-altering injuries, such therapeutic nihilism is no longer justified. The development of medical technology related to spinal cord injuries, such as the development of antibiotics and mechanical ventilators and the development of treatment for the urinary tract system, has also made gradual progress in the treatment of spinal cord injuries. Prior to

World War II, urinary tract infections were the most common mortality among acute episodes after spinal cord injury. Since the development of urodynamic test and the use of intermittent catheterization, the mortality and complications of the acute phase have been significantly reduced, and intermittent catheterization has contributed to improving the quality of life of patients with spinal cord injuries. Over the past half-century, the prospects for victims of spinal cord injury have dramatically improved.

Before World War I, there had been an unhappy military tradition of maltreatment, unpreparedness, and scandals in hospitals dating from the Napoleonic Wars to the Crimean War and the Boer War. As a result, hospitals were better organized in World War I. World War I led to the setting up of the first spinal unit in the UK, with outstanding work by Henry Head (1861–1940), George Riddoch (1888–1947), and Gordon Holmes (1876–1965). Recommendations had been made in the Medical Research Council (MRC) monograph, which set out a satisfactory method of treatment. This incorporated the outstanding work of Head, Riddoch, and Holmes. The Peripheral Nerve Committee of the Medical Research Council, chaired by George Riddoch, decided that war casualties with spinal cord injuries should be treated in special units (Sutton 1973). Treatment of patients with traumatic spinal cord injuries has been established at the King George V and Empire Hospitals followed by the Royal Star & Garter Home. Holmes was in overall charge of all neurological cases in France and worked at the base hospital, probably No 13. He arranged for patients to be transferred under the care of Head at The London Hospital. Head then arranged their transfer to either the Royal Star and Garter Home or to the Empire Hospital, which served as a spinal unit. At the time of World War I physical therapy was not a recognized speciality as it is today. However, different forms of treatment such as massage, electricity, hydrotherapy, and manipulation were used to treat the patients. After the end of the war, the military hospitals were contracted and specialist units, including spinal units, were closed (Silver 2003).

World War II led to the development of modern treatments in the UK and Guttmann's role is evaluated. During World War II, although there were spinal units in the UK, treatment was not successful. Suprapubic cystotomy was extensively practiced and used during World War II in the UK, the Soviet Union, and the other European countries as well as by the American Army (Sutton 1973). During World War II, the British Medical Research Council proposed a more aggressive approach to the management of spinal cord injury. At that time, spinal cord injury was almost universally fatal, either due to collateral injuries or the breakdown of the skin, kidney, or pulmonary systems with debilitation from the system's failure and/or secondary infection. Realizing how advanced the Americans were, Guttmann, who was not working in spinal injuries at the time, had been sent with Frank Holdsworth (1904–1969), an orthopedic surgeon from Sheffield, to visit Dr. Munro in order to observe his methods and set up spinal units in the UK incorporating Munro's ideas. Holdsworth opened a unit at Sheffield and Guttmann at Stoke Mandeville (Silver 2003).

In 1943, it was decided to set up a spinal unit at the Ministry of Pensions Hospital, Stroke Mandeville, Aylesbury. A socialized spinal cord injury unit, Stoke Mandeville Hospital, was opened in 1944 in Aylesbury, England, under the direction of Sir Ludwig Guttmann (1899–1980). Guttmann had to work as director of the Jewish Hospital and in 1939 fled to Oxford where, until 1944, he was employed in the Neurosurgical Unit under Sir Hugh Cairns, who refused to promote him. Then, when no one else wanted to employ him, he was appointed the first Director of the new Stoke Mandeville Spinal Injuries Unit (Silver 2003). In 1952, it became the National Spinal Injuries Center, part of the British National Health Service. Guttmann, Frankel, and their contemporaries have developed a comprehensive approach to the acute management and long-term rehabilitation of spinal cord injury (Frankel et al. 1969).

At an early stage, Guttmann incorporated sport into his rehabilitation program in the form of wheelchair polo and archery. In 1948, the

National Stoke Mandeville Games were started, and in 1952, the International Stoke Mandeville Games were founded (ISCoS). The most successful competed in the para-Olympics, which he devised and which eventually became a recognized and worthwhile part of the Olympic Movement (Silver 2003). In 1955, doctors from various countries who accompanied their teams to the Stoke Mandeville International Games began to meet informally to discuss their clinical work and research. As these meetings gradually became larger and more formal, the International Paraplegia Medical Society (now ISCoS) was founded in 1961 (ISCoS). The specialized centers for spinal cord injury dedicated to treating patients with spinal cord injuries have made it possible to increase the life expectancy of patients with spinal cord injuries, thereby enabling the development of specialized rehabilitation and lifelong care approaches. The survival time after spinal cord injury after Guttmann increased by about 2000%. Since the establishment of a spinal cord injury center for comprehensive treatment of spinal cord injury patients in the US and Great Britain, there has been rapid medical change and development of spinal cord injury (Guttman 1976b). In the UK including Ireland, treatment and management of spinal cord injury patients are centered on 12 specialized spinal cord injury centers (Stoke Mandeville, Oswestry, Sheffield, Southport, Middlesborough, Wakefield, Cardiff, Stanmore, Salisbury, Glasgow, Belfast, and Dublin).

Until World War I, European medicine and the burgeoning speciality of neurology, especially in Germany, led the world. In the US States, Munro (Donald Munro, 1889–1973) developed the first spinal unit in 1936 and pioneered the treatment of spinal cord injuries. Munro began his first spinal unit at the Boston City Hospital in 1936 and was subsequently responsible for the Veterans' Service at Cushing Hospital during World War II. He qualified at Harvard and served for a year and a half at Boston City Hospital where he became the first surgical resident in genitourinary surgery. Prior to the opening of the Unit at Stoke Mandeville in 1944, there was an established pattern of treatment in the Veterans' Hospitals in the US and Munro's work was recognized (Silver 2003). At the conclusion of World War II, the US government established the first comprehensive spinal cord injury unit at Hines Veterans Administration Hospital in suburban Chicago, using the British model. In Germany, the medically leading country in Europe at the end of the nineteenth century, work began with Wagner and Kocher and was further developed by the anatomical and physiological work of Foerster (Otfrid Foerster, German neurologist and neurosurgeon, 1873–1941). The failure of treatment to evolve in Germany was due to the emergence of the Nazi Party with its policies of euthanasia, anti-intellectualism, and anti-semitism. In France, the descriptive work is presented by Dupuytren, Duchenne, and Charcot. The therapeutic work of Dejerine and Marie, who set up the first French spinal units in World War I, is evaluated (Silver 2003).

In the USA, due to Dr. Guttmann's positive experience, leading spinal cord injury specialists have advocated the establishment of regional Model System Spinal Cord Injury Centers to demonstrate the benefits of a system approach to spinal cord injury care. As a result of their efforts, the Regional Centers were funded by the federal government in 1971. The National Spinal Cord Injury Statistical Center (NSCISC), centered on the American Model Spinal Cord Injury Center, which first began collecting data in 1973, collected approximately 15% of the newly developed spinal cord injuries in the US as initial data and 57.4% of all surviving individuals with spinal cord injuries in the USA. It is impossible to discuss the impact of the American Spinal Injury Association (ASIA) on spinal cord injury management without addressing and appreciating the Model Systems (Ragnarsson 2013). The ASIA was found in 1973 with its first official meeting. There are 14 model systems and 5 follow-up centers (Fig. 1.2). Each Model System Spinal Cord Injury Center is designed to meet five basic criteria: (1) a system of emergency care and early referral, (2) coordination of acute medical/surgical care, (3) rehabilitation management beginning at the onset of acute care, (4) vocational evaluation, counseling, and placement, and (5) a

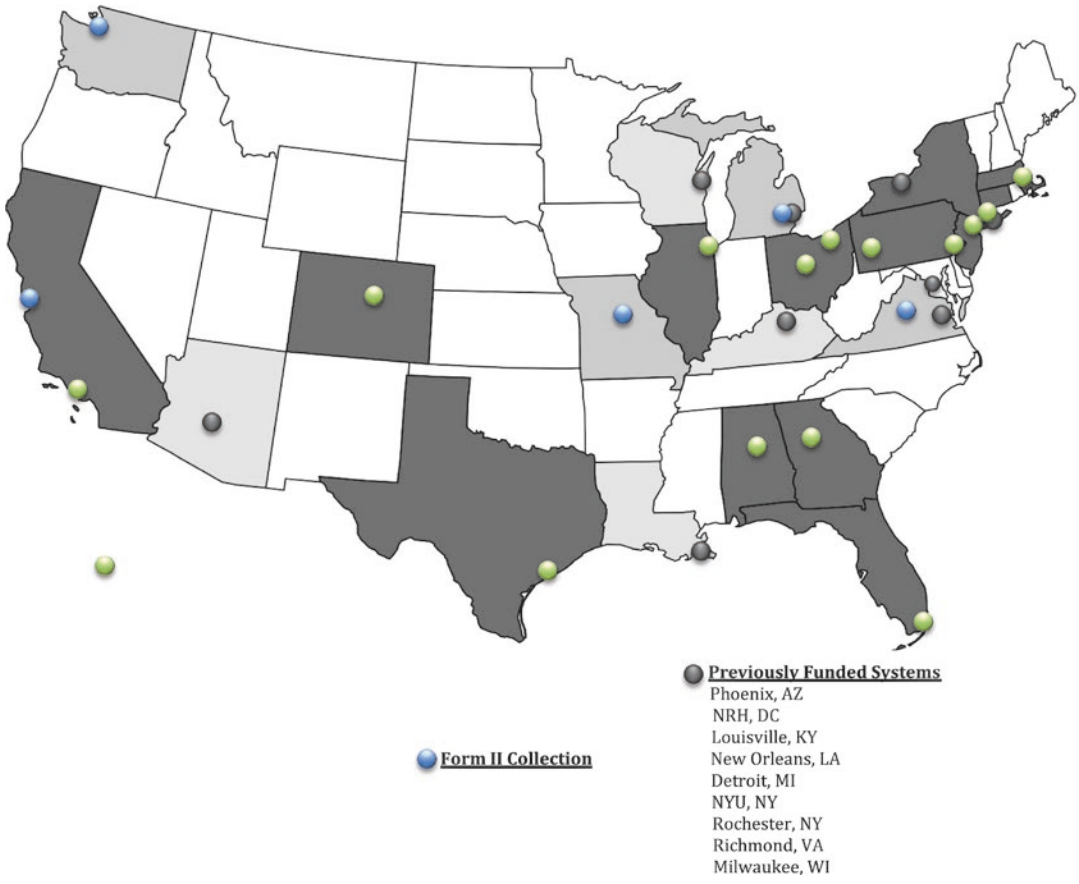


Fig. 1.2 Spinal cord injury model systems in the USA. There are 14 currently funded model systems and 5 follow-up Form II collection centers. From National Spinal Cord Injury Statistical Center

system of lifetime follow-up care. Holdsworth, Denis, and others also improved their understanding of spinal anatomy and biomechanics, and their work has served as a foundation for subsequent advances in stabilization and instrumentation (Denis 1983, 1984; Fenis 1983; Holdsworth 1970).

1.2 Characteristics of Spinal Cord Injuries

Spinal cord injuries can be caused by traumatic and nontraumatic. Traumatic causes are usually high-velocity events that lead to acute neurologic deficits. Nontraumatic lesions generally have a subacute to chronic course with a slower onset of neurologic deficits (Kupfer et al. 2015). Traumatic injuries of the spinal cord, such as fractures, dislocations, gunshot wounds, or stab wounds, are caused by direct or indirect compression, laceration, or crushing of the spinal cord. This injury directly destroys the axons or neuronal membranes constituting the spinal cord, causing neurological symptoms to appear immediately after the injury. Secondary injuries to the spinal cord after trauma appear 8–24 h after the primary injuries, creating a lesion depending on the temporal stage of the secondary injuries resulting in bleeding, edema, infarction, and necrosis. As weeks, months, or years pass after secondary injuries, Wallerian degeneration, neuroma formation, arachnoidopathy, or syringomyelia are formed. Given the anatomically corresponding levels of the vertebrae and spinal cord segments, fractures above L1 often result in a spinal cord injury

characterized by upper motor neuron lesion findings. After an initial spinal shock, an increased tone may be observed, manifested by brisk reflexes or involuntary spasms. Fractures at and below L2 often result in a cauda equina injury, characterized by symptoms of a lower motor neuron lesion such as hypotonia, flaccidity, decreased or absent reflexes, muscle atrophy, flaccid bowel and bladder. Fractures at the L1 or L2 level often involve the conus medullaris, and if the damage to the nerve roots surrounding the conus medullaris are also combined, they may present with a mixed presentation of the upper motor neuron and lower motor neuron lesion (Kupfer et al. 2015).

1.2.1 Pattern of Neurological Dysfunction

The relevant parameters determining the neurological pattern are (1) the spatial and temporal progression of symptom presentation; (2) location, quality, and severity of sensory dysfunction; (3) location and severity of motor dysfunction; (4) spasticity versus flaccid paralysis; and (5) quality and severity of bladder/bowel/cardiovascular dysfunction (Bauman et al. 2012; Gorman 2011; Weidner et al. 2017). Traumatic spinal cord injuries can affect gray matter, white matter, or nerve roots or any combination. Because the gray matter is more vascular, it is believed to be more vulnerable to mechanical trauma. Gray matter damage typically extends one or two segments rostral and caudal to the injured spinal cord segment, but can be more extensive if the spinal cord blood supply has been disrupted. Pathologic studies on spinal cord trauma show greater involvement of gray matter than white matter (Kakulas 1987). Gray matter damage leads to segmental changes with denervation muscle atrophy and impaired reflexes. White matter damage is more disabling as it results in loss of motor control and sensory input not only at but also below the injury site.

In spinal cord, the homunculus of motor and sensory area is not clear compared to the brain, and efferent and afferent neural network are densely arranged in a narrow structure, and all functions below the spinal cord injury may be damaged. Since the anatomical features of the spinal cord are laminated in each nerve pathway, there is a difference in degree of damage depending on the extent of the lesion, but it is usually accompanied by dysfunction of the distal spinal cord segments. All ascending or descending tracts of the white matter have medially caudal segment fibers and laterally rostral segment fibers. In the posterior column, however, the caudal segment fibers are medial and the rostral segment fibers are lateral. In addition, the motor neurons of the ventral horn of the gray matter also organize the motor neurons of the proximal-distal part and the extensors-flexors in the medial-lateral and anterior-posterior area, respectively. The information on the exact neuroanatomical area associated with neurological dysfunction observed and pattern of neurological dysfunction is very important for the most effective diagnosis and management, initially considering the spinal cord injury/lesion (Tator and Koyanagi 1997). For example, elderly patients with a central cord syndrome following a fall are most likely to have suffered cervical spinal cord contusion with pre-existing cervical stenosis. Subacute progressive symptoms that reflect proprioceptive dysfunction without significant motor or autonomous nerve system dysfunction are common in metabolic causes of spinal cord disease, such as subacute combined degeneration or copper deficiency (Bauman et al. 2012).

The pattern of neurological dysfunction allows us to predict the outcome. Sacral sparing means preservation of sensory or motor function in the lowest sacral segments. Patients with sacral sparing is classified as incomplete spinal cord injury according to the ASIA Impairment Scale. This means they are much more likely to recover motor and sensory function over time. The pattern of neurological dysfunction may also help to identify patients at risk for complications from spinal cord injury, including neuropathic pain. For example, pattern of changes in sensory function can indicate a risk of developing central neu-

ropathic pain. Patients with poorly defined sensory abnormality and complaints of pain or abnormal sensations that are not dependent on the dermatome or anatomical distribution below the level of injury are at high risk for neuropathic pain (Finnerup et al. 2003). Determination of the neurological level of injury is important to determine the immediate monitoring intensity. Spinal cord injury above C4 is more likely to require intensive care for the respiratory and cardiovascular complications. Whether a patient has upper motor neuron or lower motor neuron-type lesion, bowel, bladder, and sexual dysfunctions are determined by different treatment options.

1.2.2 Neurological Examination of Spinal Cord Injuries

Neurological examination of spinal cord injury, including determination of the neurological level of injury, is assessed based on the International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI), revised 2019. The ISNCSCI is detailed in Chap. 13. Neurological level of injury is important in determining some critical issues, including respiratory and cardiovascular function and significant autonomic dysfunction requiring very attentive managements during rehabilitation, as well as functional consequences depending on the level (Gorman 2011). Supraspinal parasympathetic input after spinal cord injury is usually not altered because it is transmitted through the vagal nerve, which controls heart rate and resting blood pressure (Norenberg et al. 2004). The extent of sympathetic change depends mainly on the neurological level of injury. The more rostral lesions of the T6 segment are located, the more severely control of sympathetic output is affected. Sympathetic preganglionic neurons, which innervate blood vessels in abdominal, pelvic, and lower body blood vessels, are located in segments T5 throughout L1, leading to orthostatic hypotension, hypothermia, and bradycardia. The more rostral the neurological level of injury is, the more severe orthostatic hypotension and bradycardia are (Bauman et al. 2012; Gorman 2011). Orthostatic hypotension and bradycardia in subacute and chronic spinal cord injury become less prominent, whereas autonomic dysreflexia, defined as an increase in systolic blood pressure 20–40 mmHg higher than baseline (Consortium for Spinal Cord Medicine 2001) with concomitant slowing of the pulse rate and related clinical symptoms in response to visceral or cutaneous noxious stimuli below the level of spinal cord lesion, can occur chronically recurrent.

1.2.3 Spinal Cord Injury/Lesion Type of Upper and Lower Motor Neurons

Schematically, the motor system is divided into an upper motor neuron system and a lower motor neuron system, and the lower motor neuron system is made up of anterior horn cells (motor neurons) in the ventral horn of the gray matter of the spinal cord, roots and spinal nerves, plexuses, peripheral nerves, neuromuscular junctions, and muscles (Fig. 1.3). The upper motor neuron is the upper motor control system that controls the lower motor neuron system. The upper motor neuron system from the motor cortex to the anterior horn cells consists of pyramidal tract (pathways, system) that decussates at the pyramids of the medulla to form the lateral corticospinal tract and extrapyramidal tract of the remaining fibers. The extrapyramidal fibers are distributed to the basal ganglia, thalamus, red nucleus, pons, and the medullary reticular formation (Lance 1984). The pyramidal tract itself has little influence on human muscle tone, but the cortico-reticulospinal fibers that shadow it throughout its course exert a tonic inhibitory influence on motor neurons. Upper motor neuron lesions in humans, which almost always involve the cortico-reticulospinal pathway as well as the pyramidal tract, are characterized by hyperactive motor neurons, which leads to an increase in muscle tone and tendon jerks (Lance 1984).

It is believed that the main lesion of the spinal cord is a upper motor neuron-type injury with

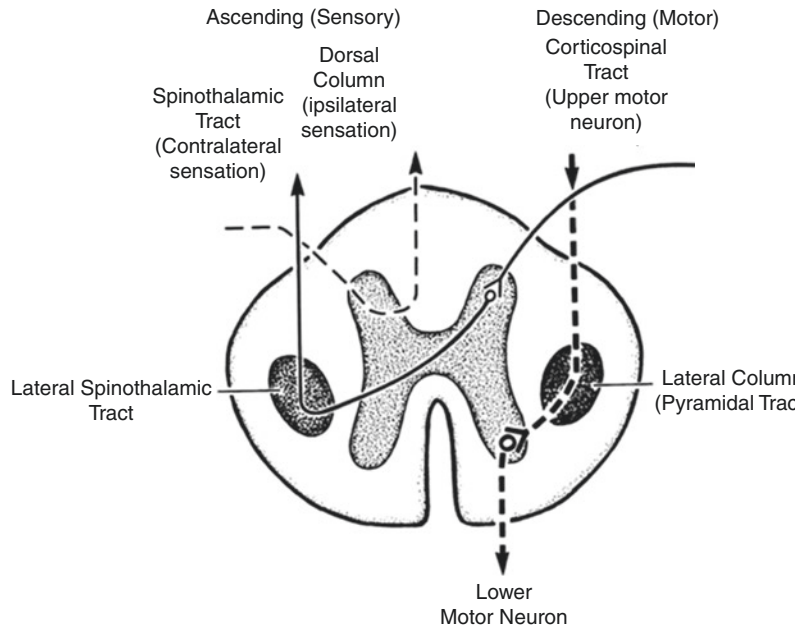


Fig. 1.3 Schematic representation of the spinal cord transverse section illustrating the main ascending and descending pathways. Depending on the level of injury and lesion site, patients may have a clinical sign of lower motor neuron lesion. Adapted from Eagler et al. (1998), with permission

expecting signs of exaggerated deep tendon reflexes, pathological reflexes, and spasticity. If the spinal cord is injured, the long descending motor tract is damaged. Depending on the location of the lesion and the extent of the lesion, motor neurons in the ventral horn and corresponding or adjacent spinal roots are directly or indirectly damaged by the mechanical lesion (Jimenez et al. 2000; Peckham et al. 1976). Spinal root avulsion by the central mechanism, combined with longitudinal or transverse movement of the spinal cord following significant spinal trauma, can result in a lower motor neuron lesion at the level or proximal or distal adjacent segments of the lesion (Moran et al. 2005) (Fig. 1.4).

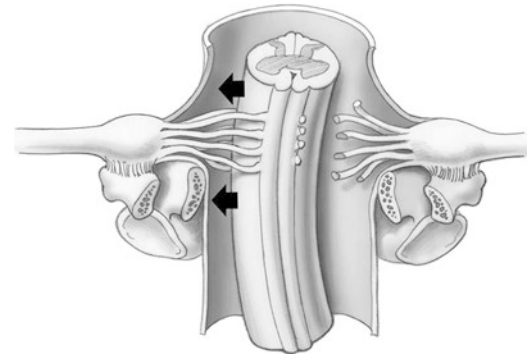


Fig. 1.4 Central mechanism of root avulsion. Central avulsions occur from direct spinal trauma. The spinal cord is moved longitudinally or transversely, causing a sheering and spinal bending that results in an avulsion of the nerve rootlets. From Moran et al. (2005), with permission

Depending on the level of spinal cord injury, patients may have a clinical sign of lower motor neuron lesion such as flaccid weakness, absent or hypoactive deep tendon reflexes, and muscle atrophy. Motor neurons of the ventral horn in the thoracic spinal cord may also be affected following injury. Motor neuron damage in the thoracic segments, however, has little functional effect since the muscles of the upper and lower extremities are spared (Anderberg et al. 2007; Peckham et al. 1976). In the lumbosacral spinal cord, the lower motor neuron damage becomes more common because damages to the surrounding nerve root of the conus medullaris and cauda equina. A retrospective study that analyzed cases of complete thoracolumbar spinal cord injury showed that the patients above the neurological level of injury T10 had predominantly upper motor neuron-type injury, while below the T12, the majority of patients had flaccid paralysis (Doherty et al. 2002).

1.2.4 Clinical Syndromes of Incomplete Spinal Cord Injuries

There are several types of clinical syndromes of incomplete spinal cord injuries according to the lesion site of the spinal cord. The characteristics of incomplete clinical syndromes are determined by anatomical features of the location and lamination of the tracts, decussation of the tract fibers, and vascular feeding areas. Central cord syndrome, Brown-Séquard syndrome, Brown-Séquard plus syndrome, anterior cord syndrome, posterior cord syndrome, subacute combined degeneration myelopathy, epiconus syndrome, conus medullaris syndrome, cauda equina syndrome, and cruciate paralysis are examples of the clinical syndrome of incomplete spinal cord injury.

1.2.5 Medical Aspects

A spinal cord injury leads to an interruption in communication between the brain and spinal cord to end organs and limbs, with resultant sensory, motor, and autonomic dysfunction. Spinal cord injuries affect the entire body system, resulting in a variety of secondary complications or medical problems (Table 1.1). Table 1.1 is the mnemonic of "N-I-B-B-L-E-S" to remember each item in the problem list related to spinal cord injury. In order to minimize the risks of morbidity, mortality, and the debilitating compromise of maximal health and function, appropriate prophylaxis, early assessment and therapeutic intervention are essential (Anderberg et al. 2007; Sezer et al. 2015).

Once it has been determined that emergency life-support measures are not indicated or the

Table 1.1 The mnemonic of the problem list for people with spinal cord injuries: N-I-B-B-L-E-S

System	Issues	Managements
*N*eurological	Neurological evaluation and classification	ISNCSCI
*I*mmobility, mobility	Function evaluation Mobility evaluation Rehabilitation goal setting	Mobility/functional training
*B*ladder/*B*owel	Evaluation of neurogenic lower urinary tract function UTI	Anticholinergic medication Clean intermittent catheterizations Antibiotics
	Dysfunctional defecation Ileus Stress ulcer Constipation Other GI complications	Bowel program H_2 blocker
*B*lood pressure	Low resting blood pressure Autonomic dysreflexia Orthostatic hypotension Supine hypertension Postvoidal syncope, postdefecation hypotension Postprandial hypotension	Beware of noxious stimuli below NLI Nonpharmacological measures Head-up while sleeping Slow voiding
*L*ung	Pneumonia Atelectasis Ventilator care	Mechanical ventilation Incentive spirometer Secretion management
*E*xtremities	Deep vein thrombosis Fracture Heterotopic ossification	LMWH prophylaxis IVC filter, etc.
*S*kin, *S*ocial, P*s*ychological	Pressure injury, burn wound Depression, anxiety, suicidal ideation, suicide Participation, discharge	Pressure ulcer management Counseling SSRI medication

ISNCSCI International Standards for Neurological Classification of Spinal Cord Injury, *UTI* urinary tract infection, *NLI* neurological level of injury, *LMWH* low molecular weight heparin, *IVC* inferior vena cava, *SSRI* selective serotonin reuptake inhibitor

patient's medical condition has been stabilized, the following areas need to be carefully assessed: (1) neurological level and extent of injury; (2) orthopedic injuries of the vertebral column; (3) cardiovascular compromise or complication; (4) respiratory complications secondary to neurological injury or associated chest injury; (5) genitourinary complications; (6) gastrointestinal complications; (7) associated injuries or complications of the head, chest, abdomen, and extremities; and (8) other significant medical history (Abrams and Ganguly 2015; Bauman et al. 2012; Burns 1998; Gorman 2011; Sezer et al. 2015).

1.2.5.1 Cardiovascular Complications

Bradycardia and hypotension are features of neurogenic shock caused by the disruption of sympathetic innervation. Peripheral dilatation, venous pooling, and decreased cardiac output decrease heart rate and blood pressure significantly (Sezer et al. 2015). The hypotension during the acute phase should be treated with aggressive IV fluids and vasopressors. Mean arterial pressure of 85–90 mmHg is generally considered a reasonable goal. Some people with cervical cord lesions may have a vasovagal response leading to profound bradycardia and cardiac arrest with abrupt change of position, prone positioning, and suctioning. These cardiac changes are thought to be caused by the loss of sympathetic innervation and the resultant parasympathetic overactivity. Anticholinergics are first-line treatments for symptomatic bradycardia following spinal cord injury. In individuals with spinal cord injury below the T6 level, bradycardia and hypotension are generally not significant, although cardiovascular assessment is necessary (Gorman 2011).

Orthostatic hypotension is a reduction in systolic blood pressure of 20 mmHg or diastolic blood pressure of 10 mmHg that occurs when moving from a supine to an upright position within 3 min of changing posture. Orthostatic hypotension is often asymptomatic. Treatment includes behavioral changes, such as moving more slowly during change of position, and physical modalities, such as abdominal binders and compressive leg stockings to help minimize venous pooling. Salt tablets are often used as a first-line treatment for hypotension. Midodrine is an α1 agonist that causes vasoconstriction and increased peripheral vascular resistance. Other vasopressors, such as ephedrine, pseudoephedrine, and phenylpropanolamine, have been used for their sympathomimetic effect. Fludrocortisone, 0.1–0.2 mg daily, has mineralocorticoid effects that cause plasma volume expansion by increasing renal sodium absorption and water retention.

Autonomic dysreflexia typically occurs in people with spinal cord injuries at T6 and above. It is defined as an increase in systolic blood pressure of 40 mmHg above the patient's baseline; or a diastolic blood pressure increase of 20 mmHg above baseline; or a systolic blood pressure of 150 mmHg, when the baseline blood pressure is not known, with an associated altered vasomotor tone. Most common causes are bladder distention and fecal impaction. However, any irritating noxious stimulus below the level of injury can trigger autonomic dysreflexia.

Deep vein thrombosis is a major cardiovascular complication of spinal cord injury. It occurs when the venous system of the lower extremities is occluded by blood clot formation. The main cause is decreased or absent muscle function in the legs and loss of sympathetic innervation after spinal cord injury, leading to vasodilation and pooling of blood in the venous system. Hypercoagulability and damage to vessel walls may also be the cause (Gorman 2011). Frequent checking for side-to-side circumference of the thigh and calf can be helpful in the diagnosis of deep vein thrombosis. D-dimer has high sensitivity but low specificity in diagnosis of deep vein thrombosis. Pulmonary embolism can be suspected by a ventilation/perfusion scan (V/Q scan). The definitive diagnosis is made by spiral CT or pulmonary angiography, the former being the more common imaging modalities.

1.2.5.2 Respiratory Complications

Respiratory complications are the leading cause of death in people with traumatic spinal cord injuries. Aggressive evaluation and prevention efforts are required to minimize the risk of death from respiratory complications (Abrams and

Ganguly 2015; Dumont et al. 2001). Atelectasis, pneumonia, and ventilatory failure can be due to the patient's inability to cough effectively, decreased diaphragmatic movement, and decreased vital capacity. A positive history of lung disease, smoking, and/or aspiration can affect respiratory problems. Prevention is the key. To compensate for loss of functional intercostal and abdominal muscles, aggressive respiratory assessment and lung care to minimize retention of pulmonary secretions are essential. Careful monitoring of pulmonary parameters and aggressive lung care can minimize or even completely eliminate the effects of respiratory complication (Anderberg et al. 2007). An additional factor in preventing pneumonia in people with spinal cord injuries is identifying dysphagia early and using appropriate aspiration precautions. Individuals with a high neurological level of injury are likely to require mechanical ventilation acutely.

People with spinal cord injuries have a high incidence and prevalence of sleep apnea compared to the general population and are at high risk for both central and obstructive sleep apnea. The most common type has been associated with obstructive sleep apnea. However, central sleep apnea patterns have also been observed, particularly in high tetraplegia (Lavis and Goetz 2019). A greater likelihood of sleeping in supine position in people with spinal cord injuries may be a contributing factor. Sleep-disordered breathing is observed in up to 60% of people with tetraplegia (Leduc et al. 2007). Although there is a correlation with the neurological level of injury of spinal cord, no clear correlation has been found with the severity or completeness of the injury. Obesity, however, correlates with sleep apnea in the general population and in the population with spinal cord injuries (Burns et al. 2005). In tetraplegia, there is an association with neck circumference, age, and body mass index, and time after injury (Stockhammer et al. 2002). There is also a high use of potentially sedating drugs used for spasticity, such as baclofen and diazepam, as well as for pain, and these should be closely monitored and reviewed with patients to be minimized as clinically appropriate (Lavis and Goetz 2019).

1.2.5.3 Urinary Complications

Flaccid paralysis of the bladder resulting from traumatic spinal cord injury persists in people with upper motor neuron lesions until resolution of the phase of spinal shock. If it is a lower motor neuron lesion, the bladder remains either atonic or hypotonic. If the patient is receiving steroids, diuretics, and IV fluid treatment, urinary output should be closely monitored. It is necessary to avoid overdistention of the bladder and maintain fluid balance (Abramson 1971; Abrams and Ganguly 2015). As soon as the diuresis phase is over, the catheter must be removed and a bladder retraining program with intermittent catheterization and fluid intake schedule with fluid restriction should be initiated. A complete urologic evaluation, including a urodynamic study, should be performed prior to the start of bladder retraining (Sezer et al. 2015). The goals of genitourinary tract management after spinal cord injury include prevention of infection, optimizing social continence and function, and prevention of deterioration of the upper urinary tract (Lavis and Goetz 2019).

Urinary tract infections are the most frequent infection after spinal cord injury, with an average of 2.5 episodes per year. Many people with spinal cord injuries who use urinary catheters for management have bacterial colonization of their bladder. The standard of care for people with spinal cord injuries does not recommend antimicrobial treatment of asymptomatic bacteriuria. A history of recurrent infections, urinary stones, or vesicoureteral reflux with hydronephrosis suggests suboptimal management associated with increased bladder pressures, inadequate emptying, or both (Lavis and Goetz 2019). Cystatin C has several advantages over serum creatinine. It is produced by all nucleated cells and is not influenced by muscle mass (Dharnidharka et al. 2002), but its value can be affected by inflammatory processes. The risk of bladder cancer in people with spinal cord injuries was estimated to be 16 times higher than in the general population (Vince and Klausner 2017).

1.2.5.4 Gastrointestinal Complications

The goals of managing neurogenic bowel dysfunction include optimal social function, in particular, minimizing incontinence and interference with activities of daily living, and preventing complications, such as abdominal pain, impaction, bowel obstruction, and hemorrhoids (Lavis and Goetz 2019). Neurogenic bowel dysfunction remains a major life-limiting problem for people with spinal cord injuries. Historical variables regarding pre-illness bowel behavior, including premorbid bowel habits, frequency of bowel movements, effects on social function, or stool consistency, are important in the management of neurogenic bowel dysfunction.

Gastrointestinal bleeding is a preventable complication in patients with spinal cord injuries. Although the specific cause of stress ulcers has not been proven, it has been hypothesized that steroid therapy, emotional stress, loss of sympathetic innervation to the gastrointestinal tract, and mechanical ventilation are the main causes. Patients with a history of ulcer disease are likely to have bleeding problems. Anticoagulation also increases the risk of gastrointestinal bleeding (Hammond et al. 2013; Sezer et al. 2015). It is important that all patients thoroughly examine the occult blood in stool and stomach contents and closely monitor hemoglobin and hematocrit levels. If the ileus persists, a gastric decompression is necessary. Careful evaluation of the gastrointestinal tract is required to determine the appropriate timing to start a bowel program (Abrams and Ganguly 2015).

Dysphagia in cervical spine injuries, nutrition, and hydration are also importantly assessed and managed. Risk factors for dysphagia include an anterior approach to cervical procedures, cervical prevertebral soft tissue edema, and cervical orthoses. Patients with a tracheostomy are increased risk of aspiration. Cervical orthoses, including collars, SOMI, and halo vest, can impair swallowing ability.

1.2.5.5 Pressure Injuries

Pressure injuries are often the most debilitating and costly complication in patients with spinal cord injuries (Sezer et al. 2015). They can also be prevented by appropriate prophylactic intervention beginning in the acute phase of care. Primary factors leading to pressure injury are pressure and shear or a combination. Pressure injury remains one of the most common reasons for rehospitalization for people with spinal cord injuries (Cardenas et al. 2004). Each member of the treatment team must assess the integrity of the skin to monitor the effects of the overall condition of treatment plan. People with spinal cord injuries and their caregivers should be educated about the importance of weight shifting every 2 h in bed and every 30 min while seated. The patient's nutritional and metabolic status can be reflected in the condition of the skin (Abrams and Ganguly 2015; Gorman 2011).

1.2.5.6 Cognitive Dysfunction

There is a high incidence of significant cognitive impairment in people with spinal cord injuries. The majority of studies report a frequency of cognitive impairment between 10% and 60%. Cognitive dysfunction after spinal cord injury is likely due to factors such as neurological level of injury, age, level of education, premorbid psychological and learning disabilities, and alcohol and substance abuse. This is also the effect of other secondary conditions commonly present in people with spinal cord injuries, including concomitant brain injury, psychological or somatic comorbidities, decentralized cardiovascular control, and sleep apnea (Sachdeva et al. 2018). 16%–59% of spinal cord injuries report a concomitant traumatic brain injury, which is associated with clinical manifestations of cognitive impairments such as attention deficit, memory loss, and reduced executive abilities (Macciocchi et al. 2008; Michael et al. 1989; Nott et al. 2014). It is often thought that traumatic brain injury is responsible for the cognitive deficit in people with spinal cord injuries.

1.2.5.7 Psychological Considerations

Psychological complications in patients with spinal cord injuries affect and are affected by all aspects of the patient care as well as their life experiences. Proper attention and care for how each patient copes with their injury psychologi-

cally are important. Denial, depression, and anger can appear in a way that compromise the patient's management plan and overall well-being (Abrams and Ganguly 2015). The consideration of the psychosocial reaction and adjustment process to the injury should not be delayed. It is important that all treatment staff have a positive attitude towards the patient (Sezer et al. 2015). The rate of depression in people with spinal cord injuries is higher than that in the general population. Depression affects about 30% of people with spinal cord injuries, and rates of major depression is estimated at 10–15% (Fann et al. 2011). Physical, pharmacological, or psychological interventions should be available to prevent or minimize the problems. In addition, the communication of the prognosis by the physician to the patient is much more than the simple transmission of information, in particular, to effectively convey negative prognostic messages to a person who has suffered a neurologically complete spinal cord injury (Kirshblum and Fichtenbaum 2008).

1.2.5.8 COVID-19 and Spinal Cord Complications

Spinal cord complications related to coronavirus infectious disease of 2019 (COVID-19) are being widely reported. The neurological manifestations included weakness, sensory deficit, autonomic dysfunction, and ataxia (Mondal et al. 2021). A variety of COVID-19-related spinal cord manifestations, such as acute transverse myelitis, acute necrotizing myelitis, SARS-CoV-2 myelitis, acute disseminated encephalomyelitis, neuromyelitis optica spectrum disorder, hypoxic myelopathy, MOG antibody-associated myelitis, spinal cord infarction, and spinal epidural abscess, have been reported. The possible mechanisms of this involvement are direct invasion, cytokine storm, coagulopathy, and an autoimmune reaction (Garg et al. 2021; Sampogna et al. 2020).

Delays in the COVID-19 pandemic tend to limit the readmission of patients with spinal cord injury and sufficient stay in rehabilitative beds. As spinal cord disease occurs in combination with COVID-19, a new approach to treatment and rehabilitation is required, and there is a need worldwide for the active introduction and utilization of telemedicine (Galea 2019) for the management and rehabilitation of people with spinal cord injuries. Therefore, a new paradigm for appropriate medical management and rehabilitation during and after a pandemic is needed.

References

Abrams GM, Ganguly K. Management of chronic spinal cord dysfunction. Continuum (Minneap Minn). 2015;21:188–200.

Abramson AS. Advances in the management of the neurogenic bladder. Arch Phys Med Rehabil. 1971;52:143–8.

Anderberg L, Aldskogius H, Holz A. Spinal cord injury-scientific challenges for the unknown future. Ups J Med Sci. 2007;112:259–88.

Bauman WA, Korsten MA, Radulovic M, et al. 31st g. Heiner sell lectureship: secondary medical consequences of spinal cord injury. Top Spinal Cord Inj Rehabil. 2012;18:354–78.

Brawanski A. On the myth of the Edwin Smith papyrus: is it magic or science? Acta Neurochir. 2012;154:2285–91.

Breasted JH. Edwin Smith surgical papyrus in facsimile and hieroglyphic transliteration with translation and commentary. Chicago: University of Chicago Oriental Institute Publications; 1930.

Burns S. Review of systems. In: Hammond MC, editor. Medical care of persons with spinal cord injury. Washington, DC: Department of Veterans Affairs; 1998. p. 17–22.

Burns SP, Rad MY, Bryant S, et al. Long-term treatment of sleep apnea in persons with spinal cord injury. Am J Phys Med Rehabil. 2005;84:620–6.

Cardenas DD, Hoffman JM, Kirshblum S, et al. Etiology and incidence of rehospitalization after traumatic spinal cord injury: a multicenter analysis. Arch Phys Med Rehabil. 2004;85:1757–63.

Consortium for Spinal Cord Medicine. Clinical practice guidelines. Acute management of autonomic dysreflexia: individuals with spinal cord injury presenting to health-care facilities. Washington, DC: Paralyzed Veterans of America; 2001.

Denis F. The three-column spine and its significance in the classification of acute thoracolumbar spine injuries. Spine. 1983;8:817–31.

Denis F. Spinal instability as defined by the three-column spine concept in acute spinal trauma. Clin Orthop. 1984;189:65–76.

Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. Am J Kidney Dis. 2002;40:221–6.

Doherty JG, Burns AS, O'Ferrall DM, et al. Prevalence of upper motor neuron vs lower motor neuron lesions in complete lower thoracic and lumbar spinal cord injuries. J Spinal Cord Med. 2002;25:289–92.

Dumont RJ, Okonkwo DO, Verma S, et al. Acute spinal cord injury, part I: pathologic mechanisms. Clin Neuropharmacol. 2001;24:254–64.

Eagler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.

Eltoral IM. Fatal spinal cord injury of the 20th president of the United States: day-by-day review of the clinical course, with comments. J Spinal Cord Med. 2004;27:330–41.

Fann JR, Bombardier CH, Richards JS, et al. Depression after spinal cord injury: comorbidities, mental health service use, and adequacy of treatment. Arch Phys Med Rehabil. 2011;92:352–60.

Fenis F. The three-column spine and its significance in the classification of acute thoracolumbar spine injuries. Spine. 1983;8:817–31.

Finnerup NB, Johannesen IL, Fulglsang-Frederiksen A, et al. Sensory function in spinal cord injury patients with and without central pain. Brain. 2003;125:57–70.

Frankel HL, Hancock DO, Hyslop G, et al. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. Paraplegia. 1969;7:179–92.

Galea MD. Telemedicine in rehabilitation. Phys Med Rehabil Clin N Am. 2019;30:473–83.

Ganz JC. Edwin Smith papyrus case 8: a reappraisal. J Neurosurg. 2014;120:1238–9.

Garg RK, Paliwal VK, Gupta A. Spinal cord involvement in COVID-19: a review. J Spinal Cord Med. 2021;11:1–15. https://doi.org/10.1080/10790268.2021.1888022.

Gorman PH. The review of systems in spinal cord injury and dysfunction. Continuum (Minneap Minn). 2011;17(3. Neurorehabilitation):630–4.

Guttman L. Spinal cord injuries. Comprehensive management and research. 2nd ed. London: Blackwell Science Ltd; 1976a.

Guttman L. Historical back ground. In: Spinal cord injuries: comprehensive management and research. 2nd ed. London: Blackwell Scientific Publication; 1976b. p. 1–8.

Hammond FM, Horn SD, Smout RJ, et al. Acute rehospitalizations during inpatient rehabilitation for spinal cord injury. Arch Phys Med Rehabil. 2013;94:S98–S105.

Holdsworth F. Fractures, dislocations and fracture-dislocation of the spine. J Bone Joint Surg. 1970;52-A:1534–51.

Howorth MB, Petrie JG. Injuries of the spine. Baltimore: The Williams & Wilkins Company; 1964.

Hughes JT. The Edwin Smith surgical papyrus: an analysis of the first case reports of spinal cord injuries. Paraplegia. 1988;26:71–82.

ISCoS. https://www.iscos.org.uk/the-history-of-iscos. Accessed 8 Sept 2021.

Jimenez O, Marcillo A, Levi AD. A histopathological analysis of the human cervical spinal cord in patients with acute traumatic central cord syndrome. Spinal Cord. 2000;38:532–7.

Kakulas BA. The clinical neuropathology of spinal cord injury. A guide to the future. Paraplegia. 1987;25:212–6.

Kirshblum S, Fichtenbaum J. Breaking the news in spinal cord injury. J Spinal Cord Med. 2008;31:7–12.

Knoeller SM, Seifried C. Historical perspective: history of spinal surgery. Spine (Phila Pa 1976). 2000;25:2838–43.

Kupfer M, DeSipio GMB, Ryan D, et al. Spinal cord injury. In: Maitan IB, editor. Current diagnosis & treatment: physical medicine & rehabilitation. New York: McGraw-Hill Education; 2015.

Lance JW. Pyramidal and extrapyramidal disorders. In: Shahani BT, editor. Electromyography in CNS disorders: central EMG. Boston: Butterworth; 1984.

Lavis T, Goetz LL. Comprehensive care for persons with spinal cord injury. Phys Med Rehabil Clin N Am. 2019;30:55–72.

Leduc BE, Dagher JH, Mayer P, et al. Estimated prevalence of obstructive sleep apnea-hypopnea syndrome after cervical cord injury. Arch Phys Med Rehabil. 2007;88:333–7.

Lifshutz J, Colohan A. A brief history of therapy for traumatic spinal cord injury. Neurosurg Focus. 2004;16:E5.

Macciocchi S, Seel RT, Thompson N, et al. Spinal cord injury and co-occurring traumatic brain injury: assessment and incidence. Arch Phys Med Rehabil. 2008;89:1350–7.

Michael DB, Guyot DR, Darmody WR. Coincidence of head and cervical spine injury. J Neurotrauma. 1989;6:177–89.

Middleton JW, Dayton A, Walsh J, et al. Life expectancy after spinal cord injury: a 50-year study. Spinal Cord. 2012;50:803–11.

Mondal R, Deb S, Shome G, et al. COVID-19 and emerging spinal cord complications: a systematic review. Mult Scler Relat Disord. 2021;51:102917.

Moran SL, Steinmann SP, Shin AY. Adult brachial plexus injuries: mechanism, patterns of injury, and physical diagnosis. Hand Clin. 2005;21:13–24.

Naderi S, Türe U, Pait TG. History of the spinal cord localization. Neurosurg Focus. 2004;16:E15.

National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord injury model systems. Birmingham: NSCISC; 2021.

Norenberg MD, Smith J, Marcillo A. The pathology of human spinal cord injury: defining the problems. J Neurotrauma. 2004;21:429–40.

Nott MT, Baguley IJ, Heriseanu R, et al. Effects of concomitant spinal cord injury and brain injury on medical

and functional outcomes and community participation. Top Spinal Cord Inj Rehabil. 2014;20:225–35.
Peckham PH, Mortimer JT, Marsolais EB. Upper and lower motor neuron lesions in the upper extremity muscles of tetraplegia. Paraplegia. 1976;14:115–21.
Ragnarsson KTG. Heiner sell distinguished lecture: American spinal injury association (ASIA) 40th anniversary: beginnings, accomplishments and future challenges. Top Spinal Cord Inj Rehabil. 2013;19:153–71.
Sachdeva R, Gao F, Chan CCH, et al. Cognitive function after spinal cord injury: a systematic review. Neurology. 2018;91:611–21.
Sampogna G, Tessitore N, Bianconi T, et al. Spinal cord dysfunction after COVID-19 infection. Spinal Cord Ser Cases. 2020;6:92.
Sezer N, Akkus S, Ugurlu FG. Chronic complications of spinal cord injury. World J Orthop. 2015;6:24–33.
Shavelle RM, DeVivo MJ, Brooks JC, et al. Improvements in long-term survival after spinal cord injury? Arch Phys Med Rehabil. 2015;96:645–51.
Silver JR. History of the treatment of spinal injuries. New York: Springer Science+Business Media, LLC; 2003.
Silver JR. History of the treatment of spinal injuries. Postgrad Med J. 2005;81:108–14.
Stockhammer E, Tobon A, Michel F, et al. Characteristics of sleep apnea syndrome in tetraplegic patients. Spinal Cord. 2002;40:286–94.
Sutton NG. Injuries of the spinal cord: the management of paraplegia and tetraplegia. Chichester: Butterworths; 1973.
Tator CH, Koyanagi I. Vascular mechanisms in the pathophysiology of human spinal cord injury. J Neurosurg. 1997;86:483–92.
van Middendorp JJ, Sanchez GM, Burridge AL. The Edwin Smith papyrus: a clinical reappraisal of the oldest known document on spinal injuries. Our Spine J. 2010;19:1815–23.
Vince RA Jr, Klausner AP. Surveillance strategies for neurogenic lower urinary tract dysfunction. Urol Clin North Am. 2017;44:367–75.
Wang D, El-Masry WS, Crumplin M, et al. Admiral Lord Nelson's death: known and unknown—a historical review of the anatomy. Spinal Cord. 2005;43:573–6.
Weidner N, Rupp R, Tansey KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.

Recommended Additional Reading

American Spinal Injury Association. International standards for neurological classification of spinal cord injury. Revised 2019. ASIA: Richmond; 2019.
Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. Wolters Kluwer: New Delhi; 2015.
Eltorai IM, Schmit JK, editors. Emergencies in chronic spinal cord injury patients. New York: Eastern Paralyzed Veterans Association; 2001.
Fulton JF, Keller AD. The sign of Babinski: a study of the evolution of cortical dominance in primates. Springfield: Charles C Thomas; 1932.
Guttmann L. Spinal cord injuries. Comprehensive management and research. Oxford: Blackwell Scientific Publications; 1976.
Maitan IB, editor. Current diagnosis & treatment: physical medicine & rehabilitation. New York: McGraw-Hill Education; 2015.
Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.
Neuburger M. The historical development of experimental brain and spinal cord physiology before Flourens. Baltimore: The Johns Hopkins University Press; 1981.
Patten J. Neurological differential diagnosis. 2nd ed. London: Springer; 1996.
Silver JR. History of the treatment of spinal injuries. New York: Springer Science+Business Media, LLC; 2003.
van Middendorp JJ, Hosman AJ, Donders AR, et al. A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: a longitudinal cohort study. Lancet. 2011;377:1004–10.
Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.
Weidner N, Rupp R, Tansey KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.
Windle WF. The spinal cord and its reaction to traumatic injury. In: Bousquet WF, Palmer RF, editors. Modern pharmacology-toxicology: a series of monographs and textbooks. New York: Marcel Dekker, Inc.; 1980.

2 Development of the Human Spinal Cord

Morphological changes in embryologic development are well documented, but understanding of regulatory mechanisms involved in cell migration and differentiation is insufficient as most human embryos cannot be dynamically studied. This comes mainly from animal experiments. The development of the human spinal cord and brain can be divided into several phases, each of which is characterized by particular developmental disorders. After implantation, the germ layers form and separate, followed by dorsal and ventral induction phases, and phases of neurogenesis, migration, organization, and myelination (ten Donkelaar et al. 2014a). The term gestational age is often used in clinical practice, starting with the first day of the last menstrual period. Usually, the number of menstrual or gestational weeks exceeds the number of postfertilization weeks by 2. In the embryonic period, postfertilization or postconceptional age is estimated by assigning an embryo to a developmental stage. In addition, a subdivision of the prenatal period into three trimester of 13 weeks each is commonly used (ten Donkelaar et al. 2014a) (Fig. 2.1). The human embryonic period, i.e., the first 8 weeks of development after fertilization, can be divided into 23

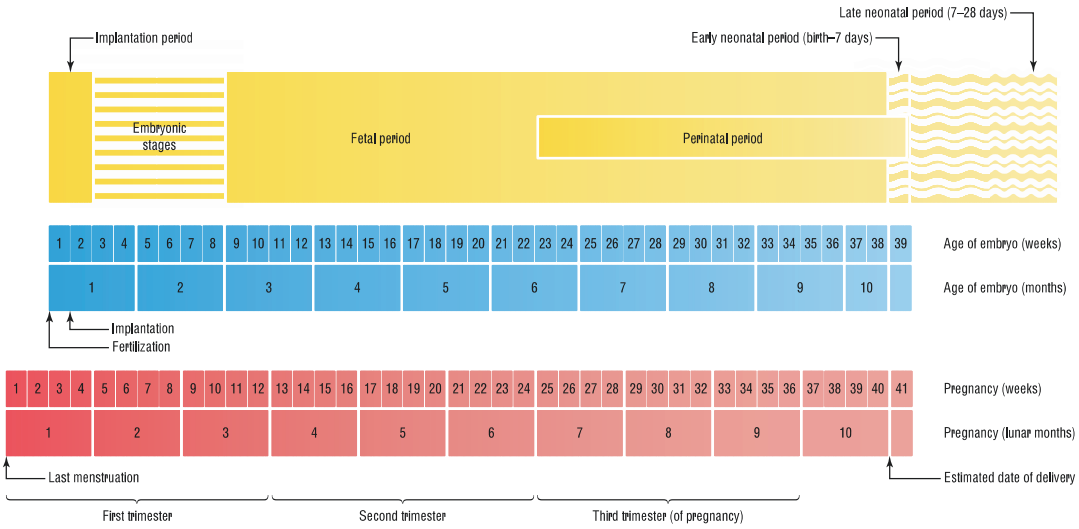


Fig. 2.1 Timescales used to describe human development. From Standring (2016)

H.-Y. Ko, *Management and Rehabilitation of Spinal Cord Injuries*,
https://doi.org/10.1007/978-981-19-0228-4_2

sages, the Carnegie stage (O'Rahilly and Müller 2010; ten Donkelaar et al. 2014a). The main external and internal features of human embryos at each Carnegie stage are summarized in Table 2.1.

All components of the central and peripheral nervous system, including the sensory organs, are derived from cells of the embryonic ectoderm and are essentially epithelial structure. The earliest derivatives of the ectoderm include the neural plate and the neural crest. The first important step in the development of spinal nervous system is the identification of dorsal ectodermal cells located along the midline of the gastrulating embryo. The folding of the neural plate, leading to the neural groove and the neural tube in sequence, is called primary neurulation. The caudal part of the neural tube does is not created by fusion of the neural folds, but develops from the so-called caudal eminence. This process is called secondary neurulation. As a result, the neural plate is formed and supports the formation of all neural cell types along the two major axes (anteroposterior and dorsoventral) that eventually form the essence of the central nervous system.

Table 2.1 Developmental stages and features of human embryo with emphasis in the nervous system

Carnegie stages	Mean length (mm)	Proposed age (postconceptional days)	External features	Internal features (with emphasis on the nervous system)
1	0.1–0.15	1	Fertilization	
2	0.1–0.2	2–3	From 2 to about 16 cells	
3	0.1–0.2	4–5	Free blastocyst	Inner cell mass and trophoblast
4	0.1–0.2	6	Attaching blastocyte	Cytotrophoblast and syncytiotrophoblast distinguishable
5	0.1–0.2	7–12	Implantation; embryonic disc circular	Amniotic cavity; primary yolk sac; extra-embryonic mesoderm
6	0.3	17	Embryonic disc elongated	Chorionic villi; primitive streak and node; prechordal plate appears; secondary yolk sac
7	0.6	19	Embryonic disc oval	Notochordal process visible; hematopoiesis starts
8	1.1	23	Primitive pit appears; neural folds may begin to form	Notochordal and neurenteric canals detectable
9	1.4	25	First somites appear; mesencephalic flexure begins; otic disc forms	Neural groove evident; 3 major subdivisions brain distinguishable; heart begins to develop
10	2.1	28	Neural folds begin to fuse; otic pit develops; 4–12 somites; pharyngeal arches 1 and 2 visible	Optic primordium begins to develop; cardiac loop appears; intermediate mesoderm
11	3.2	29	Rostral neuropore closes; 13–20 somites	Optic vesicles develop
12	3.9	30	Caudal neuropore closes; 21–29 somites; 4 pharyngeal arches visible; upper limb buds appearing	Secondary neurulation starts
13	4.9	32	Otic vesicle closed; lens disc not yet indented; 30 or more somites; 4 limb buds visible	Retinal and lens discs develop; primordium of cerebellum
14	6.5	33	Lens pit appears; upper limb buds elongated	Future cerebral hemispheres; pontine flexure; optic cup develops; adenohypophysial pouch defined

Table 2.1 (continued)

Carnegie stages	Mean length (mm)	Proposed age (postconceptional days)	External features	Internal features (with emphasis on the nervous system)
15	7.8	36	Lens pit closed; nasal pit appearing; hand plate forming	Future cerebral hemispheres become defined; retinal pigment visible
16	9.6	38	Retinal pigment visible; nasal sacs face ventrally; auricular hillocks beginning; foot plate appears	Epiphysis cerebri develops; neurohypophysial evagination; olfactory tubercle
17	12.2	41	Head relatively larger; trunk straighter; auricular hillocks distinct; finger rays	Internal and external cerebellar swellings; chondrification begins in humerus, radius and some vertebral centra
18	14.9	44	Body more cuboidal; elbow region and toe rays appearing	Oronasal membrane develops; 1–3 semicircular ducts in internal ear
19	18.2	46	Trunk elongating and straightening; ventriculus terminalis develops	Olfactory bulb develops; cartilaginous otic capsule; choroid plexus of fourth ventricle
20	20.7	49	Upper limbs longer and bent at elbows	Optic fibers reach optic chiasm; choroid plexus of lateral ventricle
21	22.9	51	Fingers longer; hands approach each other, feet likewise	Cortical plate becomes visible; optic tract and lateral geniculate body
22	25.5	53	Eyelids and external ear more developed	Olfactory tract; internal capsule; adenohypophysial stalk incomplete
23	28.8	56	Head more rounded; limbs longer and more developed; medial rotation of the lower limb to reverse the preaxial and postaxial borders	Insula indented; caudate nucleus and putamen recognizable; humerus presents all cartilaginous stages

From ten Donkelaar et al. (2014a), with permission

2.1 Gastrulation, Notochordal Formation, and Neurulation

During the first 3 weeks of development, the three germ layers (ectoderm, mesoderm, and endoderm), which form the basis of the various organs and systems of the body, are established. The second week is characterized by implantation (stage 5) and the formation of the primitive streak (stage 6). The trophoblast differentiates into the cytotrophoblast and the more peripherally situated syncytiotrophoblast that invades the endometrium. Blood-filled spaces, the lacunae, soon develop within the syncytiotrophoblast, which communicate with endometrial vessels and thus lay the foundation for the placental circulation. The embryonic cavity appears between the epiblast and the cytotrophoblast. The embryonic disc is now called the bilaminar embryo (ten Donkelaar et al. 2014a) (Fig. 2.2).

2.1.1 Gastrulation

During the first 2 weeks after fertilization, a bilaminar embryonic disc contained within an amniotic cavity is formed. The outer layer adjacent to the amniotic cavity is called the epiblast, and the inner layer adjacent to the primary yolk sac is the hypoblast. The embryonic disc migrate ventralwards along the median plane and form the primitive (primary) streak. On days 13–15, hypoblastic cells form a prechordal plate that marks the future rostral end of the embryo. In the second week gastrulation occurs, which establishes the third germ layer, mesoderm. The gastrulation, i.e., the development process until the formation of the mesoderm, proceeds as follows (Fig. 2.3). Gastrulation begins with formation of the primitive steak in the caudal region of the epiblast at about day 14 or 15. The primitive streak, a midline caudal thickening in the epiblast,

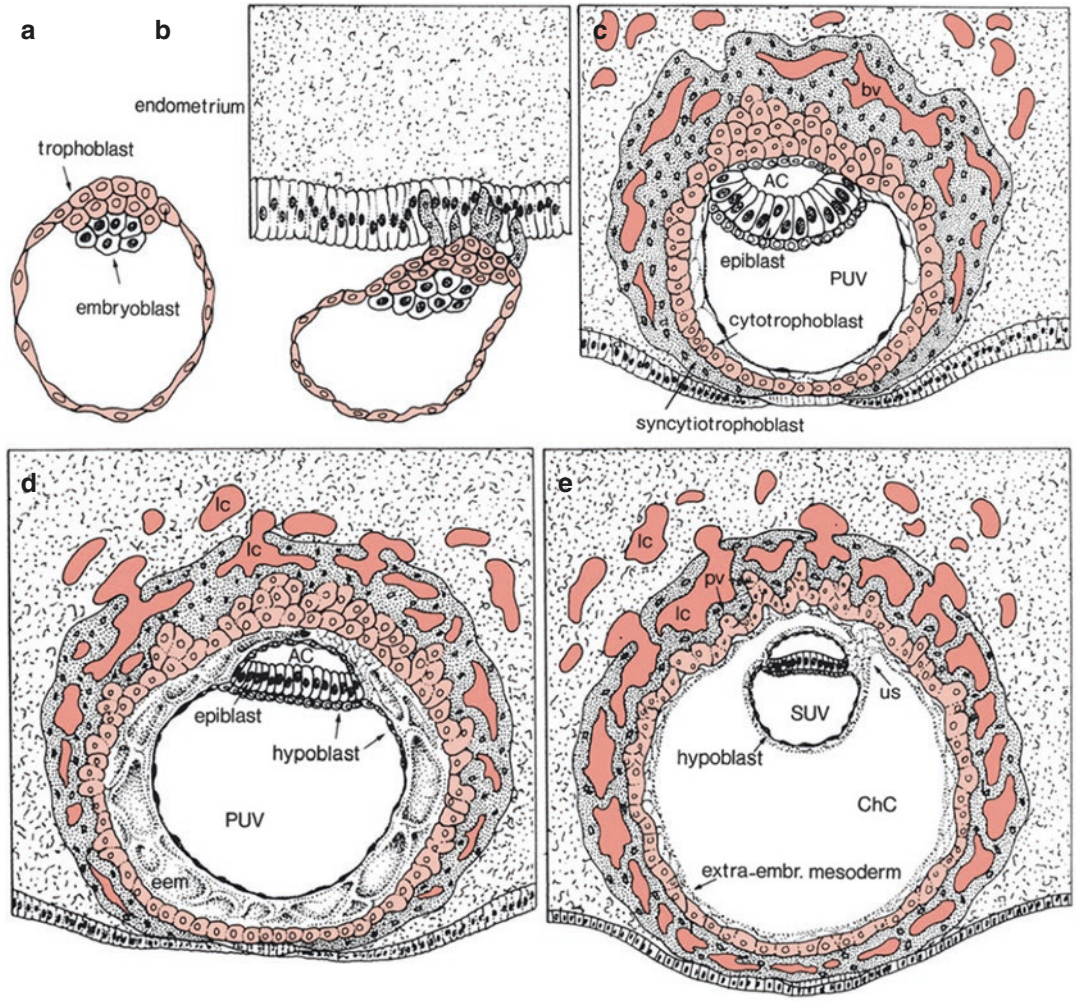


Fig. 2.2 Implantation and the formation of the bilaminar embryo: (**a**) Blastocyte; (**b**–**e**) blastocytes of approximately 4.5, 9, 12, and 13 days, respectively. The trophoblast and the cytotrophoblast are indicated in *light red*, the syncytiotrophoblast is *stippled* and maternal blood in lacunae is shown in *red*. *AC* amnionic cavity, *ChC* chorionic cavity, *eem* extra-embryonic mesoderm, *lc* lacuna, *pv* primary villi, *PUV* primary umbilical vesicle, *SUV* secondary umbilical vesicle (yolk sac), *us* umbilical stalk. From ten Donkelaar et al. (2014a), with permission

appears. The primitive streak enlarges and elongates and develops a thickening at its rostral end, the primitive node or Hensen's node. The rostral, usually distinct part of the primitive streak is known as the primitive node of Hensen. The primitive streak is a way of entrance in which cells invaginate, proliferate, and migrate to subsequently form the extra-embryonic mesoderm, the endoderm, and the intra-embryonic mesoderm (ten Donkelaar et al. 2014a). The extra-embryonic mesoderm soon covers the trophoblast, the amniotic ectoderm and the yolk sac. Simultaneously, a central depression, the primitive groove, is developed along the primitive streak to form the primitive pit at the level of Hensen's node. The proliferating cells from the epiblast migrate into the primitive streak and groove and then move rostrally between the epiblast and hypoblast to form the third embryonic layer, the mesoblast.

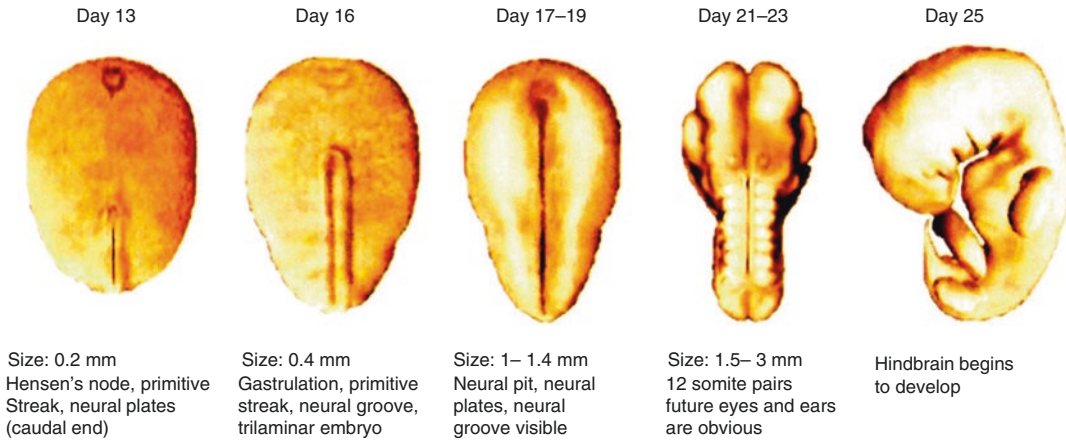


Fig. 2.3 Gastrulation and primary neurulation stages from development of Hensen's node on day 13 to closure of anterior neuropore on day 25. Gastrulation is the development process until formation of the mesoderm. Gastrulation begins with formation of the primitive streak in the caudal region of the epiblast. From Flint and Rusbridge (2014), with permission

2.1.2 Notochordal Formation

On days 16–17, mesoblastic cells migrate rostrally to Hensen's node in the midline to form the notochordal process (Fig. 2.4). In the rostral area of the primitive streak, an extension below the ectoderm, the notochordal process, arises from the primitive node and extends rostrally to the prechordal plate. The notochord is a cylindrical structure derived from mesodermal cells that specifies the midline of the embryo. It also serves as inductive signals essential for the formation of the nervous system from the overlying ectoderm. The mesoderm, which originates from the primitive streak, then condenses on both sides of this process. Subsequently, the primitive pit at Hensen's node extends into the notochordal process and creates a central notochordal canal. The canalized notochordal process is fused with the adjacent ventral entoderm (hypoblast). These two cell layers are degenerated at the fused site to create a longitudinally grooved notochordal plate in the roof of the yolk sac and allowing the notochordal canal to communicate with the yolk sac. From the cranial end, the notochordal plate is then infolded to form the solid notochord. The notochord plays a key role in inducting the overlying ectoderm to form the neural tube and acts

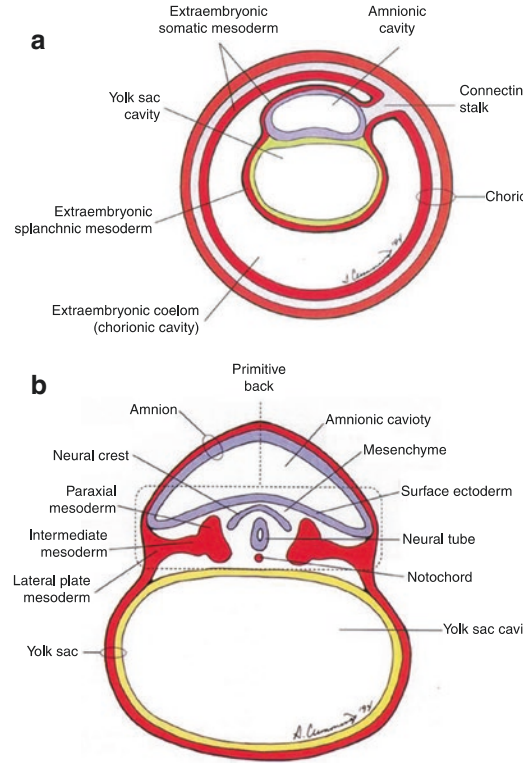


Fig. 2.4 On days 16–17, mesoblastic cells migrate rostrally to the Hensen's node in the midline to form the notochordal process. It serves as inductive signals essential for the formation of the nervous system from the overlying ectoderm. (**a**) GW 2, (**b**) GW 3

as the structure around the mesoderm to form the vertebral column. An important transitory communication between the forms of the amniotic cavity and yolk sac is known as the neurenteric canal. The neurenteric canal is of great importance for development of the spine and spinal cord. Impaired development of notochord and neurenteric canal development are mechanisms that cause complications such as diastematomyelia, neurenteric cyst, and combined anterior and posterior spina bifida (Copp and Greene 2013; Greene and Vopp 2014).

2.1.3 Neurulation

In humans, the next major step in the development of the spinal cord is around days 20 (the third week) after fertilization. Here, fusion of the opposing neural folds and subsequent formation of the neural tube occurs at the hindbrain-spinal cord junction. This event requires several days and must be coordinated simultaneously at the rostral and caudal ends. Closure of the neural tube takes 4–6 days. After the closure of the neural folds, both ends temporarily remain open and are called neuropores (O'rahilly and Müller 2002) (Fig. 2.5). Neurulation, the process of neural tube formation that will become the spinal cord and brain, occurs during days 18–27. Rostral to Hensen's node, the ectoderm that covers the notochordal process is initially thickened to form the neural plate. The edges of the neural plate are heaped to create the neural folds and the midline neural groove. Changes occur first in the middorsal region of the embryo, the site of the future cervical cord, and continue to caudal.

The precursor of spinal cord and brain is the ectodermal thickening called the neural plate (day 18). Within 24 hours after the first appearance of neural plate, the cells of the neural plate proliferate rapidly and form the neural groove by

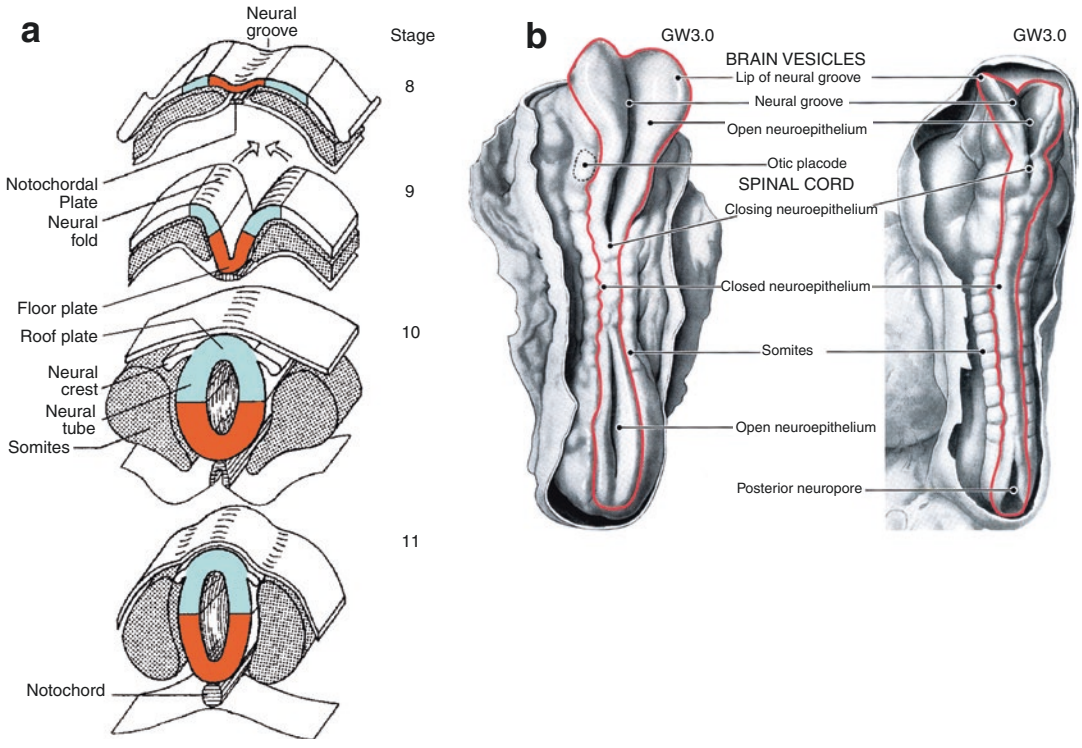


Fig. 2.5 GW 3 primary neurulation. The open neuroepithelium develops into a closed neuroepithelium. On day 18, the neural plate can be distinguished from the surrounding ectoderm. Within 24 hours of the first appearance of the neural plate, folds appear at their respective edges. Closure of the neural tube takes 4–6 days. Prior to completion of closure, the open ends of the tube form the anterior (cranial) and posterior (caudal) neuropore (**a**) cross-sectional diagram, (**b**) dorsal view. From Altman and Bayer (2001)

folding the neural plate at the time of appearance of the first mesodermal somites (Sadler 2005) (Fig. 2.6). As the neural plate develops, the mesoderm is condensed on each side of the notochord to form the paired somites. Beginning about day 20, they initially develop rostrally at the region of the future occipital bone and proceed caudally, resulting in up to 44 pairs that extend to the coccygeal level. Finally, the first occipital pair and the caudal 5–7 coccygeal ones will regress.

The neural folds on both sides of the groove gradually gather together to create a neural tube separated from the overlying embryonic sheath. The formation of the most caudal part of the neural tube occurs during days 28–48. Undifferentiated cell mass of the primitive steak caudal to the posterior neuropore develops vacuoles, which fuse to create a neural tube and connect to the rostral neural tube. Cells located at the lateral borders of the neural plate proliferate at the neural folds to form neural crests, for which the cranial, spinal, and autonomic ganglia appear (Watson et al. 2009).

Days 22–23 marks a deepening of the neural groove and convergence of the neural folds in the dorsal midline to create the neural tube. Several factors contribute to the complex event of embryonic folding, not only along the midline, but also in a dorsoventral orientation, which eventually closes and forms the neural tube. Cell intercalation in the embryonic midline leads to a narrowing along the medial-lateral axis (convergence) and concomitant rostrocaudal lengthening (extension) (Keller et al. 2008). Somites first arise at stage 9 in longitudinal rows on each side of the neural groove. The first four pairs of somites belong to the occipital region. Within the next 10 days subsequently 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and some 3–6 coccygeal somites are formed, but they are never visible together at one stage of development (ten Donkelaar et al. 2014a). Closure of the neural groove begins initially at the region of the third or fourth somite, the future cervicomedullary junction, and continues both rostrally and caudally at the same time. Rostrally and caudally, the cavity of the developing neural tube communicates via the rostral and caudal neuropores with the amniotic cavity. At days 24–25, the neural tube

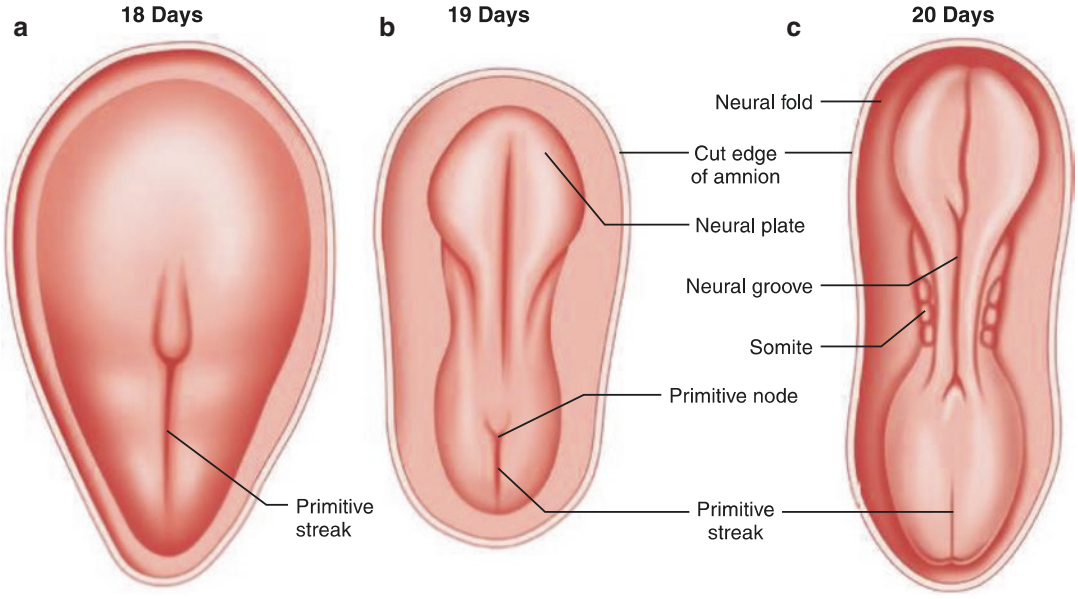


Fig. 2.6 Dorsal views of embryo showing the early stages of gastrulation and neurulation at various days after fertilization. (**a**) The primitive streak, consisting of a narrow groove, forms in the caudal part of the embryo. At the streak's cranial end is an elevation, the primary node surrounding a depression, the primitive pit. (**b**) The neural plate is induced at the cranial end of the embryo and signals the initiation of neurulation. The primitive streak of the cranial end of the embryo remains involved in the process of gastrulation. Thus, gastrulation and neurulation continue simultaneously in the human embryo. (**c**) The neural plate has now elevated to form the neural folds creating a neural groove in the midline. From Sadler (2005), with permission

completes its rostral closure at the anterior neuropore within a few hours, which becomes the site of the lamina terminalis for the development of the brain vesicle. On days 26–27, caudal closure of the neural tube occurs at the posterior neuropore, corresponding to the L1/L2 segment of the spinal cord. The closure of the neural tube in human embryos is generally described as a continuous process that begins at the level of the future cervical region, and proceeds both rostrally and caudally. This process of neural tube closure and extension of the spinal cord to S4/S5 is called primary neurulation (Fig. 2.7). The more caudal cord segments do not develop by neurulation but later by the process of canalization. Unlikely more rostral elements of the spinal cord, the conus medullaris and the film terminals form through the process of secondary neurulation. The secondary neurulation is described as the event in which more caudal levels of the spinal cord are generated by connection and fusion of mesodermal cells (Sadler 2005). The neural tube caudal to the midsacral region is continuous with the caudal end of the primary neural tube but forms by a distinct process, termed secondary neurulation (Copp and Greene 2013). Secondary neurulation is the continuing formation of the sacrocaudal part of the spinal cord without direct involvement of the surface ectoderm, i.e., without the intermediate phase of a neural plate (O'Rahilly and Müller 2006). This process involves condensation of a population of tail bud-derived mesenchymal cells to form an epithelial rod that undergoes canalization to form the lumen of the tube in the lower sacral and coccygeal regions. Secondary neurulation involves only the formation of the most caudal part of the conus medullaris, the filum terminale and a focal dilatation of the central canal, known as the ventriculus terminalis. Malformations resulting from disturbance of secondary neurulation are closed (skin covered) and often involve tethering of the spinal cord, with associated ectopic lipomatous material (Greene and Vopp 2014) (Fig. 2.8c).

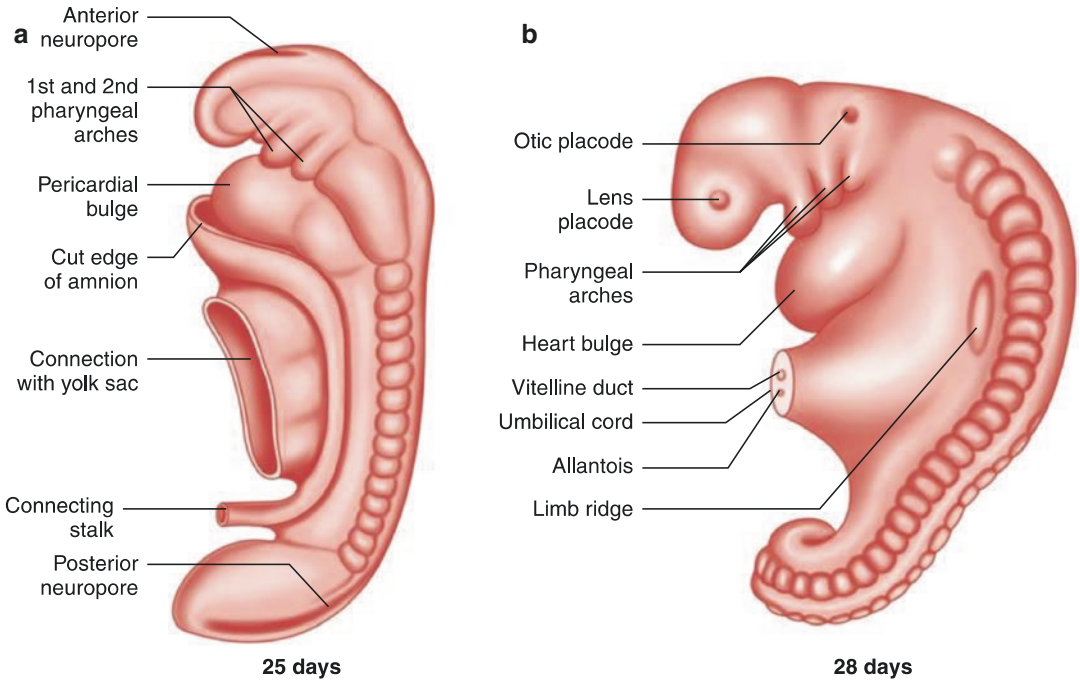


Fig. 2.7 On days 25–28, caudal closure of the neural tube occurs at the posterior neuropore. This process of neural tube closure and extension of the spinal cord to S4/S5 is called primary neurulation. (**a**) Closure of the anterior neuropore is completed on day 25. (**b**) Closure of the posterior neuropore is completed on day 28. From Sadler (2005), with permission

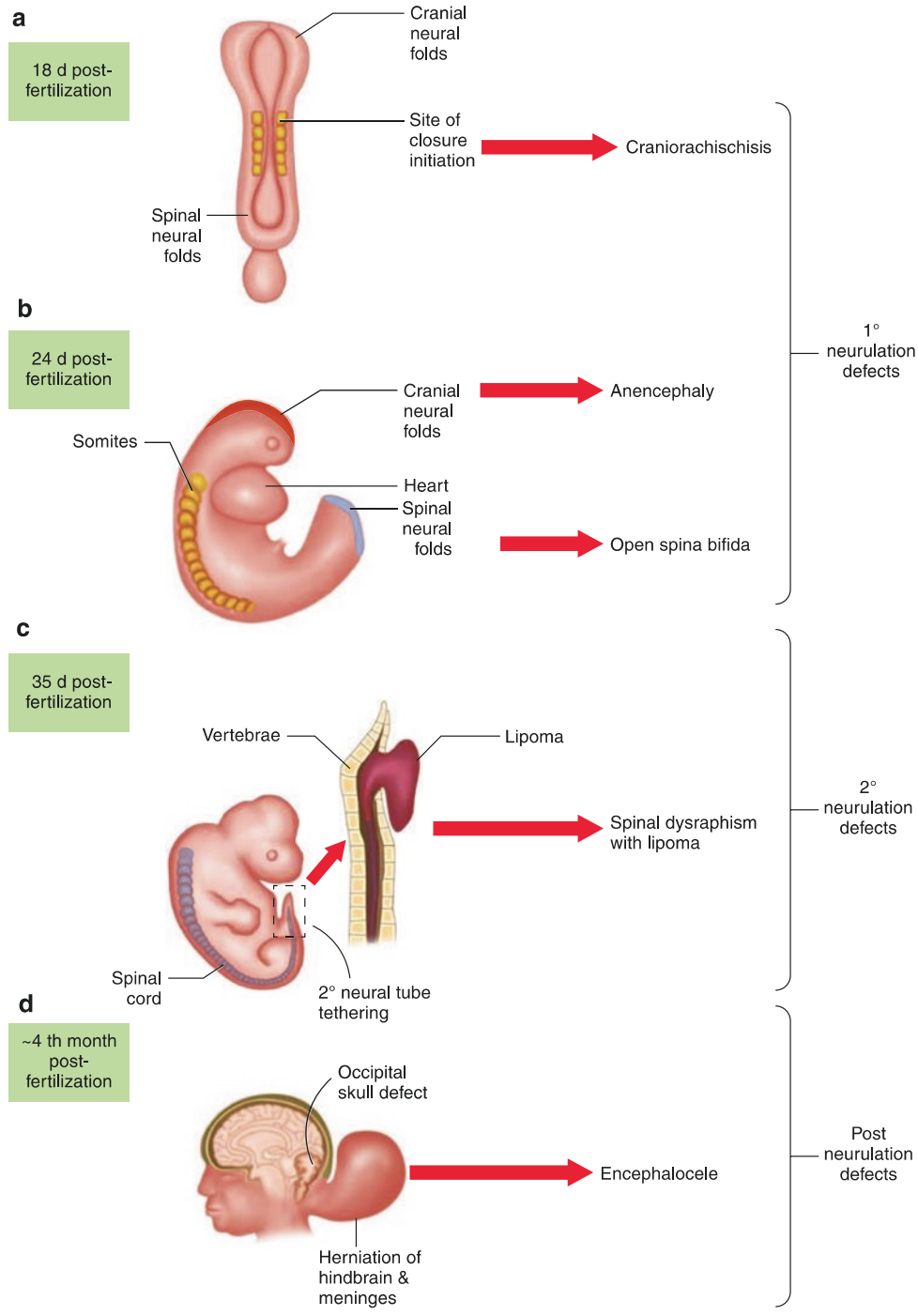


Fig. 2.8 Diagrammatic representation of the developmental origin of malformations broadly classified as neural tube defects in humans. (**a**, **b**) Disorders of primary neurulation include craniorachischisis (**a**) in which the neural tube fails to initiate closure, leaving most of the brain and the entire spine open (**b**), generating exencephaly/anencephaly and open spina bifida (myelomeningocele), respectively. (**c**) Disorders of secondary neurulation comprise failure of the neural tube to separate completely from adjacent tissues, resulting in tethering and diminished mobility. The spinal cord is covered by skin and is often associated with fatty tissue accumulation (lipoma) through as-yet-unknown mechanisms. (**d**) Postneurulation defects can arise when the bony structure of the skeleton fails to develop fully. Herniation of the meninges, with or without brain tissue, through a skull defect, generates encephalocele, while an analogous defect in the spinal region produces meningocele. From Greene and Vopp (2014), with permission

The progressive closure of the neural tube completes the basic form of the spinal cord when the last somites occur about 30 days of gestation, with the embryo being 4 mm in length. The rostral neuropore closes completely at about 30 days (stage 11) within a few hours, and caudal neuropore about 1 day later (stage 12). An opening in the central canal of the tube, the posterior neuropore, is normally closed by this time. The median and lateral hinge points are necessary for the proper folding and closing of the neural tube, and a number of neural tube closure defects along the embryo can lead to abnormalities in the spinal cord. Depending on the position of the defect, it can range from anencephaly to craniorachischisis, lumbosacral spina bifida, or spinal dysraphism and encephalocele (Copp and Greene 2013; Greene and Vopp 2014) (Fig. 2.8).

2.2 Development of the Spinal Cord

Initially, the wall of the neural tube consists of a single layer of neuroepithelial cells, the germinal neuroepithelium or the matrix layer. As this layer thickens, its nuclei are arranged in more and more layers. Mitosis occurs only on the inner ventricular side of the cell layer, and migrating cells form a second layer around the original neural tube. This layer, the mantle layer or intermediate zone, becomes progressively thicker as more cells from the germinal neuroepithelium, now called the ventricular zone. The mantle layer of the neural crest between the ventricular zone and the marginal zone is located around the primitive spinal cord and arises from multiple neuroepithelial cell divisions (ten Donkelaar et al. 2014a). The mantle layer becomes the gray matter of the spinal cord. The marginal zone eventually becomes the white matter of the mature spinal cord. Two distinct paired regions can be seen in the mantle layer: the dorsal thickening is called the alar plate (future sensory areas of the spinal cord) and the ventral thickening is the basal plate (future motor area of the spinal cord). The alar plates and incoming dorsal roots form the afferent or sensory part of the spinal cord, whereas the basal plate and its exiting ventral roots form the efferent or motor part. The spinal ganglia originate from the neural crest (ten Donkelaar et al. 2014a).

There is a ventral-to-dorsal gradient of histogenesis in the development of the spinal cord, with motor neurons appearing first, followed by neurons in the intermediate zone and, finally, neurons in the dorsal horn (Table 2.2). Motor neurons are the first neurons to develop (Bayer and Altman 2002). The motor neurons that form the nuclei of the ventral gray columns appear in the uppermost spinal segments at approximately embryonic day 27 and progresses in the caudal direction, reaching the site of the cervical enlargement at about 30 days. At this time of development also dorsal root ganglion cells are present. Dorsal root fibers enter the spinal gray matter very early in development. The subdivisions of the ventral gray column begin to appear apparent before the end of the sixth week. The neurons of the ventral horn arise from five different columnar subpopulations. The lateral motor neurons located in the cervical and lumbosacral enlargement of the spinal cord will later innervate the muscles of the extremities (Tomlinson et al. 1973). The medial motor neurons, which are found in the entire spinal cord, will later innervate axial muscles. The visceral motor neurons

Table 2.2 Time of neuron origin for the human spinal cord

Neuron	Time of neuron origin
Motor neurons	
Cervical cord	3.5–5.7 weeks of development
Thoracic cord	4.1–5.7 weeks of development
Lumbar cord	4.1–5.7 weeks of development
Intermediate zone	Fourth to fifth week
Dorsal horn (substantia gelatinosa)	6.7–7.4 weeks of development
Dorsal root ganglion cells	Fourth to fifth week
Ascending tract neurons	
Contralaterally projecting neurons	4.1–5.7 weeks of development
Ipsilaterally projecting neurons	5.8–6.6 weeks of development

occur in the intermediolateral column in the thoracic and upper lumbar segments.

The development of skeletal muscle fibers from myotomes and limb bud mesenchyme is parallel to the development of neural structures. Myofibrils appear in human myoblasts during fifth weeks, and the cross striations are visible at 7 weeks. Between the fifth and sixth weeks of development, a myotome becomes divided into a dorsal epaxial part or epimere and a ventrolateral hypaxial part, the hypomere (ten Donkelaar et al. 2014b). Figure 2.9 shows both quantitative and qualitative changes in the developing spinal cord of a GW 4.5 embryo. The quantitative change is the growth of the lateral neuroepithelium. The formation of the cluster of differentiating cell signals the onset of the exodus of postmitotic cells from the ventral neuroepithelium and the onset of differentiation of the earliest spinal cord neurons, the ventral horn motor neurons. Nerve fibers enter the primordial muscles, and simple nerve endings are present among myoblasts in human embryos at gestation 7 weeks (Fig. 2.10). There are neurons in the spinal ganglia of the human embryos before the beginning of the fifth week. The ganglion cells are initially bipolar, and their central processes reach the spinal cord, where they initiate the posterior funiculi. Interneurons are born both in the areas of the dorsal root plate as well as the ventral root plate. The posterior spinal cord forms six distinct progenitor pools (dp1–dp6). Interestingly, most of these early subtypes develop into commissural interneurons projecting to the contralateral side of the spinal cord. In the mature central nervous system, these commissural interneurons are essential components of left-right locomotor coordination and are major components of central pattern generators playing a fundamental role in the rhythmic, coordinated movement of the limbs and trunk (Vallstedt and Kullander 2013).

Regression is the process of formation of the filum terminale and the cauda equina and the migration of the conus medullaris to its adult

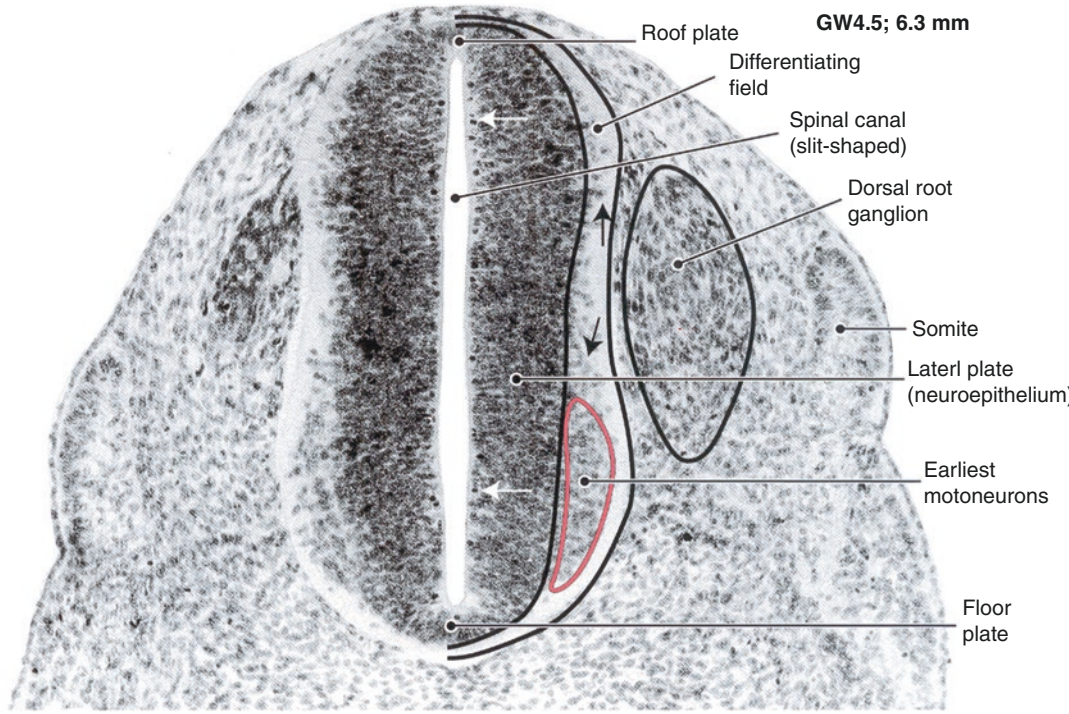


Fig. 2.9 GW 4.5. The cluster of differentiating cells that flank the ventral neuroepithelium (red outline) is the earliest motoneurons of the incipient ventral horn. From Altman and Bayer (2001)

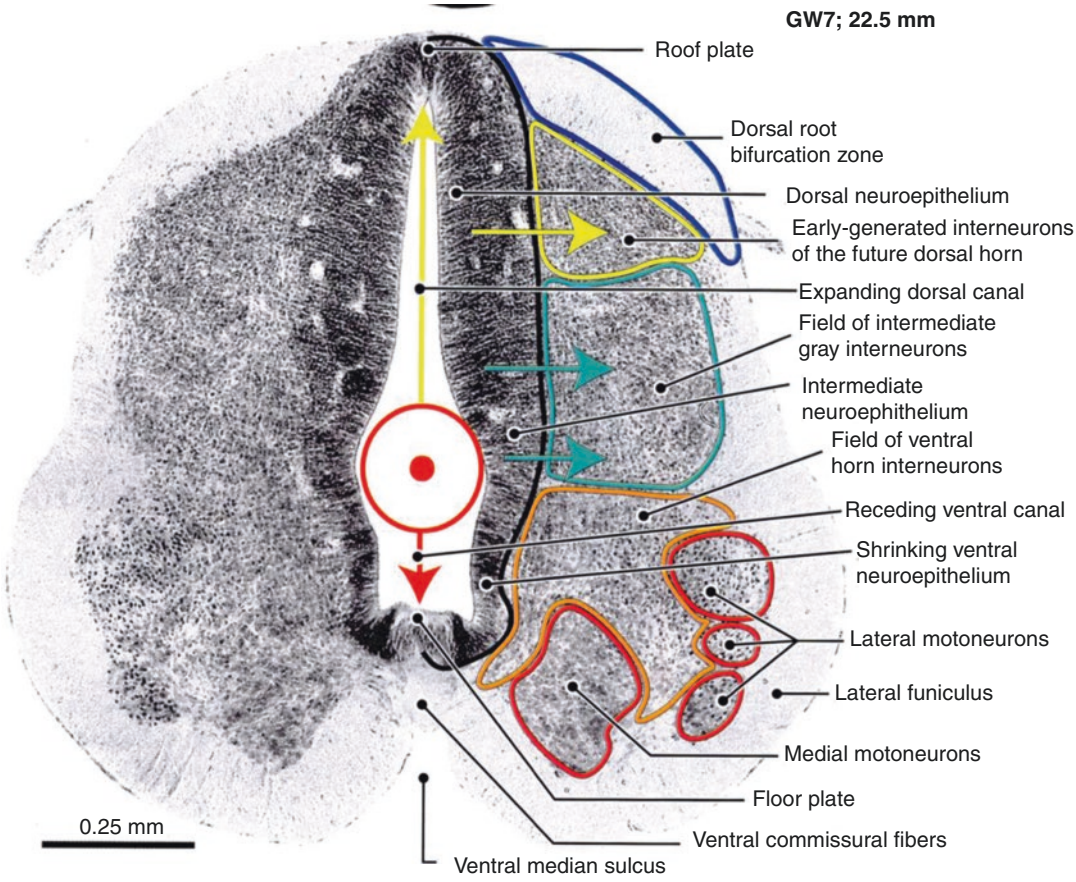


Fig. 2.10 GW 7.0. The cervical spinal cord in a GW 7.0 embryo. The ventral canal and the ventral neuroepithelium are disappearing, and the ventral horn motoneurons have grown considerably, but the population of dorsal interneurons (yellow) is small. From Altman and Bayer (2001)

level at the L1/L2 vertebral body. On days 43–48, the future site of the conus medullaris, known as the ventriculus terminalis, develops. Initially, it is located at the level of the second coccygeal vertebra. At 3 months, the appearance of the spinal cord is similar to that of the adult, but unlike the adult, it occupies the entire spinal canal. Until then, the mantle layer has a shape that characterizes mature gray columns, and the dorsal and ventral horns are connected by an isthmus, including the central canal lined by ependymal cells. The nerve fibers of the marginal layer are unmyelinated and, until the middle of the gestation period, the myelination begins to produce white matter in the spinal cord. At the end of the embryonic period (8 weeks), the spinal cord still extends to the end of the vertebral column. During the fetal period, it ascends to lumbar levels owing to disproportional growth of the spinal cord and the vertebral column. Until the 11th gestational week, the length of the spinal cord corresponds to that of the vertebral column. Then, the "ascensus medullae" begins, the filum terminale is formed, and the lower spinal nerves show a progressive obliquity due to the difference in growth between the spinal cord and the vertebral column (ten Donkelaar et al. 2014b). The caudal neural tube may then regress, and the ventriculus terminalis around the spinal canal is obliterated, thus allowing the ventriculus terminalis to rise within the spinal canal. This is 18 weeks at the level of L4 vertebral body because it is relatively fast at the beginning. Then, the rise is slowed down, and the tip of the spinal cord is at the L2–

L3 interspace at birth and reaches the adult level of the L1–L2 interspace by the first three postnatal months. When the neural tube rises, there remains a fibrous band between the ventricularis medullaris and the tip of the coccygeal vertebrae, which becomes the filum terminale. During this ascent, the nerve roots that originally leave the spinal canal opposite to their segmental origin of the spinal cord must belong to be the cauda equina (Keegan and Garrett 1948).

The discrepancy between the position of spinal cord segments with their nerve roots and corresponding bony structures due to differences in growth rates during embryonic development becomes more evident in the more caudal spinal cord segments so that the nerve roots connected to the lower lumbar, sacral, and coccygeal spinal cord segments have to travel longer distances before reaching appropriate intervertebral foramina to pass. As the nerve roots descend to their corresponding vertebral level, they become more oblique from rostral to caudal so that the lumbar and sacral nerves descend almost vertically to reach their exit points. These long spinal nerve roots surrounding the filum terminale form the cauda equina, in which most caudal segments are most centrally located. The three vertebrae (T11–L1) usually lie overall ten lumbosacral spinal cord segments (L1–S5). From C5 to C8 spinal cord segment level is 1 level higher than the corresponding vertebral body. Thus, the C5 cervical vertebral body corresponds to the level of the C6 spinal cord segment. In the upper thoracic region, the vertebral body is two segments above the corresponding cord segment. In the lower thoracic and upper lumbar regions, the difference between the vertebral level and spinal cord segment level is two or three segments so that a spinal cord sensory level at T9 would correspond to a pathologic abnormality at the T6 or T7 vertebral body. The levels of the lumbar and sacral spinal cord segments correspond to vertebral T12–L1 levels (Table 2.3).

The cord is an approximately cylindrical structure of average length 45 cm in the male and less than 43 cm in the female. The spinal cord has an uneven contour due to the presence of cervical and lumbar enlargements associated with the spinal nerves for the upper and lower extremities.

Table 2.3 Vertebral bodies in their relations to corresponding spinal cord segments

Vertebral body	Corresponding spinal cord segment
Upper cervical (C1–C4)	Same spinal cord segment
Lower cervical (C5–C7)	Add 1 segment
Upper thoracic (T1–T6)	Add 2 segments
Lower thoracic (T7–T10)	Add 3 segments
T11–T12	Lumbar segments
T12–L1	Sacral segments (conus medullaris)
Below L1	Cauda equina

The enlargements appear first in the embryo at the time of formation of the limbs. The size of the spinal cord in adults is four times longer than at birth. Its weight increases from 7 to 90 g or more, and its volume in adults increases from 6 to nearly 80 mL.

2.3 Development of the Human Pyramidal Tract

At the end of embryonic period, the pyramidal tract reaches the level of the pyramidal decussation. After reaching the level of the pyramidal decussation at the end of the embryonic period, there is a rather long waiting period occurs. Pyramidal decussation is complete by 17 weeks of gestational age, and the rest of the spinal cord is invaded the lower thoracic cord by 19 gestational weeks and the lumbosacral cord by 29 gestational weeks (Altman and Bayer 2001). Figure 2.11 shows the schematic reaching of the corticospinal tract. Following a waiting period of up to several weeks, corticospinal tract fibers progressively innervated the gray matter.

2.4 Metamerism

The spinal cord is a segmental organ. Each of the 31 pairs of spinal nerves supplies a metamere or body segment derived from an embryonic somite.

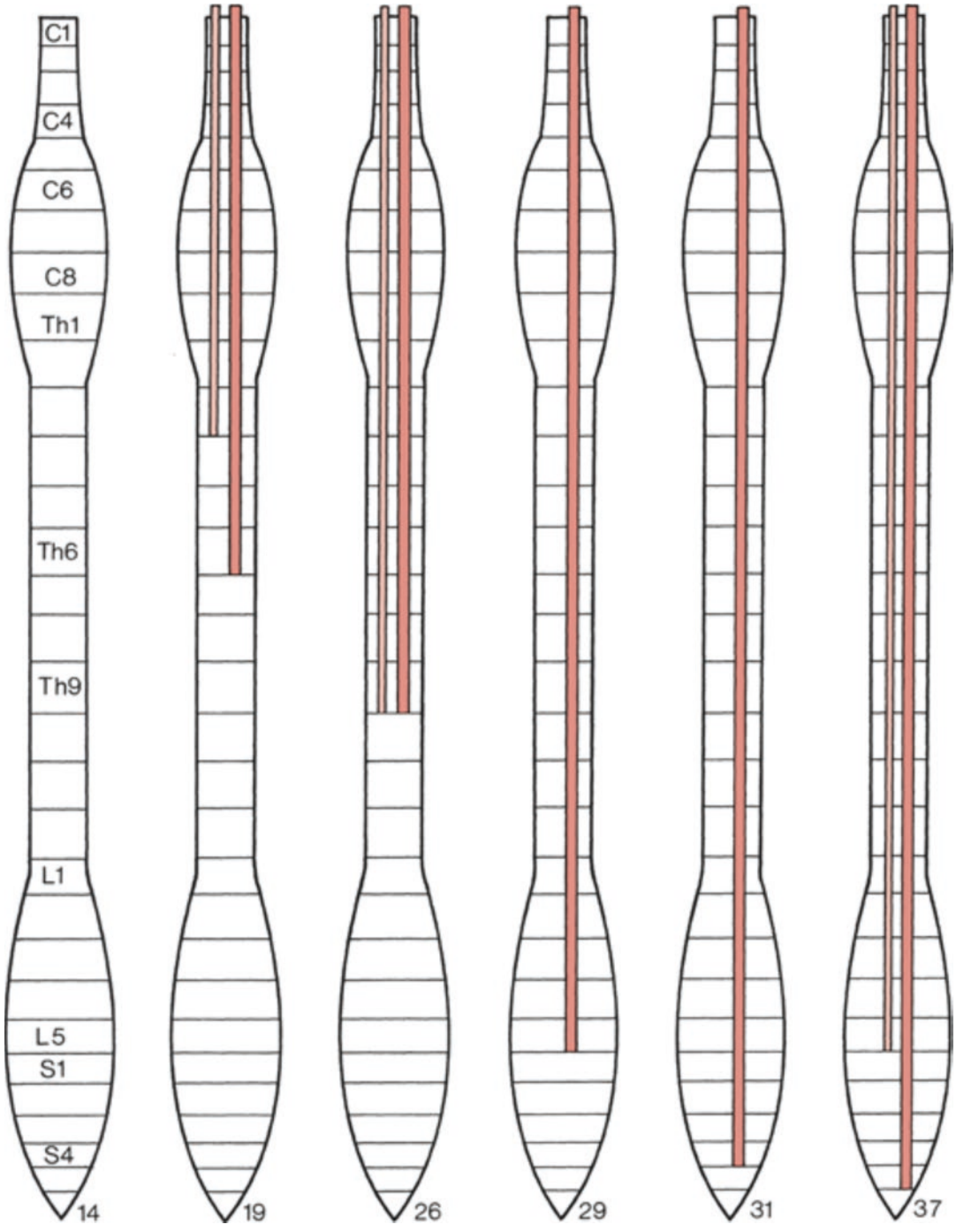


Fig. 2.11 The spinal outgrowth of the human corticospinal tract for 14, 19, 26, 29, 31, and 37 gestational weeks. Light reds show the outgrowth of the anterior corticospinal tract, and reds show the outgrowth of the lateral corticospinal tract. From Altman and Bayer (2001)

Somites appear first at days 25 (stage 9) in longitudinal rows on each side of the neural groove. The first four pairs of somites belong to the occipital region. Within the next 10 days, 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and some 3–6 coccygeal somites are formed. Each somite divides into a ventromedial sclerotome, which is involved in the formation of the vertebral column, and a dorsolateral dermomyotome that forms a myotome and the overlying dermis (dermatome). Each myotome divides into two parts: (1) a dorsal epimere, from which the erector spinae arises, and (2) a ventral hypomere, from which the ventral vertebral muscles (epaxial muscles), the muscles of the lateral and ventral body wall (hypaxial muscles) and the muscles of the extremities arise. The derivatives of the epimeres are innervated by the dorsal rami of the spinal nerves, those of the hypomeres by the ventral rami (ten Donkelaar et al. 2014a). Metamerism is more evident in the thoracic than in other regions of the adult body, and the fields of sensory innervation are easier to identify than those of motor innervation. The outgrowth of limb buds in the embryo causes complicated metameric patterns.

The body surface areas supplied by the nerve fibers from a single dorsal root ganglion are defined as a dermatome (Standring 2016). It is generally considered to arise from an initial segmental pattern in the early limb buds that corresponds to the segmental pattern in the trunk, which is subsequently rearranged in some way to correspond to the adult pattern (McLachlan 1990). The dermatomes are orderly in the embryo, but they are distorted by the outgrowth of the limbs along the ventral axial line so that the C4 dermatome is above T2 at the level of the sternal angle. Finally, the C5 dermatome is located next to the T1 dermatome (Biller et al. 2017; Vanderah and Gould 2016) (Fig. 2.12). The axial lines indicate areas in which there is no sensory overlap. A similar relationship exists in the lower extremities. Initially, each lower limb bud has a cephalic border and a caudal border. These are known as the preaxial and the postaxial borders, respectively. In the embryo, the great toe and tibia lie along the preaxial border, and little toe and fibula along the postaxial border. At the end of the embryonic period (eighth week), medial rotation of the lower limb reverses the preaxial and

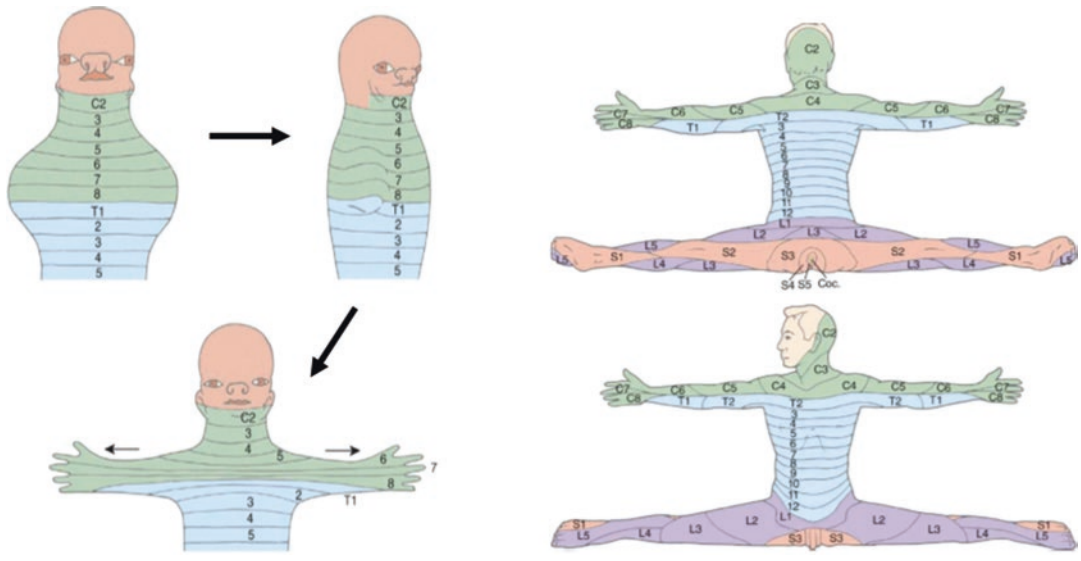


Fig. 2.12 Development of dermatomes of the upper extremity of human embryos. Outgrowth of limbbuds in the embryo results in complications of the metameric patterns. Finally, the C5 dermatome lies next to the T1 dermatome due to outgrowth of the upper extremities carrying the intervening dermatomes. From Biller et al. (2017)

postaxial borders, creating a spiral arrangement of the dermatomes (Fig. 2.13). Therefore, the great toe and tibia are carried medially, the little toe and fibula laterally. Thus, the tibial border is the original preaxial border, and the fibular border is the postaxial border of the lower limb. The great toe is supplied by nerves from a more rostral dermatome (L4) rather than the little toe (S1). The lower extremity is an extension of the trunk, and most caudal dermatomes supply the

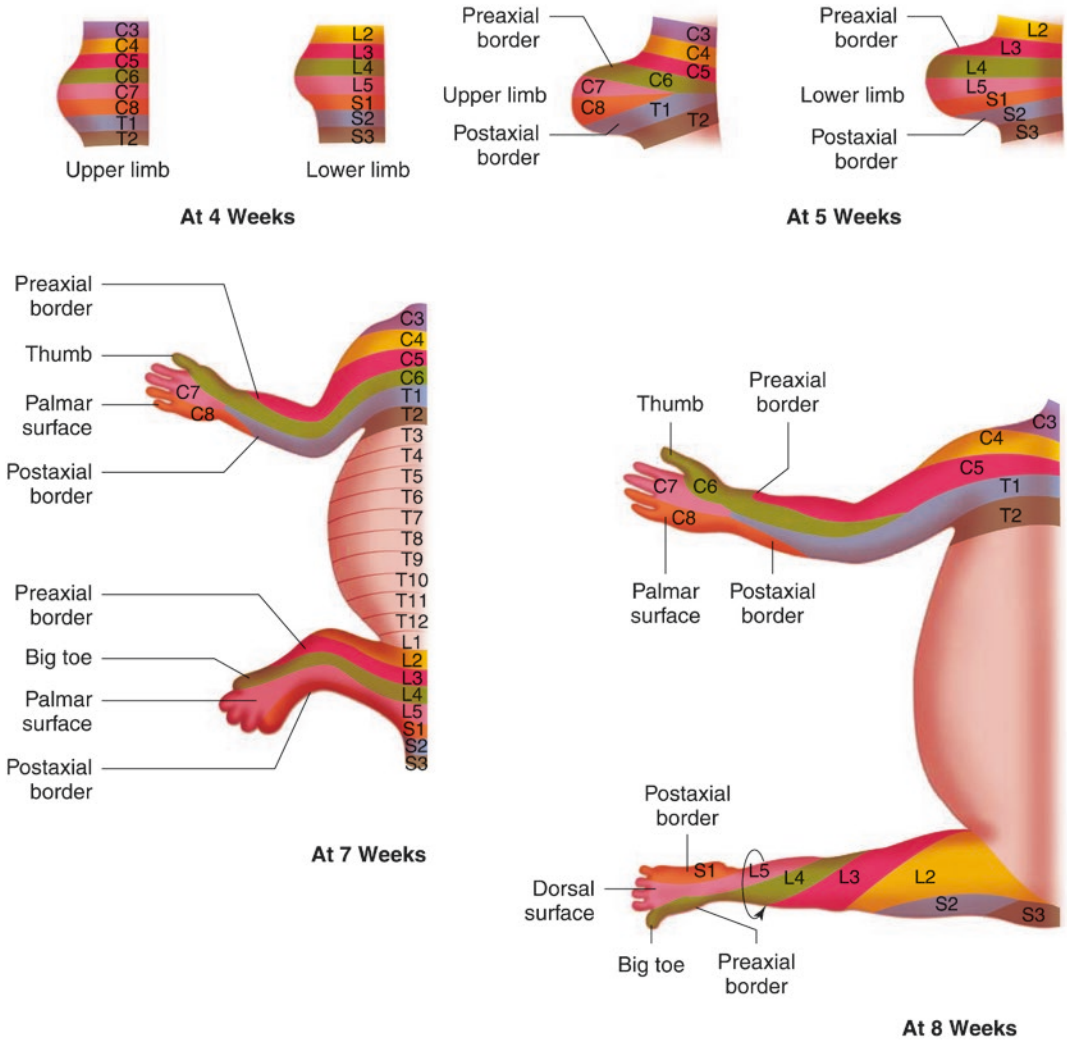


Fig. 2.13 Changes in ventral dermatome pattern during limb development with limb rotation. Rotation of the lower limb results in a reversal of the preaxial and postaxial borders, producing a spiral arrangement of dermatomes. Spinal nerve segments on the anterior surface of the lower extremity extend medially and inferiorly; the great toe (hallux) is supplied by nerves from a more rostral dermatome (L4) than the little toe (S1). The lower extremity is an extension of the trunk, and the most caudal dermatomes (sacral and coccygeal) supply the perineum, not the foot. Cervical dermatomes maintain a relatively orderly distribution to the upper extremity with minimal rotation. From Felten et al. (2016)

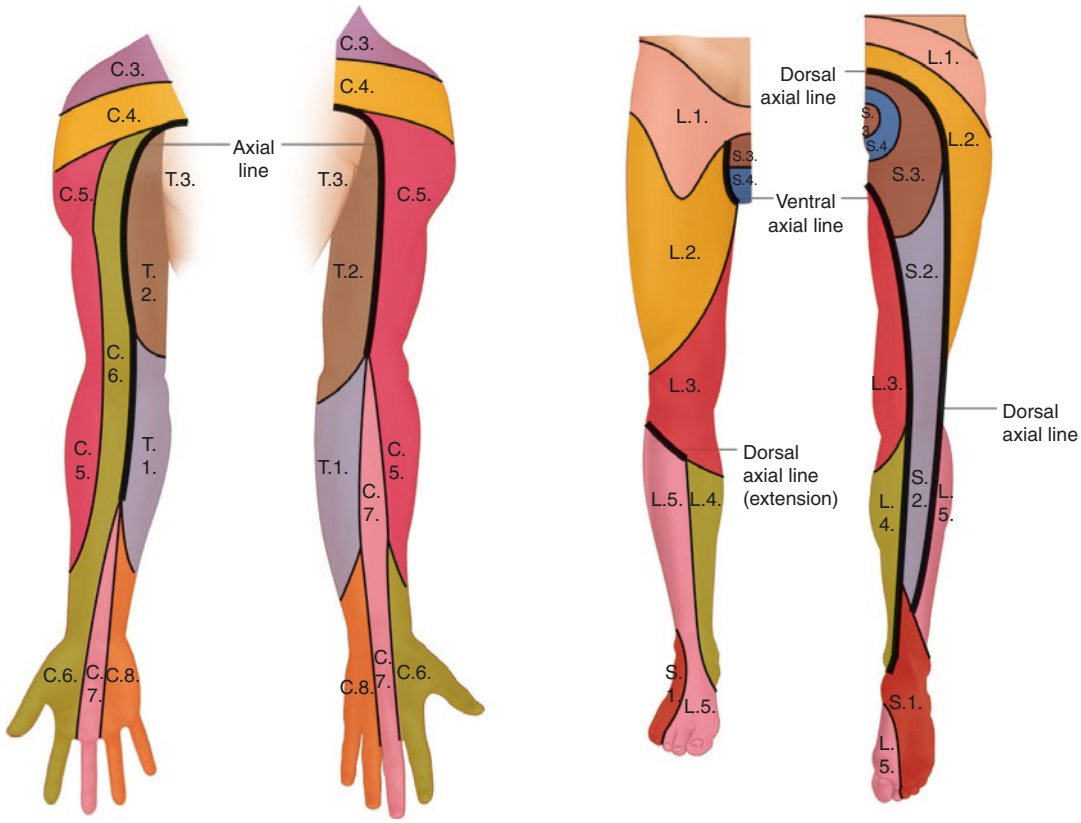


Fig. 2.14 Sensory distribution of the spinal segments to the skin of the upper and lower extremities and schematic drawing of the ventral and dorsal axial lines. From Medical Research Council (1956)

perineum, not the foot (Felten et al. 2016). Cervical dermatomes maintain a relatively orderly distribution in the upper extremity with minimal rotation. Figure 2.14 shows a showing schematic drawing of the ventral axial line (preaxial line) and dorsal axial line (postaxial line) in the upper and lower extremities. Within the same spinal cord segment, the region of the sensation is also determined by the typical topographic organization (Altman and Bayer 2001) (Fig. 2.15). Most dermatomes overlap one another to a varying extent, but there is less overlap with pain and temperature than with touch. An overlap of sensory fibers, which can reach 25–40 mm, occurs along the midline (Kellgren 1939). Due to the varying degree of overlap of adjoining dermatomes, the area of sensory loss as a result of spinal cord or nerve root injury is always smaller than the actual area of dermatomes.

Metamerism also occurs in the innervation of skeletal muscles. Few muscles have been derived from a single somite. The adductor pollicis and some of the small deep muscles of the back may have a monosegmental innervation. Other muscles receive nerve fibers from two to five ventral roots, especially in the upper and lower extremities (Keegan and Garrett 1948).

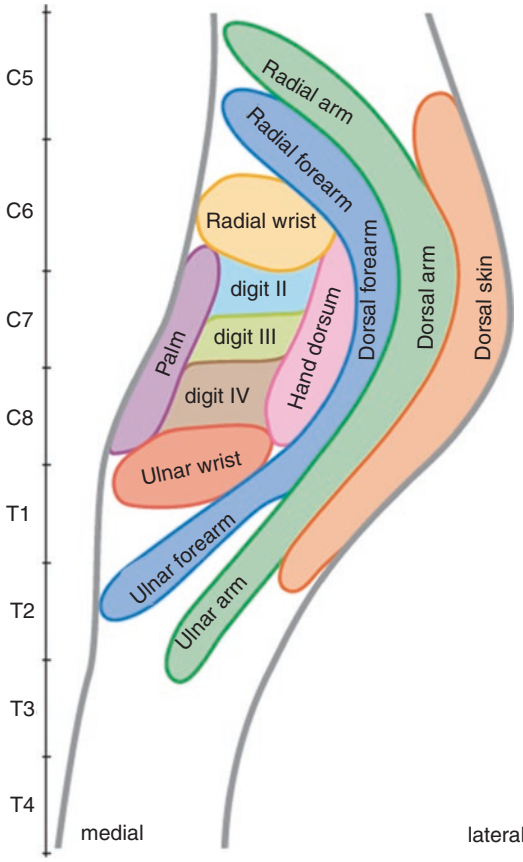


Fig. 2.15 Somatotopic organization of cutaneous afferents in laminae II–III of the cervical and upper thoracic spinal cord of the cat. Sensory fibers from the dorsal skin, arm, forearm, and hand are arranged in a lateral to medial order. Digit II, III, and IV are represented in a rostral-to-caudal order. From Altman and Bayer (2001)

2.5 Myelination

Myelin formation on nerve fibers of the spinal cord occurs only in the middle of fetal period. It is then thought to be associated with the differentiation of glioblasts into oligodendrocytes. The first myelination of axons in the human is observed in the early fetal spinal cord at less than 16 weeks of gestation. Although not in many mammals, myelination in the human is part of the postnatal developmental period. The earliest structure to myelinate is the medial longitudinal fascicles in the upper cervical spinal cord at 20 weeks, with the corticospinal tract being the last, and myelination during the first year after birth (Armand 1982; Weidenheim et al. 1996). The process of myelin formation continues for several years, but the exact time of its completion is unknown (Fig. 2.16). The development of myelination of the main fiber tracts in the human spinal cord is shown in Table 2.4.

2.6 Development of the Vertebrae

At the end of the fifth week of development, mesodermal cells that surround the notochord segment in epithelial spheres called somites. This process is called segmentation and produces 42–44 pairs of somites. The somites develop craniocaudally, and each somite develops into two parts: a sclerotome and a dermomyotome. The cells of the sclerotome are responsible for the formation of the spine, and the dermomyotomes form muscle cells and the overlying dermis of the skin. The cells of the sclerotome begin to migrate toward and around the notochord and neural tube. Once the sclerotomes surround the notochord and neural tube, each level will separate into a cranial area of loosely packed cells and a caudal area of densely packed cells. The intervertebral disc is formed between these two layers of cells. Separation or segmentation of the stacked somites occurs by the loosely packed cells in the cranial half of each somite. The cranial half becomes the disk space and the annulus fibrosus, whereas the caudal, tightly packed half of the somite becomes the vertebral body. Finally, the notochord slowly regresses to become the nucleus pulposus within the annulus fibrosus (Kaplan et al. 2005) (Fig. 2.17).

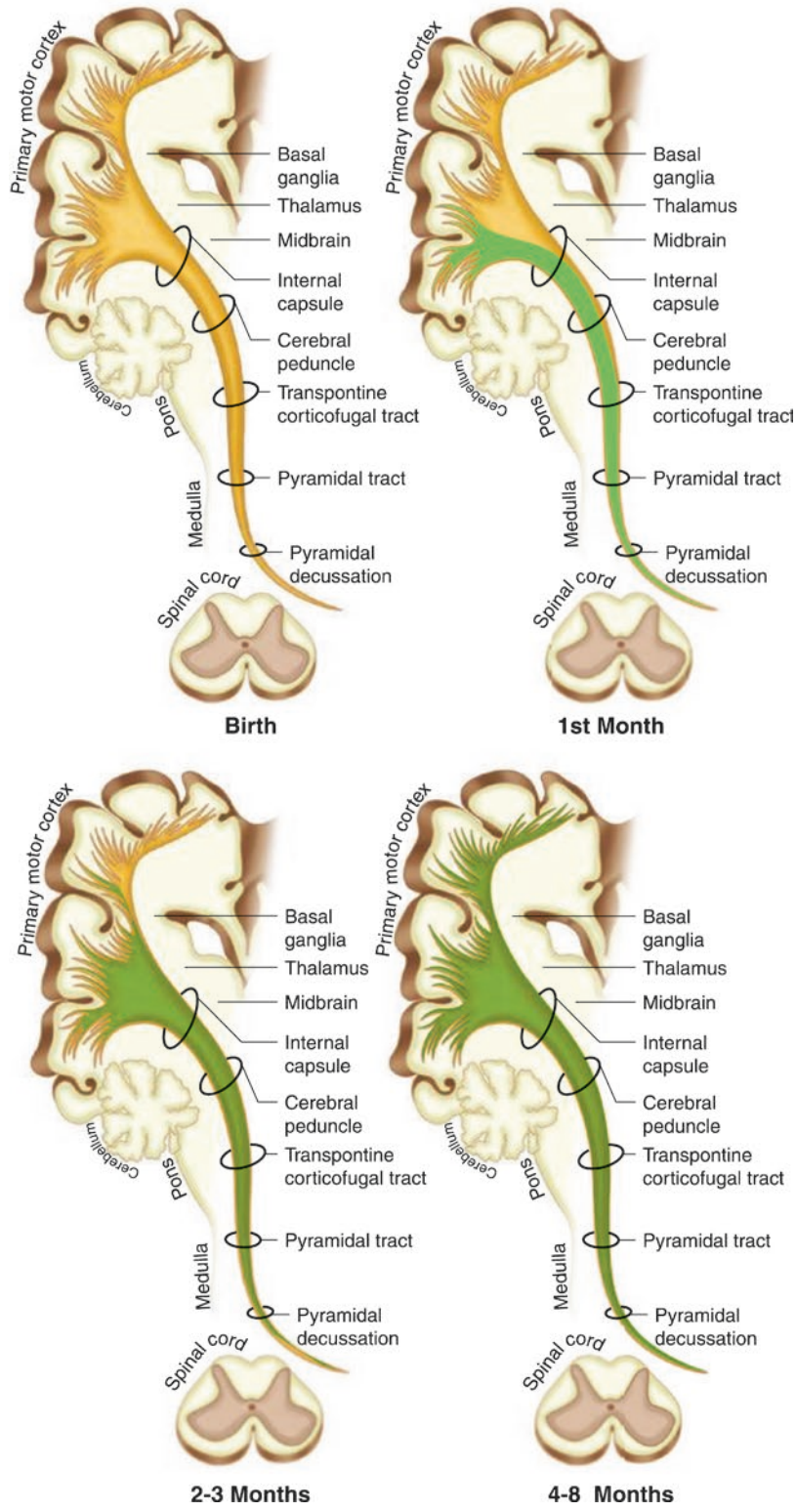


Fig. 2.16 Schematic summary of the myelination of the corticofugal tract. A corticospinal tract that descends through the internal capsule, the cerebral peduncle, the pontine gray, and crosses in the pyramid is the absence of myelin at birth. At 1 month of age, a small complement of myelinating corticofugal fibers reaches the pontine gray. But the bulk of the corticofugal tract remains unmyelinated. There is an increase in the proportion of myelinated fibers in the upper corticofugal tract between 2 and 3 months. The myelination of the bulk of the lower corticospinal tract occurs between 4 and 8 months of age. From Altman and Bayer (2001)

Table 2.4 Development of myelination of the main fiber tracts in the human spinal cord

Fiber tract	First evidence of myelin basic protein staining	Onset of reactive gliosis	Onset of myelination
Ascending tracts			
Cuneate fascicle	GW 14	GW 20	At GW 33, myelination well advanced throughout
Gracilis fascicle	GW 16	GW 20	At GW 33, wedge area myelinating
Dorsal spinocerebellar tract	GW 20	GW 26	GW 33
Ventral spinocerebellar tract	GW 20	Later than dorsal spinocerebellar tract	Late third trimester
Spinothalamic tract	GW 20	GW 33	Late-term neonate
Descending tracts			
Vestibulospinal tract	GW 9.5	By GW 20, first sign of reactive gliosis in medial vestibulospinal tract	GW 33
Reticulospinal tract	GW 9.5	Comparable to vestibulospinal tracts	GW 33
Corticospinal tracts			
Lateral corticospinal tract		At birth few glia present	After birth
Anterior corticospinal tract		At birth few glia present	After birth

GW gestational weeks
From ten Donkelaar et al. (2014b), with permission

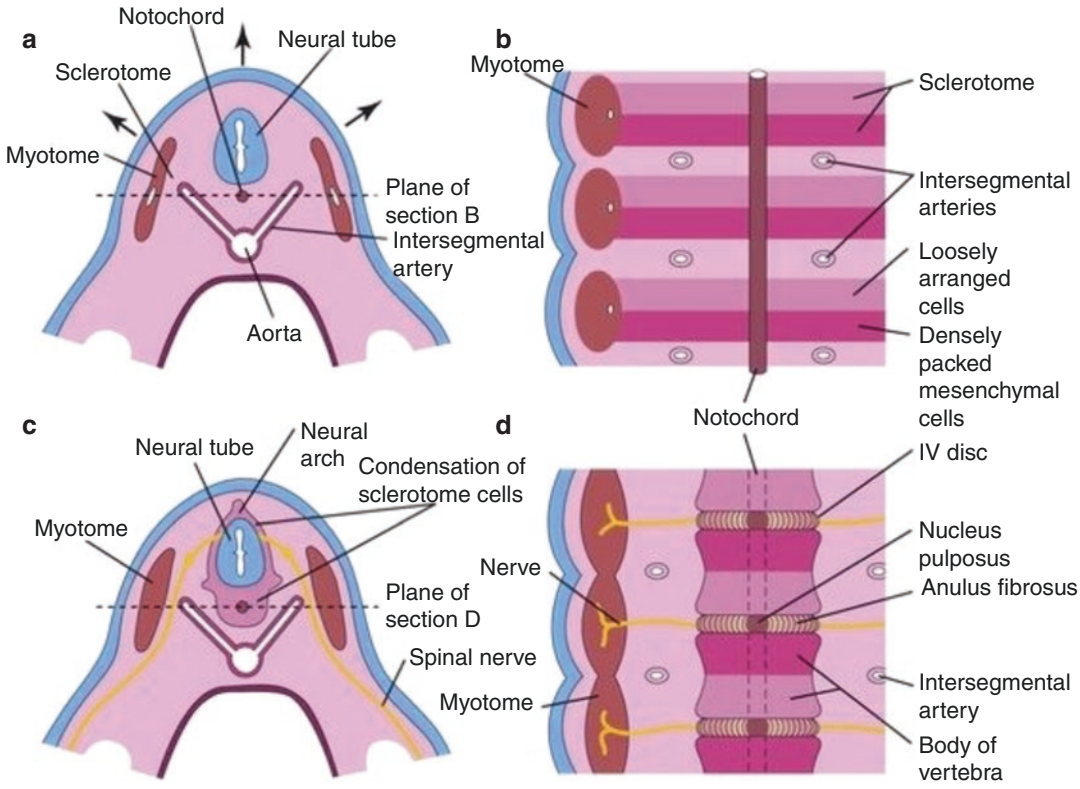


Fig. 2.17 (**a**) Transverse section through a 4-week embryo. The arrows indicate the dorsal growth of the neural tube and the simultaneous dorsolateral movement of the somite remnant, leaving behind a trail of sclerotomal cells. (**b**) Diagrammatic frontal section of this embryo showing that the condensation of sclerotomal cells around the notochord consists of a cranial area of loosely packed cells and a caudal area of densely packed cells. (**c**) Transverse section through a 5-week embryo showing the condensation of sclerotomal cells around the notochord and neural tube, which forms a mesenchymal vertebra. (**d**) Diagrammatic frontal section illustrating that the vertebral body forms from the cranial and caudal halves of two successive sclerotomal masses. The intersegmental arteries now cross the bodies of the vertebrae, and the spinal nerves lie between the vertebrae. The notochord is degenerating except in the region of the intervertebral disc, where it forms the nucleus pulposus. From Moore et al. (2013), with permission

References

Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.

Armand J. The origin, course and termination of corticospinal fibers in various mammals. Prog Brain Res. 1982;57:329–60.

Bayer SA, Altman J. Atlas of human central nervous system development series. The spinal cord from gestational week 4 to the 4th postnatal month. New York: CRC Press; 2002.

Biller J, Gruener G, Brazis P. DeMyer's the neurologic examination: a programmed text. 7th ed. New York: McGraw-Hill Education; 2017.

Copp AJ, Greene ND. Neural tube defects-disorders of neurulation and related embryologic processes. Wiley Interdiscip Rev Dev Biol. 2013;2:213–37.

Felten DL, O'Banion MK, Maida MS. Netter's atlas of neuroscience. 3rd ed. London: Elsevier; 2016.

Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.

Greene ND, Vopp AJ. Neural tube defects. Annu Rev Neurosci. 2014;37:221–42.

Kaplan KM, Spivak JM, Bendo JA. Embryology of the spine and associated congenital abnormalities. Spine J. 2005;5:564–76.

Keegan JJ, Garrett FD. The segmental distribution of the cutaneous nerves in the limbs of man. Anat Rec. 1948;102:409–37.

Keller R, Shook D, Skoglund P. The forces that shape embryos: physical aspects of convergent extension by cell intercalation. Phys Biol. 2008;5:015007.
Kellgren JH. On the distribution of pain arising from deep somatic structures with charts of segmental pain areas. Clin Sci. 1939;4:35–46.
McLachlan JC. Development of the dermatome pattern in the limb. Chin Anat. 1990;3:41–9.
Medical Research Council. Aids to the investigation of peripheral nerve injuries. War memorandum nerve injuries committee, No. 7, 2nd ed. London: Her Majesty's Stationery Office; 1956.
Moore KL, Persaud TVN, Torchia MG. The developing human clinically oriented embryology. 9th ed. Philadelphia: Elsevier; 2013.
O'rahilly R, Müller F. The two sites of fusion of the neural folds and the two neuropores in the human embryo. Teratology. 2002;65:162–70.
O'Rahilly R, Müller F. The embryonic human brain. An atlas of developmental stages. 3rd ed. Hoboken: Wiley; 2006.
O'Rahilly R, Müller F. Developmental stages in human embryos: revised and new measurements. Cells Tissues Organs. 2010;192:73–84.
Sadler TW. Embryology of neural tube development. Am J Med Genet C Semin Med Genet. 2005;135C:2–8.
Standring S, editor. Gray's anatomy. 41st ed. Philadelphia: Elsevier; 2016.
ten Donkelaar HJ, Yamada S, Shiota K, et al. Overview of the development of the human brain and spinal cord. In: ten Donkelarr HJ, Lammens M, Hori A, editors. Clinical neuroembryology. Development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014a.
ten Donkelaar HJ, Itoh K, Hori A. Development and developmental disorders of the spinal cord. In: ten Donkelarr HJ, Lammens M, Hori A, editors. Clinical neuroembryology. Development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014b.
Tomlinson BE, Irving D, Rebeiz JJ. Total numbers of limb motor neurons in the human lumbosacral cord and an analysis of the accuracy of various sampling procedures. J Neurol Sci. 1973;20:313–27.
Vallstedt A, Kullander K. Dorsally derived spinal interneurons in locomotor circuits. Ann N Y Acad Sci. 2013;1279:32–42.
Vanderah TW, Gould DJ. Nolte's the human brain. 6th ed. London: Elsevier; 2016.
Watson C, Paxinos G, Kayalioglu G. The spinal cord. London: Academic; 2009.
Weidenheim KM, Bodhireddy SR, Rashbaum WK, et al. Temporal and spatial expression of major myelin protein in the human fetal spinal cord during the second trimester. J Neuropathol Exp Neurol. 1996;55:734–45.

Recommended Additional Reading

Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.
Bayer SA, Altman J. Atlas of human central nervous system development series. The spinal cord from gestational week 4 to the 4th postnatal month. New York: CRC Press; 2002.
Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Felten DL, O'Banion MK, Maida MS. Netter's atlas of neuroscience. 3rd ed. London: Elsevier; 2016.
Mai JK, Paxinos G, editors. The human nervous system. 3rd ed. London: Elsevier; 2011.
Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.
Noback CR, Strominger NL, Demarest RJ, et al. The human nervous system: structure and function. 6th ed. Totoma: Humana Press; 2005.
Snell RS. Clinical neuroanatomy. 7th ed. Philadelphia: Wolters Kluwer; 2010.
ten Donkelaar HJ, Lammens M, Hori A. Clinical neuroembryology. Development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014.
Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.
Windle WF. The spinal cord and its reaction to traumatic injury. In: Bousquet WF, Palmer RF, editors. Modern pharmacology-toxicology: a series of monographs and textbooks. New York: Marcel Dekker, Inc.; 1980.

3 Functional Neuroanatomy of the Spinal Cord

The spinal cord is covered by three meningeal layers: the inner pial layer, arachnoid, and the outer layer of dura. Anteriorly, the spinal cord has a deep midline groove, the anterior median sulcus, while there is a shallow midline sulcus on its posterior surface. The spinal cord is supported by three ligament-like structures that are extensions of the pia and run from the pial surface of the cord to the dura. The two denticulate ligaments, one on either side, run from the midlateral aspect of the cord through the subarachnoid space and are attached laterally to the dura, which extends from the cervicomedullary junction to the tip of the conus medullaris at the lower border of the first lumbar vertebra (Bican et al. 2013). There are 20 or 21 pairs of denticulate ligaments. The spinal cord is anchored caudally by filum terminale. The filum terminale runs from the tip of the conus medullaris: the filum terminale internum inserts into the dura at the second sacral vertebra (S2) and the filum terminale externum outside the dural sac up to the coccyx. There are two symmetrical enlargements of the spinal cord and they contain the segments that innervate the limbs. The cervical enlargement (C5–Tl) gives rise to the brachial plexus, while the lumbosacral plexus arises from the lumbar enlargement (L2–S3).

The spinal cord consists of outer white matter with ascending sensory and descending motor tracts and inner gray matter with nerve cell bodies. The volume of gray matter is largest in the cervical and lumbar regions, while the white matter volume gradually tapers craniocaudally. The gray matter surrounds a central canal, which is anatomically an extension of the fourth ventricle and is lined with ependymal cells and filled with cerebrospinal fluid. In addition to the dorsal and ventral horns in the gray matter, a lateral horn (intermediolateral cell column), which contains the cell bodies of preganglionic sympathetic neurons, is visible in the thoracic and upper lumbar segments. Knowledge of both the internal and external anatomy of the spinal cord is required for the interpretation and understanding of the pathological findings of the spinal cord, as well as for the precise interpretation of the clinical findings and the localization of the lesion.

3.1 Overview of Anatomy of the Spinal Cord

The spinal cord is responsible for the motor, somatosensory, and visceral innervation of the extremities, trunk, and large parts of the neck, and inner organs. The spinal cord has a relatively simple structure and function compared to the brain and occupies about 2% of the total human nervous system. However, even a small-sized injury to the spinal cord can cause a variety of neurological symptoms and signs, including motor, sensory, and autonomic nervous system, because structures in the spinal cord are compact and concentrated in a small and narrow space.

H.-Y. Ko, *Management and Rehabilitation of Spinal Cord Injuries*,
https://doi.org/10.1007/978-981-19-0228-4_3

The topography and cytoarchitecture of the human spinal cord are well known, but the functional implications of well-described structures are difficult to explain (Cho 2015).

The spinal cord is anatomically defined as a structure of the central nervous system located between the cervicomedullary junction and the tip of the conus medullaris. Clinically, however, a spinal cord injury is defined to include the concept of the cauda equina as well as the spinal cord. The cauda equina is the structure of a bundle of lumbar and sacral nerve roots located below the tip of the conus medullaris in the spinal canal (Barson 1970). The mean length of the spinal cord from the cervicomedullary junction to the tip of the conus medullaris is 41–43 cm in females and 45 cm in males and its width ranges from 1.27 cm in cervical and lumbar regions to 64 mm in the thoracic region (Bican et al. 2013). There is no significant difference in length according to height, but a tendency for the tip of the conus medullaris to be higher in a taller person than the shorter person is noted. In the cervical and lumbar regions of the spinal cord, there are enlargements where the neurons innervate the upper and lower extremities, respectively.

The spinal canal extends from the foramen magnum to the tip of the sacrum, to the sacral hiatus of the fourth sacral spine, and contains various neural or non-neural structures. During development and up to 14 weeks after conception, the spinal cord covers the entire length of the embryo, and the spinal nerves leave the vertebral column through the corresponding intervertebral foramina. Subsequent growth and elongation of the vertebral column cause relative growth, ascensus medullae. The spinal cord extends from the foramen magnum to the lower part of the first lumbar vertebra or the space between the first lumbar spine and the second lumbar spine, where the spinal cord terminates in the adult as the conus medullaris (Barson 1970). The cervical and upper thoracic rootlets are perpendicular to the spinal cord, while the lower thoracic, lumbar, and sacral rootlets are increasingly oblique due to the difference in length between the spinal cord and vertebra. Thus, the spinal cord segment does not correspond to the vertebral level below the upper cervical spinal cord segments. This discrepancy between the spinal cord segments and vertebral levels is gradually more pronounced for the more caudal segments of the spinal cord as the spine grows faster than the spinal cord during development.

A spinal cord segment is defined as a spinal cord between the proximal and distal ends of attachment sites of the ventral and dorsal roots, with the ventral and dorsal root filaments of each nerve root attached to the spinal cord (Fig. 3.1). Thirty-one spinal cord segments, from the first cervical to the fifth sacral spinal cord segment, have different quantitative measures. The weight of each spinal cord segment is about 1 g, but the length is variable according to the regions: about 25 mm in the midthoracic spinal cord, about 12 mm in the midcervical spinal cord, and about 10 mm in the midlumbar spinal cord (Fig. 3.2). The spinal cord segment T6 is the longest with an average length of 22.4 mm. The longest segment in the cervical and lumbar spinal cord is the segments C5 and L1, respectively, with an average

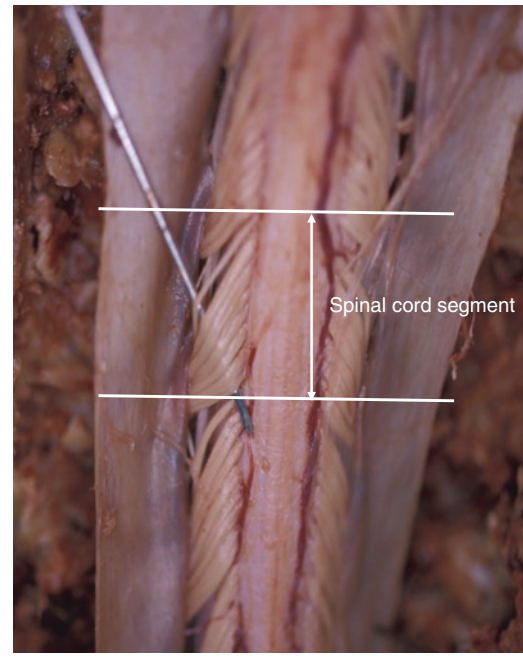


Fig. 3.1 Spinal cord segment

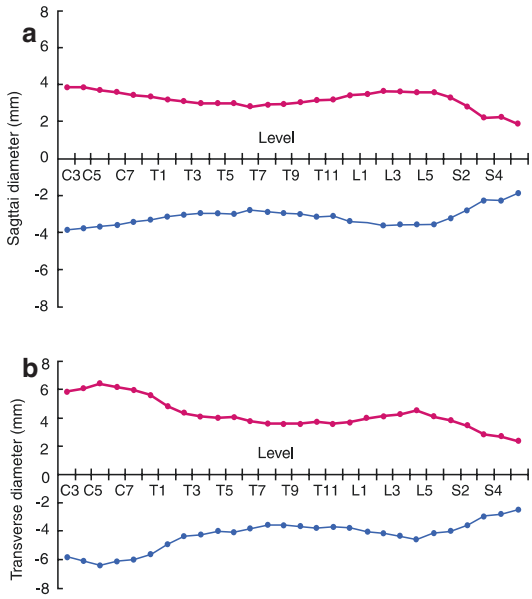


Fig. 3.2 (**a**) Sagittal diameter and (**b**) lateral diameter of each segment of spinal cord

length of 15.5 mm. The anteroposterior diameter of each spinal cord segment is 6–8 mm, relatively uniform, but there are differences in the lateral diameters. The longer the length, the shorter the lateral diameter. The diameter of the cervical and lumbar enlargements is greater than that of the other parts of the spinal cord, and the quantitative features of the cervical and lumbar enlargements are determined by the lateral diameters (Ko et al. 2004).

In the center, the gray matter forms the sensory dorsal and motor ventral horns of the nerve cells. The white matter containing the long motor and sensory tracts is distributed on the periphery. The blood supply to the spinal cord consists of one anterior and two posterior longitudinal spinal arteries. Arising from the vertebral artery at the foramen magnum, the anterior and posterior spinal arteries receive additional branches from radicular arteries that enter the spinal canal along with the nerve roots (Turnbull et al. 1966). The branches of the anterior and posterior spinal arteries form a circumferential network around the spinal cord and penetrate into the spinal cord from the outside. They are completely exposed to the cerebrospinal fluid in the subarachnoid space and can easily be damaged by tumors, infection, or toxins in the space. In the spinal cord, the anterior spinal artery feeds mainly the anterior two-thirds, and the posterior spinal arteries supply the posterior third, which distinguish the anatomical origin from the vascular ischemic lesion of the spinal cord (Cole and Weller 1998; Etz et al. 2011; Novy et al. 2006; Rubin and Rabinstein 2013).

The main descending motor pathway from the brain occupies the lateral part of the cord and enters the ventral horn to synapse with segmental motor nuclei. The lower motor neurons from the motor nuclei, both alpha and gamma, leave the spinal cord through the ventral roots to innervate their target muscle fibers (extrafusal and intrafusal). Classical clinical examination of motor function in the spinal cord is mainly concerned with the examination of the pyramidal tract. Other motor tracts from extrapyramidal system are considered to be related to more proximal automatic movements. The relationship between descending tracts and motor function is a very complex issue that is not clinically or physiologically significant in spinal cord pathology (Norenberg et al. 2004).

Sensory afferent neurons have their cell bodies in the dorsal root ganglia. The proximal parts of the sensory axons enter the cord through the dorsal roots. Large myelinated sensory fibers mediate a low threshold cutaneous mechanoreceptor and muscle and joint information, pass through the dorsal horn and ascend in the ipsilateral dorsal column nuclei to make the synapses in the dorsal column nuclei. Small myelinated and unmyelinated fibers that transmit information about temperature, pain, and muscle fatigue synapse in the laminae of the dorsal horn before ascending to the contralateral spinothalamic tracts (Bican et al. 2013). This crosses at or near the segmental level in the anterior part of the cord that is close to the central canal, making these fibers susceptible to the pressure effects associated with a syrinx and leading to classical dissociated sensory loss.

3.2 White Matter and Tracts

The white matter is located on the periphery of the spinal cord and surrounds the gray matter. The white matter includes ascending and descending tracts composed of nerve fibers from ganglia of dorsal roots, nerve fibers from nerve cells of the spinal gray matter, and nerve fibers from nerve cells at higher levels, the brain. In addition, there are short-range intrasegmental fibers that connect neurons located in the same spinal segment, or intersegmental fibers that only ascend or descend over a few spinal segments before entering the gray matter (Critchley and Eisen 1997). In addition to the nerve fibers, the white matter also has neuroglia cells with their processes and blood vessels. In addition to axonal tracts, the white matter contains a variety of glial cells: oligodendrocytes, astrocytes, and microglia. The ascending neurons in humans appear at 10 weeks of gestation (Clowry et al. 2005). At 13 weeks of gestation, the lateral corticospinal tract in humans reaches the caudal medulla oblongata. Two weeks later, the pyramidal decussation is completed (ten Donkelaar et al. 2004; Armand 1982). The lateral corticospinal tract reaches the cervical spinal cord between 14 and 16 weeks of gestation. The corticospinal tract invades the more caudal regions of the spinal cord at a later stage of development: the low thoracic spinal cord at 17 weeks and the lumbosacral spinal cord at 27 weeks (Armand 1982) (Fig. 3.3). The maturation of the spinal motor center is strongly correlated with neuronal activity according to activity-dependent pattern.

The size of white matter increases in the higher spinal cord segment. The white matter is most developed in the cervical cord region and gradually decreases in size at successive caudal levels of the spinal cord (Breig and el-Nadi 1966; Breig et al. 1966; Holmes et al. 1996) (Fig. 3.4). The cervical spinal cord segments contain more white matter because all neurons descend from the brain and ascend through the cervical cord to

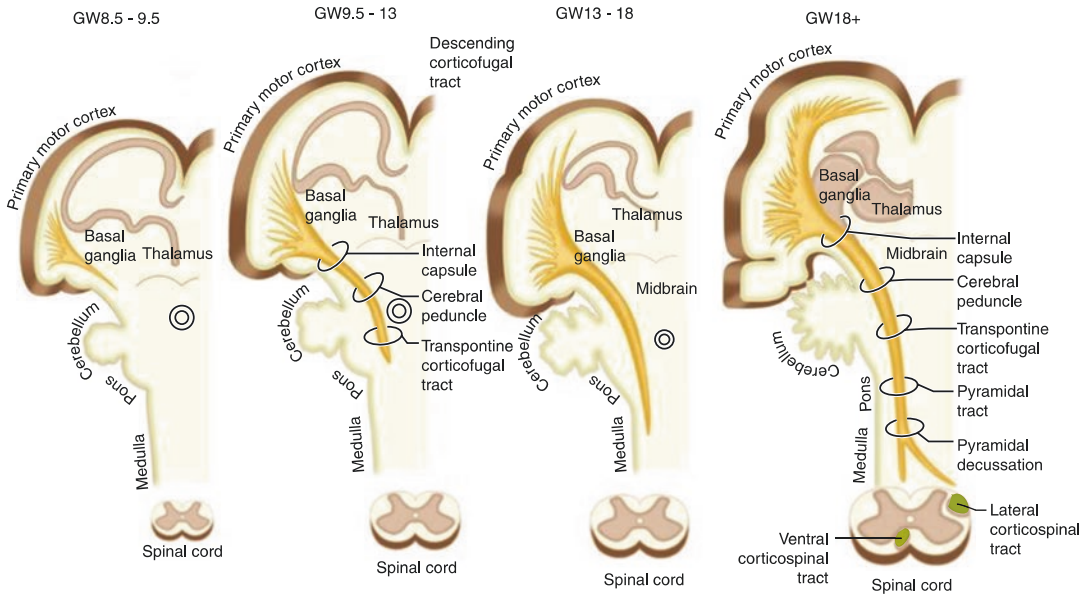


Fig. 3.3 Summary diagram of the lengthening of descending corticofugal tract. The earliest descending corticofugal fibers penetrate the basal ganglia and form the internal capsule between GW8.5 and GW9.5. The volume of the corticospinal tract increases greatly between GW13 and GW18. At about GW18, or shortly thereafter, the fibers of the corticospinal tract that form the pyramids split into two descending components, the larger contralaterally projecting lateral corticospinal tract, and the smaller ipsilateral projecting ventral corticospinal tract. From Altman and Bayer (2001)

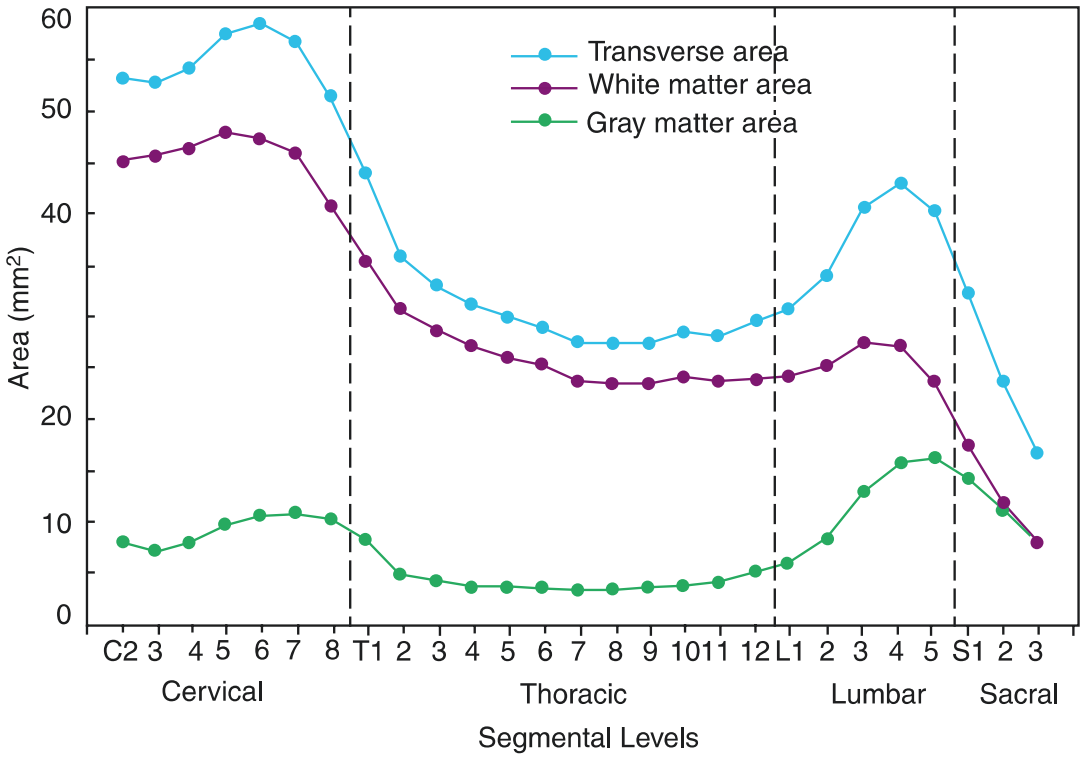


Fig. 3.4 Cross-sectional area, white matter area, and gray matter area of each spinal cord segment

the brain. As most ascending or descending fibers are contained above the sacral segments, the sacral spinal cord has the smallest white matter. The amount of gray matter increased in the cervical and lumbar enlargements as more neurons of the upper and lower extremities are included.

The white matter of the spinal cord is divided into anterior, posterior, and lateral funiculi by the ventral and dorsal horns of the gray matter (Nolte and Angevine 2013) (Fig. 3.5). In the cervical and upper thoracic regions, the posterior intermediate sulci are divided into fasciculi gracilis and cuneatus. The white matter immediately surrounding the gray matter contains most of the propriospinal fibers of the spinal cord, i.e., fasciculi proprius (Fig. 3.6), which is one of the intersegmental fibers. The ascending and descending tracts can be subdivided into functional groups (Cho 2015). The main ascending and descending tracts are reviewed in Table 3.1. The ascending pathways are composed of (1) the posterior column-medial lemniscal system that transmits sensory information on vibration and proprioception through the fasciculus cuneatus and gracilis; (2) the anterolateral system that transmits nociceptive, thermoreceptive, and tactile information via the anterior and lateral spinothalamic tracts, spinoreticular tract, etc.; and (3) the cerebellar input system responsible for proprioceptive sensibility of the upper and lower limbs by the posterior spinocerebellar tract, cuneocerebellar tract, and smaller tracts such as ventral and rostral spinocerebellar tracts (Bican et al. 2013; Patestas and Gartner 2006).

The descending pathways are grouped into (1) the lateral motor system for the movement of contralateral limbs via the lateral corticospinal tract and rubrospinal tract and (2) the medial motor system responsible for the control of bilateral trunk muscles, head/neck positioning, balance, and other posture- and gait-related movements via the anterior corticospinal tract,

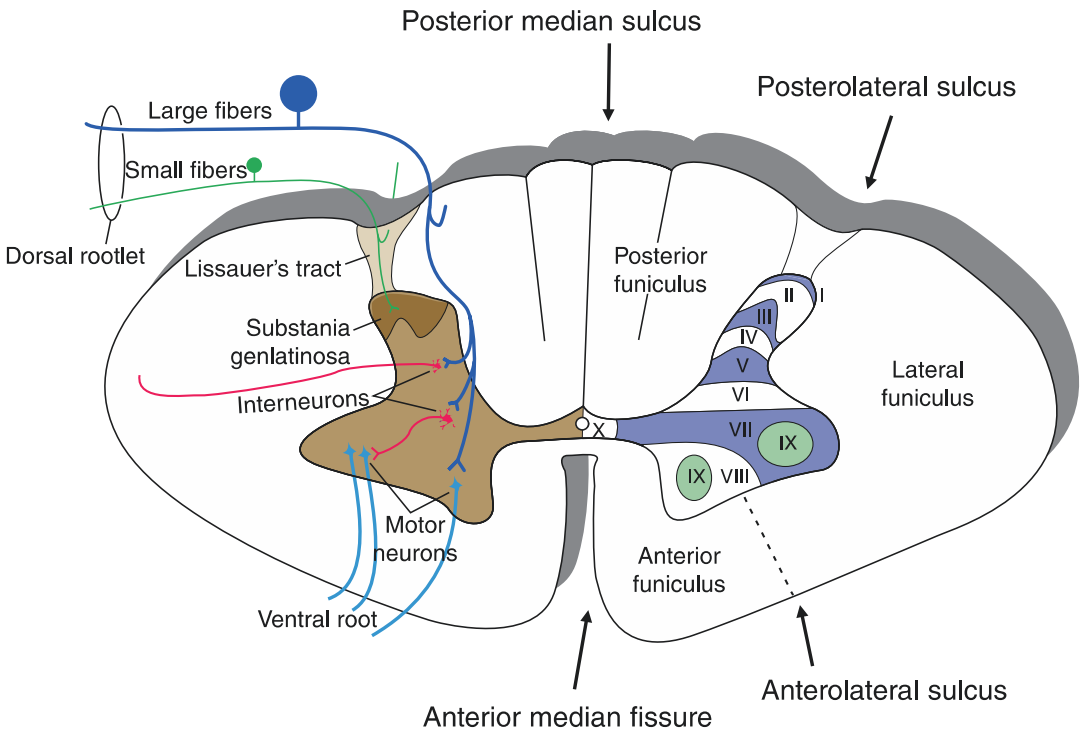


Fig. 3.5 External landmarks of the spinal cord at C8 segmental level: fissure, sulcus, and funiculus. Somatotopically organized the dorsal roots: the larger diameter fibers are medial to the smaller diameter fibers. From Nolte and Angevine (2013), with permission

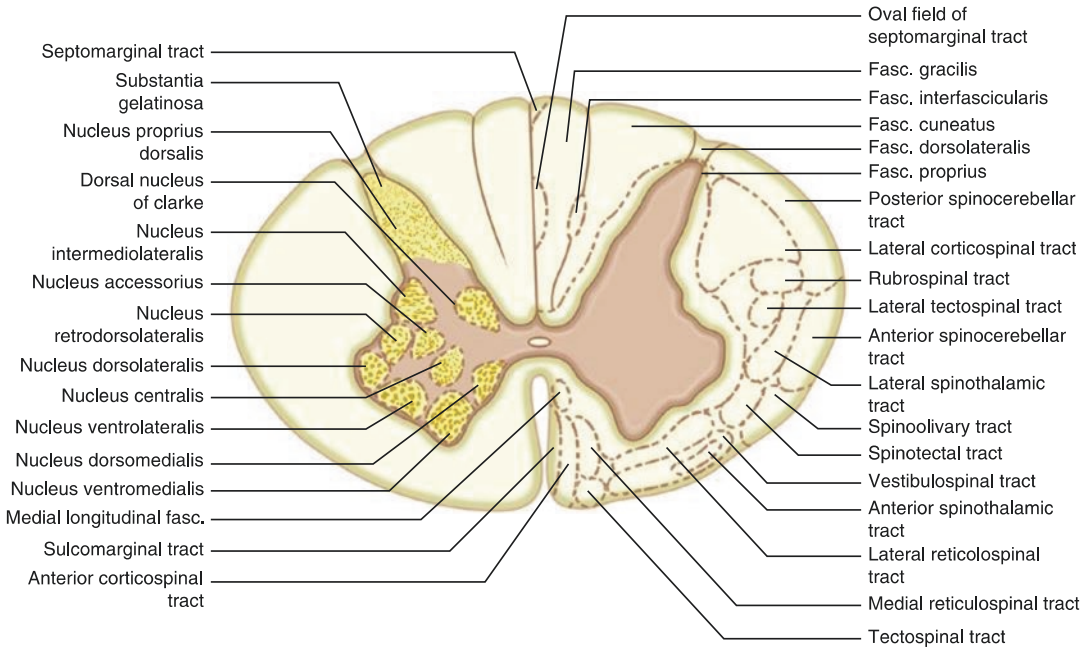


Fig. 3.6 Cross-section of the spinal cord: cellular groups of the gray matter and fiber pathways of the white matter including fasciculi proprii. From Campbell (1992)

Table 3.1 Summary of main ascending (a) and descending (b) tracts of the Spinal cord

a. Ascending tracts				
Tract	Origin	Termination	Crossed/ uncrossed	Main function
Fasciculus gracilis	Dorsal root ganglia below T6	Nucleus gracilis (medulla)	U	Proprioception and vibration
Fasciculus cuneatus	Dorsal root ganglia above T6	Nucleus cuneatus (medulla)	U	Proprioception and vibration
Posterior spinocerebellar	Clarke's nucleus	Cerebellum	U	Proprioceptive, pressure and touch input to the cerebellum
Anterior spinocerebellar	Anterior horn especially lumbosacral	Cerebellum	C	Proprioceptive, pressure and touch input to the cerebellum
Lateral spinothalamic	Rexed laminae I, III, IV, and V	Thalamus (ventral posterior nucleus)	C	Pain and temperature
Anterior spinothalamic	Rexed laminae I, III, IV, and V	Thalamus (ventral posterior nucleus)	C	Light touch and pressure
b. Descending tracts				
Tract	Origin	Termination	Crossed/ uncrossed	Main function
Pyramidal system				
Lateral corticospinal	Layer V neurons in the contralateral motor cortex (major)	Medial and lateral motor nuclei at all levels	C (85–90%)	Skilled movements mediated by distal limb muscles
Anterior corticospinal	Layer V neurons in contralateral motor cortex	Medial and lateral motor nuclei in cervical and upper thoracic levels	U	Descending motor input to motor neurons that innervate neck musculature
Extrapyramidal system				
Rubrospinal	Contralateral Red nucleus (midbrain)	Spinal neurons primarily at cervical levels	C	Posture and locomotion primarily flexor activities (small tract in man)
Reticulospinal	Bilateral reticular formation (pons and medulla)	Spinal neurons for trunk and proximal limb musculature	C and U	Posture and locomotion, respiration, modulation of pain, vasomotor tone
Tectospinal	Superior and inferior colliculi	Motor neurons for neck muscles	C	Reflex head movements toward visual and auditory stimuli
Vestibulospinal	Ipsilateral vestibular nuclei (medulla)	Spinal neurons for trunk musculature	U	Posture and locomotion primarily extensor activities
Central autonomic tract				
Sympathetic	Hypothalamus and brainstem nuclei	Preganglionic sympathetic neurons in intermediolateral nucleus (T1–L2)	C and U	Descending sympathetic outflow to entire body
Parasympathetic	Hypothalamus and brainstem nuclei	Preganglionic parasympathetic neurons in the intermediolateral nucleus (S2–S4)	C and U	Parasympathetic supply to the distal colon, rectum, bladder, and sexual organs

From Critchley and Eisen (1997), with permission

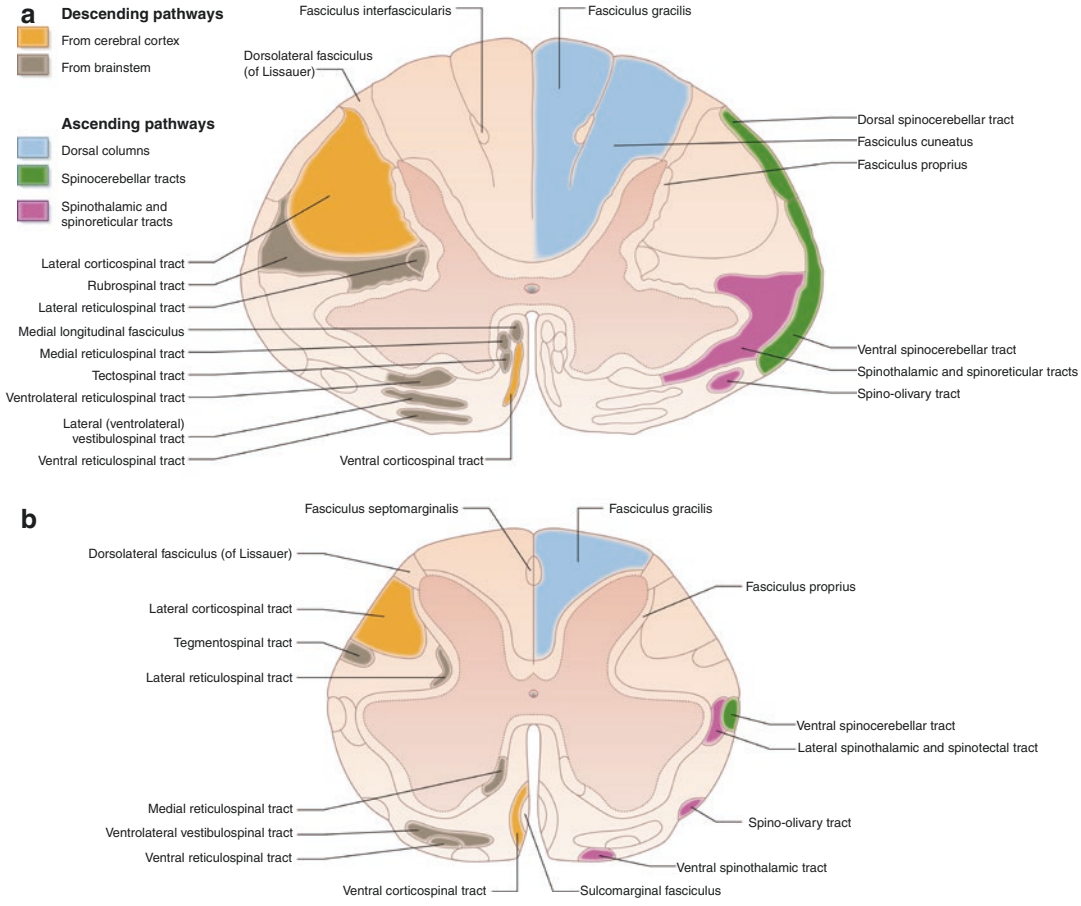


Fig. 3.7 The approximate positions of ascending and descending tracts in the spinal cord at mid-cervical (**a**) and lumbar (**b**) spinal cord levels. From Standring (2016), with permission

the medial and lateral vestibulospinal tract, the reticulospinal tract, and the tectospinal tract (Patestas and Gartner 2006) (Fig. 3.7).

The first nerve fibers that form tracts in the spinal cord of the embryo tend to be buried by subsequent similar fibers of later origin. This leads to lamination within individual fiber tracts (Blumenfeld 2010). The ascending fibers from lower segments overlap the already existing fibers at higher levels. Thus, in the cervical spinal cord, there is a laminar arrangement in which the axons of cervical origin are found to be deeper than the axons of the thoracic, lumbar, and sacral origins; the latter occupies the most superficial position (Fig. 3.8). This phenomenon is rarely seen in tracts of ascending and descending short fibers such as the fasciculi proprius. Nerve fibers of long descending tracts of the spinal cord are also laminated. They tend to grow from the brain to the surface of the spinal cord. The first descending is embedded in the white matter by fibers of later origin. In the larger lateral corticospinal tracts, fibers that terminate at cervical cord levels are most medial, and those to lumbosacral levels are most lateral (Armand 1982; Moore and Dalley 1999).

3.2.1 Ascending Tracts

The ascending tracts primarily transmit sensory information to higher relay nuclei within the main sensory pathway (e.g., thalamus) or provide sensory input (mainly proprioceptive) to the cer-

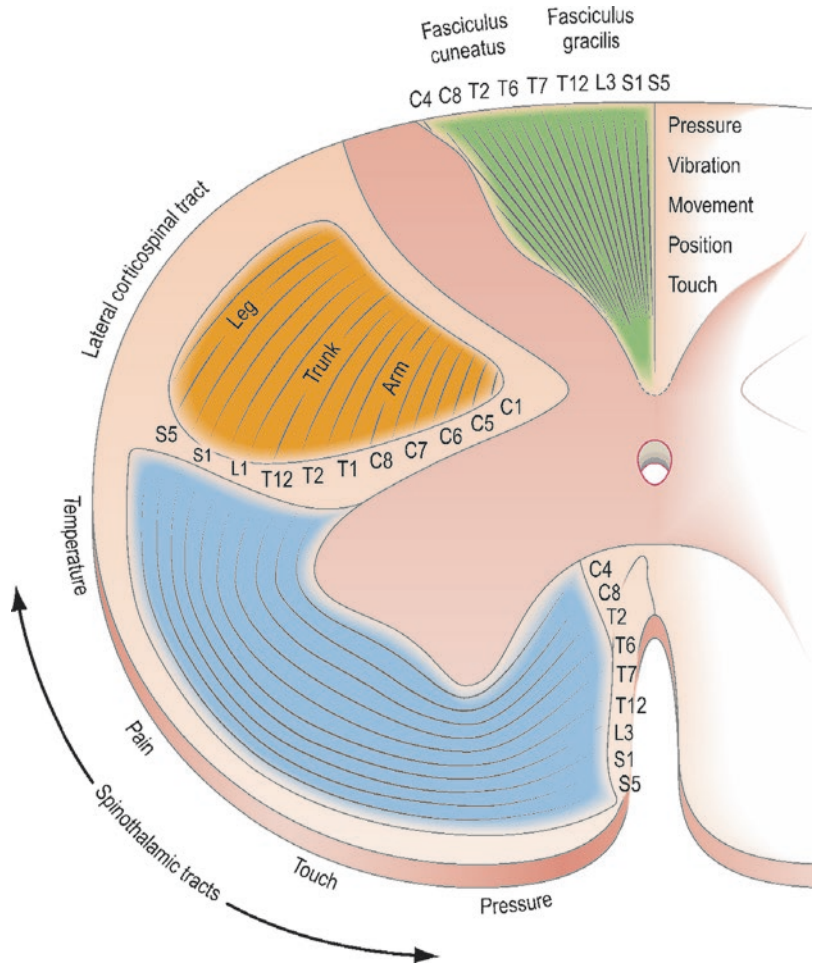


Fig. 3.8 Schematic diagram of the segmental organization of fibers in the dorsal funiculus, the lateral spinothalamic tract and the lateral corticospinal tracts. From Standring (2016), with permission

ebellum. All ascending tract consists of second-order sensory afferents originating from neurons in the gray matter, mainly from the dorsal horn. The posterior columns, in which the fasciculus cuneatus and gracilis consist of primary sensory afferents from dorsal root ganglia, are an exception. These afferents enter the spinal cord and ascend to the medulla without synapsing in the dorsal horn (Critchley and Eisen 1997).

3.2.1.1 Posterior Column-Medial Lemniscal System

Two components of the posterior funiculi appear in the cervical and upper thoracic spinal cord. It consists mainly of the central processes of dorsal root ganglions. The posterior column tract is responsible for the transmission of sensations of position, vibration, two-point discrimination, proprioception, quality of tactile sensation, and information from muscle, tendon, and joint receptors. Not all primary afferent neurons of fasciculus gracilis and cuneatus perform sensory-perceptual functions. The medial component (fasciculus gracilis) is located medially and transmits sensation for the lower half of the body, i.e., from the lower thoracic, lumbar, and sacral regions, to the brain. The lateral component (fasciculus cuneatus) is located more laterally and carries proprioceptive input on the levels rostral T5. Topographically, the sacral fibers are innermost, followed by lumbar, thoracic, and cervical. None of these fibers decussate or have synapses in the spinal cord. The fasciculus gracilis and cuneatus terminate in the nucleus gracilis and cuneatus in the posterior aspect of the lower medulla. Neurons in these nuclei give rise to

second-order sensory afferents. The axons of these second-order neurons decussate as the internal arcuate fibers and travel rostrally as the medial lemniscus to the ventral posterolateral nucleus (VPL) in the thalamus.

3.2.1.2 Anterolateral System

Small diameter Aδ-fibers and unmyelinated C-fibers carrying nociceptive and thermoreceptive information enter the spinal cord at the dorsal horns. Some primary sensory fibers branch on entering the spinal cord and ascend and descend over one or two segments within the Lissauer's tract or fasciculus before entering the gray matter. The Lissauer's tract is located between the surface of the posterolateral aspect of the spinal cord and the tip of the dorsal horn. The Lissauer's tract stains more lightly in myelin-stained preparation than the rest of the white matter because it contains the finely myelinated and unmyelinated fibers with which the substantia gelatinosa deals (Vanderah and Gould 2016). These first-order fibers are synapses in the dorsal horn after the Lissauer's tract. The fibers are immediately synapsed to second-order neurons of the gray matter, mainly in laminae I and V (dorsal horn of the gray matter). The second-order fibers then cross the anterior commissure, anterior to the central canal, and then ascend to the opposite spinothalamic tract in the anterolateral white matter (Afifi and Bergman 2005; Bican et al. 2013).

Both the anterior and lateral spinothalamic tracts are crossed tracts that originate from neurons in the principal sensory nucleus (laminae III and IV) and some neurons in laminae I and V of the posterior horn. The spinothalamic tracts ascend ipsilaterally for one or two segments before they cross to join the opposite side spinothalamic tract. The cervical fibers in the spinothalamic tract are located most medially, and sacral fibers are most lateral (Afifi and Bergman 2005; Mai and Paxinos 2011). The lateral spinothalamic tract is the pathway of pain and temperature. The fibers can also transmit impulses such as tickling, itching, sexual sensations, and feeling of muscle fatigue. The anterior spinothalamic tract is associated with light touch and pressure. The dorsal root fibers can ascend in the posterior columns (Lissauer's tract) over many segmental levels before they enter and synapse in the dorsal horn. Touch and pressure are expressed bilaterally and are not lost after the nerve fibers of the spinothalamic system are severed on one side. Small or early lesions of the spinal commissures (e.g., syringomyelia) eliminate pain and temperature sensations on both sides but do not impair tactile perception, since pain and temperature sensations are carried more dorsally compared to tough sensations.

3.2.1.3 Cerebellar Input System

The spinocerebellar tracts are the main source of input for the cerebellum. Their feedback information consists of afferent inputs about the movement of the limbs and information about the activity of the spinal interneuron during locomotion. The posterior spinocerebellar tract originating from Clarke's nucleus at levels (lamina VII) T1(C8)–L2(L3), which is an uncrossed tract containing second-order sensory afferents, are located at the dorsal periphery of the lateral funiculi (Afifi and Bergman 2005; Mai and Paxinos 2011). This tract continues into the brainstem and enters the cerebellum through the ipsilateral inferior cerebellar peduncle. The smaller and less pronounced anterior spinocerebellar tracts are also located at the periphery of the lateral funiculi. The tracts consist of crossed fibers that originate from the ventral horn and ascend through the restiform bodies to the cerebellar vermis. They ascend from the lower regions of the spinal cord, especially from neurons in the lumbar enlargement, and occupy their position in the lateral funiculi of the cervical spinal cord segments, which are more superficial than other tracts.

3.2.1.4 Others

The spinoreticular tract courses ipsilaterally, without decussating within the anterolateral portion of the spinal cord, and end in the reticular formation of the brainstem from which it projects to intralaminar thalamic nuclei and then to the limbic system.

Other ascending second-order neurons arising from the spinal gray columns terminate in infe-

rior olivary nuclei (spinoolivary tracts), pontine nuclei (spinopontine tracts), and lateral vestibular nuclei (spinovestibular tracts). The general location of most fibers is obvious and the functions of these tracts are not clearly defined in the human spinal cord.

3.2.2 Descending Tracts

The descending motor pathways are divided into lateral and medial motor systems. And the descending tracts can be divided into pyramidal (the lateral and anterior corticospinal tracts and corticobulbar tract) and extrapyramidal motor pathways, as well as the central autonomic tract. The term extrapyramidal is an inexact term, but it is still commonly encountered. The general structure of these systems is that upper motor neurons project to lower motor neurons in the spinal cord and brainstem. The motor pathway is often taught in medical school as a monosynaptic connection that begins in the motor cortex and continues to the descending corticospinal tract, then synapses with motor neurons in the ventral horn of the spinal cord before exiting through the spinal nerves. This model is grossly oversimplified, and the corticospinal tract actually projects widely to all layers of the spinal cord, including the dorsal horn, and influences nociceptive, somatosensory, autonomic, and motor functions probably more through spinal interneurons than through direct motor neuron connections (Cho and Bhattacharyya 2018; Lemon 2008).

The corticospinal tract is the largest and most important descending tract of the human spinal cord. The corticospinal tracts are the spinal components of the pyramidal system and are occupied by the neurons in the parts of the ventral medulla oblongata called pyramids (Coppola 1973; Dumitru and Lang 1986). Approximately 40% of the corticospinal tract fibers are formed in the primary motor cortex of the frontal lobes (in the precentral gyrus, Brodmann area 4). The remainder occurs in the other cortical regions of the frontal and parietal lobes. The corticospinal tract is especially important for rapid and skilled movements in an individual's digits and joints. The cervical fibers in the corticospinal tract are most medial and sacral fibers most lateral (Armand 1982; Moore and Dalley 1999). Almost 85–90% of the corticospinal tract fibers decussate at the lower end of the medulla oblongata, while the rest continue uncrossed into the spinal cord (Armand 1982) (Fig. 3.9). Of the 20% uncrossed fibers, 5% join the lateral corticospinal tract and the remaining 15% form the uncrossed anterior corticospinal tract in the anterior column of white matter. The fibers of the anterior corticospinal tract terminate on motor neurons or interneurons in medial portions of the ventral horn or intermediate gray matter, so that they preferen-

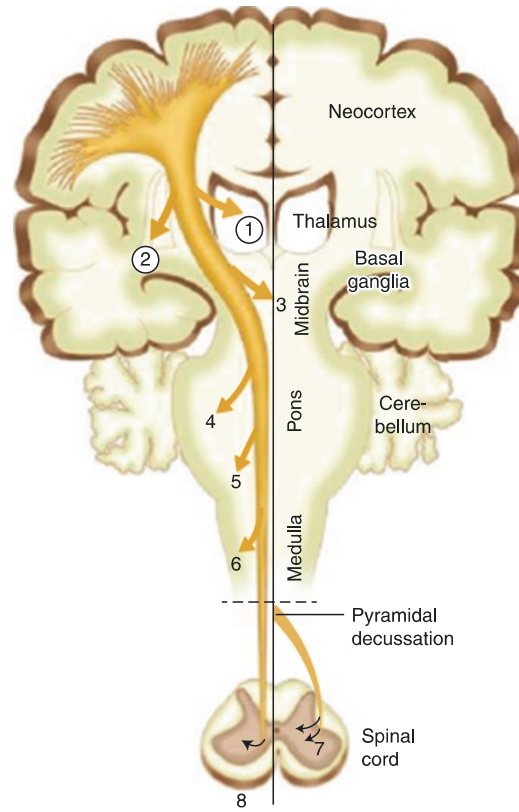


Fig. 3.9 The origin and trajectory of fibers of the descending pyramidal tract in the human brain and spinal cord. Numbers indicate the following components of the pyramidal tract: 1, corticothalamic; 2, corticostriatal; 3, corticotectal; 4, corticopontocerebellar; 5, corticoolivary; 6, corticocuneate and corticogracile. Beyond the pyramidal decussation; 7, the crossed lateral corticospinal tract, and 8, the uncrossed ventral corticospinal tract. From Altman and Bayer (2001)

tially influence the activity of motor neurons for axial muscles. Many of them cross in the anterior white commissure before they form synapses, but others do not. Most of the fibers of the anterior corticospinal tract terminate in cervical and thoracic segments, so they may have a special role in controlling the muscles of the neck and shoulder. However, damage to this tract typically does not result in obvious weakness, possibly due in part to the bilateral distribution of fibers from the contralateral tract (Vanderah and Gould 2016). The decussating fibers form the lateral corticospinal tracts occupying lateral funiculi between fasciculi proprius and posterior spinocerebellar tracts. Most of the fibers of these tracts terminate in relation to interneurons of the ventral gray columns. More than half of the axons of the lateral corticospinal tracts terminate in the cervical and upper thoracic spinal cords and only one-fourth of them reach the lumbosacral segments (Armand 1982). The lateral corticospinal tract controls voluntary movements of the opposite side. Some fibers synapse directly with motor neurons that supply the distal limb muscles and mediate the skilled movements. Bilateral lesions of the pyramidal tract at the level of the decussation only result in a loss of skilled hand movements, but the preservation of all gross locomotor function (Critchley and Eisen 1997; Lawrence and Kuypers 1968). The size of these tracts varies individually and on both sides.

Many brainstem nuclei send axons into the spinal cord. These are components of the extrapyramidal system, all of which preceded the pyramidal tracts in development. The main sources of the spinal portions of this system are cells in vestibular nuclei, red nuclei, superior colliculi, and the brain stem reticular formation. On both sides of the human spinal cord, there are four recognized tracts of this system: the medial longitudinal fasciculus, tectospinal, vestibulospinal, reticulospinal, and rubrospinal tracts. The tectospinal tract arising from the midbrain is involved in the coordination of head and eye movement. The vestibulospinal tract arises from the lateral and medial vestibular nuclei and participates in head and neck position and balance. The reticulospinal tract, which arises from the brain stem reticular formation, plays a role in automatic posture and walking-related movements by modulating spinal reflexes. The rubrospinal tract, which arises from the red nucleus in the midbrain, decussates within the brain stem and is thought to affect the muscle tone of distal extremities. The difference between the flexion posture of the upper extremities in decorticate state and the extensor posture of the upper extremities in decerebrate states corresponds to brainstem lesions above or below the red nucleus, respectively. It is believed that the greatest influence of rubrospinal projections is on flexor motor neurons of the upper extremities.

3.3 Gray Matter

3.3.1 Anatomy of the Gray Matter

Typical anatomical features of the spinal cord cross-section are an H-shaped (butterfly-shaped) form of the central gray matter and are formed by symmetrical crescent-shaped masses connected by a tissue bridge or commissure containing the central canal. The gray matter consists mainly of nerve cells, neuroglia cells, and blood vessels. It also contains numerous interweaving nerve fibers, including axons with myelin sheaths and many are unmyelinated. The gray matter is divided into ventral and dorsal columns (or ventral and dorsal horns) by an imaginary transverse line through the central canal. The gray commissure is a thin strip of gray matter that crosses the midline and connects the left and right halves of the gray matter. The central canal lined by ependyma is located in the center of this commissure. The third horn is present only in the thoracic and upper lumbar spinal cord, which is the intermediolateral (or lateral) horn containing neurons of the autonomic nervous system. The intermediate horn in the thoracic and upper lumbar spinal cord, from T1 to L2, receives visceral afferent impulses and contains cell bodies of preganglionic, visceral efferent neurons whose axons emerge in the ventral roots (Afifi and Bergman 2005; Clifton et al. 1976). The dorsal gray columns or horns contain the main receptive zones

for afferent impulses from the dorsal roots. The dorsal column or horn is directed posterolaterally and separated from the posterolateral sulcus by an important thin layer of white matter, the Lissauer's tract. The ventral gray columns or horns contain the nerve cells, the axons which emerge from the cord in ventral roots to innervate skeletal muscles. The ventral gray column is largest in cervical and lumbar enlargement, where it contains cells of motor neurons for muscles of the extremities. In particular, the thoracic lateral horn includes preganglionic sympathetic neurons (Fig. 3.10). The spinal cord plays a key role in integrating multiple peripheral and central inputs through the neurons in the gray matter. The gray matter intermingles with the white matter in the concavity of either gray mass, especially in the cervical region, to form the spinal reticular formation. The central canal is a continuation of the fourth ventricle. It is lined with ciliated columnar epithelium and filled with cerebrospinal fluid.

3.3.2 Architectural Lamination of the Gray Matter

The gray matter is divided into 10 zones or laminae labeled from I to X from dorsal to ventral.

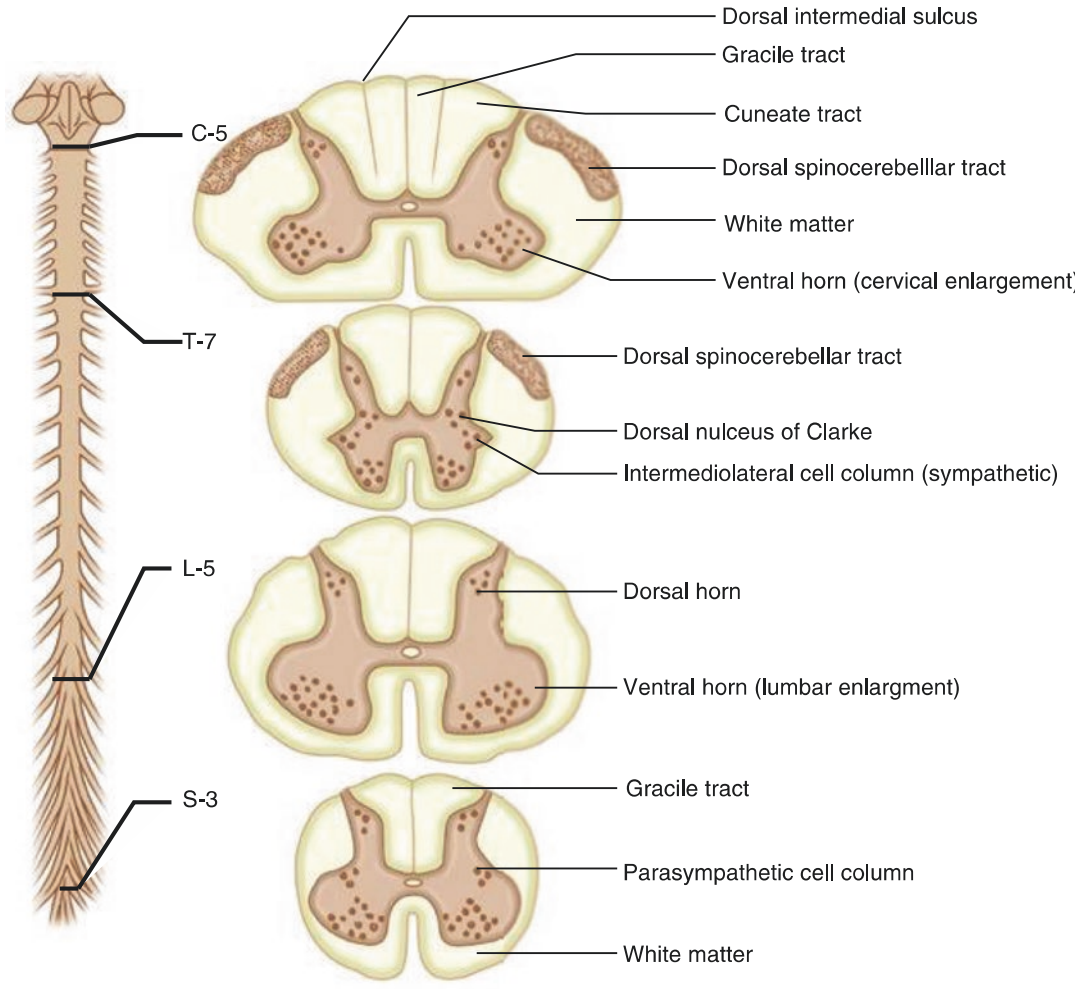
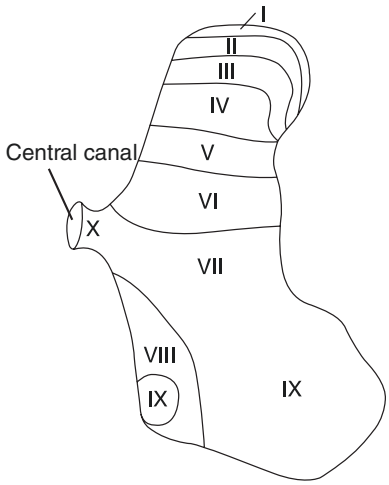


Fig. 3.10 Variations in spinal cord segments at different levels. The intermediate horn in the thoracic and upper lumbar spinal cord receives visceral afferent impulses and contain cell bodies of preganglionic, visceral efferent neurons whose axons emerge in the ventral roots



Region	Nuclei	Laminae
Dorsal horn	Marginal zone	I
	Substantia gelatinosa	II
	Nucleus proprius	III. IV
	Neck of dorsal horn	V
	Base of dorsal horn	VI
Intermediate zone	Clarke's nucleus, intermediolateral nucleus	VII
Ventral horn	Commissural nucleus	VIII
	Motor nuclei	IX
Gray matter around central canal	Grisea centralis	X

Fig. 3.11 Rexed's laminae of the gray matter and their region and nuclei

The laminar maps, Rexed's laminae, of the spinal gray matter were provided for the studies of cytoarchitecture (size, density, and morphology) of neurons based on a fundamental anatomical nomenclature for the spinal cord gray matter of cats by Rexed (Afifi and Bergman 2005; Blumenfeld 2010; Rexed 1954) (Fig. 3.11). Lamina I, also called the marginal zone, is a thin layer of gray matter that covers the substantia gelatinosa, lamina II is the substantia gelatinosa, and laminae III to VI are the body of the dorsal horn; lamina VII roughly corresponds to the intermediate gray matter including Clarke's nucleus, but also includes large extensions into the ventral horn; lamina VIII comprises some of the interneuronal zones of the ventral horn, while lamina IX consists of the clusters of motor neurons embedded in the ventral horn; lamina X is the zone of gray matter that surrounds the central canal (Vanderah and Gould 2016).

The dorsal horn contains laminae I–VI and laminae VII–X aside at the base of the ventral horn and the central region of the dorsal horn. However, not all the laminae can be clearly distinguished from each other. Laminae I–VIII extend over the entire length of the spinal cord, although the size may vary considerably from segment to segment. Lamina II corresponds to the substantia gelatinosa and plays an important role in the transmission of fibers for thermal and painful sensations. Lamina IX cannot be understood as a section in the classical sense but can be understood as interspersed motor neuron pools within laminae VII and VIII. Lamina IX is not a true lamina, but a set of columns in laminae VII and VIII and along the edge of X. It is a major site for large α-motor neurons (innervate striated musculature) and smaller **γ**-motor neurons (innervate muscle spindles) in the spinal cord. They are surrounded by certain types of interneurons, namely, Renshaw cells, which induce a recurrent inhibition for motor neurons and thus provide an essential negative feedback mechanism for motor neuron activity. Lamina VII occupies the intermediate gray zone and contains Clarke's nucleus. Lamina X, the central gray of the spinal cord, extends along the entire spinal cord and surrounds the region around the central canal (Table 3.2).

3.3.2.1 Dorsal Gray Horn (Laminae I–IV)

The dorsal horn is the entry site of afferent sensory information into the central nervous system. Laminae I to IV are located in the dorsal horn. Rexed lamina I is the tip of the dorsal horn. Each dorsal and intermediate horn contains two anatomically distinct nuclei, the substantia gelatinosa (lamina II), and the nucleus dorsalis (Clarke's nucleus, lamina VII) (Zeman and Innes

Table 3.2 Important subdivisions of spinal cord gray matter: their segmental levels and function

Nucleus	Levels	Rexed lamina	Main function
Marginal zone	All	I	Modulate nociceptive sensory input Some spinothalamic tract cells
Substantia gelatinosa	All	II	Modulate nociceptive sensory input Modulate transmission of pain and temperature information
Body of posterior horn	All	III–VI	Sensory processing Origin of main secondary sensory afferents to higher centers (e.g. spinothalamic tract)
Clarke's nucleus	T1–L2	VII	Origin of posterior spinocerebellar tract
Intermediolateral nucleus	T1–L3	VII	Origin of preganglionic sympathetic fibers
Intermediolateral nucleus (sacral parasympathetic nucleus)	S2–S4	VII	Origin of preganglionic parasympathetic fibers
Medial motor nuclei	All	IX	Motor neurons innervating trunk musculature
Lateral motor nuclei	C5–T1 and L2–S3	IX	Motor neurons innervating upper and lower limb musculature

Modified from Vanderah and Gould (2016) and Critchley and Eisen (1997)

1963). The remainder of the gray matter forms the so-called nucleus proprius (laminae III and IV) of the dorsal gray column. Lamina II is the part of the spinal gray matter with the highest neuronal density. The substantia gelatinosa present in all segments of the spinal cord is prominent, since it contains few elements stained with dyes for staining myelin sheathes, and many cells are very small (Golgi II). The small cells are interneurons that are part of the pain pathway in the spinal cord. Their axons synapse immediately with larger neurons in the nucleus proprius, which adjoin the nucleus, and lead to axons to the lateral spinothalamic tract (Bican et al. 2013). Laminae I, II, and V receive input from noxious stimuli. Laminae III and IV (together as the nucleus proprius) receive light touch and position input. Lamina VI receives mechanical input from the skin and joints (Bican et al. 2013).

3.3.2.2 Intermediate Gray Horn (Laminae V–VIII and Autonomic Nuclei)

The intermediate zone presents in the thoracic and upper lumbar segments. It contains preganglionic autonomic neurons for the sympathetic nervous system that receive input from hypothalamic and brainstem nuclei via the descending central autonomic tract. Lamina VII of the gray matter in the thoracic and upper lumbar segments includes the nucleus containing cells projecting from preganglionic sympathetic fibers and cells of the nucleus dorsalis (Clarke's nucleus), which form the posterior spinocerebellar tract (Rexed and Brodal 1951). The nucleus dorsalis occupies a medial area near the base of the dorsal horn in the T1 to L2 segments of the spinal cord. It is largest in the lower thoracic and upper lumbar segments. The nucleus consists of large nerve cells, which receive collateral nerve fibers from the medial divisions of dorsal roots. The Clarke's nucleus is an important relay nucleus for transmitting information to the cerebellum and can also play a role in forwarding proprioceptive information from the leg to the thalamus. Because of its prominent role in sensory processing, it is treated as part of the dorsal horn (Vanderah and Gould 2016). Axons of the small nerve cells in this column leave the spinal cord in ventral roots and synapse with postganglionic sympathetic neurons in the ganglia of the sympathetic chain. Other visceral efferent neurons are located in the S2 to S4 segments of the spinal cord and form a parasympathetic efferent column lateral to the central gray matter and central canal in the intermediate zone of the spinal cord. They give rise to the pelvic splanchnics, which provide parasympathetic input to the distal colon, rectum, bladder,

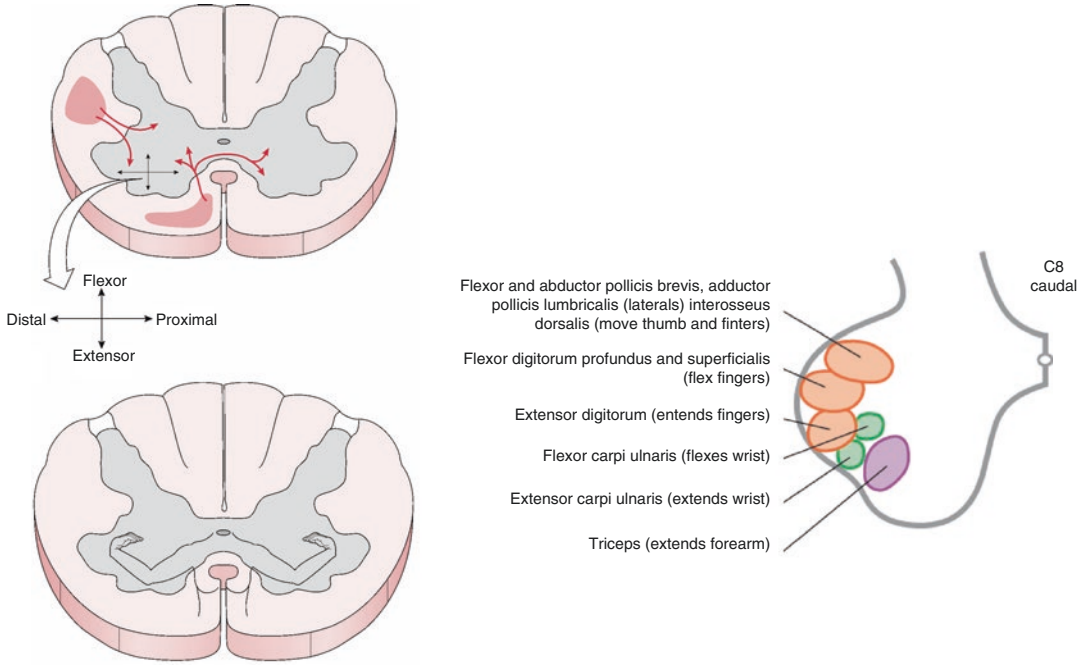


Fig. 3.12 Somatotopical arrangement of neurons of the ventral gray column. The more medially located neurons innervating the axial and proximal limb muscles and the more laterally located neurons innervating the distal limb muscles. More ventrally located neurons innervate to the extensor muscle and more lateral neurons innervate to the flexor muscles. The diagram on the right side is an example of the C8 segment caudal portion

and sexual organs, and their fibers synapse with postganglionic parasympathetic neurons located in the walls of these target organs.

3.3.2.3 Ventral Gray Horn (Lamina IX)

The ventral horns of the spinal cord contain large α-motor neurons (innervate striated musculature) and smaller γ-motor neurons (innervate muscle spindles) in the spinal cord. The axons of the α-motor neurons supply skeletal muscle fibers. Those of the γ-motor neurons innervate the intrafusal fibers of muscle spindles, so they are also referred to as fusimotor neurons (Vanderah and Gould 2016). A third type of nerve cells, intrasegmental neurons (interneurons) with short axons, is present in the ventral gray matter, especially in the medial region. Neurons of the ventral gray column (lamina IX) are somatotopically arranged, with the more medially located neurons innervating the axial and proximal limb muscles and the more laterally located neurons innervating the distal limb muscles. More anteriorly located neurons innervate to the extensor muscle, and more lateral neurons innervate to the flexor muscles (Craw 1928) (Fig. 3.12). There is an anatomical characteristic that affects the difference between the degree of motor paralysis and the degree of recovery of motor function of the muscles in case of partial damage to a spinal cord segment because of a difference in the size of the motor neuron group and length of the motor neuron column in the same or adjacent spinal cord segments (Figs. 3.13 and 3.14). Due to the difference in the length or size of the motor neuron column of each muscle, the smaller the size or length of the motor neuron column of a muscle, the less likely it is to be damaged, but the degree of damage can be more serious once injured (Elliott 1942; Sharrard 1955).

3.3.2.4 Central Canal (Lamina X)

Lamina X is the neurons that surround the central canal. The lamina X consists of the posterior and anterior gray commissures. The central canal,

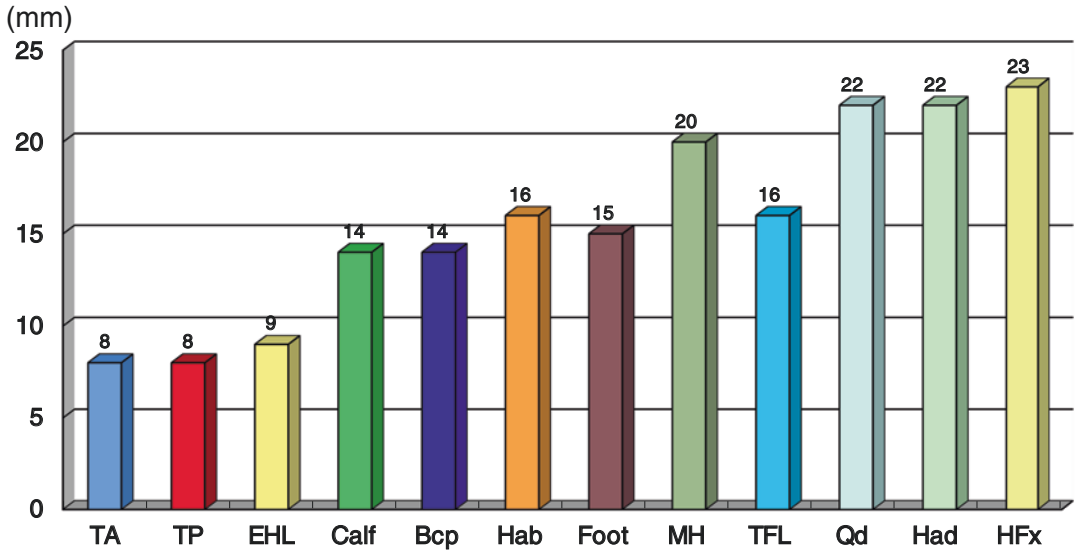


Fig. 3.13 Length of the motor neuron cell column of the muscles in the leg. Modified from Sharrard (1955)

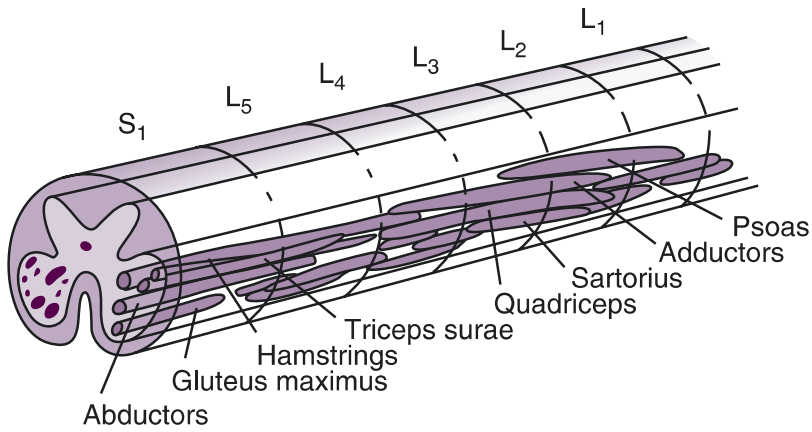


Fig. 3.14 Approximate location in the transverse plane and longitudinal extent of the anterior horn cell groups innervating muscles, in the lumbosacral segments of the human spinal cord. Note the S1 cluster of triceps surae, hamstrings, and gluteals and the S2–3 cluster of quadriceps, hip flexors, and adductors. Based on clinicopathological studies of poliomyelitis. From Hsu et al. (2008). This figure from Hsu et al. (2008) was modified from Sharrard (1955)

which is lined by ependymal cells, runs the entire length of the spinal cord, opens into the fourth ventricle in the medullar oblongata, and passes caudally into the upper end of the filum terminale. A small dilatation of the central canal called the terminal ventricle occurs in the conus medullaris during early life but is obliterated about the age of 40.

3.4 Spinal Nerves and Roots

There are 31 spinal nerves to each corresponding spinal cord segment. Each spinal nerve consists of a sensory root and a motor root. At each segmental level, the ventral and dorsal roots arise from the anteriolateral and posterolateral surfaces of the spinal cord, respectively. The first

cervical nerve and coccygeal nerve have no dorsal root with no dermatomal presentation. Each root is formed by the union of three or more small rootlets (filaments). Usually, the ventral root consists of 4–7 filaments, which exit the cord at the anterolateral sulcus. The dorsal root enters the cord at the posterolateral sulcus and consists of 4–10 filaments. At each level of the ventral root, there are axons of motor neurons, while at levels T1–L2 (sympathetic) and S2–S4 (parasympathetic), these roots also carry preganglionic autonomic fibers that originate from the intermediolateral nucleus. The dorsal root contains the central process of bipolar sensory neurons. These neurons are located in the dorsal root ganglion. Some primary sensory afferents, particularly those of visceral origin, enter the spinal cord through the ventral root but still terminate in the dorsal horn. All ventral roots contain a large number of unmyelinated axons that they make up 27% of the total population of ventral root axons. The function of these unmyelinated axons in the ventral roots is not well defined, but for various reasons, it is likely that a significant number are sensory (Coggeshall et al. 1975).

The ventral roots are the motor output from the spinal cord. These ventral roots are large-diameter α-motor neuron axons to the extrafusal striated muscle fibers, and **γ**-motor neuron axons supply the intrafusal striated muscle spindles as well as preganglionic autonomic fibers. The dorsal roots consist of several types of afferent fibers, which are somatotopically organized so that the largest diameter fibers are medial to the smaller ones (Fig. 3.5). These largest afferent fibers (Ia and Ib) are heavily myelinated fibers that conduct the afferent limb of muscle stretch reflexes and carry information from muscle spindles and Golgi tendon organs. Medium-sized fibers (A-β) convey impulses from mechanoreceptors in the skin and joints. Small, thinly myelinated A-***δ*** and unmyelinated C-fibers convey noxious and thermal sensations. After the dorsal and ventral roots join to form spinal nerves, they divide into a smaller primary dorsal ramus and a larger primary ventral ramus. Each ramus contains motor, sensory, and autonomic fibers. The dorsal ramus consists of a medial sensory branch and a lateral motor branch to supply the skin and paraspinal muscle, respectively, at the segmental level. The ventral ramus is much larger and contributes to the brachial and lumbosacral plexuses as well as to segmental branches such as intercostal nerves (Bican et al. 2013).

The nerve roots are covered by a thin layer of arachnoid cells which enclose the endothelial compartment of the nerve and include myelinated and unmyelinated nerve fibers that accompany Schwann cells and endoneurial blood vessels. The dura forms dural sleeves in each intervertebral foramen and blends with the epineurium of each spinal nerve. The roots are surrounded by pia and cross the subarachnoid space until they reach their respective dural sleeve, which emerges from the anterolateral surface of the dural sac. Nerve roots have no dural covering in the subarachnoid space, lacking epineurium coverage. Nerve roots in the subarachnoid space are more sensitive and more susceptible to injury than spinal nerves.

The first seven cervical spinal nerves exist above the same-numbered cervical vertebra. The C8 nerve emerges between the seventh and first thoracic vertebrae, and the remaining spinal nerves caudal to that level, all emerge below their respective same-numbered vertebra. In the upper cervical region, the nerve roots pass out of the spinal canal through the intervertebral foramen, almost at the level where they leave the spinal cord. However, since the spinal cord extends only to L1 or L2 vertebra, the segmental level of the cord is located above the intervertebral foramen at most levels. Thus, at progressively more caudal levels, the roots have a more oblique and downward course in the subarachnoid space from the cord to the intervertebral foramen. Therefore, the lower sacral roots leave the cord at L1 and extend several centimeters to the sacral region before leaving the spinal canal. When determining the level of affected nerve roots, the level of dissociation must be considered. In the supine position, the nerve roots in the lower lumbar spine lie in a U-shaped configuration in the posterior part of the dural sac. The sacral roots are located dorsally and medially, the lumbar roots lie more laterally and anteriorly.

3.5 Meninges, Subarachnoid Space, and Cerebrospinal Fluid

The connective tissue membranes surrounding the spinal cord, dura mater, arachnoid, and pia mater from the most superficial layer to the closest to the spinal cord, respectively, arise as condensation of the embryonic mesenchyme around the neural tube. Together the arachnoid and pia are called leptomeninges (the Greek word *lepto*, meaning "thin") (Bican et al. 2013). The meninges (the Greek word *meninx*, meaning "membrane") of the spinal cord are continuous with those of the brain. The dura mater is apparent until 8 weeks of gestation. The dura is a dense membrane of fibrous connective tissue, and the inner surface is a layer of simple squamous epithelium. Its outer surface merges with the epidural areolar and adipose tissues separating it from the walls of the spinal canal. The outer layer of the dura mater serves as the cranial periosteum at the foramen magnum. The dura mater is sparsely vascularized and contains a few nerve fibers. The dural sac is attached to the skull of the foramen magnum. The dural sac ends caudally at the lower border of the second sacral vertebra, but its fibrous wall extends to the coccyx and merges with the periosteum of the dorsal surface of this bone as a coccygeal ligament, anchoring the spinal cord to the spinal canal. Unlike the skull anatomy, the dura mater of the spine is separated from the periosteum of the vertebrae by the epidural space with fatty and loose connective tissue and the epidural venous plexus (Batson's venous plexus). Batson's venous plexus is believed to be relevant to the spread of infection or metastatic cancer (Bican et al. 2013). Adipose tissue located in the epidural space between the dura and the bony lining of the spinal canal is more abundant posteriorly than anteriorly. Because the nerve roots from the spinal cord or cauda equina pass through the intervertebral foramen, they are ensheathed by an extension of the dura mater. The dura forms an important barrier that largely prevents the invasion of metastatic tumors from the bone or the epidural space into the spinal cord. The spread of infection from the extradural compartment into the subarachnoid space is also likely to be delayed by the dura.

The spinal arachnoid is a thin, avascular connective tissue membrane covered with squamous cells. The arachnoid lines the dura and ends as a sac at the level of the second sacral vertebra. In contrast to the brain, there is little space between the dura mater and the arachnoid membrane of the spinal cord. Unlike the brain, therefore, there are a few lesions such as subdural hemorrhage (Fig. 3.15). It is mainly attached to dura mater at the denticulate ligaments and spinal nerve roots. The subarachnoid space is filled with spinal fluid that forms a hydraulic cushion for the spinal cord and is connected with a large cistern above the foramen magnum. Caudally, the subarachnoid space between the second lumbar and second sacral vertebrae surrounding the cauda equina and the filum terminale is enlarged. This enlarged subarachnoid space is called the lumbar cistern.

The pia mater of the spinal cord is a thin membrane that consists of two distinctly divisible layers, an outer connective tissue sheath and an inner, more delicate component that includes terminal processes of neuroglia cells, thus forming the so-called pia-glial membrane. The outer fibers of the pia mater tend to be arranged longitudinally. The pia mater narrows distally to the conus medullaris and continues the filum terminale (Barson 1970). The filum terminale internum extends downward from the conus medullaris and consists mainly of connective

Fig. 3.15 In contrast to the brain, there is little space between the dura mater and the arachnoid membrane of the spinal cord

tissue, glia, and leptomeninges. Usually, it measures 2 mm or less in diameter. It has a branch of the anterior spinal artery that causes enhancement after admission of a contrast agent. It perforates the caudal end of the dural sac. The filum terminale internum anchors the caudal end of the spinal cord to the caudal end of the spinal dural sheath. The extradural continuation is called filum terminale externum, which attaches to the dorsum of the first or second coccygeal segment. The caudal end of the dural sheath is anchored to the caudal end of the spinal canal by the filum terminale externum. The spinal pia mater forms two fibrous bands, the denticulate ligaments, on each side of the cord, midway between dorsal and ventral spinal nerve roots. Each of these bands is scalloped and, projecting through the arachnoid, attached to the dura mater by a series of pointed processes, usually 21 on both sides. The denticulate ligaments help suspend the spinal cord in a fluid-filled sac.

In the sheath of the spinal cord, there are three presumptive spaces: the epidural, subdural, and subarachnoid. The epidural space is located outside the dura containing mainly loose connective tissue, epidural adipose tissue, and the internal vertebral venous plexus. The epidural space is reduced at the foramen magnum and at the sacral hiatus. The spinal dura mater merges with the endosteal dura of the cranium and at the sacral hiatus. In the cervical and thoracic area, the epidural space is filled with a large basivertebral vein. Under normal conditions, the subdural space has no actual potential space (Heines et al. 1993). The subarachnoid space lies between the arachnoid and the pia mater. The subarachnoid space extends from the cranium to the second sacral vertebra. It contains cerebrospinal fluid and a loose network structure of collagen fibers and fibroblast, the arachnoid trabeculae. Vessels on the surface of the spinal cord are also exposed to the cerebrospinal fluid in the subarachnoid space. Therefore, toxic, infectious, or therapeutic agents introduced into the subarachnoid space contact both spinal nerve roots and the blood vessels supplying the spinal cord. The cerebrospinal fluid supports the spinal cord, which is further stabilized by the presence of the denticulate ligaments and the dorsal and dorsolateral ligaments of the arachnoid. In normal individuals, cerebrospinal fluid freely passes between the cranium and the subarachnoid space. Disruption of this free passage can lead to disorders of the spinal cord such as syringomyelia. Dorsal and ventral nerve roots arising from the spinal cord occupy a large part of the subarachnoid space.

3.6 Vascular Anatomy of the Spinal Cord

The spinal cord is richly supplied with blood. The blood supply of the neonatal spinal cord is much greater than at maturity. The average spinal cord volume, which is only 6 mL in the neonate, increases at least 13 times in mature individuals (d'Amato 2005; Etz et al. 2011). However, the diameter of vessels supplying the spinal cord increases by less than half. The maximum diameter in Adamkiewicz's artery is 1.2 mm, and most of all other vessels are in the range of 0.1–0.8 mm (Melissano et al. 2010, 2015).

3.6.1 Arteries

The arterial supply of the spinal cord comes from the vertebral arteries and from branches, ultimately from the thoracic and abdominal aorta, called radicular arteries. The vertebral artery arises from the subclavian artery, the innominate artery, or directly from the aorta (Williams et al. 2017). The course of the vertebral artery is divided into four segments (Fig. 3.16). The V1 segment represents the segment from the origin to the entry of the vertebral artery into its first transverse foramen. This is at the C6 level in 87.5% of cases (Daseler and Anson 1959). The V2 segment is the section that traverses the transverse foramen and ends after the C2 transverse foramen. It is the most vulnerable segment of the vertebral artery in most common cervical spine surgeries. The V2 segment can be tortuous and these anomalies must be identified radiographically before performing cervical surgery. The V3 segment continues until the vertebral artery

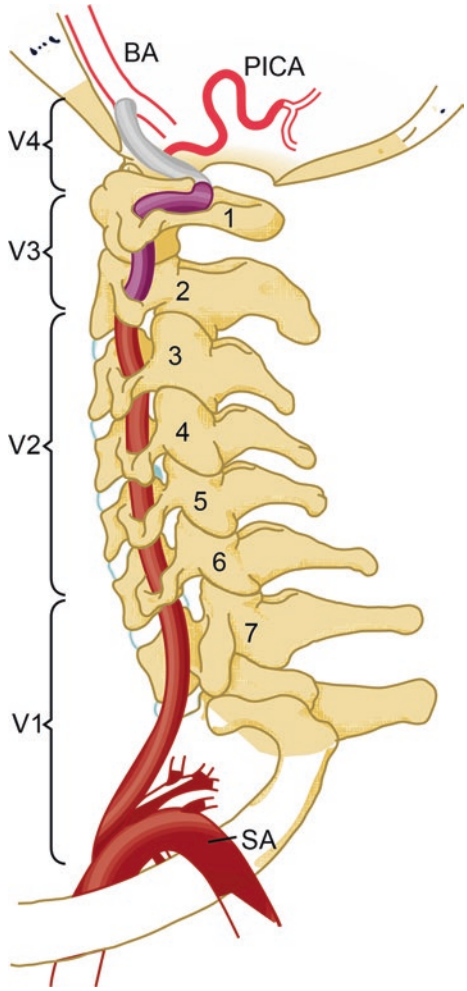


Fig. 3.16 Vertebral artery anatomy. BA, basilar artery; PICA, posterior inferior cerebellar artery; SA, subclavian artery. From Williams et al. (2017), with permission

penetrates the dura. The V4 segment is the intradural part of the vessel and ends at the vertebrobasilar junction (Williams et al. 2017). Each vertebral artery gives rise to an anterior spinal artery. The two anterior spinal arteries merge to form a single midline vessel, the longest artery in the body, which runs along the anterior median fissure of the spinal cord. The vertebral or posterior inferior cerebellar artery on each side also gives rise to posterior spinal arteries, which run along the line of attachment of the dorsal rootlets, bilaterally (Vanderah and Gould 2016). The anteriorly located anterior spinal artery and the posteriorly located two posterior spinal arteries supply the spinal cord directly. Along the length of the vertebrae, these vessels receive input from the subclavian artery via the vertebral artery, the thyrocervical trunk, and the costocervical trunk (Thron 2016) (Fig. 3.17). The origin of the main arterial supply of the spinal cord is variable, but usually, the anterior spinal artery is a derivative of two branches of the vertebral arteries at the level of the pyramidal decussation. During embryonic development, the anterior spinal artery is derived from 31 bilateral segmental arteries. From the end of the fourth month of gestation, most of the segmental arteries of the anterior spinal artery are regressing and are obliterated (Fig. 3.18). Only a few of these arteries (2–14, mean 6) are left in the adult. An average of 2–3 is found at the cervical level (left = right), 2–3 at the thoracic level (left > right), and 0–1 at the lumbosacral level (left > right) (Melissano et al. 2010, 2015). The segmental arteries of the vertebral column at the thoracic and lumbar regions originate from the dorsal surface of the aorta and are called intercostal and lumbar arteries.

Medullary feeder arteries arise from the segmental arteries of the vertebral column and traverse the intervertebral foramen with the spinal nerves. Radicular arteries (not to be confused with feeders), which feed the spinal nerve roots, develop along with medullary feeder arteries from the segmental arteries as well as from the longitudinal arterial trunks (Windle 1980). The dorsal medullary feeder arteries are more numerous than the ventral feeder arteries but smaller in size. The number of ventral medullary feeder arteries varies from 2 to 17, and their locations were also variable. The medullary feeder arteries in the thoracic region are smaller and less than those at higher and lower levels of the spinal cord. The parenchyma of the spinal cord receives blood through small branches of the ventral longitudinal arterial trunk (anterior spinal artery), so-called sulcal arteries that enter the cord through the ventral sulcus (Fig. 3.19). The sulcal arteries pass posteriorly through the anterior median sulcus before they laterally diverge to supply one-half of the cord at each level. There are 2–12 sulcal arteries per centimeter of the ventral longitudinal arterial trunks, more at the

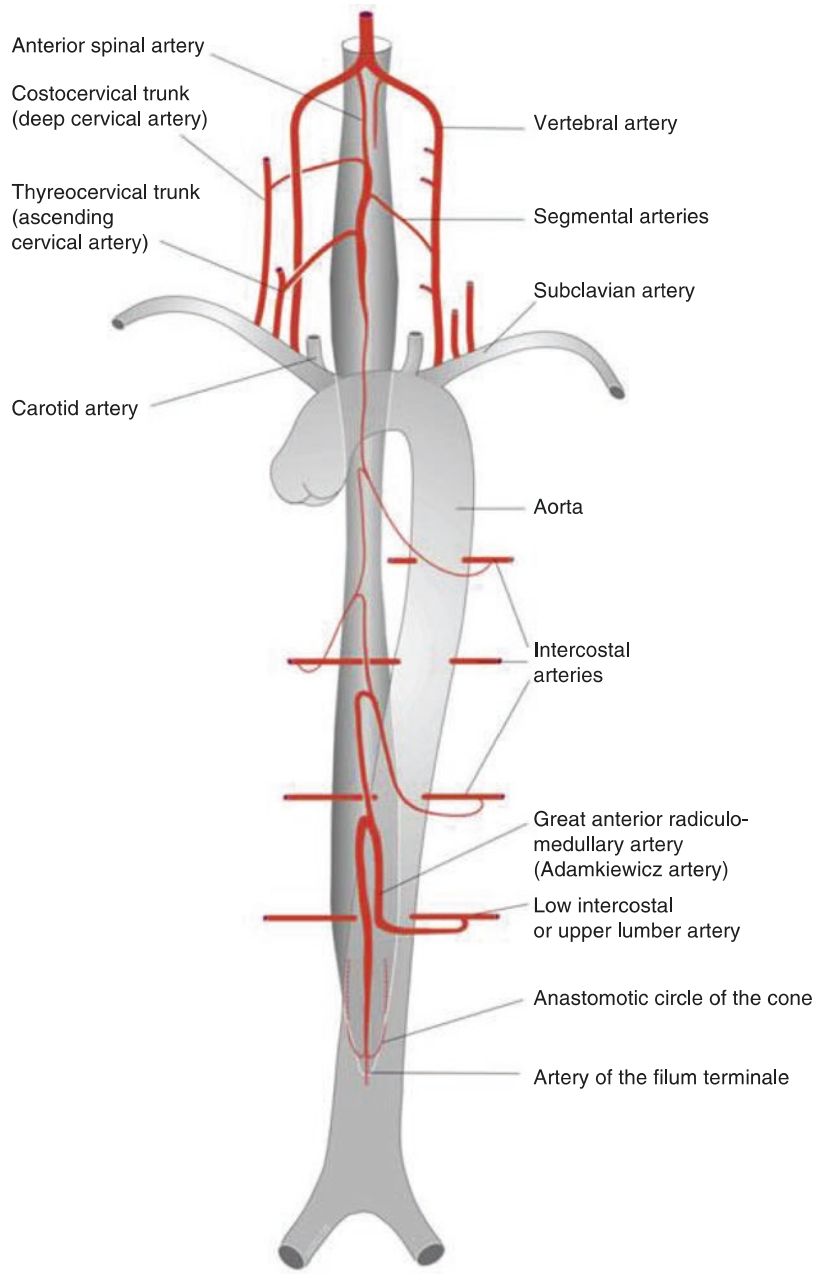


Fig. 3.17 Main source of arterial supply to the anterior spinal artery. From Thron (2016)

cervical and lumbosacral enlargements than in the thoracic cord where spinal gray matter is smaller.

The radicular branches of segmental arteries approach the spinal column, which runs along with the ventral nerve roots through the intervertebral foramina. There are more radicular branches that feed the cervical and lumbar enlargements. The thoracic cord is supplied by a few radicular arteries, which probably reflect the reduced metabolic requirement, as less gray matter is present. The anterior spinal artery may be discontinuous in these regions. Another important factor is the alteration of the subclavian artery that feeds the radicular arteries to direct aortic supply in the upper thoracic region. This

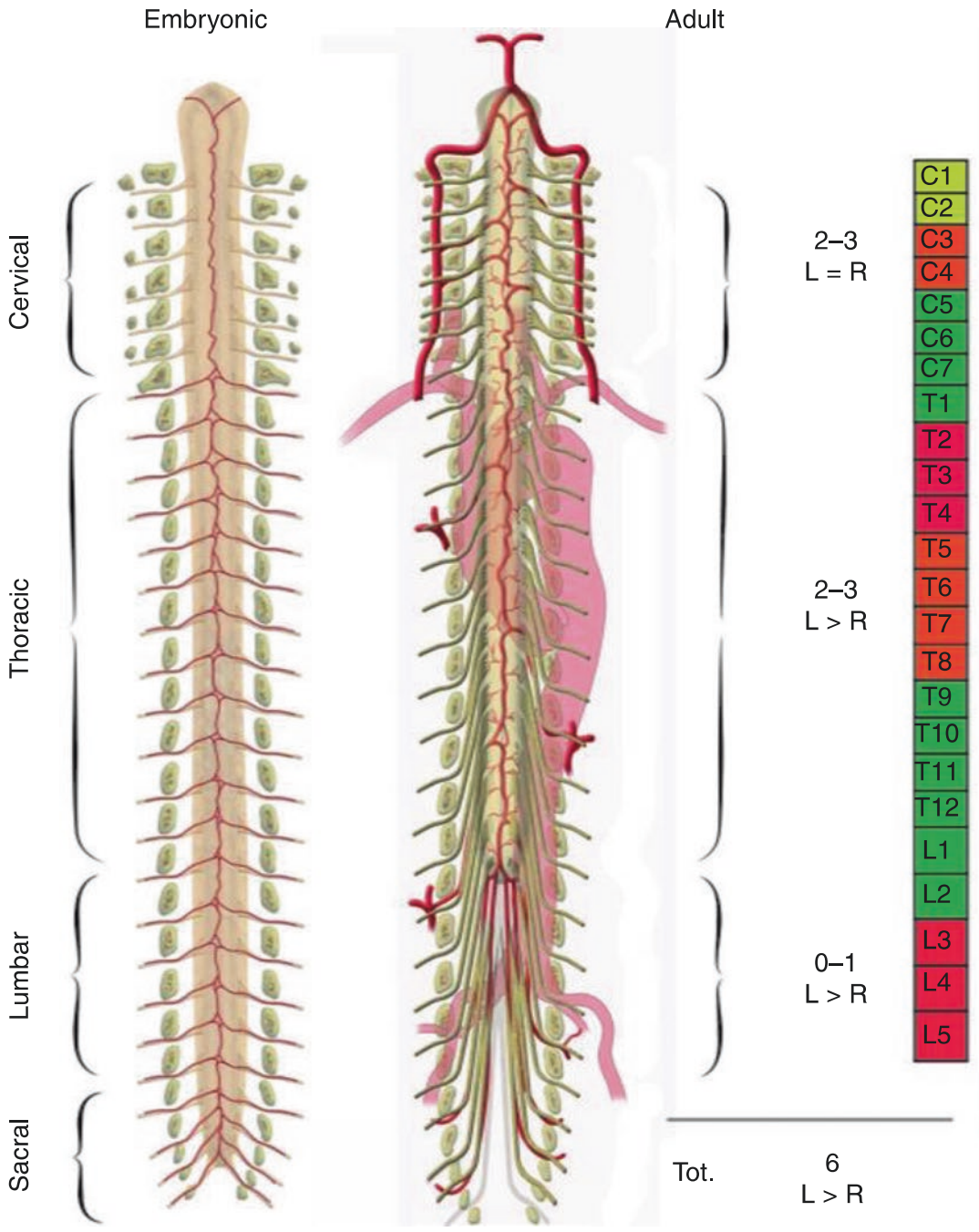


Fig. 3.18 Embryonic development (GW 16) of the anterior spinal artery from 31 bilateral segmental feeders. In the adult, most of the segmental feeders of anterior spinal artery regress. Only a few (2–4, mean 6) of these feeders are left in the adult). From Melissano et al. (2015), with permission

low arterial supply to the upper and midthoracic levels represents a watershed area that is susceptible to systemic hypotension or occlusion of a single vessel. The relatively midthoracic region (T4–8) watershed area is between the rostral region, where the anterior spinal artery is more

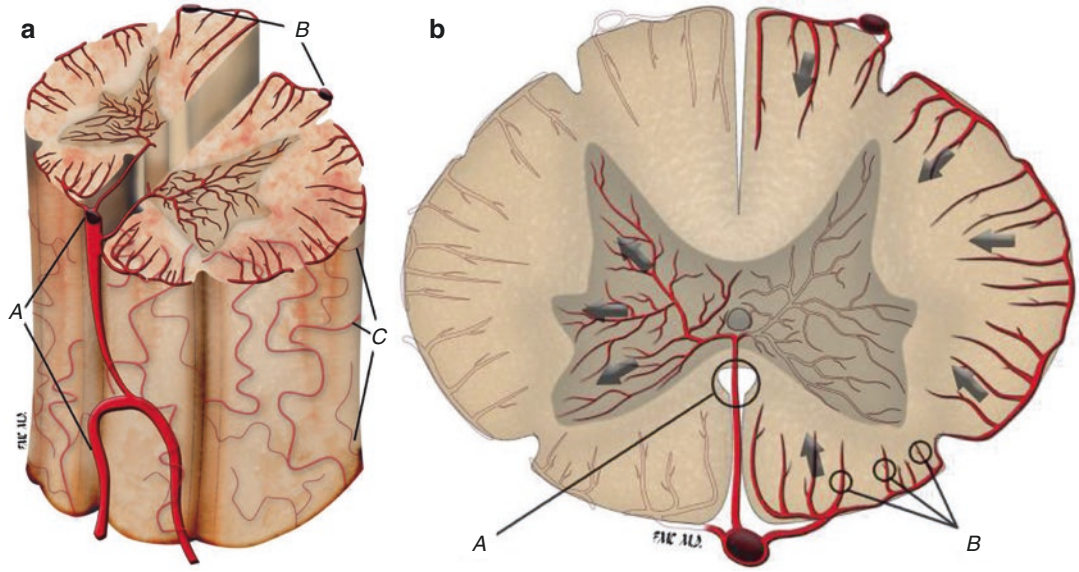


Fig. 3.19 (**a**) The spinal cord is covered by a net-like anastomosing vascular system in which the anterior spinal artery (A) and the two posterior spinal arteries (B). The pial network (C) and intramedullary anastomoses may only be important for slower circulatory adjustments. (**b**) The intrinsic arterial system of the spinal cord is divided into a central (centrifugal) system. The central system is represented by the sulcal arteries, which approach from the anterior arterial tract, pass into the anterior median fissures (A). The peripheral system consists of numerous small arteries "rami perforantes" (B). From Melissano et al. (2015), with permission

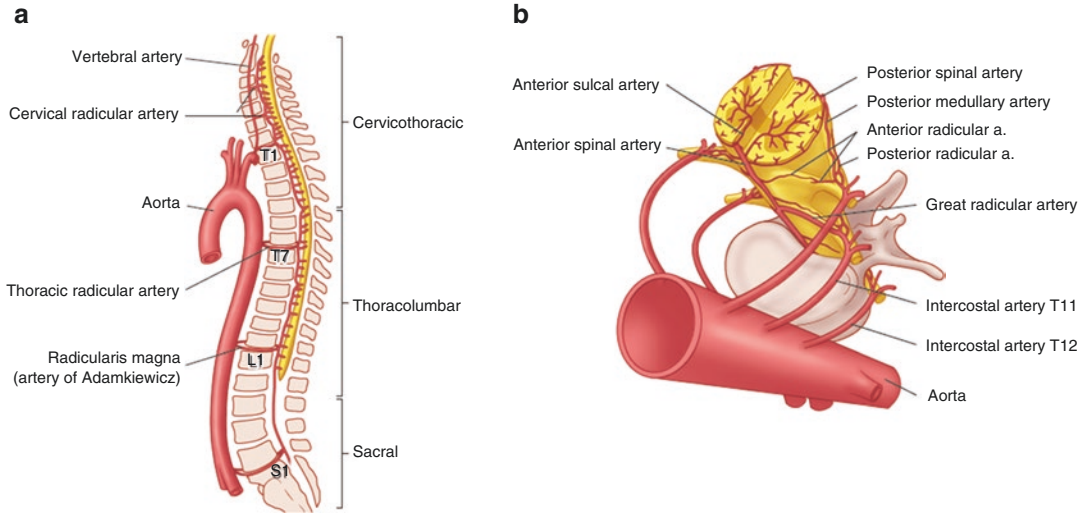


Fig. 3.20 Main arterial vasculature of the spinal cord. (**a**) sagittal aspect, and (**b**) axial view

robust, and the caudal region, where blood supply is supplemented by the relatively large radicular artery of Adamkiewicz. From the lower thoracic to upper lumbar regions, the larger radicular artery of Adamkiewicz supplies the anterior spinal artery. It originates in the abdominal aorta at T9, transverses the intervertebral foramen, and finally anastomoses with the anterior spinal artery (Nijenhuis et al. 2006). The Adamkiewicz artery is located more often on the left side than on the right and maybe anywhere between the T7 and L4 segments of the spinal cord (Murthy et al. 2010) (Figs. 3.20 and 3.21). It accompanies the left T10 ventral root in 30% of patients and the

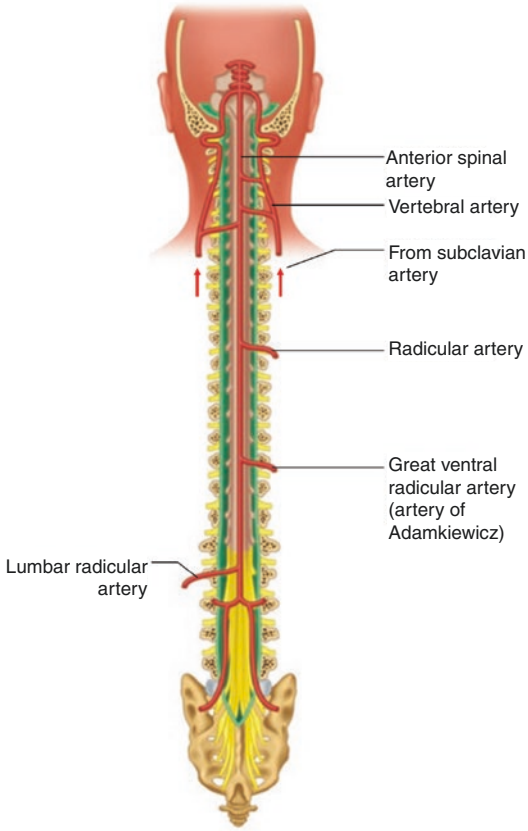


Fig. 3.21 Ventral view of the spinal cord. The great ventral radicular artery (artery of Adamkiewicz) is the largest, albeit inconsistent, of the radicular arteries. From Patestas and Gartner (2006)

rest are accompanied by any root from T9 to L1 (Hughes 1989). The artery of Adamkiewicz is generally cranially oriented.

The anterior spinal artery feeds most of the ventral two-thirds of the spinal cord, including the nucleus dorsalis (Clarke's) and the corticospinal tracts. The posterior one-third of the spinal cord, that is, the posterior funiculi and dorsal gray matter, receives blood from pia-penetrating arteriolar branches of the dorsolateral longitudinal arterial trunks (posterior spinal artery). The arteries entering the spinal cord have no anastomoses except at the conus medullaris, which are end arteries. At the level of the conus medullaris, there is an anastomotic ring containing segmental branches of lumbar and iliolumbar arteries connecting the anterior and posterior arterial systems.

The posterior spinal arteries are derived directly from the vertebral artery in the neck region or from the posterior inferior cerebellar artery on the posterolateral surface of the medulla oblongata (Zhang et al. 2013). Immediately after the origin, each artery is divided into two anastomotic tracts. There are two posterior spinal arteries on the dorsal surface, which arise from the dorsal radicular branch arteries, and these form small vessel plexus. The posterior spinal arteries also receive blood from segmental arteries (ascending cervical artery, profound cervical artery, posterior intercostal artery, and lumbar arteries). There are also circumflex vessels connecting the two systems. The posterior spinal arteries, which are much less often affected than the anterior system, also arise from the vertebral arteries rostrally, with additional contributions from the dorsal radicular branches at each level. The posterior spinal artery supplies approximately the posterior one-third of the cord, and especially the posterior columns, through the pial arterial plexus penetrating from the surface of the cord.

Within the gray and white matter of the spinal cord, a complex capillary network is formed and is significantly more complicated in the gray matter (Scharrer 1945). Some regions also appear to contain more capillaries than others. For example, the corticospinal tract contains about twice as many capillaries as the fasciculus cuneatus (Zeman and Innes 1963).

3.6.2 Veins

Venous drainage is through a series of six irregular, plexiform channels: one along the anterior and posterior midlines and one along the attachment line of the dorsal and ventral rootlets of each side. These are drained through radicular veins, which in turn flow into the epidural venous plexus (Vanderah and Gould 2016).

The venous systems are divided into intrinsic (internal) and extrinsic (external) systems: intrinsic system is the outflows from the vertebral body through the basilar vein and others are extrinsic (external) systems. Similar to the arterial system,

an anterior and posterior spinal vein extends along the longitudinal axis of the spinal cord but can exhibit significant caliber variations (Fig. 3.22). The venous drainage of the ventral cord tends to accompany the anterior spinal artery. The typical difference is that the arterial

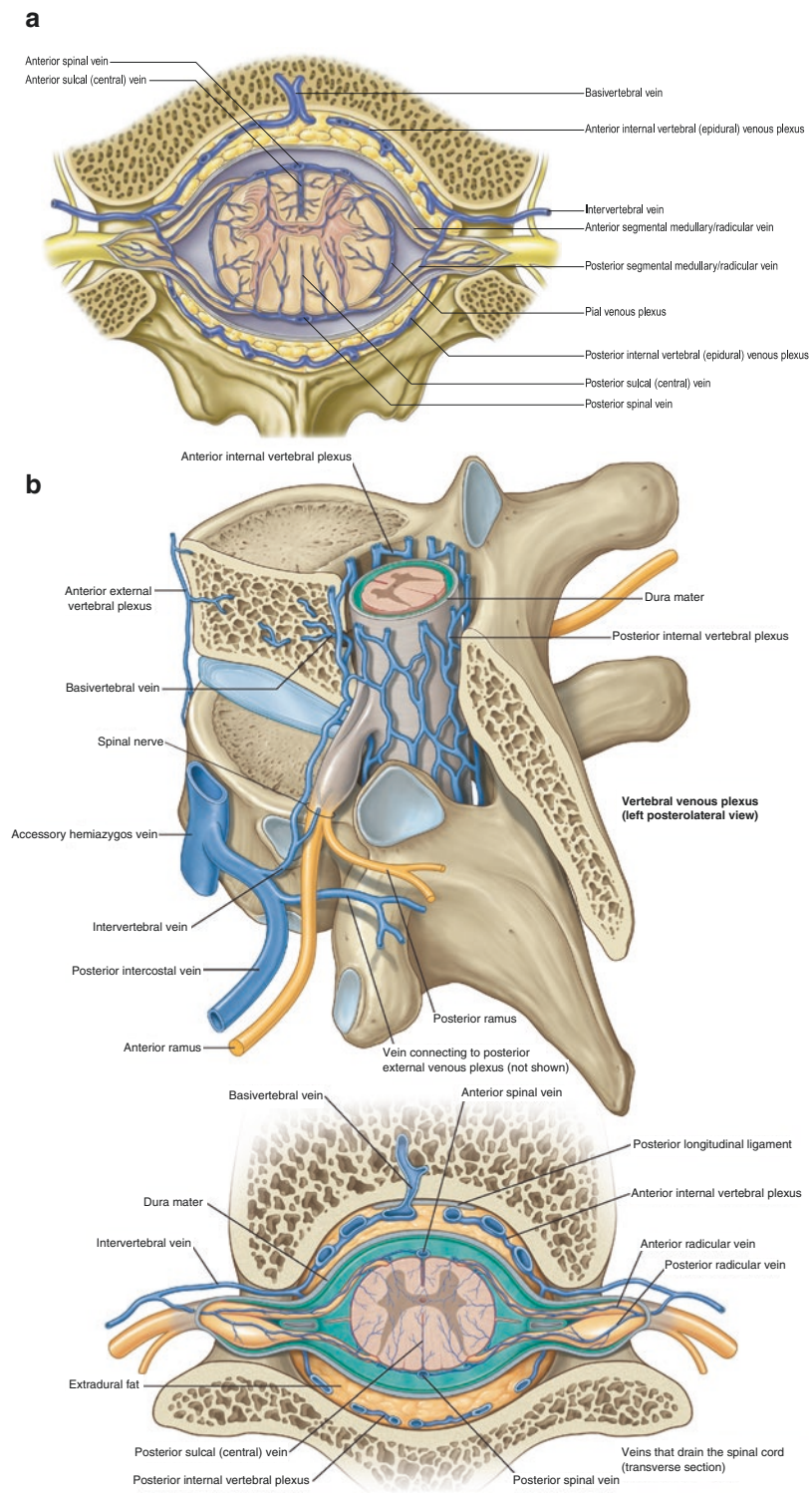


Fig. 3.22 (**a**) Venous drainage of the spinal cord. From Mancall and Brock (2011), with permission. (**b**) Venous drainage of the spinal cord. From Darke et al. (2021), with permission

network is denser on the anterior portion of the cord and the venous network is denser on the posterior portion. In the posterior, the more prominent veins run separately to the spinal arteries, draining into posterior radicular veins with every second or third root. The venous plexus is particularly prominent in the lumbar enlargement. These anterior and posterior venous plexuses drain into the segmental veins and then drain into the ascending lumbar veins, the azygos system, and the pelvic venous plexuses.

References

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.

Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.

Armand J. The origin, course and termination of corticospinal fibers in various mammals. Prog Brain Res. 1982;57:329–60.

Barson AJ. The vertebral level of termination of the spinal cord during normal and abnormal development. J Anat. 1970;106:489–97.

Bican O, Minagar A, Pruitt AA. The spinal cord: a review of functional neuroanatomy. Neurol Clin. 2013;31:1–18.

Blumenfeld H. Neuroanatomy through clinical cases. 2nd ed. Sunderland: Sinauer Associates; 2010.

Breig A, el-Nadi AF. Biomechanics of the cervical spinal cord. Relief of contact pressure on and overstretching of the spinal cord. Acta Radiol Diagn (Stockh). 1966;4:602–24.

Breig A, Turnbull I, Hassler O. Effects of mechanical stresses on the spinal cord in cervical spondylosis. A study on fresh cadaver material. J Neurosurg. 1966;25:45–56.

Campbell WW. DeJong's the neurologic examination. 7th edn. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Cho TA. Spinal cord functional anatomy. Continuum (Minneap Minn). 2015;21:13–35.

Cho TA, Bhattacharyya S. Approach to myelopathy. Continuum (Minneap Minn). 2018;24(2, Spinal Cord Disorders):386–406.

Clifton GL, Coggeshall RE, Vance WH, et al. Receptive fields of unmyelinated ventral root afferent fibres in the cat. J Physiol. 1976;256:573–600.

Clowry GJ, Moss JA, Clough RL. An immunohistochemical study of the development of sensorimotor components of the early fetal human spinal cord. J Anat. 2005;207:313–24.

Coggeshall RE, Applebaum ML, Fazen M, et al. Unmyelinated axons in human ventral roots, a possible explanation for the failure of dorsal rhizotomy to relieve pain. Brain. 1975;98:157–66.

Cole J, Weller R. Introduction to the clinical presentations of spinal cord disease from a pathophysiological perspective. In: Engler GL, Cole J, Merton WL, editors. Spinal cord diseases. Diagnosis and treatment. New York: Marcel Dekker, Inc; 1998. p. 1–13.

Coppola AR. "Cruciate paralysis": a complication of surgery. South Med J. 1973;66:684.

Craw CH. The distribution of the nerve cells in the ventral columns of the spinal cord. J Comp Neurol. 1928;45:283–99.

Critchley E, Eisen A, editors. Spinal cord disease. Basic science, diagnosis and management. London: Springer; 1997.

d'Amato C. Pediatric spinal trauma: injuries in very young children. Clin Orthop Relat Res. 2005;432:34–40.

Darke RL, Vogl AW, Mitchell AWM. Gray's atlas of anatomy. 3rd ed. Philadelphia: Elsevier; 2021.

Daseler EH, Anson BJ. Surgical anatomy of the subclavian artery and its branches. Surg Gynecol Obstet. 1959;108:149–74.

Dumitru D, Lang JE. Cruciate paralysis. Case report. J Neurosurg. 1986;65:108–10.

Elliott HC. Studies on the motor cells of the spinal cord, I. Distribution in the normal human cord. Am J Anat. 1942;70:95–117.

Etz CD, Kari FA, Mueller CS, et al. The collateral network concept: a reassessment of the anatomy of spinal cord perfusion. J Thorac Cardiovasc Surg. 2011;141:1020–8.

Heines DE, Harkey HL, Al-Mefty O. The "subdural" space: a new look at an outdated concept. Neurosurgery. 1993;32:111–20.

Holmes A, Han ZH, Dang GT, et al. Changes in cervical canal spinal volume during in vitro flexion-extension. Spine (Phila Pa 1976). 1996;(21):1313–9.

Hsu JD, Michael JW, Fisk JR. AAOS atlas of orthoses and assistive devices. 4th ed. Philadelphia: Mosby; 2008.

Hughes JT. In: Vinken PJ, Bruyn GW, Klawans HL, editors. Vascular diseases, part III. London: Elsevier; 1989.

Ko HY, Park JH, Shin YB, et al. Gross quantitative measurements of spinal cord segments in human. Spinal Cord. 2004;42:35–40.

Lawrence DG, Kuypers HG. The functional organization of the motor system in the monkey. I. The effects of bilateral pyramidal lesions. Brain. 1968;91:1–14.

Lemon RN. Descending pathways in motor control. Annu Rev Neurosci. 2008;31:195–218.

Mai JK, Paxinos G, editors. The human nervous system. 3rd ed. London: Elsevier; 2011.

Mancall E, Brock DG, editors. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.

Melissano G, Civilini E, Bertoglio L, et al. Angio-CT imaging of the spinal cord vascularisation: a pictorial essay. Eur J Vasc Endovasc Surg. 2010;39:436–40.

Melissano G, Bertoglio L, Rinaldi E, et al. An anatomical review of spinal cord blood supply. J Cardiovasc Surg. 2015;56:699–706.
Moore KL, Dalley AF. Clinically oriented anatomy. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 1999.
Murthy NS, Maus TP, Behrns C. Intraforaminal location of the great anterior radiculomedullary artery (artery of Adamkiewicz): a retrospective review. Pain Med. 2010;11:1756–64.
Nijenhuis RJ, Mull M, Wilmink JT, et al. MR angiography of the great anterior radiculomedullary artery (Adamkiewicz artery) validated by digital subtraction angiography. AJNR Am J Neuroradiol. 2006;27:1565–72.
Nolte J, Angevine JB. The human brain in photography and diagrams. 4th ed. Philadelphia: Elsevier; 2013.
Norenberg MD, Smith J, Marcillo A. The pathology of human spinal cord injury: defining the problems. J Neurotrauma. 2004;21:429–40.
Novy J, Carruzzo A, Maeder P, et al. Spinal cord ischemia. Arch Neurol. 2006;63:1113–20.
Patestas MA, Gartner LP. A textbook of neuroanatomy. Oxford: Blackwell Publishing; 2006.
Rexed B. A cytoarchitectonic atlas of the spinal cord in the cat. J Comp Neurol. 1954;100:297–379.
Rexed B, Brodal A. The nucleus cervicalis lateralis: a spinocerebellar relay nucleus. J Neurophysiol. 1951;14:399–407.
Rubin MN, Rabinstein AA. Vascular diseases of the spinal cord. Neurol Clin. 2013;31:153–81.
Scharrer E. Capillaries and mitochondria in neutrophil. J Comp Neurol. 1945;83:237–43.
Sharrard WJW. The distribution of the permanent paralysis in the lower limb in poliomyelitis: a clinical and pathological study. J Bone Joint Surg. 1955;37:540–58.
Standring S. Spinal cord: internal organization. In: Standring S, editor. Gray's anatomy: the anatomical basis of clinical practice. 41st ed. London: Elsevier; 2016.
ten Donkelaar HJ, Lammens M, Wesseling P, et al. Development and malformations of the human pyramidal tract. J Neurol. 2004;251:1429–42.
Thron AK. Vascular anatomy of the spinal cord. 2nd ed. Cham: Springer; 2016.
Turnbull IM, Brieg A, Hassler O. Blood supply of cervical spinal cord in man. A microangiographic cadaver study. J Neurosurg. 1966;24:951–65.
Vanderah TW, Gould DJ. Nolte's the human brain. Introduction to its functional anatomy. 7th ed. Philadelphia: Elsevier; 2016.
Williams KA, Rauschning W, Prasad S. Applied anatomy of the cervical spine. In: Steinmetz MP, Benzel EC. Benzel's spine surgery. 4th ed. Philadelphia: Elsevier; 2017.
Windle WF. The spinal cord and its reaction to traumatic injury. In: Bousquet WF, Palmer RF, editors. Modern pharmacology-toxicology: a series of monographs and textbooks. New York: Marcel Dekker, Inc.; 1980.
Zeman W, Innes JRM. Craigie's neuroanatomy of the rat. New York: Academic; 1963.
Zhang S, Wadhwa R, Haydel J, et al. Spine and spinal cord trauma: diagnosis and management. Neurol Clin. 2013;31:183–206.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.
Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.
Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Crossman A, Neary D. Neuroanatomy: an illustrated colour test. 5th ed. Philadelphia: Elsevier; 2015.
Cramer GD, Darby SA, editors. Clinical anatomy of the spine, spinal cord, and ANS. St. Louis: Elsevier; 2014.
Felten DL, O'Banion MK, Maida MS. Netter's atlas of neuroscience. 3rd ed. London: Elsevier; 2016.
Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.
Kirshbrum S, Lin VW, editors. Spinal cord medicine. 3rd ed. New York: Demos Medical Publishing; 2019.
Mai JK, Paxinos G, editors. The human nervous system. 3rd ed. London: Elsevier; 2011.
Mancall E, Brock DG, editors. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.
Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia: Elsevier; 2016.
Noback CR, Strominger NL, Demarest RJ, et al. The human nervous system: structure and function. 6th ed. Totoma: Humana Press; 2005.
Parent A. Carpenter's human neuroanatomy. 9th ed. Philadelphia: Williams & Wilkins; 1996.
Patestas MA, Gartner LP. A text book of neuroanatomy. Oxford: Blackwell Publishing; 2006.
Patten J. Neurological differential diagnosis. 2nd ed. London: Springer; 1996.
Standring S. Development of nervous system. In: Standring S, editor. Gray's anatomy. 42nd ed. Philadelphia: Elsevier; 2020.
Thron AK. Vascular anatomy of the spinal cord. 2nd ed. Cham: Springer; 2016.
Vanderah TW, Gould DJ. Nolte's the human brain. Introduction to its functional anatomy. 7th ed. Philadelphia: Elsevier; 2016.
Watson C, Paxinos G, Kayalioglu G, editors. The spinal cord. A Christopher and Dana Foundation text and atlas. New York: Elsevier; 2009.

4 Kinematics of Extremity Muscles for Functional Utilization After Spinal Cord Injuries

Successful rehabilitation for the potential functional goal utilizing the remaining musculoskeletal functions after spinal cord injuries requires an understanding of both the basic anatomy and the dynamic relationship of the anatomical structures to one another, referred to as functional anatomy. Kinesiology requires an understanding of functional anatomy and combines the sciences of kinetics and kinematics as well as biomechanics, anatomy, and physiology in the study of movement (Feeko and Mallow 2015).

People with spinal cord injuries can have a variety of disabilities, including loss of upper and lower extremity function, bladder and bowel dysfunction, pain, sexual dysfunction, and many other dysfunctions. Priority studies that are expected to restore in people with cervical spinal cord injuries have described upper limb function as a function they primarily wanted to restore compared to other dysfunctions (Anderson 2004; Huh and Ko 2020; Snoek et al. 2004). For functional training with the muscles of the remaining spinal cord segments after a spinal cord injury, we need knowledge of the functional anatomy and kinematics of the remaining muscles involved in upper limb, standing, and walking activities. The origin and insertion of the muscles to use or replace the main movements with the muscles of the segments involved is a very important factor in determining the functional role of each muscle. In order to be able to perform certain movements, it is also necessary to carry out training to enable joint fixation and the effective weight load in a closed kinetic chain that can cope with the muscle activities. Autonomy after tetraplegia is based on upper extremity movements and is achieved both by relearning open chain movement such as grasping and by learning new closed chain movement such as manual wheelchair propulsion or sitting pivot transfer (Mateo et al. 2015).

The neurological level of injury and the severity of the injury are very important in function retraining after spinal cord injury and restoration of lost function. In addition, functional training using the muscle strength of the remaining muscles or the muscles of the zone of partial preservation below the neurological level of injury is essential for effective functional rehabilitation. Although they have the same neurological level of injury and a similar ASIA Impairment Scale, the functional difference in sitting, transfer, standing, and personal care activities can be compared to the difference between the general population that may or not do usual activities such as swimming and cycling.

4.1 Potential Functions

Depending on the neurological level of injury, outcomes for activities of daily living including personal care and mobility can be predicted (Consortium for Spinal Cord Medicine 1999) (Table 4.1). However, there is a significant differ-

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Table 4.1 Expected outcomes of mobility

NLI	Bed	Transfers	Wheelchair (W/C) use	Standing/Walking
C1–C4	Total assist	Total assist	• Independent in Power recline and/or tilt W/C with head, chin, or breath control • Total assist in manual W/C	Total assist Standing in tilt table
C4	Total assist	Total assist	• Independent in power recline and/or tilt W/C with head, chin, or breath control • Total assist in manual W/C	Total assist Standing in tilt table
C5	Some assist	Some to total assist	• Independent in power recline and/or tilt W/C with arm drive control • Total assist to independent in manual W/C	Total assist Standing in tilt table
C6	Some assist	Some assist to independent	• Independent in power W/C • Total assist to independent depending on terrain	Total assist Standing in tilt table
C7–C8	Independent	Independent	Independent	Total assist Standing in tilt table
T1–T9	Independent	Independent	Independent	• Some assist to independent in standing using HKAFOs or KAFOs • Not typical of walking using HKAFOs or KAFOs and bilateral Lofstrands or walker
T10–L1	Independent	Independent	Independent	• Independent in standing using KAFOs • Some assist to independent in walking using KAFOs and bilateral Lofstrands or walker
L2–S5	Independent	Independent	Independent	• Functional ambulation with KAFOs or AFOs and Lofstrand(s) or cane(s)

ence in the outcome of each activity depending on the individual. Voluntary motor function has a major impact on a person's functional capacity, but it is not the only determinant. The expected outcome is one that is approximately set according to the neurological level of injury, and various factors including the disadvantageous body build (e.g., short arms), an individual's motivation, psychological and environmental situation are affected. Therefore, it is not necessary to strictly apply the generally expected outcome as a guideline for goal-setting.

In practice, the duration of the rehabilitation period is not sufficient to achieve the expected neurological recovery and functional results, which limits the time-consuming functional training. It should also be considered that the activity achieved in the hospital after discharge often becomes not functional if the activity obtained during the rehabilitation stay is not sufficiently functional for the patient and the patient's motivation is not good.

4.2 Relevant Kinematics

4.2.1 Movement and Kinetic Chains

Degrees of freedom indicate the number of allowed for angular motions on a joint. A joint can have up to three degrees of freedom, corresponding to the three cardinal planes (sagittal, frontal, and horizontal or transverse planes). Each rotational motion in the three cardinal planes consists of six degree of freedom. The movement of the joints or body along the degrees of freedom is centered at the fulcrum of the angular motion of the body or parts of the body, called the axis of rotation. The axis of rotation is located within or very close to the joint. The movement of the body, translation or rotation, can be performed by active movement with muscle contraction and passive movement with no active muscle contraction.

Physical laws of motion are also applied to the human body to describe movements. Rigid lever systems can be used to describe how joint motion

takes place. The fulcrum (pivot) of a lever is the point around which movement takes place and is often the joint center between two articulating bones in the human body. The lever also includes two arms or distances from the fulcrum that work in opposition to one another as motion takes place (Sliwinski and Druin 2008). Different arrangements of the fulcrum, load and force arms produce different classes of lever. There are three possible arrangements: a first-class lever has the fulcrum between the load and force arms; a second-class lever has the fulcrum at one end and the force applied at the other, with the load between them; a third-class lever again has the fulcrum at one end but the load at the other with the force applied force between them (Palastanga et al. 2002) (Fig. 4.1).

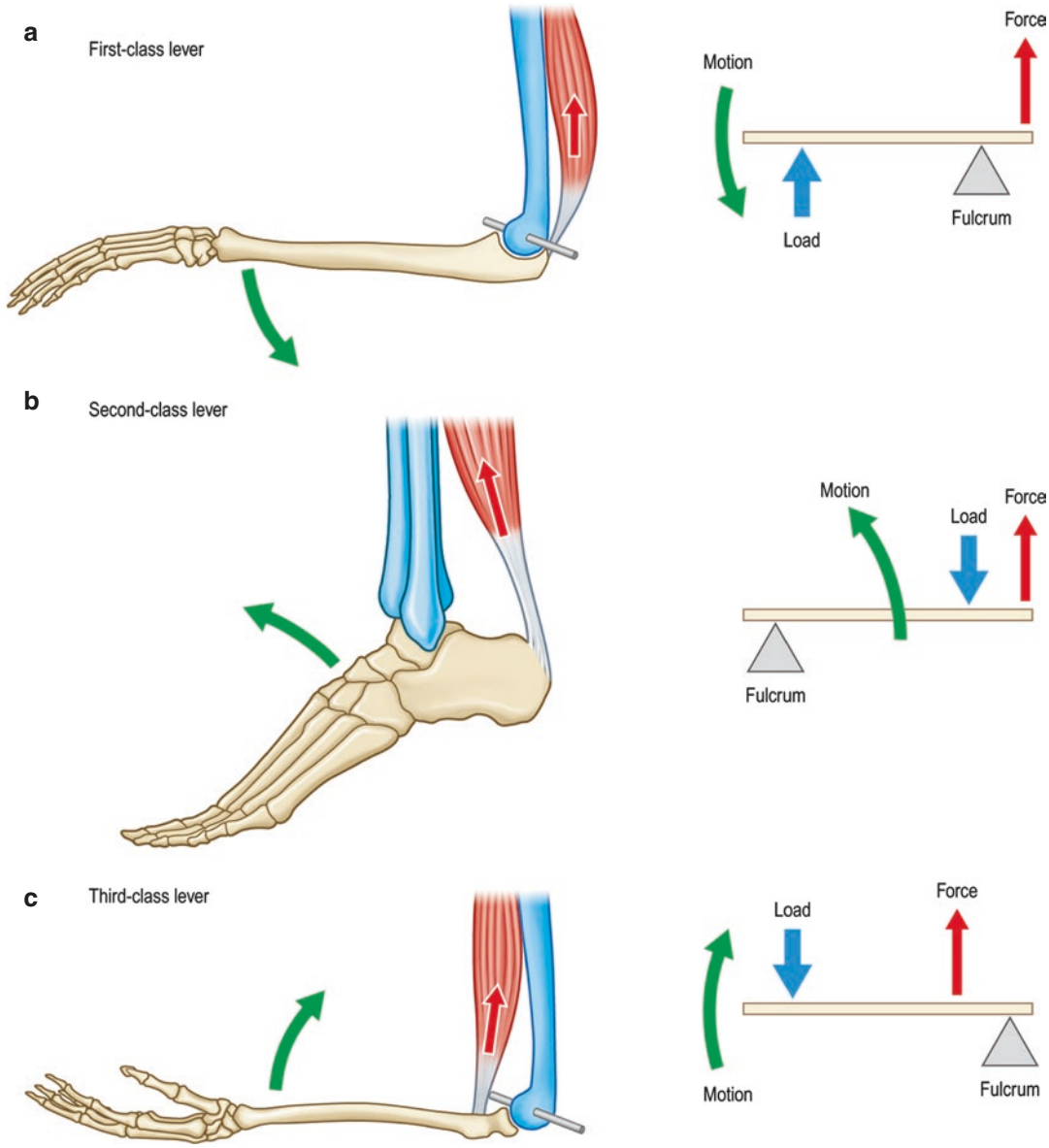

Fig. 4.1 Classes of lever. (**a**) First-class lever demonstrates the forces on either side of the fulcrum. (**b**) Second-class lever demonstrates the muscle or the internal force having greater leverage than the external force because it is further from the pivot than the external force but they are both on the same side of the fulcrum. (**c**) Third-class lever demonstrates the muscle of internal force is closer to the axis of rotation than the external force. From Standring (2016), with permission

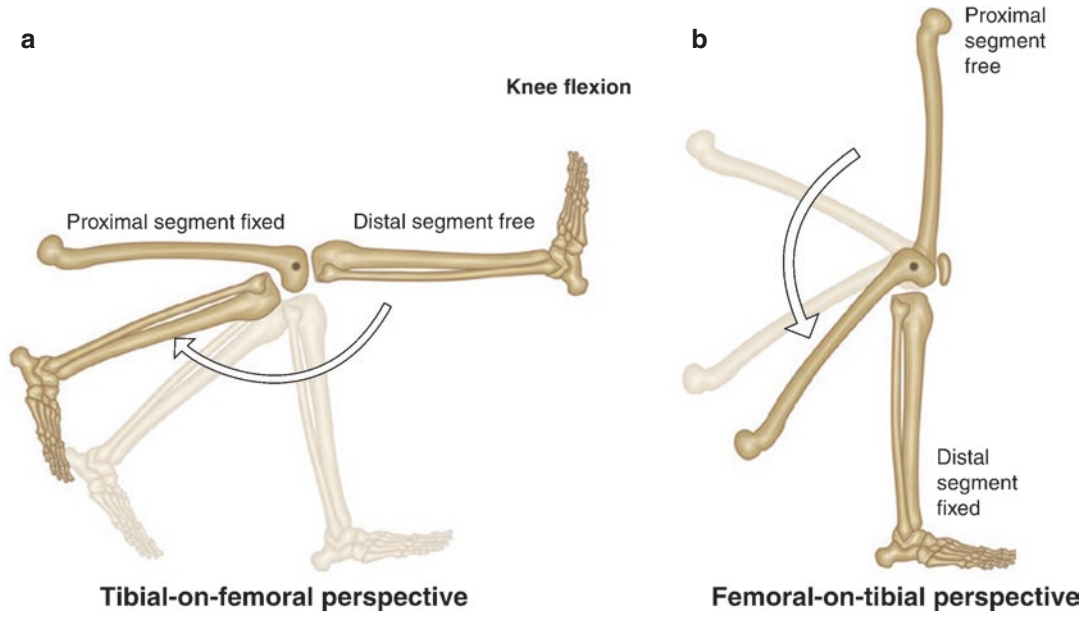

Fig. 4.2 Sagittal plane osteokinematics at the knee shows an example of (**a**) distal-on-proximal segment kinematics and (**b**) proximal-on-distal segment kinematics. The axis of rotation is shown as a circle at the knee. Adapted from Neumann (2010)

Movement of a joint is performed in two kinematics: a movement of the distal segment against the relatively fixed proximal segment; movement of the proximal segment against the relatively fixed distal segment (Fig. 4.2). As shown in Fig. 4.2, knee flexion is the relative movement between the thigh and the lower leg, the proximal-on-distal segment kinematics, or the distal-on-proximal kinematics (Karandikar and Vargas 2011). In the upper extremity, during usual activities, the proximal segment is stabilized by muscles or ligamentous structures, gravity, its inertia, while the distal segment rotates relatively easily, as an example of distal-on-proximal segment kinematics. The upper extremities are certainly able to perform proximal-on-distal segment kinematics, such as flexing and extending the elbows when pushing up or transferring the seat (Neumann 2010). A kinetic chain refers to a series of articulated segmented links, such as the connected pelvis, thigh, leg, and foot of the lower extremity. The terms *open* kinetic chain and *closed* kinetic chain are defined by whether the distal end of an extremity is fixed to the ground or some other immovable object. An *open kinematic chain* refers to a situation in which the distal segment of a kinematic chain is not fixed to the ground or other immovable object, like distal-on-proximal segment kinematics described above. The distal segment can, therefore, move freely (Fig. 4.2a). A *closed kinematic chain* describes a situation in which the distal segment of the kinematic chain is fixed to the ground or another immovable object. Therefore, the proximal segment can move freely (Neumann 2010) (Fig. 4.2b).

Applying the closed kinetic chain kinematics to people with spinal cord injuries can help with pressure relief, transfers, and wheelchair propulsion in individuals with injuries as high as C5 or C6. The major barrier to gaining independence in performing daily activities in high tetraplegics is the lack of active antigravity strength of elbow extension. The anterior deltoid, biceps, and brachialis muscles, all innervated by the C5 and/or C6 segments are used in a closed kinetic chain to convert the movement of the elbow and shoulder flexion into a movement of elbow extension when

the hand is fixed on the wheelchair hand rim by friction or floor (Little et al. 2000; Karandikar and Vargas 2011). The mechanism for this motion does not involve active extension of the triceps, but rather a substitution of muscles with intact innervation that can cause elbow extension in a closed chain system.

4.2.2 Muscle Contraction

Muscle contraction or activation can occur with actual shortening, lengthening, or remaining at a constant length. A muscle produces a force by muscle contraction in one of three ways: isometric, concentric, and eccentric. When the muscle is producing a force while maintaining a constant length, this type of activation is called isometric. Concentric activation occurs as a muscle produces a force as it contracts (shortens). Eccentric contraction, in contrast, occurs as a muscle produces an active force while being elongated (Hamill et al. 2015; Neumann 2010) (Fig. 4.3).

4.2.3 One- and Two-Joint Muscles

Anatomically, the origin and insertion sites of a muscle are determined by which site is relatively more mobile. That is, the origin tends to be less mobile compared to the insertion site, and the insertion tends to be more mobile compared to the origin site. The movement and function accomplished by the origin site and the insertion site of a muscle can vary the joint movement between the origin and insertion of the muscle

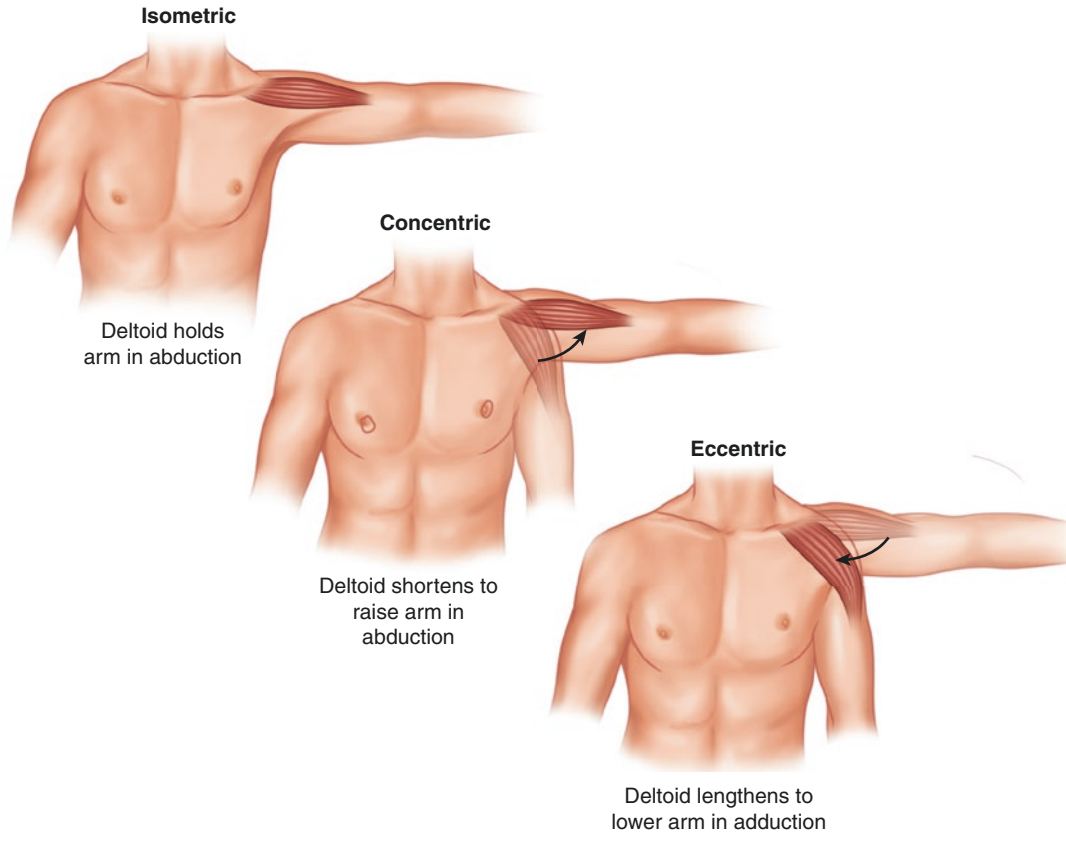

Fig. 4.3 A muscle action is isometric when the tension creates no change in joint position. A concentric muscle action occurs when the tension shortens the muscle. An eccentric muscle action is generated by an external force when the muscle lengthens. Adapted from Hamill et al. (2015)

depending on which site is stabilized. A muscle action can move a segment at one end of its attachment or two segments at both ends of its attachment. Most muscles cross only one joint, so the dominating action of the one-joint muscle is on the joint it crosses. For example, the soleus is a plantarflexor of the ankle, but it can also force the knee into extension, even though it does not cross the knee joint. The soleus contracts, creating plantarflexion of the ankle. When the foot is on the ground, the plantarflexion movement requires extension of the knee joint. The two-joint muscle is a special case in which the muscle crosses two joints and creates a multitude of movements that often occur in opposite sequences. For example, the rectus femoris is a two-joint muscle that creates both hip flexion and knee extension. The action of a two-joint muscle depends on the position of the body and the interaction of the muscle with external objects such as the ground. In the rectus femoris, the muscle mainly contributes to the extension of the knee due to the position of the hip joint. This position causes the force of the rectus femoris to act close to the hip, limiting the action of the muscle and its effectiveness in producing hip flexion (Hamill et al. 2015).

The two-joint muscle is restricted in its function at certain joint positions. When the two-joint muscle is restricted in elongation, this is known as passive insufficiency. This occurs when the antagonistic muscle cannot be elongated any farther and the full range of motion cannot be achieved. An example of passive insufficiency is the prevention of the full range of motion in knee extension by a tight hamstring. A two-joint muscle can also be restrained in contraction by active insufficiency, where the muscle is slackened to the point where it has lost its ability to generate maximum tension. An example of active insufficiency is seen at the wrist, in which the finger flexors cannot generate maximum force in a grip if they are shortened by an accompanying flexion movement of the wrist (Hamill et al. 2015).

4.2.4 Muscle Substitution

Movement by muscle substitution is common in people with spinal cord injuries. If a muscle that is involved in a specific joint motion is weak or absent, muscles that not involved or that have relatively stronger strength can be used to substitute the motion. Substitution by tensioning the other structures (e.g., tenodesis grip), using gravity (e.g., forearm pronation/supination by shoulder motion), and closed kinetic chain kinematics (e.g., locking the elbow extension for a weak triceps) can be used (Fig. 4.4). In addition, the muscles of the secondary mover of the joint motion can substitute the motion when the prime movers are weak or absent, such as the tensor fascia lata for a weak gluteus medius in hip abduction or anconeus and extensor carpi radialis longus for an absent triceps.

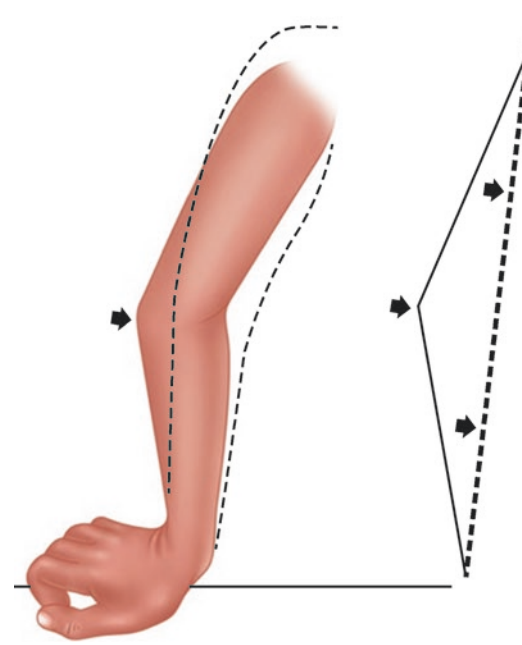

Fig. 4.4 Substitution using closed kinetic chain Kinematics with fixation of the distal segment. Adduction of the humerus and supination of the forearm result in elbow extension. Adapted from Somers (2010)

4.2.4.1 Substitution Using Tension to Nonfunctioning Musculature or Tendon

The tenodesis grip is an example of substitution using tension to the nonfunctioning muscle or tendon. The exquisite balance of muscle forces crossing the wrist and fingers creates a reciprocal motion called tenodesis. Finger extension occurs when the wrist is flexed due to increased tension on the extrinsic extensor muscles. Conversely, when the wrist extends by activation of the extensor carpi radialis longus and brevis, tension is increased in the extrinsic flexor muscles (flexor digitorum profundus, flexor digitorum superficialis, and flexor pollicis longus) that flex the fingers (Fig. 4.5). Shortening of the finger flexors lead to a passive whole hand grip and shortening of the flexor politic longus to a passive lateral grip (Mateo et al. 2015). This reciprocal action can establish the functional grasp and release pattern of the hand against gravity or some resistance (Harvey 1996). This substitution, tenodesis, can lead to a more forceful motion than the substitution using gravity.

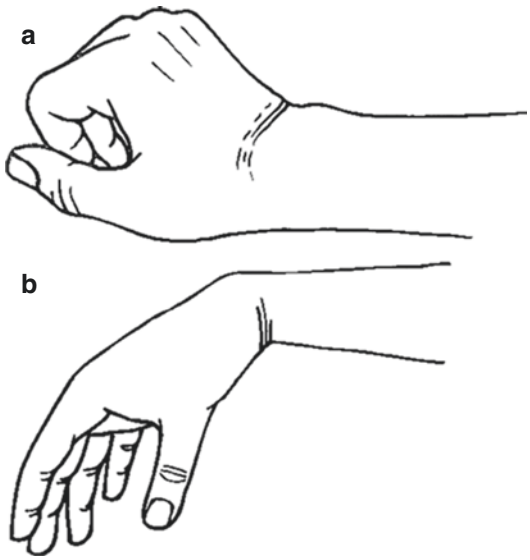

Fig. 4.5 Tenodesis grasp with wrist extension and flexion. (**a**) When the wrist extends, tension is increased in the extrinsic flexor muscles that flex the fingers. (**b**) Finger extension occurs when the wrist is flexed due to increased tension on the extrinsic extensor muscles

In people with C6 spinal cord injury, stretching of the extrinsic finger flexors should be avoided in order to achieve a more effective tenodesis, and the MP, DIP, and PIP joints of the fingers as target joints in tenodesis are allowed to have a mild to moderate flexion contracture (Little et al. 2000). An overstretching of the long finger flexors leads to a loss of the functional tenodesis grip. Simultaneous wrist and finger extension or flexion should be avoided to ensure adequate tension in the long finger flexors. ROM exercises should include finger extension to neutral with the wrist fully flexed and full finger flexion with the wrist fully extended. A person using a tenodesis grip should keep the interphalangeal joints flexed when bearing weight on the palms in a closed kinetic chain.

4.2.4.2 Substitution Using Gravity

Functional muscles of the rostral segment in spinal cord injuries can cause a position change of the distal part using gravity effect, for example, pronation of the forearm by shoulder abduction and/or internal rotation. The force of substitution movement using gravity is very limited and the movement is restricted by any resistance (Somers 2010).

4.2.4.3 Substitution Using Closed Kinetic Chain Kinematics

Fixation or stabilization of the distal segment can establish motion at an intermediate joint using the proximal muscles. If the hands are stabilized with fixing on the mat floor, activation of the anterior deltoid and clavicular fibers of pectoralis major may lead to extension of the elbow (Gagnon et al. 2003; Mulroy et al. 2004). Persons with tetraplegics with paralysis of the triceps brachii lift themselves by generating active shoulder flexor and adductor moments in performing a weight-relief maneuver and transfer (Harvey and Crosbie 2000). Using closed kinetic chain kinematics placing the palms on the mat surface or wheelchair wheel handrim, the elbow can lock in extension while weight-bearing activity such as push-up and transfer. This movement is per-

formed more effectively by external rotation of the shoulder and supination of the forearm (Marciello et al. 1995; Harvey and Crosbie 1999; Harvey and Crosbie 2000; Somers 2010). In tetraplegic patient, the functions of the anterior deltoid and serratus anterior in the sagittal plane, the pectoralis major in the transverse plane, and the latissimus dorsi in the coronal plane can cause passive extension of the elbow by pulling the proximal humerus forward and adduction of the proximal humerus, respectively, while distal limb is fixed (Feeko and Mallow 2015). It is important to avoid simultaneous extension of the wrist and hand when bearing weight on the palm in a closed kinetic chain, since stretching the long finger flexors. Flexion of the DIP and PIP of the fingers when extending the elbow with the palm on the floor should be kept (Somers 2010). In the lower extremity, when the foot is fixed to the ground, the gastrocnemius and hamstring muscles can help extend the knee by pulling back the distal femur and the proximal tibia, respectively.

4.3 Contributing Muscles to Mobility Depending on the Motor Level

Functional mobility activities including bed activity, transfer, wheelchair use, and ambulation are largely determined by voluntary motor function according to the neurological level of injury. Function, innervation, and the consequences of neurological level of spinal cord injury are summarized in Table 4.2.

4.3.1 Neurological Level of Injury: C4

People with C5 spinal cord injuries do not have a helpful voluntary motor function for transfers. All transfer activities are totally dependent. Fully innervated trapezius (CN XI) and partially innervated rhomboids (C4, C5) and levator scapulae (C3, C4, C5) offer a limited function in postural control.

Although people cannot propel a manual wheelchair, it is possible to drive an electric power wheelchair with movements of the head, chin, tongue, or breath. If the muscles of C5 have some voluntary motor functions, they can control a hand-held joystick to control the power wheelchair in very limited cases.

4.3.2 Neurological Level of Injury: C5

People with C5 spinal cord injuries are dependent in all transfers. However, some people can be independent or some assist level using a transfer board or overhead loops or trapezes. They are independent or some assist level indoors on non-carpeted floors in propelling manual wheelchair. They can use high-friction or pegged handrims (handrim projection bars). Propelling manual wheelchairs in the community may be inadequate. A pressure relief activity in the manual wheelchair using lateral lean method is independent or some assist level.

The biceps brachii (C5, C6), brachialis (C5, C6), and brachioradialis (C5, C6), partially innervated by C5, allow the elbow flexion to pull. The deltoids (C5, C6) partially innervated by C5 help to extend the elbows by muscle substitution, and additional functions with the infraspinatus (C5, C6) and teres minor (C5, C6) allow the extended elbow to be locked in a closed kinetic chain. The serratus anterior (C5, C6, C7) minimally innervated by C5 contributes minimal function to stabilize the scapulae against the thorax.

4.3.3 Neurological Level of Injury: C6

People with C6 spinal cord injuries are independent or some assist level in transfers with or without transfer board including transfers between the wheelchair and mat or bed. Propelling manual wheelchair indoors on non-carpeted level is independent. Wheelchair mobility in the community may be insufficient. Pressure relief in the manual wheelchair by depression, forward lean, or lateral lean method is independent or some assist level.

Table 4.2 Upper limb muscles function, innervation, and the consequences of neurological level of spinal cord injury on muscle innervation

			Innervation				SCI level					
Joint	Muscles	Function	Nerve	Roots			C4	C5	C6	C7	C8	T1
Shoulder scapulo-thoracic	Serratus anterior	Protraction and upward rotation	Long thoracic	C5	C6	C7	–	±	±	±	+	+
	Trapezius upper part	Elevation	Accessory spinal	XI			+	+	+	+	+	+
	Trapezius middle part	Retraction					+	+	+	+	+	+
	Trapezius lower part	Downward rotation					+	+	+	+	+	+
	Pectoralis minor	Depression and anterior tipping	Medial pectoral	C8	T1		–	–	–	–	±	±
Shoulder gleno-humeral	Deltoïd anterior part and Coracobrachialis	Flexion	Axillary	C5	C6		–	±	±	+	+	+
	Deltoïd medius part	Abduction					–	±	±	+	+	+
	Deltoïd posterior part	Extension					–	±	±	+	+	+
	Pectoralis major upper part	Flexion/Adduction/ Medial rotation	Lateral pectoral	C5	C6	C7	–	±	±	±	+	+
	Pectoralis major middle and lower parts	Flexion/Adduction/Medial rotation	Medial pectoral	C8	T1		–	–	–	–	±	±
	Lattissimus dorsi	Extension/Adduction/Medial rotation	Thoracodorsal	C6	C7	C8	–	–	±	±	±	+
	Teres major	Extension/Adduction/Medial rotation	Subscapularis	C5	C6	C7	–	±	±	±	+	+
	Subscapularis	Medial rotation					–	±	±	±	+	+
	Supraspinatus	Abduction					–	±	±	±	+	+
	Infraspinatus	Lateral rotation					–	±	±	±	+	+
	Teres minor	Lateral rotation	Axillary	C5	C6		–	±	±	+	+	+
Elbow	Biceps brachii	Flexion	Musculo-cutaneous	C5	C6		–	±	±	+	+	+
	Brachialis	Flexion					–	±	±	+	+	+
	Brachioradialis	Flexion					–	±	±	+	+	+
	Triceps brachii	Extension	Radial	C7	C8	T1	–	–	–	±	±	±
Wrist	Extensor carpi radialis longus and brevis	Extension	Radial	C6	C7	C8	–	–	±	±	±	+
	Extensor carpi ulnaris	Extension		C7	C8		–	–	–	±	±	+
	Flexor carpi radialis	Flexion	Median	C6	C7		–	–	±	±	+	+
	Flexor carpi ulnaris	Flexion	Ulnar	C7	C8		–	–	–	±	±	+
Fingers &thumb	Flexor digitorum superficialis	Flexion	Median	C7	C8	T1	–	–	–	±	±	±
	Flexor digitorum profundus	Flexion	Median and ulnar	C8	T1		–	–	–	–	±	±
	Extensor digitorum	Extension	Radial	C6	C7	C8	–	–	±	±	±	+
	Flexor pollicis longus and brevis	Flexion	Median	C8	T1		–	–	–	–	±	±
	Extensor pollicis longus and brevis	Extension	Radial	C7	C8		–	–	–	±	±	+
	Abductor pollicis longus	Abduction					–	–	–	±	±	+
	Abductor pollicis brevis	Abduction	Median	C8	T1		–	–	–	–	±	±
	Opponens pollicis	Opposition					–	–	–	–	±	±
	Adductor pollicis and intrinsic	Adduction	Ulnar	C8	T1		–	–	–	–	±	±
	Abductor digitorum minimi	Abduction	Ulnar	T1			–	–	–	–	–	±

From Mateo et al. (2015)

The fully innervated biceps brachii (C5, C6) allow stronger elbow flexion. The deltoids (C5, C6), infraspinatus (C5, C6), teres minor (C5, C6), and clavicular part of the pectoralis major (C5, C6), which are fully innervated in NLI C6, allow a stronger elbow extension and locking of the extended elbow by muscle substitution. The partially innervated serratus anterior (C5, C6, C7) makes it possible to stabilize the scapulae against the thorax. The possibility of scapular protraction and stability of the scapula improves the wheelchair propelling and self-positioning in the wheelchair. Minimally innervated latissimus dorsi (C6, C7, C8) and triceps brachii (C6, C7, C8) assist in depression of the shoulder girdle to allow the buttocks to lift for pressure relief and to contribute to transfers and wheelchair skills.

4.3.4 Neurological Level of Injury: C7

People with C7 spinal cord injuries are independent in transfers without a transfer board and between the wheelchair and the bed. Limited people are independent in transfers between the wheelchair and the floor using a side-approach transfer. They are independent indoors and outdoors on level terrain for long distances using manual wheelchair. They can negotiate 1:12 ramps independently or with some assist. Pressure relief is independent.

Partially innervated triceps brachii (C6, C7, C8) allow stronger elbow extension. The latissimus dorsi (C6, C7, C8) and sternocostal part of the pectoralis major (C7, C8, T1) increase shoulder girdle depression to enable a stronger buttock lifting for pressure relief. Fully innervated serratus anterior (C5, C6, C7) offers more stable scapulae against the thorax and a stronger protraction of the shoulders.

4.3.5 Neurological Level of Injury: C8

Most people with C8 spinal cord injuries can be independent in transfers between the wheelchair and the floor. They are independent in negotiating 1:12 ramps.

Fully innervated triceps brachii (C6, C7, C8) allow normal strength in elbow extension. Fully innervated latissimus dorsi (C6, C7, C8) and more innervated pectoralis major (C7, C8, T1) compared to NLI C7 provide a stronger shoulder girdle depression. The muscles, flexor digitorum superficialis, flexor digitorum profundus, flexor pollicis longus and breves, partially or almost fully innervated by C7, C8, and T1, allow a grasp without muscle substitution and provide easier handling of the legs.

4.3.6 Neurological Level of Injury: T1–9

Fully innervated upper extremities allow all transfers easier and lifting the body's weight using elbow extension and scapular depression. They may walk for exercise with KAFOs or HKAFOs.

4.3.7 Neurological Level of Injury: T10–T12

They can be independent functional ambulators using KAFOs within the home and for very limited distance in the community, but mostly use a wheelchair for mobility due to the high energy requirements of the ambulation.

4.3.8 Neurological Level of Injury: L1

People with L1 spinal cord injuries can be independent functional ambulators using KAFOs within the home and for very limited distance in the community, but mostly uses a wheelchair for mobility due to the high energy requirements of the ambulation.

Minimally innervated psoas major (L1–L3) and iliacus (L1–L3) allow weak but active hip flexion during swing phase.

4.3.9 Neurological Level of Injury: L2

Independent functional ambulation with KAFOs can be possible within the home and for limited distances in the community, but mostly uses a wheelchair for mobility due to the high energy consumptions of the ambulation.

The psoas major (L1, L2, L3), iliacus (L1, L2, L3), pectineus (L2, L3), and sartorius (L2, L3), which are partially innervated, allow an active hip flexion, but weak. The sartorius and gracilis (L2, L3, L4) allow a limited knee flexion, which is capable for swing limb. There may be minimal knee extension movement using minimally innervated quadriceps (L2, L3, L4).

4.3.10 Neurological Level of Injury L3

People with L3 spinal cord injuries are likely to ambulate independently in the community using AFOs with plantar flexion stops and forearm crutches, but may choose a wheelchair for long distances due to the high energy consumption of ambulation.

The iliacus (L1, L2, L3), pectineus (L2, L3), psoas major (L1, L2, L3), and sartorius (L2, L3), which are fully innervated and partially innervated gracilis (L2, L3, L4), allow a normal hip flexion. Partially innervated quadriceps offer the potential for active knee extension.

4.3.11 Neurological Level of Injury: L4

They may ambulate independently within the community with AFOs with dorsiflexion stops or dorsiflexion assist if the dorsiflexion strength is inadequate for eccentric control of plantar flexion after initial contract or dorsiflexion fatigue, and forearm crutches or canes.

Fully innervated sartorius (L2, L3) and gracilis (L2, L3, L4) and quadriceps (L2, L3, L4) allow normal knee flexion during swing and stance, respectively. Partially innervated tibialis anterior (L4, L5, S1) and peroneus tertius (L4, L5, S1) allow active dorsiflexion during swing phase and a potential for eccentric control of ankle plantar flexion at early stance. The tensor fascia lata (L4, L5, S1), gluteus medius (L4, L5, S1), and gluteus maximus (L5, S1, S2) partially innervated provide limited hip abduction capacity that is inadequate for stabilizing the pelvis in the frontal plane during stance.

4.3.12 Neurological Level of Injury: L5

People with L5 spinal cord injuries are independent in community ambulation using AFOs with dorsiflexion stop and standard canes.

The tibialis anterior (L4, L5, S1) is almost completely innervated and allows ankle dorsiflexion during swing and eccentric control of plantar flexion during early stance. Almost complete innervation of the tensor fascia lata (L4, L5, S1) and partial innervation of the gluteus medius (L4, L5, S1) and gluteus maximus (L5, S1, S2) ensure a stronger abduction of the hip to stabilize the pelvis in the frontal plane during stance phase. Partially innervated hamstrings (L5, S1, S2) improve active knee flexion for swing limb advancement. Almost complete innervation of the peroneus tertius (L4, L5, S1) and extensor digitorum longus (L4, L5, S1) and partial innervation of the extensor hallucis longus (L4, L5, S1), peroneus longus and brevis (L4, L5, S1), tibialis posterior (L5, S1), flexor digitorum longus (L5, S1), and flexor hallucis longus (L5, S1, S2) allow a limited stabilizing capacity of the subtalar joint and the foot during stance phase.

4.3.13 Neurological Level of Injury: S1

People with S1 spinal cord injuries are independent in community ambulation with no walking aid. If the strength of the plantar flexors is not sufficient to control the forward progression during late stance, AFOs with dorsiflexion stops are required.

Partial innervation of the gastrocnemius (S1, S2) and soleus (S1, S2) ensures active plantar flexion, with potential for eccentric control of dorsiflexion during midstance and terminal stance. The tensor fascia lata (L4, L5, S1), gluteus medius (L4, L5, S1), and gluteus maximus (L5, S1, S2), which are fully innervated, enable a strong hip abduction to stabilize the pelvis in the frontal plane during stance. The hamstrings (L5, S1, S2) and gluteus maximus (L5, S1, S2), which are partially innervated, ensure strong knee flexion and sagittal plane stabilization of the pelvis in early stance, respectively. Fully innervated peroneus longus and brevis (L4, L5, S1), extensor hallucis longus (L4, L5, S1), peroneus tertius (L4, L5, S1), extensor digitorum longus (L4, L5, S1), tibialis posterior (L5, S1), and flexor digitorum longus (L5, S1); partially innervated flexor hallucis longus (L5, S1, S2) ensure strong inversion and eversion to stabilize the subtalar joint and foot during stance.

4.4 Functional Anatomy of the Extremity Muscles

4.4.1 Muscles of the Upper Extremity

4.4.1.1 Movements

The movements of the scapula include elevation, depression, protraction, and rotation. The scapula is elevated by the upper fibers of the trapezius and the levator scapulae muscles. The levator scapulae muscle lies deep to the trapezius and is attached to the medial border above the scapular spine and superiorly to the cervical transverse processes. In depression of the scapula, the serratus anterior, pectoralis minor, latissimus dorsi, lower fibers of the trapezius, and pectoralis major may all participate. The serratus anterior rotate the scapula upward, whereas the pectoralis minor rotates it downward. Upward rotation of the scapula is produced by the combined actions of the trapezius and the serratus anterior. Downward rotation of the scapula is by the rhomboids and levator scapulae in raising the medial border of the scapula, whereas the pectoralis minor and major and latissimus dorsi are aided by the effect of gravity on the free limb pulling down the lateral angle. Protraction of the scapula is produced by the serratus anterior and pectoralis minor and major. Retraction is by the middle fibers of the trapezius with the rhomboids and latissimus dorsi.

Flexion of the shoulder joint is produced by the clavicular head of the anterior fibers of the deltoid, coracobrachialis, and pectoralis major muscles. Of these, the anterior part of the deltoid is the most important. The biceps brachii muscle helps flexion of the arm because the biceps brachii cross the shoulder joint. Extension occurs through the posterior fibers of the deltoid, the sternoclavicular head of the pectoralis major, latissimus dorsi, teres major, and the long head of the triceps muscles. Abduction is initiated by the supraspinatus and continued by the deltoid muscles, especially its middle or more lateral part. Abduction in external rotation is stronger than it is in internal rotation. Adduction is produced mainly by the pectoralis major, latissimus dorsi, and teres major. Internal rotation is by the subscapularis, pectoralis major, the anterior fibers of the deltoid and latissimus dorsi, and teres major muscles. External rotation is by the infraspinatus, the posterior fibers of the deltoid, and teres minor muscles and the infraspinatus muscles.

The elbow is flexed by the biceps and brachialis muscles, assisted by brachioradialis and the muscles attached to the common flexor origin. As the biceps supinates as the elbow flexes, flexion from the pronated forearm is carried out by the brachialis alone, unless there is strong resistance. Extension is by the anconeus and triceps muscle, with a weak contribution from the muscles of common extensor origin. The anconeus acts first to extend the elbow, and the triceps are recruited for more strength: first medial, then the lateral, then the long head. The biceps and supinator muscles supinate and the pronator teres and pronator quadratus pronate. The brachioradialis muscle brings the forearm into the midprone position.

The wrist is flexed mainly at the midcarpal joint and is produced by the flexor carpi radialis and flexor carpi ulnaris, which are aided by the

long digital flexor muscles. Extension occurs mainly at the wrist and is produced by the extensor carpi radialis longus and brevis and the extensor carpi ulnaris, assisted by the long digital extensor muscles. Abduction occurs mainly at the midcarpal joint and is produced by flexor carpi radialis and extensor carpi radialis longus and brevis. Adduction is mainly at the wrist and is produced by the flexor carpi ulnaris and extensor carpi ulnaris.

Flexion of the thumb is combined with internal rotation and is generated by flexor pollicis longus and brevis and opponens pollicis. Extension is combined with external rotation and is produced by extensor pollicis longus and brevis and abductor pollicis longus. The abduction is produced by abductor pollicis brevis, adduction by adductor pollicis, and opposition by opponens pollicis.

4.4.1.2 Muscles

Scapula and Shoulder

The *trapezius* muscle has an extensive origin from the medial half of the superior nuchal line of the occipital bone, the ligamentum nuchae and the spines and spinous process of the lower cervical and all the thoracic vertebrae. Laterally the muscle is attached to the lateral third of the clavicle and to the length of the acromion and the spine of the scapula. The wide origin of the muscle produces a wide range of scapular movements, raising, externally rotating and drawing the scapula medially.

The *deltoid* muscle is the most prominent intrinsic muscle of the shoulder. The deltoid muscle takes its medial attachments from the lateral third of the clavicle, the acromion, and the spine of the scapula. Laterally, it is attached to the deltoid tubercle on the lateral aspect of the humerus. It is the prime abductor of the arm, its anterior fibers contributing to flexion and internal rotation, and posterior fibers to extension external rotation of the arm.

The *pectoralis major* muscle has two medial heads. The clavicular head is attached to the medial two-thirds of the clavicle and the sternocostal head to the anterior surface of the sternum, the upper five to seven costal cartilages, and the upper part of the aponeurosis of the external oblique muscle (the most superficial of the lateral abdominal muscle). Laterally, the two heads converge on a narrow tendon that runs deep to the deltoid muscle to be attached to the lateral lip of the biceps groove on the humerus. The tendon of insertion is bilaminar. The tendon from the fibers of the clavicular head blends with the tendon from the upper part of the sternocostal head to form an anterior lamina. The fibers of the lower sternocostal and the abdominal parts pass upward deep to the insertion of the upper portion to form the posterior layer of the pectoralis tendon. The lowest fibers are inserted highest on the humerus. The muscle as a whole is a powerful adductor and internal rotator of the arm. The clavicular head, acting with the anterior fibers of deltoid, flexes the arm. In contrast, the sternocostal head is an extensor from the flexed position of the arm, acting with latissimus dorsi.

The *latissimus dorsi* muscle also has a wide medial attachment to the lower six thoracic and all the lumbar and sacral spinous processes, lumbar fascia, and posterior half of the iliac crest. Its fibers pass upwards and laterally to the floor of the bicipital groove on the humerus. The muscle is also attached to the inferior angle of the scapula, producing internal rotation, and helps to prevent this angle from jutting out from the chest wall during shoulder movements. The latissimus dorsi is a powerful adductor of the arm. The muscle is used for chopping wood and for the overhand swimming stroke.

The *teres major* and the *subscapularis* muscles run in front of the shoulder, the latter to an insertion on the lesser tuberosity, and are internal rotators of the shoulder joint. The *infraspinatus* and *teres minor* muscles pass posterior to the shoulder to the greater tuberosity and are external rotators. The insertion of the teres minor muscle is on the greater tuberosity directly inferior to the insertion of the infraspinatus. The infraspinatus is attached medially to the posterior aspect of the scapula below its spine and the teres minor to its lateral border.

The *supraspinatus* muscle is attached to the posterior aspect of the scapula above the spine

(supraspinous fossa). It passes laterally under the acromion to the greater tuberosity of the humerus. It stabilizes the shoulder joint and is important for the initiation of abduction, since the deltoid muscle does not have sufficient mechanical advantage to initiate abduction from adducted position. The supraspinatus tendon is compressed between the greater tuberosity of the humerus and the acromion in mid-abduction, therefore, the arm has to be externally rotated for full abduction.

Arm

The *short head of the biceps* is attached to the coracoid process and the *long head* runs between the greater and lesser humeral tuberosities, within the biceps groove, and is attached to the superior aspect of the glenoid fossa. Inferiorly the muscle is attached to the bicipital tuberosity on the radius. It has no attachments on the humerus. The muscle flexes the elbow and is a strong supinator of the forearm. Since the biceps supinates when the elbow flexed, flexion from the pronated position is only performed by the *brachialis*, unless there is strong resistance. The action of the *coracobrachialis* is to flex and adduct the arm. It cannot produce forearm movement because it does not cross the elbow.

The *triceps* is attached to the posterior shaft of the humerus above (lateral head) and below (medial head) the radial groove and, by its long head below glenoid fossa of the scapula (infraglenoid tubercle). The long head of the triceps passes distally between the teres minor and the teres major. The muscle is attached distally to the ulnar olecranon and is a strong extensor of the elbow. The long head, not the other two heads, aids in extension and adduction of the arm as it crosses the glenohumeral joint. The *anconeus* is too small to supply much power, its action is not only to extend the elbow, but also to stabilize the elbow against flexion or pronation-supination.

Forearm

The extensor muscles of the forearm are conveniently divided into superficial and deep groups. All muscles of the superficial group originate in the humerus on or around the lateral epicondyle, but most of the deep group do not. In the distal part of the posterior forearm, some of the muscles in the deep group (muscles to the thumb) become superficial and cover some of the superficial muscles. The superficial extensor forearm muscles are the brachioradialis, extensor carpi radialis longus, extensor carpi radialis brevis, extensor digitorum, extensor digiti minimi, and extensor carpi ulnaris. The deep extensor muscles are the supinator, extensor indicis, and the three thumb muscles: abductor pollicis longus, extensor pollicis brevis, and extensor pollicis longus.

The *brachioradialis* muscle is the most superficial muscle of the lateral forearm group and it is attached proximally to the upper two-thirds of the lateral supracondylar ridge of the humerus and distally to the lateral aspect of the distal end of the radius. Its primary action is to flex the forearm. It pronates and supinates the forearm into the midprone position. It can pronate better than supination. Flexion of the elbow joint is most powerful in this position. The *extensor carpi radialis longus* muscle is attached to the lower third of the lateral supracondylar ridge of the humerus. The extensor carpi radialis longus supports the brachioradialis in flexion of the elbow, but arises too low on the humerus to be just as important for flexion. It has an insertion at the base of the second metacarpal bone.

The common extensor origin muscles on the lateral epicondyle are the *extensor carpi radialis brevis*, *extensor digitorum*, *extensor digiti minimi,* and *extensor carpi ulnaris*. These muscles are weak extensors of the elbow joint. The extensor carpi radialis brevis is inserted at the base of the third metacarpal bone. The *supinator* is also attached to the common extensor origin at a deeper level and receives a head from the lateral aspect of the upper end of the ulna. Of the deep muscles, the supinator is the most proximal.

The flexor muscles of the forearm can be divided into superficial, intermediate, and deep groups. The superficial group consists of four muscles: pronator teres, palmaris longus, flexor carpi radialis, and flexor carpi ulnaris. These muscles arise from the medial epicondyle as a common flexor tendon. The intermediate layer consists of only one muscle, the flexor digitorum

superficialis. The deep group of muscles consist of the flexor digitorum profundus, flexor pollicis longus, and pronator quadratus.

The *pronator teres* is the uppermost muscle of the superficial group of the forearm. The pronator teres muscle is attached proximally just above the common flexor origin, on the anterior surface of the medial epicondyle. The common flexor origin gives attachment to the *flexor carpi radialis*, *palmaris longus*, *flexor digitorum superficialis,* and *flexor carpi ulnaris*. The *pronator teres* gains an additional head from the coronoid process of the ulna, and the *flexor carpi ulnaris* one from the posterior subcutaneous border of the ulna. The pronator teres muscle is attached distally to the lateral aspect of the mid-shaft of the radius and pronates the forearm. Because of its relatively high origin on the humerus, it is also a weak elbow. The tendons of the other common flexor origin muscles pass to the hand. The *flexor pollicis longus*, *flexor digitorum profundus* and, distally, the *pronator quadratus* muscles are placed deep in the forearm and are not palpable. These muscles are supplied by the anterior interosseous branch of the median nerve. The flexor digitorum profundus receives an additional supply from the ulnar nerve. The pronator quadratus arises more distally on the forearm and is positioned posterior to the tendons of the other two muscles.

The *flexor carpi radialis* is attached distally to the base of the second and third metacarpal bones. The *palmaris longus* muscle is attached to the flexor retinaculum and the apex of the palmar aponeurosis, it is occasionally absent. The *flexor carpi ulnaris* muscle is attached to the pisiform bone, hamate, and the base of the fifth metacarpal bones. The flexor retinaculum is a 2.5–3 cm rectangular fibrous band between the pisiform and the hook of the hamate medially and the tubercle of the scaphoid and ridge of the trapezium laterally. The *flexor digitorum profundus* is attached to the base of the distal phalanx. Each tendon of the *flexor digitorum superficialis* splits into two slips around the associated tendon of the flexor digitorum profundus. The two slips interchange some fibers behind this profundus tendon, and then each has an attachment to the middle phalanx. The *flexor pollicis longus* tendon is attached to the distal phalanx of the thumb and has its own synovial and fibrous sheaths.

Each extensor digitorum tendon forms a triangle (the dorsal expansion) over the metacarpophalangeal joint. The corresponding *interossei* and *lumbrical* muscles are attached to the base of this expansion. The long tendon reforms at the apex of the triangle and then divides into three slips over the proximal interphalangeal joint. The middle slip is attached to the base of the middle phalanx and outer slips reunite before being attached to the base of the distal phalanx. There are two more tendons on the wrist dorsum. The *extensor digiti minimi* lies medial to the long tendon of the little finger and is inserted into its dorsal tendinous expansion. The tendon of the *extensor indicis* lies medial to the long tendon of the index finger and is also inserted into the dorsal expansion.

Hand

The *abductor, flexor, and opponens pollicis* muscle are attached to the scaphoid tubercle, the ridge of the trapezium, and the adjacent flexor retinaculum. These three muscles form the thenar eminence. The *abductor pollicis brevis* and *flexor pollicis brevis* both pass to the radial side of the proximal phalanx of the thumb and the *opponens pollicis* to the whole length of the radial margin of the first metacarpal bone. The *adductor pollicis* is deeply placed in the palm and is attached medially by two heads to the capitate and second and third metacarpals. Distally it passes laterally to the proximal phalanx of the thumb. The muscle bulk in the first intermetacarpal space includes adductor pollicis, the first dorsal and palmar interossei, and the first lumbrical.

The hypothenar eminence is formed by the *abductor digiti minimi*, *flexor digiti minimi,* and *opponens digiti minimi*, arising from the flexor retinaculum and adjacent medial carpal bones, and passing distally to the ulnar side of the proximal phalanx and the ulnar margin of the fifth metacarpal bone. The little finger is less mobile than the thumb.

Abduction and adduction of digits 2–5, away from and toward the midline of the middle finger, are brought about by the palmar and dorsal inter-

osseous muscles arising from the side of the length of the metacarpals. The three *palmar interosseous* muscles are attached to the palmar surfaces of the second, fourth, and fifth metacarpal bone. The palmar interossei are the adductors of the index, ring, and little fingers. Since three fingers and a thumb have to be adducted toward the middle finger, four muscles are required to perform the adduction movement. The thumb has its own adductors, the adductor pollicis. Therefore, there are only three palmar interossei. The four *dorsal interosseous* muscles are larger and more powerful compared to the palmar interossei. The dorsal interossei are arranged to abduct the fingers from the midline of the hand. There are two interossei around the middle finger, so that this middle finger can be abducted in either a radial or ulnar direction. Four more adductors are required to move the remaining four fingers, but both the thumb and little finger have their own abductors. Therefore, there are only four dorsal interossei in all, one for the index and one for the ring finger, in addition to the two attached to the middle finger. The distal tendons of all interossei are attached to the corresponding proximal phalanx and extensor expansion. The interossei also flex the proximal phalanx at the metacarpophalangeal joint and extend the proximal and distal interphalangeal joints due to their attachment to the extensor expansion.

The *lumbricals* are four slender muscles and have origins from the lateral side of each flexor digitorum profundus tendon in the palm. They are attached to the lateral side of the expanded extensor tendons on the proximal phalanges of the same finger. Their action is to flex the metacarpophalangeal joint and extend the proximal and distal interphalangeal joints, aided by the interosseous muscles. Further flexion of the metacarpal and interphalangeal joints of the fingers is performed by the long flexor tendons, the flexor digitorum profundus alone acts on the distal interphalangeal joint. Extension of the fingers is mainly by the long digital extensor muscles aided by extensor indicis and extensor digiti minimi. The collateral slips of the extensor expansion over the proximal interphalangeal joint reunite beyond the expansion. The reformed tendon is attached to the base of the distal phalanx and extends the distal interphalangeal joint.

4.4.2 Muscles of the Lower Extremity

4.4.2.1 Movements

The muscles involving extension of the hip joint are located in the gluteal region and the posterior aspect of the thigh. The gluteus maximus is a powerful extensor of the hip. The extension movement is assisted by the part of the adductor magnus and the posterior fibers of the gluteus medius. The hamstring muscles, the semimembranosus, semitendinosus, and biceps femoris, are also hip extensors because the muscles attach proximally to the ischial tuberosity. However, they can contribute strongly to hip extension when the knee is flexed. From the point of view of supporting the pelvis, there are only two good abductors of the hip: gluteus medius and gluteus minimus. Other muscles assisting abduction are the tensor fasciae lata, sartorius, piriformis, obturator internus, and the upper fibers of the gluteus maximus. The gluteus maximus is a powerful external rotator of the hip. Internal rotation of the hip is produced primarily by the tensor fasciae lata, gluteus minimus, and anterior fibers of the gluteus medius. Internal rotation is aided by the semitendinosus and semimembranosus. The iliopsoas is a powerful flexor, but is only used when strong movement is required. The rectus femoris, pectineus, adductor longus, adductor brevis, and the anterior fibers of the adductor magnus assist the flexion. The adductors of the hip include the pectineus, adductor longus and brevis, and the obturator portion of the adductor magnus.

The movements of the knee are flexion, extension, and a little rotation. Flexion occurs through the hamstring muscles, which is supported by gastrocnemius. The gastrocnemius helps to extend the knee when the leg is supporting weight. Extension is produced mainly by the quadriceps muscles. The gluteus maximus also helps extend the leg when extending the weight-bearing limb or keep it extended. The main part of the iliotibial tract runs in front of the center of

the knee joint on the lateral side of the knee, therefore, the tensor fasciae lata and gluteus maximus exert an effect of knee extension. Hyperextension is caused by medial rotation of the femur on the tibia around a taut anterior cruciate ligament.

Dorsiflexion of the ankle is produced by the tibialis anterior and other muscles of the anterior (extensor) compartment of the lower leg. Plantar flexion occurs mainly by the gastrocnemius and soleus muscles. The subtalar and talocalcaneonavicular joint act as a single unit at which inversion and eversion occur. Inversion is produced by the tibialis anterior and posterior, and limited by tension in the peroneus longus and brevis muscles as well as the interosseous talocalcaneal ligament. The movement is increased in plantar flexion and movement at the midtarsal joint. Eversion is produced by the peroneal muscles and limited by the tibialis anterior and posterior muscles, and the medial ligament of the ankle joint. The movement is increased in dorsiflexion and by movement at the midtarsal joint. When the foot is weight-bearing, there is an additional movement of supination and pronation of the distal tarsus and metatarsus (forefoot) relative to the tarsus and calcaneus (hindfoot).

4.4.2.2 Muscles

Hip

The iliopsoas muscle consists of two muscles, the *iliacus* and the *psoas major*. These muscles blend together as they go toward a common insertion and have a common action. The *iliopsoas* muscle is attached proximally to the medial aspect of the ilium and to the lateral aspect of the lumbar vertebrae. Distally, the tendon passes to the lesser trochanter of the femur. The iliopsoas muscle is powerful flexors and internal rotators of the hip joint. The *pectineus* muscle is attached to the superior pubic ramus and, distally, just below the iliopsoas tendon on the femur. The *sartorius* muscle passes from the anterior superior iliac spine distally, across the thigh, and is attached to the medial surface of the upper tibia below the tuberosity. At its insertion, its tendon is closely associated with the tendon of the gracilis, medially, and the semitendinosus, posteriorly. The sartorius acts as a hip flexor because it crosses anterior to the hip joint, and participates in flexion of the knee as it crosses posterior to the axis of motion of the knee joint. Its function is best described as producing the crossed-leg position. The *adductor longus* muscle passes from the body of the pubis to the linea aspera of the femur. The *adductor magnus* is attached medially along the ischiopubic ramus and ischial tuberosity and, laterally, to the length of the linea aspera and the medial supracondylar ridge and by a strong tendon to the adductor tubercle on the femur.

The *gluteus maximus* has an extensive proximal attachment, including the lateral surface of the ilium behind the posterior gluteal line, the sacrum, the coccyx, and the sacrotuberous ligament. The gluteus maximus passes downwards and laterally to the iliotibial tract and the gluteal tuberosity on the femur. The muscle is a powerful external rotator and extensor of the hip joint and, through the iliotibial tract, it extends and stabilizes the knee joint. The *tensor fasciae lata* is attached to the iliac crest just posterior to the anterior superior iliac spine and is distally attached to the iliotibial tract. The tensor fasciae lata is to assist in flexion of the hip joint and it also works as an internal rotator of the hip joint. The *gluteus medius* and *gluteus minimus* muscles have a similar action, which consist in strongly abducting the thigh. When walking, the muscles on both sides should alternately contract, as the weight is shifted from side to side. Although the major function of both muscles is hip abduction, the muscles are involved in other movements. The anterior fibers of the gluteus medius act in internal rotation and flexion of the hip, while posterior fibers act in external rotation and extension of the hip joint. The gluteus minimus rotates the thigh internally and may assist in flexion.

Thigh

The *quadriceps* has four attachments. The *rectus femoris* is attached by a straight head to the anterior inferior iliac spine, and by an oblique head to just above the acetabulum. The *vastus medialis and lateralis* take their attachment from their

respective sides of the intertrochanteric line, encircle the subtrochanteric femur, then coverage to their respective sides of the linea aspera of the femur and the *vastus intermedius* from the anterior aspect of the femoral shaft. The quadriceps muscle is attached inferiorly to the patella and is extended beyond it to form a strong tendon, the patellar ligament, attached to the tibial tuberosity.

The three muscles of the posterior thigh are known as the *hamstring* muscles and include the semimembranosus, semitendinosus, and biceps femoris. It is called as posterior hamstrings when the sartorius and gracilis are also called hamstrings. The *hamstring* muscle arises from the ischial tuberosity. The *semimembranosus* crosses deep to the semitendinosus and long head of the biceps femoris and attached distally to a groove on the posteromedial aspect of the tibial condyle and also by a tendinous expansion to the lateral femoral condyle. The *semitendinosus* muscle is attached distally to the upper subcutaneous medial surface of the tibia and the biceps to the head of the fibula. The *biceps femoris* muscle receives an additional short head from the linea aspera. The tendon by union of the two heads is inserted on the fibular head. The all three hamstring muscles have similar actions as powerful hip extensors and knee flexors. The short head of the biceps does not act in hip extension because it does not cross the hip joint. The semimembranosus and semitendinosus act as weak internal rotators of the hip and internal rotators of the lower leg when the knee is flexed. The long head of the biceps can act as an external rotator of the hip.

Lower Leg and Foot

The muscles of the lower leg are divided into anterior, lateral, and posterior groups by the tibia, the fibula, the interosseous membrane, and the anterior and posterior intermuscular septa. Of the four muscles of the anterior compartment (*tibialis anterior*, *extensor hallucis longus*, *extensor digitorum longus,* and *peroneus tertius*), only *tibialis anterior* is attached to the tibia, over the upper two-thirds of the lateral surface and adjacent interosseous membrane. Its distal tendon passes to the medial cuneiform and the base of the first metatarsal bones. The muscles of the anterior compartment dorsiflex the ankle and in addition the extensor hallucis longus and the extensor digitorum longus dorsiflex the toes.

The two lateral compartment muscles are the *peroneus longus* and *peroneus brevis*, which are attached to the upper two-thirds and lower third of the lateral surface of the fibula, respectively. The *peroneus longus* is attached to the base of the fifth metatarsal and adjacent medial cuneiform bone. The tendon of the *peroneus brevis* passes to the tuberosity of the base of the fifth metatarsal bone. The two muscles evert and plantar flex the foot.

The posterior compartment muscles are primarily plantar flexors of the ankle and toes. The *gastrocnemius* is superficial to the soleus and it has medial and lateral heads attached to the respective femoral condyles. The gastrocnemius acts as a powerful plantar flexor of the ankle and can help the knee when the leg is not supporting weight. If the foot is fixed in weight-bearing, the gastrocnemius acts in knee extension by pulling the distal femur backwards at the knee. The *soleus* has a continuous upper attachment from the head of the fibula, a tendinous arch over the posterior tibial vessels and tibial nerve, and to the soleal line on the tibia.

The pattern of the small muscles of the foot is similar to that of the hand, but here are no opponens muscle and the flexor digitorum accessorius has no upper limb counterpart. The *flexor digitorum accessorius* muscle is attached to the calcaneus posteriorly and to the lateral aspect of the tendon of the flexor digitorum longus anteriorly. The medial plantar nerve supplies abductor hallucis, flexor hallucis brevis, flexor digitorum brevis and the first lumbrical, the remaining muscles are supplied by the lateral plantar nerve.

References

Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. J Neurotrauma. 2004;21:1371–83.

Consortium for spinal cord medicine. Outcomes following traumatic spinal cord injury: clinical practice

guidelines for health-care professionals. Washington, DC: Paralyzed Veterans America; 1999.
Feeko KJ, Mallow M. Kinesiology. In: Maitin IB, editor. Current diagnosis & treatment. Physical medicine & rehabilitation. New York: McGraw-Hill Education; 2015.
Gagnon D, Nadeau S, Gravel D, et al. Biomechanical analysis of a posterior transfer maneuver on a level surface in individuals with high and low-level spinal cord injuries. Clin Biomech. 2003;18:319–31.
Hamill J, Knutzen KM, Derrick TR. Biomechanical basis of human movement. 4th ed. Philadelphia: Wolters Kluwer; 2015.
Harvey L. Principles of conservative management for a non-orthotic tenodesis grip in tetraplegics. J Hand Ther. 1996;9:238–42.
Harvey LA, Crosbie J. Weight bearing through fixed upper limbs in quadriplegics with paralyzed triceps brachia muscles. Spinal Cord. 1999;37:780–5.
Harvey LA, Crosbie J. Biomechanical analysis of a weight-bearing maneuver in C5 and C6 quadriplegia. Arch Phys Med Rehabil. 2000;81:500–5.
Huh S, Ko HY. Recovery target priorities of people with spinal cord injuries in Korea compared with other countries: a survey. Spinal Cord. 2020;58:998–1003.
Karandikar N, Vargas OO. Kinetic chains: a review of the concept and its clinical applications. PM R. 2011;3:739–45.
Little JW, Goldstein B, Hammond MC. Spinal cord injury rehabilitation. In: Belandres PV, Dillingham TR, editors. Rehabilitation of the injured combatant. Washington, DC: Department of the Army; 2000.
Marciello MA, Herbison GJ, Cohen ME, et al. Elbow extension using anterior deltoids and upper pectorals in spinal cord-injured subjects. Arch Phys Med Rehabil. 1995;70:426–32.
Mateo S, Roby-Brami A, Reilly KT, et al. Upper limb kinematics after cervical spinal cord injury: a review. J Neuroeng Rehabil. 2015;12:9.
Mulroy SJ, Farrokhi S, Newsam CJ, et al. Effects of spinal cord injury level on the activity of shoulder muscle during wheelchair propulsion: an electromyographic study. Arch Phys Med Rehabil. 2004;85:925–34.
Neumann DA, editor. Kinesiology of the musculoskeletal system: foundations for rehabilitation. 2nd ed. St. Louis: Mosby; 2010.
Palastanga N, Field D, Soames R. Anatomy and human movement. Structure and function. 4th ed. Oxford: Butterworth-Heinemann; 2002.
Sliwinski MM, Druin E. Intervention principles and position changes. In: Sisto SA, Druin E, Sliwinski MM, editors. Spinal cord injuries: management and rehabilitation. 1st ed. St. Louis: Mosby; 2008.
Snoek GJ, Ijzerman MJ, Hermens HJ, et al. Survey of the needs of patients with spinal cord injury: impact and priority for improvement in hand function in tetraplegics. Spinal Cord. 2004;42:526–32.
Somers MF. Spinal cord injury: functional rehabilitation. 3rd ed. New York: Pearson; 2010.
Standring S, editor. Gray's anatomy. 41st ed. Philadelphia: Elsevier; 2016.

Recommended Additional Reading

Bromley I. Tetraplegia and paraplegia. A guide for physiotherapists. 6th ed. Philadelphia: Churchill Livingstone; 2006.
Harvey L. Management of spinal cord injuries. A guide for physiotherapists. Philadelphia: Butterworth Heinemann; 2008.
Hislop HJ, Avers D, Brown M. Daniels and Worthingham's muscle testing. 9th ed. St. Louis: Elsevier; 2014.
Ford JR, Duckworth B. Physical management for the quadriplegic patient. 2nd ed. Philadelphia: F.A. Davis Company; 1987.
Jenkins DB. Hollinshead's functional anatomy of the limbs and back. 9th ed. St. Louis: Saunders; 2009.
Neumann DA, editor. Kinesiology of the musculoskeletal system: foundations for rehabilitation. 2nd ed. St. Louis: Mosby; 2010.
O'Sullivan SB, Schmitz TJ, editors. Improving functional outcomes in physical rehabilitation. 2nd ed. Philadelphia: F.A. Davis Company; 2010.
Somers MF. Spinal cord injury: functional rehabilitation. 3rd ed. New York: Pearson; 2010.
Stone RJ, Stone JA. Atlas of skeletal muscles. 2nd ed. Dubuque: Wm. C. Brown Publishers; 1997.

5 Functional Assessments and Predicted Functional Outcomes After Spinal Cord Injuries

Neurological recovery after spinal cord injury occurs due to the anatomical, biological, and pathophysiological nature of the mechanism. In terms of the anatomical basis of clinical recovery, neurological recovery from spinal cord injury may be the result of a recovery of the nerve roots at the injury level or of recovery of the spinal cord itself. Spinal cord recovery may be the anatomical basis for improved function of the local circuits at the injury level, or it may be the basis for improved function of caudal structures innervated by the long tracts at the injury level. In terms of the pathophysiological mechanisms involved in recovery, restoration of neurological function may be the result of the resolution of acute injury events such as hemorrhages or resolution of secondary injury processes such as ischemia, edema, or inflammation. Recovery can occur through regrowth or regeneration of the nervous tissue (Tator 1998). Motor functions are known to recover rapidly in the first 2 months after injury, but slowly after 3–6 months.

In the forward to one of the reports of Consortium for Spinal Cord Medicine, "Outcomes following traumatic spinal cord injury," Dr. Whiteneck wrote the following questions faced by patients with spinal cord injury: What outcomes can be expected after spinal cord injury? What extent of recovery can be anticipated? What activities can be performed independently? What equipment and assistance will be needed? What degree of productivity and community integration can be accomplished? What quality of life can be achieved? (Consortium for Spinal Cord Medicine 1999). The question he suggested is both a question to the rehabilitation team during the spinal cord injury rehabilitation process, and it is also the task of the rehabilitation team. In practice, the questions most frequently asked by patients with spinal cord injuries are "Can I walk again?" "When will I get better?" and "Will I be able to get back to my life?"

Long-term outcomes in people with spinal cord injuries are primarily determined by the neurological level of injury and the severity of the injury; however, in many cases, preexisting diseases and conditions can affect the rehabilitation process and interfere with the achievement of the outcomes (Horn et al. 2013). Expected outcome and their measurement for individuals with spinal cord injuries are divided into four domains: motor recovery, functional independence, social integration, and quality of life. The ideal outcome for each patient cannot always be achieved. The functional outcomes may be below target performance levels as the functional goal of people with spinal cord injuries can be affected by various coexistent conditions such as cognitive impairment, obesity, age, upper extremity injury, or preexisting medical conditions. Secondary conditions such as depression, spasticity, or contractures can also hinder the achievement of long-term outcomes (Consortium for Spinal Cord Medicine 1999). However, the long-term

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outcomes are largely determined by the neurological level of injury and severity of the injury, particularly the state of motor function. It is generally accepted that the prediction of long-term outcomes after traumatic spinal cord injury can be more accurately predicted with neurological examinations performed days to weeks after injury. The timing of the baseline neurological examination at 4 h or less after the injury is more likely to be associated with increased conversion rates of the ASIA Impairment Scale (Evaniew et al. 2020). It is believed that patients assessed very early after spinal cord injury have a greater potential for spontaneous neurological recovery, and it is intuitive that their prognosis may vary compared to patients assessed much later (Fawcett et al. 2007). During the first 24 h after spinal cord injury, there are various factors that affect neurological examination, such as unstable vital signs including pain, anxiety, and sedation. Therefore, neurological evaluation after 72 h after the injury is important in predicting future neurological recovery (Alexander et al. 2009; Herbison et al. 1992).

The International Classification of Functioning, Disability, and Health (ICF) published by the WHO in 2001 serves as a comprehensive and universally accepted conceptual framework when discussing functional outcomes and the classification and description of functioning, disability, and health in people with spinal cord injuries (Post et al. 2010). This classification eliminated most of the negative connotations of the 1980 classification. Disease/pathology became a health condition, impairment change to body structure/function, and self-care/mobility was combined into activities, but functional limitation was removed again. Although this offered many needed changes to the 1980 classification, such as the elimination of the word handicap, clarification is required, particularly in the activity domain (Ditunno 2010; Marino 2007). The ICF comprises four components: impairments of body functions, impairments of body structures, activity limitations and participation restrictions, and environmental factors (WHO 2001). Table 5.1 outlines the similarities and differences among the domains of Impairment, Capability/Functional Limitation, Activity, and Participation (Marino 2007).

5.1 Initial Neurological and Functional Assessment After Spinal Cord Injury

The initial neurological examination in the emergency department after a spinal cord injury can be difficult because the patient has combined other injuries or is under the influence of drugs or alcohol. The neurologic status may change over the first hours or few days and is influenced by various factors, including unstable vital signs including pain, anxiety, and sedation. The 72 h to 1 week post-injury period is the earliest time after injury for reliable neurological assessment and predicting neurological

Table 5.1 Characteristics of domains of outcome in modified International Classification of Functioning, Disability, and Health model

Domain	Level of operation	Example	Can use adaptive Aids?	Can use another Person's assistance?
Impairment	Organ System	Strength of finger flexors	No	No
Functional Limitation Activity	Individual as whole	Grasp cylindrical object	No	No
Capacity	Individual in standardized environment	Drink from 6 oz glass without handle	Preferably not	Preferably not
Performance	Individual in usual environment	Get drink (any method, i.e., cup, glass, straw)	Yes	Yes
Participation	Individual fulfilling life roles in usual environment	Dine out with friends	Yes	Yes

From Marino (2007), with permission

recovery to some extent (Alexander et al. 2009; Herbison et al. 1992). The neurological examination is assessed using the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI).

5.2 Factors Affecting Neurological Recovery and Functional Outcomes

Neurological function, particularly motor function, is the main determinant of overall functional outcomes after spinal cord injury. Additional factors such as age, pain, spasticity, comorbid conditions, body habits, and environmental and psychosocial factors may also affect the function and play an important role in determining functional outcomes (AlHuthaifi et al. 2017; Behrman and Harkema 2007). Recovery of motor function has been reported for up to 2 years or more after spinal cord injury (Ditunno et al. 1992; Kirshblum et al. 2004). However, in the first 2 months after the injury, the recovery rate of the motor function is fast but slow after 3–6 months. One-half to two-thirds of the one year's motor recovery occurs within the first 2 months after injury. The recovery rate and recovery prognosis are better for patients with incomplete injuries than for complete injuries (Fig. 5.1).

Clinically, it may be difficult or impossible to distinguish between different types of caudal neurological recovery, to determine whether recovery is the result of root or spinal cord recovery, or both. The increase in the anatomic propensity for recovery is in the order of roots, gray matter, and then white matter. This hierarchy is probably based on an inherent combination of increasing vulnerability to injury and decreasing ability to recover among these structures, in the order of roots, gray matter, and then white matter. In addition, motor roots and tracts have increased vulnerability to injury and decreased propensity for recovery, compared with sensory roots and tracts (Tator 1998). Neurological deterioration can also occur due to cord tethering or syringomyelia. Regular neurological status assessment can facilitate early detection and appropriate intervention. In addition, maximum spinal cord compression, spinal cord hemorrhage, and spinal cord swelling in MR imaging findings of an acute traumatic cervical spinal cord injury are associated with a poor prognosis for neurologic recovery (Miyanji et al. 2007). The vertical diameter of the T2 high-intensity area on the MRI after an injury is reported as a better predictive finding for neurological outcomes (Farhadi et al. 2018; Matsushita et al. 2017). There is a study that the Brain and Spinal Injury Center (BASIC) score,

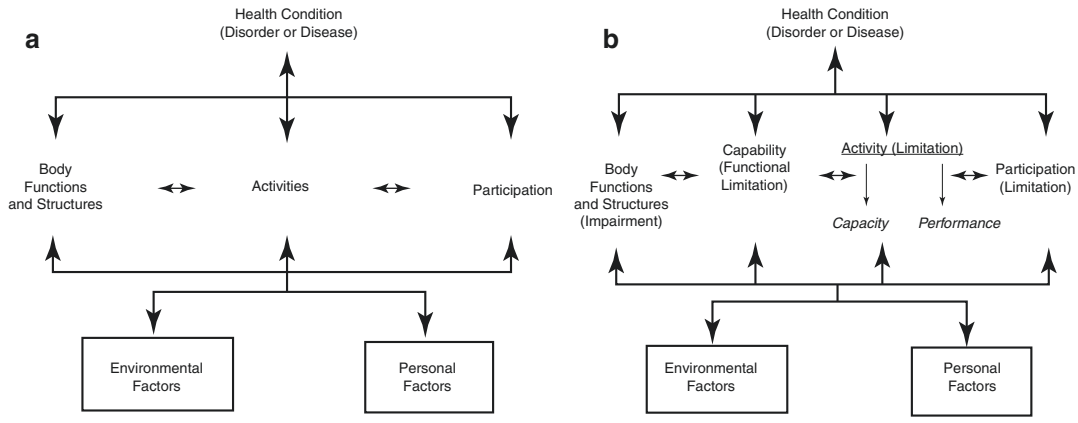


Fig. 5.1 (**a**) WHO International Classification of Functioning, Disability, and Health model of functioning. (**b**) Modified International Classification of Functioning, Disability, and Health model of functioning. Model extracts Capability/Functional Limitation from Activity and explicitly divides Activity into Capacity and Performance subdomains. From Marino (2007), with permission

which is based on the extent of axial T2-weighted MR images, is the best predictor of both neurological severity and ASIA Impairment Score (AIS) conversion (Farhadi et al. 2018).

While 10–20% of patients with complete injury (AIS A) recovered to incomplete injury at 1 year, only 3–6% of leg strength recovered to functional muscle strength (Maynard et al. 1979). In most patients with complete tetraplegia, muscle strength in the 2–3 spinal cord segments below the neurological level of injury in the upper extremity is improved, and the key muscle of one spinal cord segment just below the level of injury is likely to recover more than grade 3. Muscles with a muscle strength of at least grade 1 or 2 recover rather than muscles without muscle strength. If the muscles of the segment just below the level of injury have grade 1 or 2 of muscle strength, it is estimated that 90% will recover above grade 3 by 1 year after injury. If, on the other hand, there is no muscle strength in the segment immediately below the level of injury, the probability to recover to grade 3 or more by 1 year drops to 45%, and the probability that grade 3 will recover by 2 years is 64% (Waters et al. 1998). Regardless of the neurological level of injury, the prognosis of individual muscle recovery for muscles with grade 0 strength 1 month after injury is poor. Only 5% of these muscles recover to grade 3 or greater strength 1 year after injury. The prognosis for muscles with some strength at 1 month is good; muscles with grade 1 or 2 have a 64% chance of achieving functional strength at 1 year (Waters et al. 1998).

5.3 Recovery of the Upper Extremity Function

The cervical spinal cord injury directly affects the functioning of the upper extremities, although injuries at the thoracic level also affect, to some degree, the function of the upper limb and trunk stability during upper extremity tasks. Priority studies that are expected to be restored in people with cervical spinal cord injuries have described upper limb function as a function that they primarily wanted to restore compared to other dysfunctions (Anderson 2004; Huh and Ko 2020; Snoek et al. 2004). The upper extremity function plays an important role in the autonomy of the person in activities of daily living and quality of life (Boakye et al. 2012; Rudhe and van Hedel 2009). Although the ability to grasp and manipulate objects primarily depends on neurological impairment determined by the neurological level of injury, compensatory strategies, such as passive tenodesis grasp by learning during rehabilitation or enhancement of active tenodesis grasp by surgical reconstruction of the hand, are necessary for person's functioning in everyday life (Mateo et al. 2015).

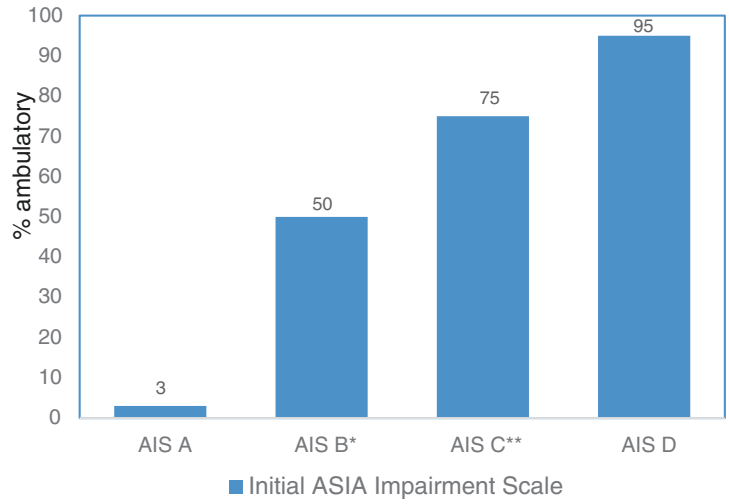
Autonomy after tetraplegia is based on upper limb movements and is achieved by both relearning open-chain movements such as grasping and learning new closed-chain movements such as manual wheelchair propulsion or sitting pivot transfer (Koontz et al. 2011). A C5 spinal cord injury preserves the innervation of the shoulder and elbow flexors, while C6 injuries retain control of elbow flexors and wrist extensors and C7 injuries also preserve elbow extensors. Thus, functionally, C5 and C6 injuries impair active elbow extension against gravity, while C5 to C7 injuries are absent active grasping. Fortunately, since wrist extension is preserved in injuries at C6 or below, tenodesis can replace active grasp by passive whole hand and lateral grips. During wrist extension, tenodesis leads to passive tendon shortening of flexor digitorum superficialis and profundus, which leads to passive finger-to-palm flexion, and of flexor pollicis longus, leading to thumb-to-index lateral face adduction (passive lateral grasp) (Mateo et al. 2013; Woolsey 1985). Autonomy, performed by open-chain or closed-chain movement in tetraplegia, is achieved by rehabilitation and can be complemented or enhanced by a surgical tendon transfer which involves transferring a tendon from a spared muscle that is stronger than 4/5 manual muscle test to that of a paralyzed muscle (Fridén and Gohritz 2015).

5.4 Recovery of Ambulatory Function

A community ambulator is defined as one who is possible to walk more than 40 m (130 feet), sit alone, stand alone, and don and doff the orthoses alone. At initial assessment, 3% of patients with AIS A recovered to an ambulatory in a year of injury. However, the majority of people with incomplete motor injuries on initial examination regain the ability to ambulate. Fifty percent of AIS B will be able to walk, especially if there is a pinprick sensation in the lower sacral segments, and it is very likely that they will recover to AIS C or D (Hussey and Stauffer 1973). Without the pinprick sensation of the lower sacral segments, the probability of recovery for walking is 10–33%. Seventy-five percent of AIS C become community ambulators. Ninety-five percent of initially with AIS D will be able to walk. Age and the amount of preserved spinal cord function below the lesion influence recovery of ambulation. The greater the amount of function preserved, the better the prognosis for recovery of ambulation. Patients aged 50–60 years or older have a poor prognosis for functional recovery (Burns et al. 1997; Daverat et al. 1988; Waters et al. 1994) (Fig. 5.2).

5.5 Functional Assessment Measures for Spinal Cord Injuries

In people with spinal cord injuries, body functions and structures are assessed using the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), the gold standard for neurological assessment of spinal cord injuries. First published by ASIA in 1982, the eighth edition of the standards is now available. The most commonly used elements to determine neurological and functional outcomes are the sensory scores, motor scores, and ASIA impairment scale, although the sensory or motor levels are occasionally utilized (Marino 2005). The details of ISNCSCI are described in Chap. 13. The evaluation of activities uses tools such as Spinal Cord Independence Measure (SCIM), Quadriplegia Index of Function (QIF), Modified Barthel Index (MBI), and Functional Independence Measure (FIM) (Anderson et al. 2008). The Craig Handicap Assessment and Reporting Technique (CHART) has been developed to assess participation. The SCIM III, QIF, MBI, and FIM are summarized in Table 5.2. Refer to Chap. 44 for functional assessment measures of upper limb function in spinal cord



*Prognosis influenced by presence or absence of pin prick sensation.
**Prognosis influenced by age.
Modified fromConsortium for Spinal Cord Medicine (1999)

Fig. 5.2 Prognosis for ambulation after traumatic spinal cord injuries. *Prognosis influenced by presence or absence of pin prick sensation. **Prognosis influenced by age. Modified from Consortium for Spinal Cord Medicine (1999)

Table 5.2 Measures for functional assessment of people with spinal cord injuries

Scale	Evaluation contents	Scoring	Remarks
Spinal Cord Independence Measure (SCIM-III)	• 19 items in 3 subscales: (a) self care (6 items, subscore 0-20), respiration and sphincter management (4 items, subscore 0–40), and mobility ("room and toilet" and "indoors and outdoors", nine items, subscore 0–40)	• All items are weighted in terms of their assumed clinical relevance • Total score range: 0–100	• Developed specifically for people with SCI • Most commonly used scale in people with SCI
Quadriplegia Index of Function (QIF)	• Ten items: 9 ADL tasks and a question for understanding of personal care	• The items are weighted according to their assumed clinical relevance. • For the first seven tasks: 0–4 each • The last three tasks have separate set of scoring criteria. • Total QIF score: 0–100	• Developed specifically for assessment of people with tetraplegia. • No item for locomotion • Limitation of this scale use for ambulatory tetraplegic
Modified Barthel Index (MBI)	• 10 ADL functions in three areas (self-care, continence, locomotion)	• Total score range: 0–100 • Each item is weighted in terms of its assumed clinical relevance.	• Not developed for people with SCI, limited use in SCI • Not suitable for a detailed function evaluation as limited to the basic ADL functions
Functional Independence Measure (FIM)	• 18 tasks (13 motor, 5 cognitive) in 6 areas (self-care, sphincter management, transfers, locomotion, communication, and social cognition)	• Each task range 1–7 • 1–5 as levels needing helper(s) • 1 total assist, 2 maximum assist, 3 moderate assist, 4 minimal assist, 5 supervision, 6 modified independence using device, 7 complete independence • Total score range: 18–126	• Not specified for people with SCI • No respiratory task • Less applicable cognitive tasks for SCI • Score ceiling effect

injuries such as the Graded Redefined Assessment of Strength, Sensibility, and Prehension (GRASSP) Test, Capabilities of Upper Extremity Questionnaire (CUE-Q), and Capabilities of Upper Extremity Test (CUE-T). Measures for the ambulation function, such as Walking Index for Spinal Cord Injury II (WISCI II), Spinal Cord Injury-Functional Ambulation Inventory (SCI-FAI), 6-Minute Walking Test (6MWT), 10-Meter Walk Test (10MWT), and Timed Up and Go (TUG), are described in Chap. 45. WISCI II and 10MWT are the most valid and clinically useful tests as primary outcome measures for gait and ambulation for incomplete spinal cord injury, as they have shown criterion-oriented validity, reliability, and sensitivity to change (Alexander et al. 2009).

The SCIM is a scale specifically designed for people with spinal cord injuries to assess their ADL performance and to make functional assessments. The latest version of the SCIM, SCIM III (Itzkovich et al. 2007, 2018), consists of 19 items in 3 subscales: self-care (6 items, subscore 0–20), respiration and sphincter management (4 items, subscore 0–40), and mobility (9 items, subscore 0–40). The total score ranges from 0 to 100. Mobility is divided into "room and toilet" and "indoors and outdoors." The items are weighted according to their assumed clinical relevance (Anderson et al. 2008). Reliable variables in pre-

dicting the SCIM-III total score at 6 months after injury have been reported such as age at injury, three key muscles (C6 wrist extensors, C8 finger flexors, and L3 knee extensors), and two mobility assessments (WISCI and SCM-item13), which are clinical factors collected at 1 month after injury (Ariji et al. 2020).

The QIF was specifically developed for the assessment of people with tetraplegic spinal cord injuries (Anderson et al. 2008). The QIF measures the level of independence in nine tasks of ADL (transfers, grooming, bathing, feeding, dressing, wheelchair mobility, bed activities, bladder program, bowel program) and a question about understanding of personal care. The tasks consist of up to ten items each, and all items are weighted according to their relative contribution to the total score. Each item represents a different activity. For the first seven tasks, each item is scored separately from 0 to 4 (independent, independent with devices, supervision, assistance needed, dependent). The last three tasks have separate scoring criteria. The total QIF score ranges from 0 to 100 (Anderson et al. 2008; Gresham et al. 1986). The QIF has limited use for ambulatory tetraplegics as it does not contain an item (category) for assessing locomotion.

The MBI measures ten ADL functions in the areas of self-care, continence, and locomotion. The MBI does not assess the most difficult functions for someone with spinal cord injuries, such as respiratory function. Each item has five categories. The maximum score of each item represents the weighting of that item for its relative contribution to the total score. For example, personal hygiene scores a maximum of 5 of 100 points, dressing 10 of 100 points, and chair/bed transfers 15 of 100 points. The total MBI score ranges from 0 to 100.

The FIM was developed to assess functional ability in daily activities that are primarily represented by the burden of caring for a disability. It was not developed specifically for people with spinal cord injuries. It evaluates six areas of function (self-care, sphincter management, transfers, locomotion, communication, and social cognition) based on 18 tasks. The FIM consists of 13 motor and 5 cognitive items. There is no assessment task for respiratory function. Assessment of cognitive function is less applicable to people with spinal cord injuries. The given score has a ceiling effect in the continuous evaluation. The score of each task ranges from 1 to 7: 1, total assist; 2, maximum assist; 3, moderate assist; 4, minimal assist; 5, supervision; 6, modified independence using the device; 7, complete independence (Table 5.3). The total score ranges from 18 to 126.

Table 5.3 Independence level of FIM

Level	Descriptions	Remarks
7	Complete independence (timely, safely)	No helper
6	Modified independence (device)	
Modified dependence		Helper
5	Supervision	
4	Minimal assist (subject = 75% or more)	
3	Moderate assist (subject = 50%–74%)	
Complete dependence		
2	Maximal assist (subject = 25%–49%)	
1	Total assist (subject = 0%–24%)	

5.6 Expected Functional Outcomes of Spinal Cord Injuries

As described above, various factors affect neurological and functional recovery, and there are cases in which the expected outcome cannot be reached depending on individual characteristics. However, the initial neurological evaluation and, in particular, the degree of motor function is very important in determining the functional outcome.

It should be recognized that these outcomes reflect the level of independence that can be achieved under optimal conditions without considering other personal and environmental factors that may be applied to individual patients. An interdisciplinary approach, consideration of unique barriers and facilitators, and inclusion of the patient as an active participant in setting goals are important elements in establishing an individualized rehabilitation program (Gittler et al.

2002; Jones et al. 2012). That is, although the typical degree of independence expected for each neurological level of spinal cord injury can be specified for large groups of individuals, any general expectations must be individualized based on the unique characteristics of the case. Patients with spinal cord injuries may have functional changes over time as a result of factors such as aging, comorbid conditions, changes in neurological status, changes in environment and residence status, and changes in psychological status (Consortium for Spinal Cord Medicine 1998, 1999). Periodic evaluation of functional capabilities and the impact of these factors is important to optimize functional gains and minimize potential functional losses (Hachem et al. 2017; Horn et al. 2013). Patients, families, and clinicians can learn about the ultimate functional ability of an individual after a rehabilitation program. Physicians must be able to give cautious but realistic advice. The functional goals and the level of assistance by others according to the neurological level of injury listed in Table 5.4 are based on patients with complete injuries/lesions.

5.6.1 C2–C4 Tetraplegia

Patients with C2–C4 lesions are the most severely injured spinal cord injuries and are commonly referred to as "high tetraplegics." These patients do not have significant strength in any limb. Many patients are dependent on the ventilator. These patients require assistance in all activities of daily living and instrumental activities of daily living. Caregivers should be available 24 h a day. Intermittent catheterization by caregivers or health care providers is ideal, but most high tetraplegics have permanent urethral or suprapubic catheters.

Advances in technology such as talking tracheostomy, computer-controlled environmental control system, motorized wheelchairs controlled by sip-puff or chin control mechanisms, and AI-assisted environmental control have improved the quality of life of patients. In some cases, the phrenic nerve pacing with an electrical stimulator may release a high tetraplegic from the ventilator for at least part of the day.

5.6.2 C5 Tetraplegia

C5 tetraplegics preserved the biceps muscles. They should be able to help them in their personal self-care activities. These people will need adaptive devices such as universal cuffs to feed themselves independently. C5 tetraplegics cannot perform intermittent self-catheterization. They will need assistance for transfers. They can partly use the passive tenodesis effect with the gravitational extension of the wrist in supination posture of the forearm.

5.6.3 C6 Tetraplegia

Preservation of the C6 myotome provides important functional advantages. They can use the active tenodesis effect because they retain the extension of the wrist. The result is a type of prehension that will increase functional independence. C6 males may be able to perform self-catheterization. Transfer can be completed without the assistance of a caregiver. C6 tetraplegics can drive a modified vehicle.

5.6.4 C7 and C8 Tetraplegia

With an intact triceps function, transfers must be independent without a sliding board. They should be independent in most functional tasks at a modified level (3–5 of FIM level). Both male and female patients should be able to perform intermittent catheterization.

5.6.5 Thoracic Paraplegia

Patients with lower thoracic injuries (T10) will have better trunk stability in wheelchairs than patients with higher lesions (T2). Lower thoracic paraplegics result in more intact abdominal and

Table 5.4 The functional goals and the level of the assistance according to the neurological level of injury

Activity		C1–C3	C4	C5	C6	C7–C8	T1–T9	T10–L1	L2–S5
Breathing		(T/S) bedside ventilator, portable ventilator, suction device, backup battery, vent tray for w/c	(I/S/T) according to vent use	(I)	(I)	(I)	(I)	(I)	(I)
Eating		(T)	(T)	(I/S/T) long opponens splint, adaptive devices	(I/S) adaptive devices, U-cuff, tenodesis splint, adapted utensils, plate guard	(I)	(I)	(I)	(I)
Bathroom functions	Bowel care	(T)	(T)	(T)	(S/T)	(S/T)	(I)	(I)	(I)
	Bladder care	(T)	(T)	(T)	(S/T)	(I/S)	(I)	(I)	(I)
Personal care	Dressing	(T)	(T)	(T)	(I) for upper exts (I/S) for lower exts	(I) for upper exts (I/S) for lower exts	(I)	(I)	(I)
	Grooming	(T)	(T)	(S/T) long opponens splint, adaptive devices	(I/S) adaptive devices, U-cuff, adaptive handles	(I)	(I)	(I)	(I)
	Bathing	(T)	(T)	(T)	(I) for upper exts (I/S) for lower exts adaptive devices	(I) for upper exts (I/S) for lower exts	(I)	(I)	(I)
Position/Pressure relief	Wheelchair	(I/S/T) for power recline (T) For manual w/c	(I/S/T) for power recline (T) for manual w/c	(I)Power recline (I/S) for manual w/c	(I) with adapted techniques	(I)	(I)	(I)	(I)
	Bed	(T)	(T)	(S/T)	(I/S)	(I)	(I)	(I)	(I)

(continued)

Table 5.4 (continued)

Activity		C1–C3	C4	C5	C6	C7–C8	T1–T9	T10–L1	L2–S5
Mobility	Bed	(T)	(T)	(S)	(S)	(I/S)	(I)	(I)	(I)
	Transfers	(T)	(T)	(T)	(I/S/T)	(I/S) some assist on uneven surfaces	(I)	(I)	(I)
	Wheelchair use (power)	(I) Power recline	(I)	(I)	(I)	NA	NA	NA	NA
	Wheelchair use (manual)	(T)	(T)	(I/S/T)	(I/S/T)	(I)	(I)	(I)	(I)
	Transportation	(T)	(T)	(S/T)	(I/S)	(I/S)	(I)	(I)	(I)
	Walking	NA	NA	NA	NA	NA	NA	(I/S)	(I/S)
Driving		(T)	(T)	(I) with highly specialized car/van	(I) with a modified car/van	(I) with hand controls	(I) with hand controls	(I) with hand controls	(I) with or without hand controls
Communication (handwriting and keyboard, telephone use)		(I/S/T) mouth stick, head mouth, environmental controls	(I/S/T)	(I/S)	(I) Adaptive devices	(I)	NA	NA	NA
Homemaking		(T)	(T)	(T)	(S/T)	(I/S)	(I/S)	(I/S)	(I/S)

Remarks: I, independent; S, some assist; T, total dependent

intercostal muscles that improve coughing and secretion clearance. Patients with lesions below the T6 are not at risk for autonomic dysreflexia.

5.7 Quality of Life After Spinal Cord Injury

Quality of life (QOL) and life satisfaction of people with spinal cord injuries have a positive impact on social participation, social support, and perceived control over life. On the other hand, there was no consistent or strong association between QOL and biomedical factors such as completeness of injury or neurological level of injury (Boakye et al. 2012). QOL improvement is a common goal of spinal cord injury care and rehabilitation, but measuring and defining precision or consistency is a difficult concept. In addition, the usefulness of many popular measures of QOL is limited in people with spinal cord injuries, for example, because of inappropriate questions for people with motor impairments related to walking (Gurcay et al. 2010).

There are many components that contribute to QOL, only one of which is health-related quality of life (HRQOL). An example of an instrument measuring HRQOL is the Short Form (SF)-36, which is also available in the modified version. Another aspect of QOL is subjective well-being and life satisfaction (Cooper and Cooper 2010). The tool used to describe overall subjective well-being is the Diener Satisfaction with Life Scale (SWLS), which allows the normative data from the Spinal Cord Injury Model Systems and other sources (Boakye et al. 2012).

References

Alexander MS, Anderson KD, Biering-Sorensen F, et al. Outcome measures in spinal cord injury: recent assessments and recommendations for future directions. Spinal Cord. 2009;47:582–91.

AlHuthaifi F, Krzak J, Hanke T, et al. Predictors of functional outcomes in adults with traumatic spinal cord injury following inpatient rehabilitation: a systematic review. J Spinal Cord Med. 2017;40:282–94.

Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. J Neurotrauma. 2004;21:1371–83.

Anderson K, Aito S, Atkins M, et al. Functional recovery outcome measures work group. Functional recovery measures for spinal cord injury: an evidence-based review for clinical practice and research. J Spinal Cord Med. 2008;31:133–44.

Ariji Y, Hayashi T, Ideta R, et al. A prediction model of functional outcome at 6 months using clinical findings of a person with traumatic spinal cord injury at 1 month after injury. Spinal Cord. 2020;58:1158–65.

Behrman AL, Harkema SJ. Physical rehabilitation as an agent for recovery after spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:183–202, v.

Boakye M, Leigh BC, Skelly AC. Quality of life in persons with spinal cord injury: comparisons with other populations. J Neurosurg Spine. 2012;17:29–37.

Burns SP, Golding DG, Rolle WA Jr, et al. Recovery of ambulation in motor-incomplete tetraplegia. Arch Phys Med Rehabil. 1997;78:1169–72.

Consortium for Spinal Cord Medicine. Depression following spinal cord injury: clinical practice guideline for health care professionals. Washington, DC: Paralyzed Veterans of America; 1998.

Consortium for Spinal Cord Medicine. Outcomes following traumatic spinal cord injury. Clinical practice guidelines for health care professionals. Washington, DC: Paralyzed Veterans of America; 1999.

Cooper RA, Cooper R. Quality-of-life technology for people with spinal cord injuries. Phys Med Rehabil Clin N Am. 2010;21:1–13.

Daverat P, Sibrac MC, Dartigues JF, et al. Early prognostic factors for walking in spinal cord injuries. Paraplegia. 1988;26:255–61.

Ditunno JF. Outcome measures: evolution in clinical trials of neurological/functional recovery in spinal cord injury. Spinal Cord. 2010;48:674–84.

Ditunno JF Jr, Stover SL, Freed MM, et al. Motor recovery of the upper extremities in traumatic quadriplegia: a multicenter study. Arch Phys Med Rehabil. 1992;73:431–6.

Evaniew N, Sharifi B, Waheed Z, et al. The influence of neurological examination timing within hours after acute traumatic spinal cord injuries: an observational study. Spinal Cord. 2020;58:247–54.

Farhadi HF, Kukreja S, Minnema A, et al. Impact of admission imaging findings on neurological outcomes in acute cervical traumatic spinal cord injury. J Neurotrauma. 2018;35:1398–406.

Fawcett JW, Curt A, Steeves JD, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. Spinal Cord. 2007;45:190–205.

Fridén J, Gohritz A. Tetraplegia management update. J Hand Surg Am. 2015;40:2489–500.

Gittler MS, McKinley WO, Stiens SA, et al. Spinal cord injury medicine. 3. Rehabilitation outcomes. Arch Phys Med Rehabil. 2002;83(3 Suppl 1):S65–71, S90–98.

Gresham GE, Labi ML, Dittmar SS, et al. The quadriplegia index of function (QIF): sensitivity and reliability

demonstrated in a study of thirty quadriplegic patients. Paraplegia. 1986;24:38–44.
Gurcay E, Bal A, Eksioglu E, et al. Quality of life in patients with spinal cord injury. Int J Rehabil Res. 2010;33:356–8.
Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: from point of injury to rehabilitation. J Spinal Cord Med. 2017;40:665–75.
Herbison GJ, Zerby SA, Cohen ME, et al. Motor power differences within the first two weeks post-SCI in cervical spinal cord-injured quadriplegic subjects. J Neurotrauma. 1992;9:373–80.
Horn SD, Smout RJ, DeJong G, et al. Association of various comorbidity measures with spinal cord injury rehabilitation outcomes. Arch Phys Med Rehabil. 2013;94(4 Suppl):S75–86.
Huh S, Ko HY. Recovery target priorities of people with spinal cord injuries in Korea compared with other countries: a survey. Spinal Cord. 2020;58:998–1003.
Hussey RW, Stauffer ES. Spinal cord injury: requirements for ambulation. Arch Phys Med Rehabil. 1973;54:544–7.
Itzkovich M, Gelernter I, Biering-Sorensen F, et al. The Spinal Cord Independence Measure (SCIM) version III: reliability and validity in a multi-center international study. Disabil Rehabil. 2007;29:1926–33.
Itzkovich M, Shefler H, Front L, et al. SCIM III (Spinal Cord Independence Measure version III): reliability of assessment by interview and comparison with assessment by observation. Spinal Cord. 2018;56:46–51.
Jones ML, Harness E, Denison P, et al. Activity-based therapies in spinal cord injury: clinical focus and empirical evidence in three independent programs. Top Spinal Cord Inj Rehabil. 2012;18:34–42.
Kirshblum S, Millis S, McKinley W, et al. Late neurologic recovery after traumatic spinal cord injury. Arch Phys Med Rehabil. 2004;85:1811–7.
Koontz AM, Kankipati P, Lin YS, et al. Upper limb kinetic analysis of three sitting pivot wheelchair transfer techniques. Clin Biomech (Bristol, Avon). 2011;26:923–9.
Marino RJ. Neurological and functional outcomes in spinal cord injury: review and recommendations. Top Spinal Cord Inj Rehabil. 2005;10:51–64.
Marino RJ. Domains of outcomes in spinal cord injury for clinical trials to improve neurological function. J Rehabil Res Dev. 2007;44:113–22.
Matsushita A, Maeda T, Mori E, et al. Can the acute magnetic resonance imaging features reflect neurologic prognosis in patients with cervical spinal cord injury? Spine J. 2017;17:1319–24.
Maynard FM, Reynolds GG, Fountain S, et al. Neurological prognosis after traumatic quadriplegia. Three-year experience of California Regional Spinal Cord Injury Care System. J Neurosurg. 1979;50:611–6.
Mateo S, Revol P, Fourtassi M, et al. Kinematic characteristics of tenodesis grasp in C6 quadriplegia. Spinal Cord. 2013;51:144–9.
Mateo S, Roby-Brami A, Reilly KT, et al. Upper limb kinematics after cervical spinal cord injury: a review. J Neuroeng Rehabil. 2015;12:9.
Miyanji F, Furlan JC, Aarabi B, et al. Acute cervical traumatic spinal cord injury: MR imaging findings correlated with neurologic outcome–prospective study with 100 consecutive patients. Radiology. 2007;243:820–7.
Post MW, Kirchberger I, Scheuringer M, et al. Outcome parameters in spinal cord injury research: a systematic review using the International Classification of Functioning, Disability and Health (ICF) as a reference. Spinal Cord. 2010;48:522–8.
Rudhe C, van Hedel HJA. Upper extremity function in persons with tetraplegia: relationships between strength, capacity, and the spinal cord independence measure. Neurorehabil Neural Repair. 2009;23:413–21.
Snoek GJ, Ijzerman MJ, Hermens HJ, et al. Survey of the needs of patients with spinal cord injury: impact and priority for improvement in hand function in tetraplegics. Spinal Cord. 2004;42:526–32.
Tator CH. Biology of neurological recovery and functional restoration after spinal cord injury. Neurosurgery. 1998;42:696–707; discussion 707-8.
Waters RL, Adkins R, Yakura J, et al. Donal Munro lecture: functional and neurologic recovery following acute SCI. J Spinal Cord Med. 1998;21:195–9.
Waters RL, Adkins RH, Yakura JS, et al. Motor and sensory recovery following incomplete paraplegia. Arch Phys Med Rehabil. 1994;75:67–72.
WHO. International classification of functioning. Disability and Health (ICF); 2001. https://www.who.int/docs/default-source/classification/icf/icfchecklist.pdf?sfvrsn=b7ff99e9_4
Woolsey RM. Rehabilitation outcome following spinal cord injury. Arch Neurol. 1985;42:116–9.

Recommended Additional Reading

Bromley I. Tetraplegia and paraplegia. A guide for physiotherapists. 6th ed. Philadelphia: Churchill Livingstone; 2006.
Buchanan LE, Nawoczenski DA, editors. Spinal cord injury-concepts and management approaches. Baltimore: Williams & Wilkins; 1987.
Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Harvey L. Management of spinal cord injuries. A guide for physiotherapists. Philadelphia: Churchill Livingstone; 2008.
Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.
Sisto SA, Druin E, Sliwinski MM. Spinal cord injuries: management and rehabilitation. 1st ed. St. Louis: Mosby; 2008.
Somers MF. Spinal cord injury. Functional rehabilitation. 3rd ed. New York: Pearson; 2010.

6 Biomechanics of the Spine and Spinal Cord and Pathophysiology of Spinal Cord Injury

In traumatic spinal cord injuries, the neurological level of injury, clinical features, and neurological prognosis are determined by the biomechanical characteristics of the spinal cord through the response of the spinal cord to external forces and the pathophysiology occurring in the spinal cord. Understanding the kinematics of the spine, which includes the anatomical and biomechanical properties of the spinal cord and the surrounding spine, is very important for the mechanism of the fractures and degeneration of the spine and lesions associated with the spinal cord. Since the structure of the anterior and posterior elements is different in the cervical, thoracic, and lumbar spine, resistance and reaction to external forces are different. The anatomy and biomechanics of the spinal cord exhibit various types of symptoms and signs, correlating with the internal structure and physical characteristics, including the somatotopic organization of the spinal cord in each region. This chapter describes the anatomy that is important for understanding the biomechanics of the spine which may have a characteristic effect on the spinal cord injury, the biomechanics of the spinal cord itself, and the pathophysiology of the spinal cord injury.

6.1 Biomechanically Relevant Spine Anatomy

The basic spinal unit (motion unit or motion segment) (Fig. 6.1) consists of two intact vertebrae joined by an intervertebral disc, two posterior articulations, and several ligaments. With an understanding of the natural behavior mechanics of the spinal motion segment, it may be possible to better understand the limitations of the system and the conditions under which tissue damage occurs and subsequent pain would be likely.

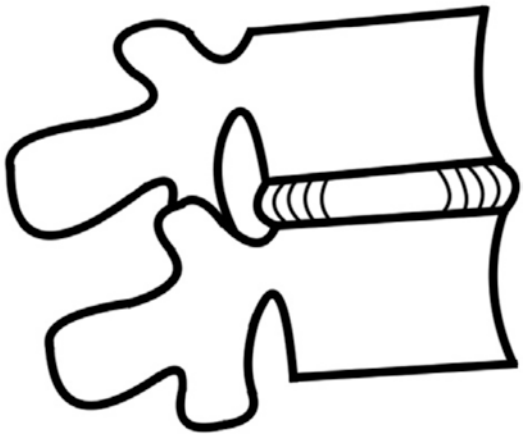


Fig. 6.1 A single spinal unit (motion unit)

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From a biomechanical point of view, the spine accomplishes three major functions: The spine provides a structure through which loads can be transmitted through the body; the spine enables motion in multidimensional space; the spine provides a structure to protect the spinal cord (Bernhardt et al. 2006). Each regions of a spine relates to one or more of the functions of the vertebral column. The vertebral bodies help with support, whereas the pedicles and laminae protect the spinal cord. The superior and inferior articular processes help determine spinal motion by facing of their facets. The transverse and spinous processes aid movement by acting as lever arms that the muscles of the spine act on (Fig. 6.2). A typical biomechanical study examines the load and deformation of a motion segment using a cadaver. Since the effect of muscles in in vivo movement of the spine cannot be excluded, there may be a significant difference from the information obtained in the laboratory.

6.1.1 Bony Vertebrae

The shape of the vertebrae changes from level to level in the spine. The vertebral body shape and the orientation of the posterior elements change as their shapes and contact angles change. The biomechanical role of the posterior elements is to control the position of the vertebral bodies. These elements provide attachment points for muscles to control the position of the vertebra and provide lever arms to give mechanical advantage, control motion, and prevent excessive movement of the vertebral body. The pedicles provide a robust support structure to transmit force between the posterior elements and the anterior element (vertebral body). The lamina projects from each pedicle and coverage at the midline of the body to form a neural arch.

There are two sets of articulation surfaces in the posterior elements. A bony extension, known as the superior articular process, protrudes from

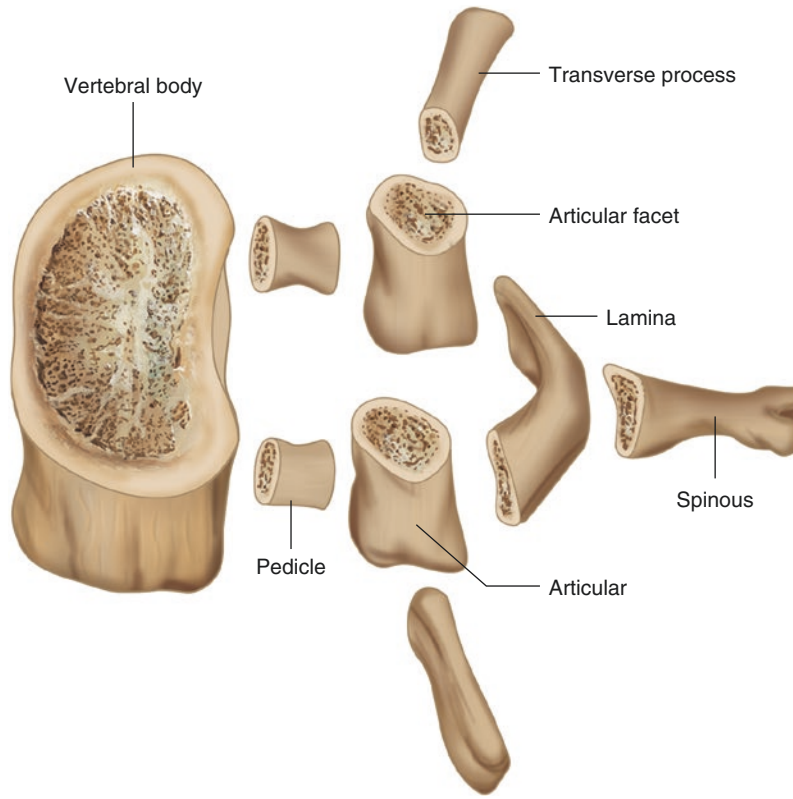

Fig. 6.2 Functional components of a typical vertebra. The vertebral body serves the function of support. The pedicles and laminae serve the protective function of the spinal cord in the cervical and thoracic regions and cauda equina below the level of L1. The spinous process, transverse processes, articular processes, and particularly the articular facets serve the function of movement. Adapted from Cramer and Darby (2014)

each of the cephalic lateral corners of the lamina. The superior articular process from the lower vertebra interacts with the inferior articular process of the above vertebra to form a synovial joint known as the zygapophyseal joint (facet joint). The inclination of the facet joint changes from the cervical spine to the thoracic spine to the lumbar spine. The different orientation of these facet joints restricts movement in different planes of motion (Fig. 6.3), allowing certain motions and limiting other motions of the spine (Steinmetz and Benzel 2017).

6.1.2 Intervertebral Disc

The vertebral bodies are connected by discs that serve several biomechanical purposes, including absorbing shock between the vertebrae, transmitting mechanical load, and permitting motion segmental motion. Functionally, the intervertebral discs provide a separation between consecutive vertebrae. This separation makes space between the vertebrae so that the vertebral bodies can independently change their orientation and perform bending movements. The outer lamellae of the intervertebral disc, the anulus fibrosus, consists of alternating 10–20 fiber layers that are oriented at an angle of 60°–65° to the vertical. The lamellae are stiff and can withstand significant compression loading. When the nucleus pulposus is compressed, it expands radially and places the anulus fibrosus under tension, which provides stiffness (Steinmetz and Benzel 2017).

The end plate is located at the intersection of the intervertebral disc and the vertebral body. The end plates are composed of cartilage and cover the upper and lower portions of the intervertebral disc. They are composed of concave surfaces of approximately 1.3-mm-thick cortical bone. These structures bind the intervertebral disc fibers to the vertebral bones and play an important in the

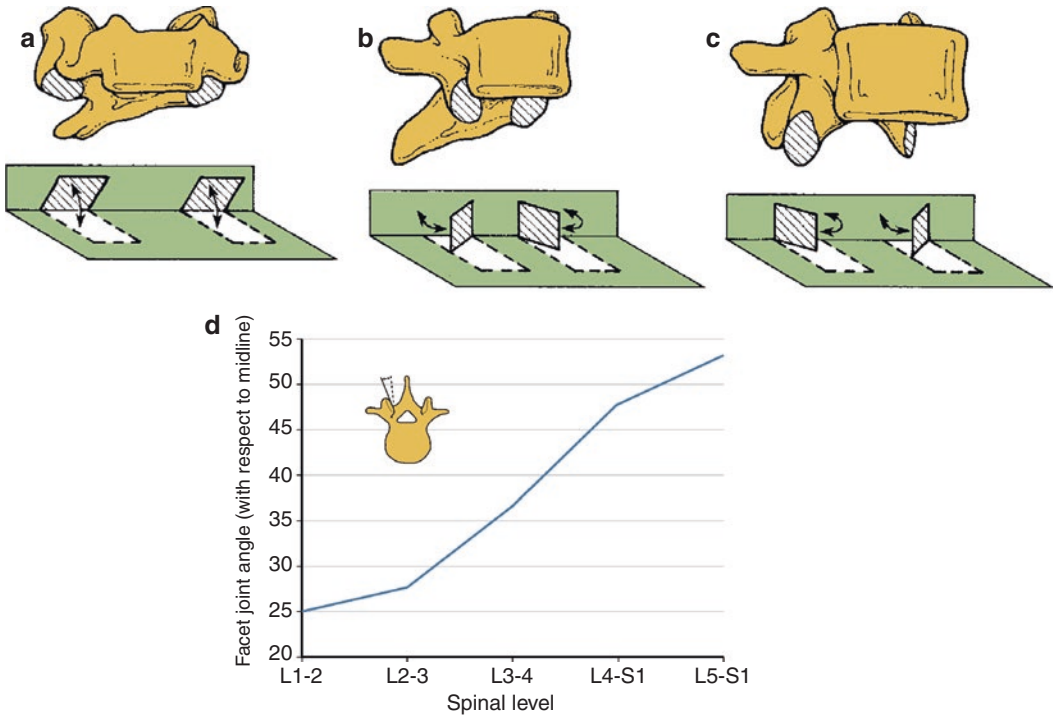

Fig. 6.3 Facet joint orientation. (**a**) The relative coronal plane orientation in the cervical spine. (**b**) The intermediate orientation in the thoracic spine. (**c**) The relative sagittal orientation in the lumbar spine. (**d**) The facet orientation changes substantially in the lumbar spines. From Steinmetz and Benzel (2017), with permission

nutritional transport to the intervertebral disc, which nutrients for the intervertebral disc penetrate through the small pores at the lamina cribs.

6.1.3 Ligamentous Structures

There are seven major spinal ligaments that stabilize the subaxial spine in its physiological range of motion. These ligaments also work to limit the motion of the spine to well-defined limits while allowing adequate motion and fixed postures to protect the spinal cord. Starting anteriorly and moving posteriorly, the ligaments are the anterior longitudinal ligament, posterior longitudinal ligament, capsular ligaments, intertransverse process ligaments, ligamentum flavum, interspinous ligament, and supraspinous ligament (Ozapinar et al. 2022) (Fig. 6.4).

The *anterior longitudinal ligament* spans the entire length of the vertebral column. It begins at the occiput, the ventral border of the foramen magnum (basion), as the anterior occipitoatlantal membrane and continues down to the sacrum and covers one fourth to one third of the ventral circumference of the vertebral bodies and intervertebral discs. The *posterior longitudinal ligament* also traverses the entire length of the spinal column. It begins at C2 as the tectorial membrane and continues to the sacrum, with the fibers spreading out at the disc level and narrowing in the middle of the vertebral body. While the ligament closely adheres to the disc anulus, it attaches only marginally to the vertebral body. This ligament is much thinner over the vertebral body and over the intervertebral disc and is thickest in the thoracic region. The function of the posterior longitudinal ligament is to prevent hyperflexion. The *ligamentum flavum* is broad paired ligaments that connect spinal laminae. They arise from the ventral surface of the caudal lamina and attach to the dorsal margin of the adjacent rostral lamina. They are discontinuous at midvertebral levels and in the midline. They extend laterally to the joint capsules and become confluent. These ligaments extend from C1–2 to L5–S1 levels. The ligamentum flavum is the most elastic tissues in the human body and is not lax except under hyperextension resulting in minimizing buckling during extension (Yoganandan et al. 2022). In general, the ligaments farthest from the instantaneous axis of rotation show the greatest strength due to the relatively longer lever arm length of ligament (Fig. 6.5).

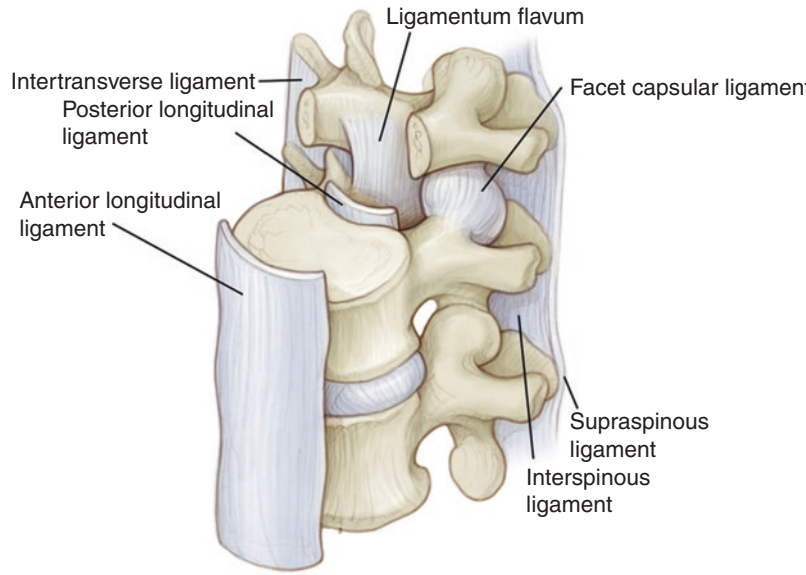

Fig. 6.4 Ligaments of the spine. From Ozapinar et al. (2022), with permission

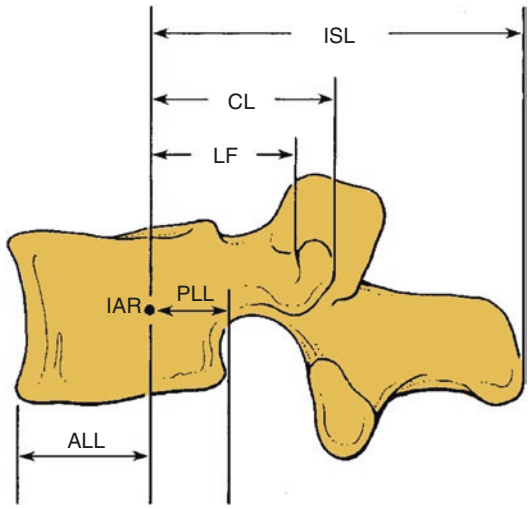

Fig. 6.5 The relative lever arm length of ligaments causing flexion. This length depends on the location of the instantaneous axis of rotation (IAR, dot). ALL, anterior longitudinal ligament; PLL, posterior longitudinal ligament; LF, ligamentum flavum; CL, capsular ligament; ISL, interspinous ligament. From Yoganandan et al. (2022), with permission

6.2 Biomechanics of the Spine

6.2.1 Movement of the Spine

In order to accurately describe the movement and force transmission through tissue, it is necessary to describe accurately the direction of movement as well as the direction and magnitude of the force acting on the tissue. The origin or center of the coordinate system is at the base of the spine. The coordinate system is defined as a traditional three-dimensional Cartesian coordinate system with three mutually perpendicular axes, i.e., *x*, *y*, and *z* axes. Cartesian coordinate system with the *z*-axis oriented along the caudal to rostral direction, the *x*-axis along the dorsal to ventral direction, and the *y*-axis along the right-to-left direction. For the right-handed system, this results in a positive moment of flexion (extension is negative), a positive moment for a left-to-right lateral bending (right-to-left lateral bending is a negative moment), and positive twisting for a right axial rotation moment (left axial rotation is a negative moment) (Yoganandan et al. 2017). All movements of the spine are described relative to the origin of the central coordinate system. Flexion and extension are typically described in the sagittal plane, lateral bending occurs in the coronal plane, and rotation occurs along the horizontal or transverse plane. Most activities are combinations of movements in these planes. Figure 6.6 shows the coordinate system with the instantaneous axis of rotation (Marras et al. 2018). If a hypothetical line is extended from the constant point inside a vertebra, the point at which these two lines meet when the vertebra moves between two different positions is called the instantaneous axis of rotation (Fig. 6.7).

When the spinal motion units are subjected to forces of different magnitude and direction, damage occurs by forces of different magnitude and direction: compression, flexion, extension, lateral flexion, rotation, and horizontal shear (Roaf 1960). Spinal column motion is determined by the bony structures such as the interverterbral bodies/discs and the facet joints. Spine motion is also limited by the bony structures and ligamentous structures (Cramer and Darby 2014; White and Panjabi 1990; Standring 2016) (Table 6.1). The anatomical features of the intervertebral disc and facet that determine the spine motion are as follows: the possible moments in the spine are determined by the size of the intervertebral discs.; the direction of movement is determined by the orientation of the facet joints. The orientation of the surfaces of the facet joint varies from one area to another, and the main motion in each region depends on the plane of facet orientation. The ability of the spine to resist the stiffness imposed by the load is determined by the design of the facet joints (White and Panjabi 1990). The spine gradually becomes stiff from T7 to L4 and has a peak between T12 and L1. At this level, the facet joints interfere with rotation. This is a level of high stress concentration and can cause mechanical failure as evidenced by the high incidence of spinal injury at the thoracolumbar junction (Breig 1970).

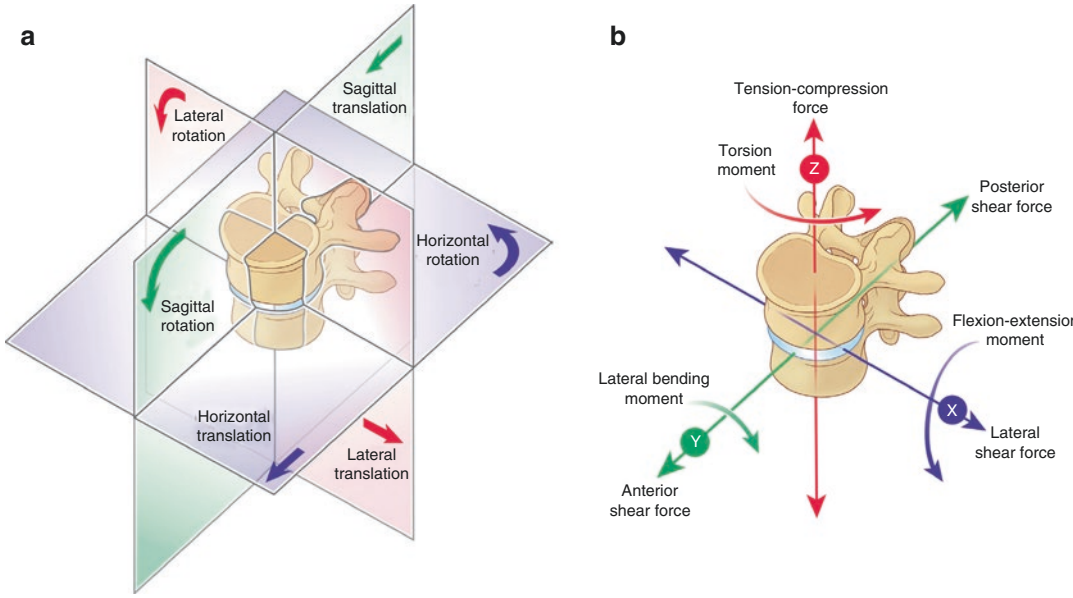

Fig. 6.6 The coordinate system with the instantaneous axis of rotation as the center. (**a**) Spinal motion segment planes and directions of motion. (**b**) Biomechanical coordinate system and direction of forces and moments. From Marras et al. (2018), with permission

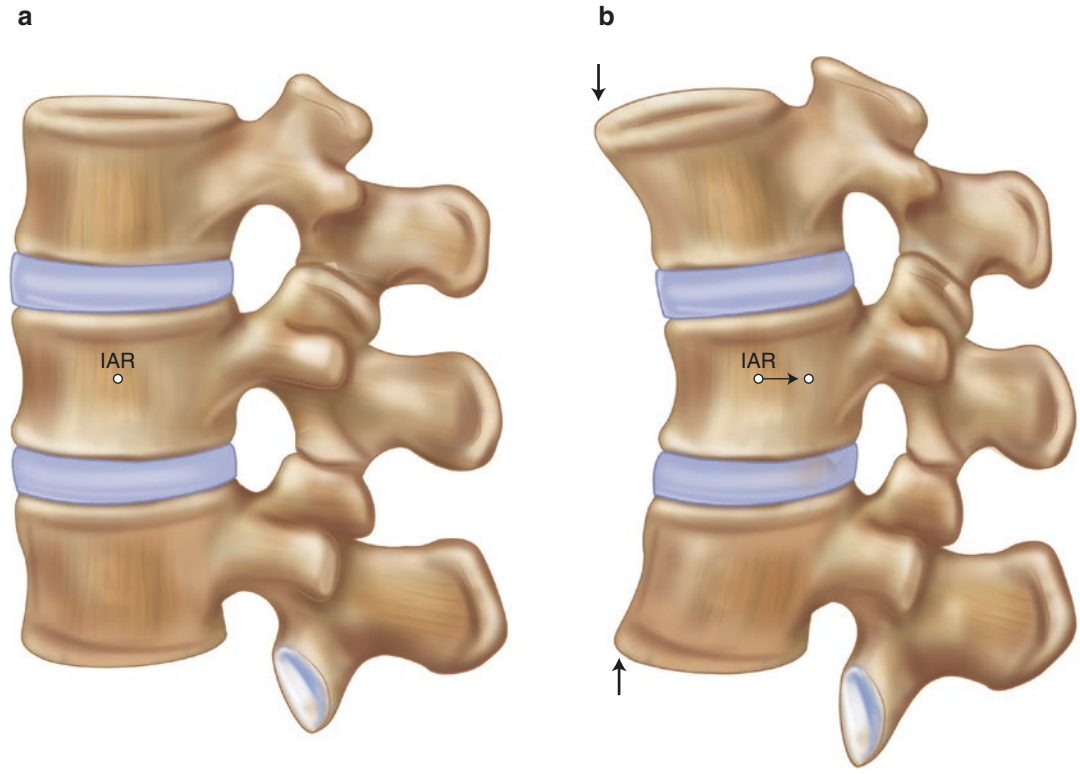

Fig. 6.7 A depiction of an applied bending moment altering the location of the IAR from the (**a**) preload situation to the (**b**) postload situation. During sagittal plane flexion, the IAR moves backward. IAR, instantaneous axis of rotation. Adapted from Benzel (2015)

Table 6.1 Structures or situations limiting spine motion

Spine motion	Structures or situations limiting motion
Flexion	Posterior longitudinal ligament Ligamentum flavum Articular capsule Posterior fibers of intervertebral disc Interspinous ligament Supraspinous ligament Tension of back extensor muscles Anterior surface of inferior articular facet against posterior surface of superior articular facet
Extension	Anterior longitudinal ligament Anterior aspect of intervertebral disc Approximation of spinous processes, articular processes, and laminae
Lateral flexion	Contralateral side of intertransverse ligament and intervertebral disc Approximation of articular processes Approximation of uncinate processes (cervical region) Approximation of costovertebral joints (thoracic region) Antagonist muscles
Rotation	Tightening of lamellar fibers of anulus fibrosus Orientation and architecture of articular processes

Adapted from Cramer and Darby (2014), White and Panjabi (1990), and Standring (2016)

Maximum flexion and extension movements occur between C4 and C6 (White and Panjabi 1990). The thoracic region is less flexible and more stable than the cervical spine because of the limitation by the ribs, spinous processes, and the joint capsules in this region. All directional movements are possible but are limited by changes in the facet orientation from the upper to lower thoracic region. Flexion and extension are limited in the upper thoracic region but increase in the lower thoracic spine. Rotation is not limited in the upper thoracic spine, but is more limited in the lower thoracic spine. The lumbar facets prefer flexion and extension and limit lateral flexion and rotation. Flexion is more limited than extension in the lumbar spine. Lateral flexion and rotation gradually decrease in the lower region of the lumbosacral spine.

6.2.2 Coupled Motion

Movements are considered coupled when one motion is accompanied by motion in a different plane. Motion in the primary, or intended, plane of movement is called the primary motion; the accompanying motions are called coupled motions. Coupling is a function of the geometric characteristics of specific vertebrae, limitations of the tissue properties of the intervertebral disc and ligaments, and spine curvature (Marras et al. 2018). Coupling is clinically important for understanding the effect of various pathologies, such as scoliosis and various spine traumas. Coupling occurs most often in the cervical and lumbar spine, but can also occur in the thoracic spine. Coupling in the cervical and lumbar spine involves axial rotation coupled with lateral bending. Motion of the lumbar spine may involve a cross coupling in all three directions of rotation. Coupled motions of the lumbar spine vary with the spine level and with the spine posture (White and Panjabi 1990).

The cervical spine shows a noticeable coupling, as the lateral bending of the neck is accompanied by significant cervical rotation. This becomes clear by observing the position of the spinous processes during lateral bending. If there is a left lateral bend, the spinous processes point to the right; when right lateral bending occurs, the spinous processes go to the left. It is generally assumed that the angle of inclination of the facet joints in the sagittal plane increases from the head toward the lower spine (White and Panjabi 1990). Coupling patterns in the lumbar spine appear to be different from those of the cervical and thoracic spine. The most dominant coupling pattern of the lumbar spine appears to be lateral bending coupled with axial rotation. In this case, the spinous process moves in the same direction as lateral bending. This is exactly opposite to the pattern found in the cervical and upper thoracic spine (Marras et al. 2018). In vitro studies have reported that lateral bending motion is coupled with flexion motions between L1 and L3, while in vivo studies have reported that lateral motions

are coupled with extension movements in these vertebrae (Cholewicki et al. 1996).

6.2.3 Spinal Stability

In biological systems, stability depends on circumstances rather than all-or-none phenomenon. It must be defined both for static conditions, in which the system is in equilibrium, and for dynamic situations, in which the system moves on a given trajectory. The classical definition of clinical stability is "the ability of the spine under physiological loads to limit patterns of displacement so as not to damage or irritate the spinal cord or nerve roots and, in addition, to prevent incapacitating deformity or pain caused by structural changes" (White and Panjabi 1990).

Stability is maintained by three mechanisms: (1) the active subsystem (musculoskeletal system), (2) the passive subsystem (the spinal column), and (3) the neural system (activation of the active system through neurological control). Under normal conditions, the three subsystems maintain mechanical stability while the spinal column translates and rotates about the three cardinal anatomical axes (Breig 1970; Vinken and Bruyn 1976).

6.2.4 Mechanism of Spine Injury

Hyperflexion, hypertension, axial loading, and penetrating wounds are the four mechanisms responsible for spinal injuries. Each can occur alone or in combination with one or more of the others.

6.2.4.1 Hyperflexion

Forward contact with forces acting on the front of the body or with an immovable object can create the mechanism of hyperflexion. And when a hyperflexion mechanism occurs, the most flexible levels of the spine act as a fulcrum with the maximum stress (Breig 1970). For example, the largest forward bending moment in the cervical spine is C5–C6. The posterior longitudinal ligament may stretch or tear and may cause the intervertebral disc to herniate or tear. More than one vertebral body may be compressed causing fractures and/or dislocation (subluxation). If the integrity of the spinal canal is compromised by bone fragments or by the movement of one or more vertebral bodies, the spinal cord may be damaged.

6.2.4.2 Hyperextension

Sufficient force on the posterior surface of the body or backward movement through contact with a fixed object will cause hyperextension. Hyperextension usually occurs when an individual is involved in a car accident in which the car is rear-ended. In its mildest form, hyperextension caused by this type of accident is commonly referred to as whiplash injury.

When the hyperextension mechanism occurs, the most flexible elements of the spine act as a fulcrum. The greatest bending movement in hyperextension of the cervical spine occurs at C4–C5. The anterior longitudinal ligament may be stretched or torn, the intervertebral disc may become torn or herniated, the posterior elements of the spine may compress and fracture, and there may be subluxation. Damage to the integrity of the spinal canal can damage the neural elements of the spinal cord (Breig 1970).

6.2.4.3 Axial Loading

The axial loading mechanism occurs when sufficient force acts vertically through the vertebral column. The force transmitted along the spine does not itself cause spinal cord damage. However, if the force is sufficient, one or more vertebral bodies "burst" literally by absorbing the strength of the force. When this happens, the vertebral body bursts in all directions, including damage to the spinal cord (White and Panjabi 1990).

Injuries due to axial loading occur most often when an individual hits his head against the bottom of the shallow water. The resulting injury is usually a burst fracture of C4 or C5 with complete tetraplegia. In such cases, there is usually no concomitant head injury. If the skull were fractured during the diving, the head would act as a shock absorber for the cervical spine. When a

person jumps or falls from a height and falls on a foot, an injury due to axial loading is also observed. Damage usually results in a burst fracture of T10, T11, or T12 with paraplegia. In this case, bilateral calcaneal fractures are often accompanied (White and Panjabi 1990).

6.2.4.4 Penetrating Wounds

Low-velocity penetrating wounds and high-velocity penetrating wounds use two different mechanisms of spinal cord injury. A low-velocity penetrating wound can be manually stabbed by a foreign body such as a knife or an ice pick, pushed into the body, or a low-velocity bullet from a small caliber handgun. The mechanism of injury from low-velocity penetrating wounds is usually mechanical. The foreign body pieces or cuts the spinal cord or the neural element at the contact point. The stability of the spine should always be carefully assessed, but the fracture of bony elements may or may not be present, and stability of the spine is rarely compromised.

High-velocity penetrating wounds can be caused by bullets from high-powered rifles or explosive foreign bodies that are forced into the body. In high-velocity penetrating wounds, the foreign material may not penetrate the spine or the spinal cord to damage the neural elements. This is an important consideration in the evaluation process. The concussive impact of the missile through the body can be sufficient to cause complete damage to the spinal cord. The concussive force alone can cause the pathophysiological disruption of hemorrhage, edema, and necrosis without physical destruction of the spine or spinal cord (Harrison et al. 1999).

6.3 Biomechanics of the Spinal Cord

Knowledge of the mechanics of spinal cord injuries and the interactions between different anatomical components during trauma provides valuable information on the pathophysiology of injury and potential management strategies. The spinal cord is a dynamic structure that undergoes significant geometric changes without negative sequelae during normal physiological movements (Mattucci et al. 2019; Miele et al. 2012). Most biomechanical outcomes occurring in the spinal cord are determined by motion of the spinal column and impact on the spine and intrinsic physical properties of the spinal cord and associated structures, including the nerve roots, pia and dura mater, and dentate ligament. The spinal cord participates with the spinal column in configuration changes due to the alteration of the body positioning. The structures of the spinal cord participate in physical alterations, the predominant effects occurring at the local level of distraction and the biomechanical response of a functional spinal unit.

The spinal cord can be damaged by various types of mechanical pathomechanisms: concussion, contusion or compression, dislocation, distraction, and laceration (Fig. 6.8). Of these injury

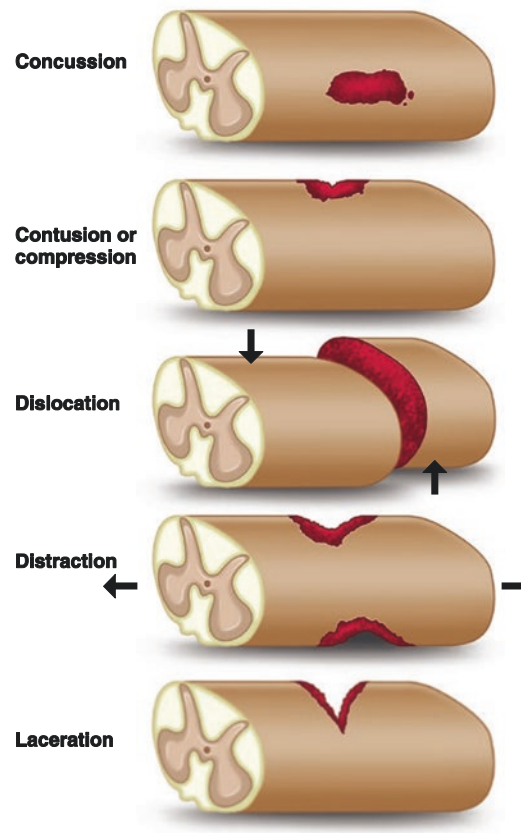

Fig. 6.8 Types of physical damage mechanisms to the spinal cord

mechanisms of the spinal cord, transverse contusion, distraction, and dislocation are commonly encountered mechanism. These injury patterns can occur as a combination. Distraction injuries were more evenly distributed throughout the spinal cord compared to contusion and dislocation. Distraction injury has also been associated with an increased caudal-cranial injury severity compared to contusion. It also often results in the greatest strains in the dorsal column while the ventral column experienced the least strain. Compared to contusion, dislocation is associated with compressive lateral strains and increased strains in the lateral columns (Choo et al. 2007; Miele et al. 2012).

With small force levels, large initial displacements occur that demonstrate the elastic flexibility of the spinal cord. This initial flexibility is followed by stiffening, with additional stretching or distraction requiring higher load levels (Cusick 1991; Yoganandan et al. 2022).

The folding/unfolding zone of the spinal cord reaches 70–75% of the length changes between flexion and extension, with the remainder of the length changes occurring in the elastic deformation zone (White and Panjabi 1990). When flexed, the spinal cord elongates in the spinal canal and decreases in the AP diameter. This induces increased axial tension in the axonal cylinders of the white matter tracts and lesions of the spinal canal that affect the cross-sectional area. In extension, the spinal cord shortens and the AP diameter increases with relative relaxation of the axonal cylinders. In extension, the reduced cross-sectional area of the spinal canal due to the dorsal protrusion of the anulus and the infolding of the ligament flavum and scaffolding of the lamina can lead to a pincer-like effect on the spinal cord (Yoganandan et al. 2022). Irreversible spinal cord damage may occur when the compression exceeds about 30% of the initial spinal cord diameter. The gray matter fails at lower strains than the white matter, which implies that gray matter is more fragile (Ichihara et al. 2001). Spinal cord injury is primarily a result of direct damage to the spinal cord neural and supportive glial tissue but is also the result of changes in vascular physiology and metabolic dysfunction (Carlson et al. 2003; Harrison et al. 1999). When the spinal cord is deformed, the axonal membrane is subjected to varying degrees of local stretch damage.

6.4 Pathophysiology of Spinal Cord Injuries

Based on pathophysiological changes the early acute phase is defined to be 2–48 h after the injury, the subacute phase from 2 days to 2 weeks, and the intermediate phase from 2 weeks to 6 months (Rowland et al. 2008). An understanding of the pathophysiological processes that occur after spinal cord injury is essential to development of effective therapies that can minimize or reverse lesions. In addition to local pathophysiological processes that cause secondary injury at the injured site, systemic factors also contribute. Strategies include immediate resuscitation, minimization of prolonged hypoxia, as well as the prevention and management of neurogenic shock and hypotension in the acute phase after spinal cord injury and the limitation of secondary damage to the spinal cord (Cadotte and Fehlings 2011).

Traumatic injury of the spinal cord causes mechanical destruction of neural tissue and hemorrhage in the epicenter within the spinal cord. This axonal loss due to direct physical deformation is called primary injury. The initial loss of axons has a centrifugal pattern which is explained by a longitudinal displacement of the central content of the spinal cord (Onose et al. 2009). This primary injury triggers a cascade of pathochemical events leading to significant further axonal loss, which is secondary injury (Anderson and Hall 1993). Hemorrhages occur almost immediately in the gray matter and spread in a few minutes to the white matter, which affects the microcirculation. A few minutes after injury, small hemorrhages appear in the central gray matter, followed by the leakage and filtration of erythrocytes in the perivascular spaces. These small hemorrhages soon merge to form a central hemorrhagic necrosis and evolve into a centrifugal pattern involving the surrounding white mat-

ter. The result of this cascade is cell death due to neuronophagia caused by polymorphonuclear leukocytes. Emphasis was placed on the lipid derangements of posttraumatic axonal membrane because of the possibility of pharmacological interruption of this cascade, possibly limiting the secondary injury. The events in question are activation of membrane phospholipases and lipases leading to release of fatty acid and the lipid peroxidation induced by free radicals (Anderson and Hall 1993). The temporal mechanisms of the primary and secondary injuries of spinal cord injury are shown in Fig. 6.9.

For several minutes after severe impact injury to the spinal cord, the spinal cord may appear grossly and histologically normal. Detailed animal studies of impact injury to the spinal cord, however, defined the sequence of pathologic events that transform this normal appearance into complete focal necrosis and inflammation within 24–48 h of injury (Table 6.2).

Subarachnoid and subpial hemorrhage occurs on the surface of the spinal cord just under the injury site. Petechial hemorrhages in the central cord gray matter are observed within 30 min after injury. Initially confined to the areas in the

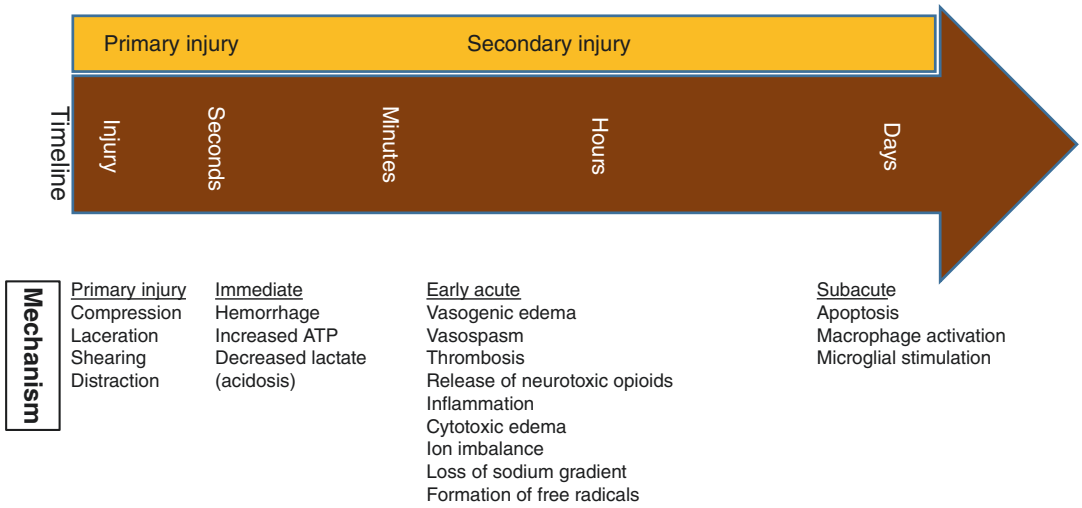

Fig. 6.9 Primary and secondary injuries mechanisms of spinal cord injury. Adapted from Wilson et al. (2013)

Table 6.2 Pathophysiologic response to spinal cord injury

Time	Anatomical change	Physiological change	Biochemical change
Immediate	• Cord deformation		
1 min		• Loss of evoked potentials	• Lipid peroxidation • Free-radical formation
5 min	• Axonal swelling	• Vasoconstriction	
15 min		• Decreased gray and white matter blood flow	• Increased thromboxane levels • Increased tissue norepinephrine levels
30 min	• Central hemorrhages	• Ischemia	• Profound tissue hypoxia
1 h			
4 h	• Blood vessel necrosis • White matter edema		
8 h	• Central hematoma formation		
24 h	• White matter necrosis		

From Wilberger (1986), with permission

anterior horns and around the central canal, these hemorrhages coalesce for several hours and extend into the posterior gray matter and white matter. Hemorrhages in the corticospinal tracts are first observed at about 4 h. Eight hours after injury, white matter tracts are characterized by a nonhemorrhagic necrosis associated with edema (Okazaki et al. 2018). The edema obliterates the subarachnoid space and compresses pial vein and spreads to several segments from the initial lesion in both directions. There is no initial change in axons or myelin sheaths, but this process eventually leads to extensive tissue necrosis and shrunken axons. After 48 hours, the tissues of the spinal cord become soft and liquefied as the myelin degraded to neutral fat. Macrophages quickly enter the lesion to clean the necrosis. After several weeks, fully developed cavities will form, and after 3–6 weeks, the central cavity will completely remove the debris. The primary lesions, which extended over several segments, were in the form of multiloculated cysts, including glial cells and remaining white matter tracts (Okazaki et al. 2018).

Ischemia, edema, and hemorrhages are responsible for most of the delayed injuries that may occur after spinal cord injury (Lammertse 2004). Ischemia due to release of vasoactive substances causing local vasoconstriction and microvascular injury sustained at the time of the injury. Inflammatory responses with wounds cause edema. Edema causes compression of the neurological structures, causing additional damage to the microvasculature of the spinal cord, perpetuating the cycle, and promoting neurological deficits.

6.4.1 Primary Injury

The primary injury results from direct physical trauma to the spinal cord due to various mechanisms classified as either penetrating or blunt injuries. The primary injury is the initial alteration of the tissue and damages to the spinal cord that occurs at the time of impact. Penetrating injuries include gunshot wounds, fragmentation injury from a blast mechanism, or low-velocity injuries (e.g., knife wounds). Blunt injuries are most often caused by falls, crush injuries, collisions, or tertiary injuries from a blast (Hachem et al. 2017). The main mechanical impact on the spine and spinal cord is related to the forces caused by flexion, extension, axial loading, rotation, and/or distraction. Physical injury to the spinal cord causes laceration, contusion, compression, shear, and traction of the neural tissue of the spinal cord, resulting in traumatic axonal damage (Kwon et al. 2004).

6.4.2 Secondary Injury

Spinal cord injuries cause delayed damage and death of surviving cells in the initial trauma. A cascade of physiologic, extracellular biochemical, and intracellular insults comprises the secondary injury phase. For hours to days, the cells continue to undergo cell death, which releases potent pro-apoptotic signals and recruits regional microglia. Together, these events introduce numerous cytotoxic by-products (e.g., ATP, potassium ions, DNA, reactive oxygen species, etc.) into the local microenvironment which further propagates cell death (Hachem et al. 2017). Secondary response occurs within days to weeks following the injury (Kwon et al. 2011b). The processes contributing to secondary injury after spinal cord injury include vascular perfusion abnormalities, edema, inflammation, free radical generation, lipid peroxidation, excitotoxicity with changes in local ionic concentrations and calcium influx, and cell death (Borgens and Liu-Snyder 2012; Rowland et al. 2008).

6.5 Discomplete Injury

The term “discomplete” was first introduced by Dimitrijevic et al. (1983) to explain their finding of electrophysiological transmission of signals across the lesion in clinically complete patients who have lost all sensation and voluntary motor functions below the level of the lesion. They were clinically complete but in which a variable number of intact nerve fibers cross the level of the

lesion. These patients can be considered "anatomically discomplete." The finding that a large proportion of these cases shows some anatomical continuity of the spinal cord white matter across the lesion in clinically incomplete and "discomplete" patients emphasizes the relative sparing of the tracts even in the most severe cases of spinal cord injury (Kakulas 1999).

6.6 Neuroprotection

Despite the exponential growth in research, there was no accepted or approved treatment by the FDA to improve neurological function after spinal cord injury (Kwon et al. 2011a; Lammertse et al. 2007). High-dose methylprednisolone, which was administered intravenously within 8 h of injury, was the only drug widely used clinically for a period of time after the publication of positive results after spinal cord injury in the 1990s (Cadotte and Fehlings 2011; Kwon et al. 2011a). But the study did subject to much controversy and lack of consensus (Cadotte and Fehlings 2011; Curt 2012). The guidelines for management of acute cervical spine and spinal cord injury by the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS), updated in 2013, now explicitly recommend not to administer methylprednisolone for the treatment of spinal cord injuries. It should be noted that there are many studies that the ketogenic diet is effective for neuroprotection, including acute spinal cord injury (Demirel et al. 2020; Koh et al. 2020; Sayadi et al. 2021; Tan et al. 2020; Veyrat-Durebex et al. 2018).

References

Anderson DK, Hall ED. Pathophysiology of spinal cord trauma. Ann Emerg Med. 1993;22:987–92.

Benzel EC. Biomechanics of spine stabilization. 3rd ed. New York: Thieme; 2015.

Bernhardt M, White AA, Panjabi MM. Biomechanical considerations of spinal stability. In: Herkowitz HN, Garfin SR, Eismont FJ, editors. Rothman-Simeone the spine. Philadelphia: WB Saunders; 2006.

Borgens RB, Liu-Snyder P. Understanding secondary injury. Q Rev Biol. 2012;87:89–127.

Breig A. Overstretching of and circumscribed pathological tension in the spinal cord-a basic cause of symptoms in cord disorders. J Biomech. 1970;3:7–9.

Cadotte DW, Fehlings MG. Spinal cord injury: a systematic review of current treatment options. Clin Orthop Relat Res. 2011;469:732–41.

Carlson GD, Gorden CD, Nakazawa S, et al. Sustained spinal cord compression: Part II: effect of methylprednisolone on regional blood flow and recovery of somatosensory evoked potentials. J Bone Joint Surg Am. 2003;85-A:95–101.

Cholewicki J, Crisco JJ 3rd, Oxland TR, et al. Effects of posture and structure on three-dimensional coupled rotations in the lumbar spine. A biomechanical analysis. Spine (Phila Pa 1976). 1996;21:2421–8.

Choo AM, Liu J, Lam CK, et al. Contusion, dislocation, and distraction: primary hemorrhage and membrane permeability in distinct mechanisms of spinal cord injury. J Neurosurg Spine. 2007;6:255–66.

Cramer GD, Darby SA. Clinical anatomy of the spine, spinal cord, and ANS. St. Louis: Elsevier; 2014.

Curt A. The translational dialogue in spinal cord injury research. Spinal Cord. 2012;50:352–7.

Cusick JF. Pathophysiology and treatment of cervical spondylotic myelopathy. Clin Neurosurg. 1991;37:661–81.

Demirel A, Li J, Morrow C, et al. Evaluation of a ketogenic diet for improvement of neurological recovery in individuals with acute spinal cord injury: study protocol for a randomized controlled trial. Trials. 2020;21:372.

Dimitrijevic MR, Faganel J, Lehmkuhl D, et al. Motor control in man after partial or complete spinal cord injury. Adv Neurol. 1983;39:915–26.

Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: from point of injury to rehabilitation. J Spinal Cord Med. 2017;40:665–75.

Harrison DE, Cailliet R, Harrison DD, et al. A review of biomechanics of the central nervous system-part II: spinal cord strains from postural loads. J Manipul Physiol There. 1999;22:322–32.

Ichihara K, Taguchi T, Shimada Y, et al. Gray matter of the bovine cervical spinal cord is mechanically more rigid and fragile than the white matter. J Neurotrauma. 2001;18:351–67.

Kakulas BA. A review of the neuropathology of human spinal cord injury with emphasis on special features. J Spinal Cord Med. 1999;22:119–24.

Koh S, Dupuis N, Auvin S. Ketogenic diet and Neuroinflammation. Epilepsy Res. 2020;167:106454.

Kwon BK, Tetzlaff W, Grauer JN, et al. Pathophysiology and pharmacologic treatment of acute spinal cord injury. Spine J. 2004;4:451–64.

Kwon BK, Okon E, Hillyer J, et al. A systematic review of non-invasive pharmacologic neuroprotective treatments for acute spinal cord injury. J Neurotrauma. 2011a;28:1545–88.

Kwon BK, Okon EB, Plunet W, et al. A systematic review of directly applied biologic therapies for acute spinal cord injury. J Neurotrauma. 2011b;28:1589–610.

Lammertse DP. Update on pharmaceutical trials in acute spinal cord injury. J Spinal Cord Med. 2004;27:319–25.

Lammertse D, Tuszynski MH, Steeves JD, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: clinical trial design. Spinal Cord. 2007;45:232–42.

Marras WS, Mageswaran P, Khan SN, et al. Biomechanics of the spine motion segment. In: Garfin SR, Eismont FJ, Bell GR, et al., editors. Rothman-Simeone and Herkowitz's the spine. 7th ed. Philadelphia: Elsevier; 2018.

Mattucci S, Speidel J, Liu J, et al. Basic biomechanics of spinal cord injury–how injuries happen in people and how animal models have informed our understanding. Clin Biomech (Bristol, Avon). 2019;64:58–68.

Miele VJ, Panjabi MM, Benzel EC. Anatomy and biomechanics of the spinal column and cord. Handb Clin Neurol. 2012;109:31–43.

Okazaki T, Kanchiku T, Nishida N, et al. Age-related changes of the spinal cord: a biomechanical study. Exp Ther Med. 2018;15:2824–9.

Onose G, Anghelescu A, Muresanu DF, et al. A review of published reports on neuroprotection in spinal cord injury. Spinal Cord. 2009;47:716–26.

Ozapinar A, Joseph JR, Kanter AS. Functional anatomy of the spine. In: Steimetz MP, editor. Benzel's spine surgery. 5th ed. Philadelphia: Elsevier; 2022.

Roaf R. A study of the mechanics of spinal injury. J Bone Jt Surg. 1960;42(B):810–23.

Rowland JW, Hawryluk GW, Kwon B, et al. Current status of acute spinal cord injury pathophysiology and emerging therapies: promise on the horizon. Neurosurg Focus. 2008;25:E2.

Sayadi JJ, Sayadi L, Satteson E, et al. Nerve injury and repair in a ketogenic milieu: a systematic review of traumatic injuries to the spinal cord and peripheral nervous tissue. PLoS One. 2021;16:e0244244.

Standring S, editor. Gray's anatomy. 41st ed. London: Elsevier; 2016.

Steinmetz MP, Benzel EC. Benzel's spine surgery. Techniques, complication avoidance, and management. 4th ed. Philadelphia: Elsevier; 2017.

Tan BT, Jiang H, Moulson AJ, et al. Neuroprotective effects of a ketogenic diet in combination with exogenous ketone salts following acute spinal cord injury. Neural Regen Res. 2020;15:1912–9.

Veyrat-Durebex C, Reynier P, Procaccio V, et al. How can a ketogenic diet improve motor function? Front Mol Neurosci. 2018;11:15.

Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part I. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976.

White AA, Panjabi MM. Clinical biomechanics of the spine. 2nd ed. Philadelphia: Lippincott; 1990.

Wilberger JE, editor. Spinal cord injuries in children. New York: Futura Publishing Company; 1986.

Wilson JR, Forgione N, Fehlings MG. Emerging therapies for acute traumatic spinal cord injury. CMAJ. 2013;185:485–92.

Yoganandan N, Arun MWJ, Dickman CA, et al. Practical anatomy and fundamental biomechanics. In: Steimetz MP, Benzel EC, editors. Benzel's spine surgery. 4th ed. Philadelphia: Elsevier; 2017.

Yoganandan N, Arun MWJ, Dickman CA, et al. Practical anatomy and fundamental biomechanics. In: Steimetz MP, editor. Benzel's spine surgery. 5th ed. Philadelphia: Elsevier; 2022.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.

Benzel EC. Biomechanics of spine stabilization. 3rd ed. New York: Thieme; 2015.

Buchanan LE, Nawoczenski DA, editors. Spinal cord injury-concepts and management approaches. Baltimore: Williams & Wilkins; 1987.

Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.

Eagler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.

Garfin SR, Eismont FJ, Bell GR, et al. Rothman-Simeone and Herkowitz's the spine. 7th ed. Philadelphia: Elsevier; 2018.

Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.

Lee BY, Ostrander LE, editors. The spinal cord injured patient. 2nd ed. New York: Demos; 2002.

Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.

Patten J. Neurological differential diagnosis. 2nd ed. London: Springer; 1996.

Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.

Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.

Wilberger JE, editor. Spinal cord injuries in children. New York: Futura Publishing Company; 1986.

Traumatic Spine Fractures

7

Almost all traumatic spinal cord injuries, except for spinal cord injury without radiographic abnormality (SCIWORA) or spinal cord injury without radiologic evidence of trauma (SCIWORET), involve spinal fractures around the epicenter of the spinal cord injury. Therefore, understanding the mechanism and classification of spinal fractures is very important for predicting the severity and neurological symptoms of spinal cord injury and understanding the related symptoms. A typical mechanism of mechanical injury that causes spinal fractures is the four loads of flexion, extension, rotation, and compression. A more complicated movement with combinations of the basic four external loads leads to fractures (Breig and el-Nadi 1966). These fractures and dislocations of the spine due to these external forces, along with damage to the blood vessels, spinal cord blood flow, and ligaments, lead to various clinical symptoms and consequences (Breig et al. 1966). As a result, secondary spinal cord damage is caused by concussion, contusion or compression, dislocation, distraction, and laceration.

Table 7.1 Summary of loads and fractures on the spine

Primary loading	Injury mechanism	Spinal injury
Flexion	Diving injury, motorcycle injury	• Bilateral facet dislocation • Anterior wedge fracture • Flexion teardrop fracture • Anterior dislocation • Clay-Shoveler fracture
Extension	Fall of elderly person Hyperextension injury in a car accident	• Hangman's fracture • Hyperextension fracture-dislocation • Laminar fracture
Axial compression	Fall onto head or feet	• Jefferson fracture of atlas • Burst fracture • Uncinate process fracture
Flexion-rotation	Car rollover accident	• Unilateral facet dislocation
Flexion-distraction	Seat-belt injury	• Chance fracture

7.1 Classification of the Spinal Fractures by Injury Mechanisms

The basic load of the mechanical injury mechanism described above, and the combination of these basic loads, is the injury mechanism caused by the force applied to the vertebrae and the resulting vertebral fracture (Table 7.1).

H.-Y. Ko, *Management and Rehabilitation of Spinal Cord Injuries*,
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7.1.1 Flexion Injuries

Diving injuries in shallow water or damage due to motorcycle accidents are examples of the flexion injuries. These injuries are caused by bilateral facet dislocation, anterior wedge fracture, flexion teardrop fracture, anterior dislocation, and Clay-Shoveler's fracture. Bilateral facet dislocations are considered to be locked facets in the form of a leapfrog in which the facet joint surface is dislocated or the upper facet joint surface of the lower vertebra is protruded. When the upper and lower vertebrae are dislocated more than 50%, this is called bilateral facet dislocation. This suggests that both the anterior longitudinal ligament and posterior longitudinal ligament and the facet joints are damaged. Anterior wedge fracture is often a stable fracture, and compression fracture of more than 50% is accompanied by posterior longitudinal ligament injury and flexion instability (White et al. 1976). In the case of a flexion teardrop fracture, it occurs most commonly in C2 and occurs often in the lower anterior vertebral body. In this case, the visible fracture seems to be mild but may be accompanied by severe ligament injury and the entire vertebral body may be pushed back to the spinal canal causing severe spinal cord injury. A Clay-Shoveler's fracture is an avulsion fracture of the spinous process of the lower cervical vertebrae and is a stable fracture.

7.1.2 Extension Injuries

This is a common form of damage that occurs when the head hits a window in the event of a car accident or when the elderly person falls from the floor and hits the chin or forehead first. Hyperextension fractures due to hyperextension, dislocation of vertebral bodies and folds of the posterior longitudinal ligament, or spinal cord injury may occur. In this case, spinal cord injuries are more likely to occur as a central spinal cord syndrome. A hangman's fracture is due to bilateral fractures of the pars interarticularis of C2. Fortunately, spinal cord injury can be minor because of the large diameter of the spinal canal at this level. In the case of extension teardrop fracture, unlike flexion teardrop fracture which often involves C2, it occurs in the lower cervical spines, and the fracture site is located at the upper part of the vertebral body. Other extension injuries may cause damage to the lamina fracture or widening of the anterior aspect of the disc with no facet dislocation (Fig. 7.1).

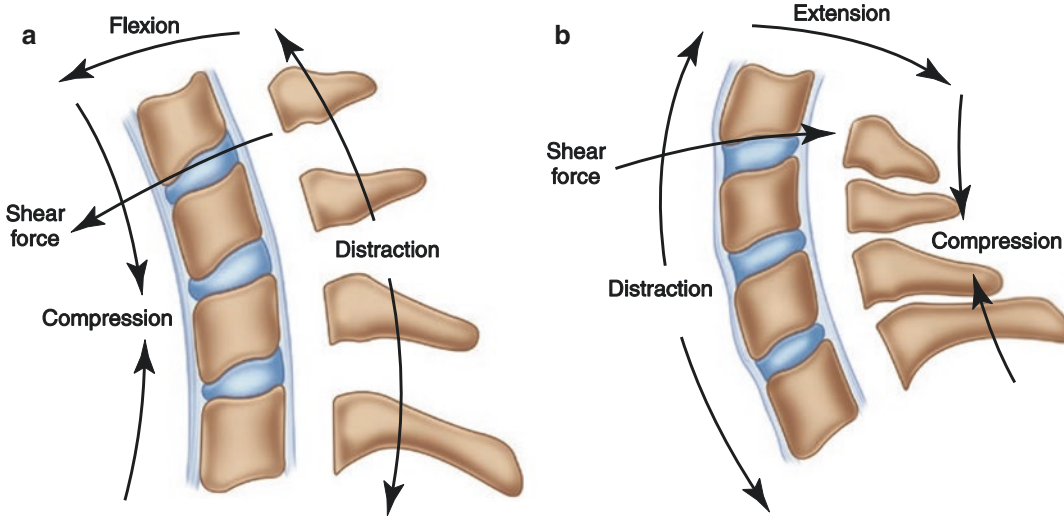

Fig. 7.1 Basic spinal load leading to spine fracture. (**a**) Flexion causes anterior compression and backward distraction load. (**b**) Extension causes compression and load to be reversed, and opposite shear force is generated. From Holtz and Levi (2010)

7.1.3 Axial Compression

Spinal fracture due to axial compression appears in the form of a Jefferson fracture or burst fracture. Jefferson fracture is the fracture of C1, which is an injury to the anterior and posterior arches. If the transverse ligament is not damaged, there is usually no neurological symptoms or instability (Fielding et al. 1974). An open-mouth view or CT showing a widening of more than 7 mm between C1 and C2 indicates the transverse ligament damage. The burst fracture is the most common fracture in T12 or L1 and is more likely to occur in C5 in the cervical spine.

7.1.4 Flexion-Rotation Injuries

An example is damage caused by rolling a car accident. This is a type of unilateral facet dislocation and shows a malalignment in the lateral X-ray film. It is usually a stable fracture and causes incomplete spinal cord injury or nerve root injury.

7.1.5 Flexion-Distraction Injuries

Chance fractures are typical fractures caused by flexion-distraction injuries. It is an unstable fracture parallel to the vertebral body in L1 and L2, usually accompanied by abdominal injuries.

7.1.6 Other Injuries

Other causes include odontoid fracture, atlantoaxial instability, and uncinate process fracture due to lateral flexion injury. The odontoid fractures are classified into three types according to the fracture site. Type 2 fractures are the most unstable and most likely to have nonunion. If the distance between C1 and C2 is more than 3 mm in adults and 5 mm or more in children, atlantoaxial instability is considered to be present (Jackson et al. 2002).

Spinal cord injury due to rotational or torsional injury can result in death or brain damage if injury to the carotid and vertebral artery occurs. The carotid artery can be compressed by the lower cervical vertebrae and the upper thoracic vertebrae or the internal carotid artery adjacent to the carotid tubercle on the C1 level. The vertebral artery enters the transverse foramen directly from the subclavian artery or the aortic arch and enters the foramen magnum under the occipital condyle at C1. Excessive rotation, flexion, or extension stress can cause the vertebral artery to be pulled or squeezed causing cerebral ischemic injury (Shedid and Benzel 2007). Although vertebral artery lesions are common in the C6 region, it may occur in the occipital condyle region.

7.2 Spine Stability

The stability of the vertebrae should consider anatomical abnormalities and clinical symptoms, but the stability of vertebral fractures is not clearly defined. In general, a stable state is defined as a state in which no progress of deformation or deterioration of neurological symptoms over time is observed. The fracture stability of the occipital condyle, atlas, and axis is determined by the pattern of fracture. Spine stability of fractures of the lower cervical spine (C3 to C7) can be assessed according to the criteria described by White and Panjabi (White and Punjabi 1987). Stability defined by White and Panjabi is the ability of the spine to maintain structural form without pain, deformity, or neurologic deficit under normal physiological loads. This system requires evaluation of translation and angulation in cervical flexion and extension films. Relative sagittal plane translation of 3.5 mm and relative sagittal plane angulation of 11 degrees or more are related to instability based on two-column spine concept (Panjabi et al. 1975; Steinmetz and Benzel 2017; White and Punjabi 1987) (Fig. 7.2 and Table 7.2).

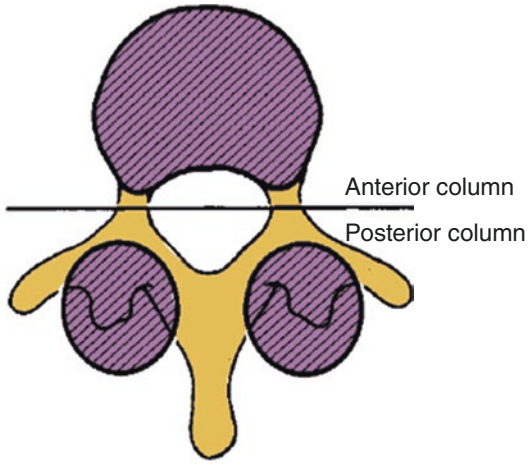

Fig. 7.2 Two-column spine concept (Louis concept). The concept described by Louis assigns significance to the vertebral body and the facet joint complex (lateral masses) on either side of the dorsal spine. From Steinmetz and Benzel (2017), with permission

Table 7.2 Clinical instability of thoracolumbar spine injuries

Injury	Score
Anterior element disruption	2
Posterior element disruption	2
Sagittal translation >2.5 mm	2
Rotation > 5°	2
Damage to spinal cord or cauda equina	2
Costovertebral disruption	1
Anticipated dangerous loading	1

A score >5 indicates instability
From White and Punjabi (1987)

The stability of thoracic and lumbar injuries is assessed using Denis's three-column model. The anterior column consists of the anterior longitudinal ligament, anterior vertebral body, and anterior annulus fibrosus. The middle column consists of the posterior vertebral body, posterior annulus fibrosus, and posterior longitudinal ligament. The posterior column includes the spinous process, laminae, facets, pedicles, and posterior ligamentous structures. If only one column is damaged, the fractures are stable. If two or more columns are compromised, the spine is considered unstable. The Denis classification of vertebral fractures is not suitable for cervical vertebral fractures, but may be used to determine the stability of lower cervical vertebral fractures (Fig. 7.3).

7.3 Fractures in the Upper Cervical Spines (Occipitocervical Junction)

The cervical spine region differs from the thoracolumbar region in that the upper and lower cervical spine show different injury patterns and mechanisms. The upper cervical spine, i.e., occipitocervical junction, consists of the occipital bone/condyles (C0), C1, C2, and the associated ligamentous, muscular, neural, and vascular structures. In the cervical spine classification system, injuries to the upper cervical injuries are defined as fractures that occur in the occipital, C1, and C2 regions.

7.3.1 Occipital Condyle Injuries

Occipital condyle (C0) fractures generally occur with axial trauma and are almost always unilateral (>90%). Occipital condyle injuries are rare and can be classified into three groups (Anderson–Montesano classification) (Anderson and Montesano 1988) (Fig. 7.4). Type I injuries are a burst-type impaction fracture of the condyle related to an axial loading. Type II injuries are associated with occipital basal skull fractures. Type III injuries are secondary to violent lateral or rotational forces and are associated with avulsion fracture of the alar ligament (Anderson and D'Alonzo 1974). Type 1 and type 2 fractures are stable and can be treated with a cervical orthosis (Philadelphia or SOMI). Type III injuries are a potentially unstable fracture and should be considered surgery or rigid immobilization in a halo vest.

7.3.2 Occiput-C1 Injury

This injury rarely develops clinically and is usually fatal due to injury to the medulla oblongata or spinomedullary junction. Survival of this injury has been reported in varying degrees of neurological deficit. Displacement can occur anteriorly or dislocation of C1 and C2 in the opposite direction (Menezes and Traynelis 2008). If patient survives the injury, treatment with

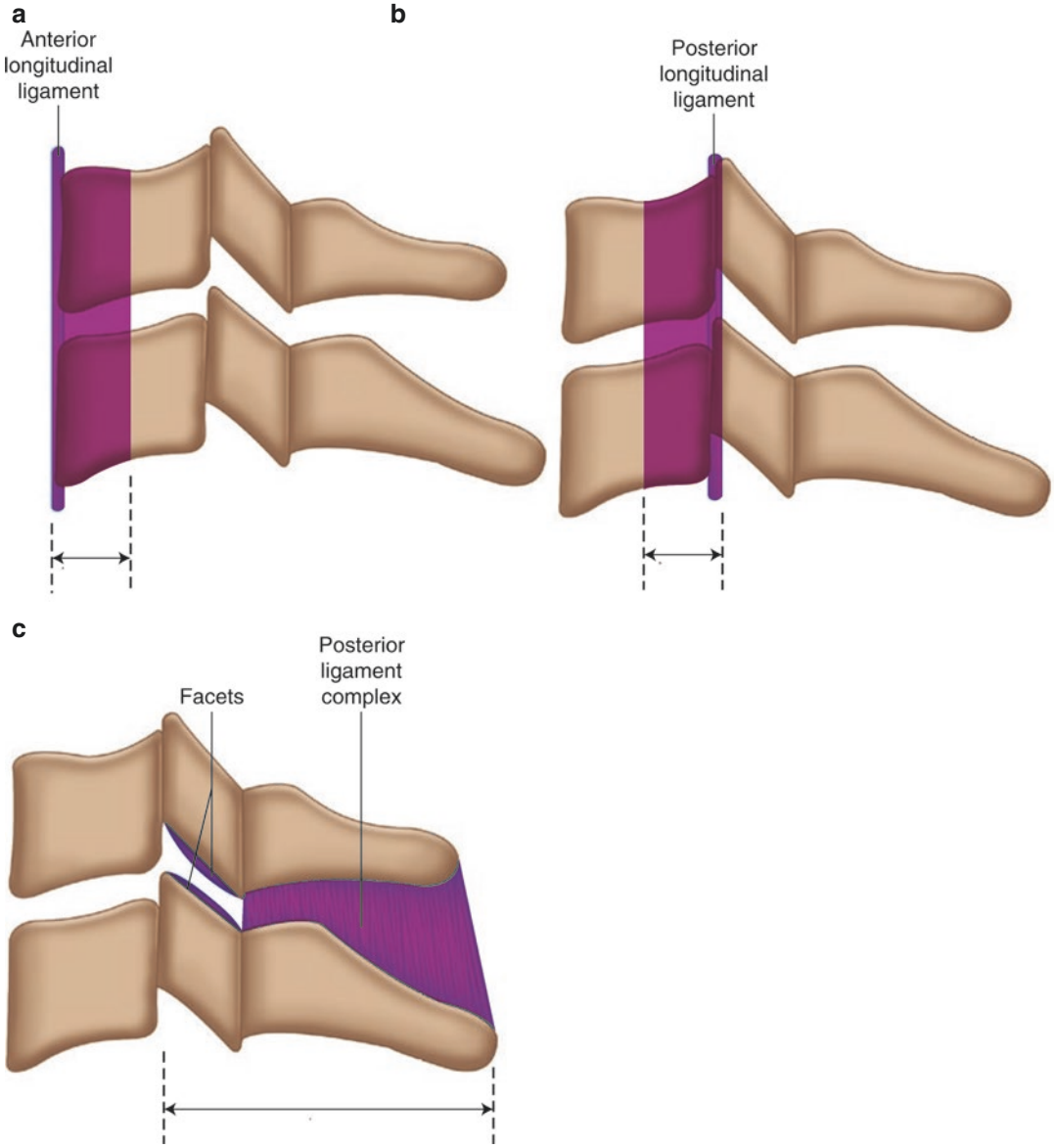

Fig. 7.3 Three-column spine concept: (**a**) anterior column, (**b**) middle column, and (**c**) posterior column. Denis's three-column concept assigns significance to the region of the neural axis and the integrity of the posterior vertebral body wall (middle column). From Holtz and Levi (2010) and Steinmetz and Benzel (2017)

internal fixation and fusion is recommended. Traction for occiput-C1 dislocation is not recommended because of the high risk of neurological deterioration.

7.3.3 C1 Fracture

Isolated C1 fractures occur with axial trauma with or without lateral bending (Hadley et al. 1988). Fracture of the posterior arch of C1 is the most common fracture of C1. The fractures occur just posterior to the lateral masses of the thinnest part of the bone. This part of the C1 ring has the least cross-sectional inertia against a vertical compression force. This fracture is usually diagnosed by a high-quality lateral radiography of the C1. This fracture is stable and is treated with orthotic immobilization until the fracture heals.

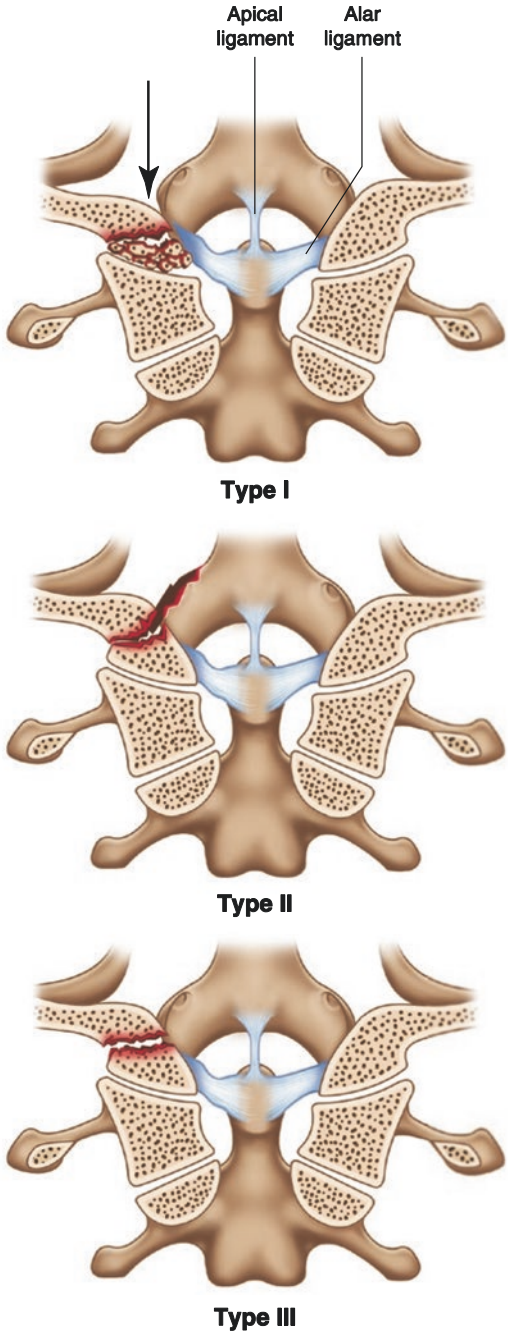

Fig. 7.4 Occipital condyle fractures. Type I, II, III. From Holtz and Levi (2010)

Hyperextension force or axial load applied to the top of the head and transferred through the condyles of the occiput can fracture the ring of the C1. This is known as a Jefferson fracture. Jefferson burst fractures of C1 result from injuring forces of relatively high magnitude directed caudally. The lateral masses of C1 are separated by the occipital condyles. The classic fracture pattern of a Jefferson fracture consists of two fractures of the anterior ring and two posterior, i.e., four-part fractures of bilateral anterior and posterior ring fractures (Fig. 7.5). However, most commonly, there is one anterior fracture and one posterior fracture. The main radiographic feature of this injury is that the lateral masses of C1 are spread on the open-mouth view. The assessment of these injuries is focused on evaluating the integrity of the transverse ligament (transverse cruciate ligament). If this spread exceeds 7 mm, the transverse ligament is most likely ruptured with resultant C1–C2 instability (Spence et al. 1970). Treatment of C1 burst fracture depends on the degree of displacement. Displacement less than 5 mm can be treated with orthotic protection until healed. If there is a significant displacement, reduction with halo traction is indicated. This traction is continued up to 6 to 8 weeks until early healing occurs. Neurologic injury in C1 fractures is rare.

7.3.4 C1–C2 Dislocation

Traumatic displacement of C1 on C2 may be anterior or posterior or rotational subluxation. The primary restraint of anterior displacement is the transverse ligament between tubercles on the lateral masses of the atlas. The alar ligaments serve as secondary restraints. Experimentally anterior subluxation of C1 on C2 is produced by a force of 84 kg rupturing the transverse ligament (Fielding et al. 1974). If this is not visible on static lateral films, it can usually be detected on flexion-extension films, although initial spasm of the cervical musculature can lead to a false-negative examination. Mild displacement of less than 5 mm indicates a stretch injury of the transverse ligament. Rupture of the transverse ligament is complete at a displacement of 5–10 mm. The transverse ligament rupture of C1

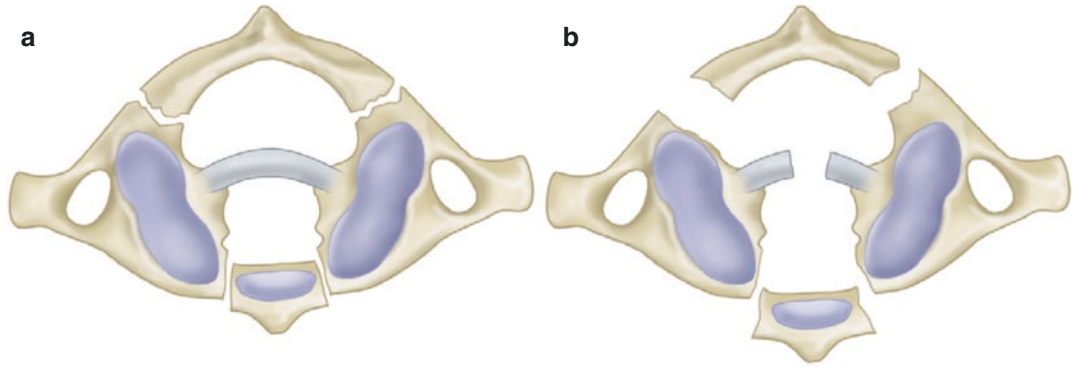

Fig. 7.5 Jefferson burst fracture of C1. The classic fracture pattern consists of two fractures of the ring anteriorly and two posteriorly. (**a**) Axial view of stable Jefferson fracture (intact transverse ligament). (**b**) Axial view of unstable Jefferson fracture (ruptured transverse ligament). From Williams (2021), with permission

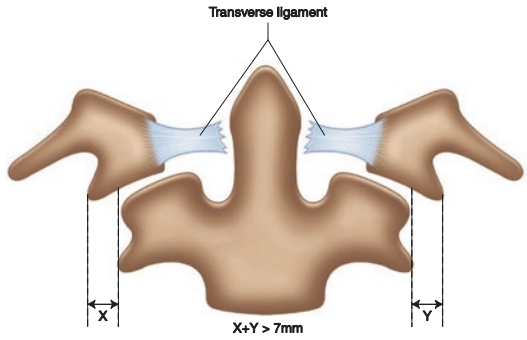

Fig. 7.6 C1–C2 overhang relationship illustrating Spence's rule. Spence's rule suggests the loss of integrity of the transverse ligament if combined overlap of lateral masses more than 7 mm on open-mouth view. From Holtz and Levi (2010)

is defined when the sum of the bilateral distance of displacement of the lateral mass of C1 (Spence distance) is more than 7 mm (Spence et al. 1970) (Fig. 7.6). A displacement of 10 mm or more means that the entire ligament complex is disrupted. This degree of displacement is at a high risk of spinal cord injury. Treatment of this lesion usually requires surgical stabilization and fusion. Orthotic immobilization does not result in stabilization of the C1–C2 complex. This injury more common in the elderly may not be recognized after minor injury until clinical symptoms of chronic myelopathy occur (Sweeney 1995).

7.3.5 Odontoid Fracture (Dens Fracture)

Fractures of the C2 odontoid are caused by a combination of shear and compression loads and can result from a blow to the back of the head. Odontoid fractures are the most common cervical fractures in patients older than 70 years and account for 10–15% of all fractures of the cervical spine (Ryan and Henderson 1992). Odontoid process fractures of C2 typically occur in two groups: in the young as a result of high-energy trauma such as a motor vehicle accident and less commonly in the elderly as the result of falls. Odontoid fractures usually present with muscle spasms and suboccipital pain, and sometimes there is pain in the distribution of the greater occipital nerve. Fortunately, the neural canal at the C1–C2 level is the most capacious of the entire cervical spine, with a low incidence of neurological injury. The majority of these patients are neurologically intact, and up to 20% will exhibit a variety of motor and/or sensory deficits including high tetraplegia. The open-mouth view shows most odontoid fractures.

Anderson and D'Alonzo classified odontoid fractures into three types (Anderson and D'Alonzo 1974) (Fig. 7.7). Type I is an oblique avulsion fracture of the upper portion of the dens. Stability of the motion segment is not disturbed because

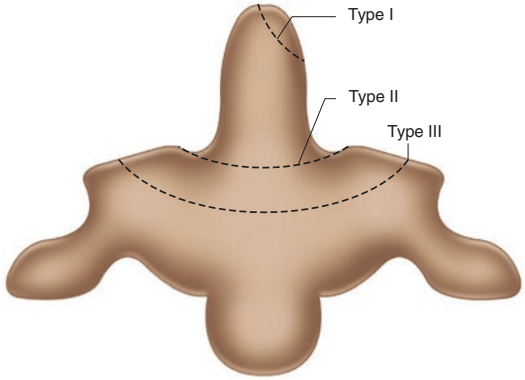

Fig. 7.7 Odontoid fracture. Type II fracture occurs at the junction of the dens is most common odontoid fracture. The fracture interrupts the blood supply to the dens, with significant risk of nonunion. From Wilberger (1986), with permission

the transverse ligament and alar ligaments are not damaged. Treatment uses a rigid cervical orthosis, such as Philadelphia collar. The type II fracture occurs at the junction of the dens with the vertebral body of the axis. This is the most common odontoid fracture, accounting for 60% of odontoid fractures, and the most difficult to treat (Karlstrom and Olerud 1987). Anterior displacement is clinically more common. Because the fracture interrupts the blood supply to the dens, there is a significant risk of nonunion that increases with age. Nonunion occurs in 30–50% in the elderly and those with significant displacement: angulation of more than 10° or translation of more than 5 mm. If the displacement is greater than 4 mm in patients older than 50 years, stabilization surgery by screw fixation is recommended (Karlstrom and Olerud 1987). Type III fractures occur through the body of the axis at the base of the dens, allowing the atlas and the occiput to move as a unit. These fractures are usually mildly displaced and once it is reduced, it is stabled.

7.3.6 Traumatic Spondylolisthesis of the Axis

C2 spondylolisthesis is commonly referred to as a "hangman's fracture," which is the fracture of the C2 through bilateral fractures of the pars interarticularis separating the anterior and posterior elements. The use of the submental knots results in an extension-distraction type injury with disruption of the C2–C3 disc and transection of the cord. This injury most commonly occurs as a result of a motor vehicle accident. The major injury vector is usually extension without significant distraction. The injury force produces an extension moment on the dens and body with a balancing joint reaction force at the C2–C3 joint, and breakage occurs at the pars interarticularis due to the relatively low area moment of inertia to bending in the sagittal plane. Neurological injury is rare because spinal canal is actually widened from this injury.

There are numerous classification systems for a hangman's fracture. Levine and Edwards's classification is most widely used for traumatic spondylolisthesis of the axis (Fig. 7.8). Type I fractures, the most common injury type, are fractures with no angulation and displacement less than 3 mm between the posterior cortex of the dens and the posterior cortex of the C3 vertebral body. This is considered a stable fracture. Type II fractures are fractures with significant translation (>3 mm) and angulation (>10°) of C2 with respect to C3. Also seen is anterior displacement of the C2 body with disruption and asymmetrical widening of the C2–C3 disc space. The posterior longitudinal ligament is disrupted, whereas the anterior longitudinal ligament usually intact. This is considered unstable. A subset of these fractures involves a distraction component with flexion angulation of the C2–C3 disc (type IIa), with less displaced <3 mm and more angulated. Type III fractures are additionally comprised of bilateral pars interarticularis fracture as well as bilateral C2–C3 facet dislocations. The management of hangman's fractures is nonsurgical and has a high success rate. Surgical care is recommended if there is angulation or instability (Jackson et al. 2002).

7.4 Fractures of the Subaxial Cervical Spine (C3–C7)

The subaxial cervical spine consists of the C3–7 vertebrae. Many systems have been proposed to classify traumatic subaxial cervical spine inju-

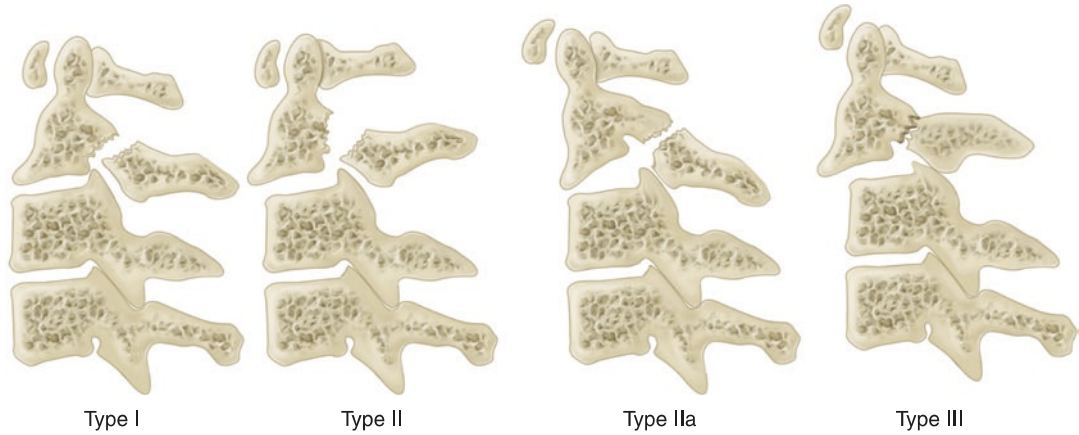

Fig. 7.8 Hangman fracture (Levin and Edwards classification). From Williams (2021), with permission

Table 7.3 Subaxial injury classification (SLIC) scale

	Points
Morphology	
No abnormality	0
Compression + burst	1 + 1 = 2
Distraction (e.g., facet perch, hyperextension)	3
Rotatimi or translation (e.g., facet dislocation, unstable teardrop or advanced staged flexion compression injury)	4
Discoligamentous complex	
Intact	0
Indeterminate (e.g., isolated interspinous widening, MRI signal change only)	1
Disrupted (e.g., widening of anterior disk space, facet perch or dislocation)	2
Neurological status	
Intact	0
Root injury	1
Complete cord injury	2
Incomplete cord injury	3
Continuous cord compression (neuro modifier in the setting of a neurologic deficit)	+ 1

From Dvorak et al. (2007)

ries. The subaxial region of the cervical spine accounts for about 65% of all cervical spine injuries and most cervical spinal cord injuries. The old classification and descriptions that Magerl used for the thoracolumbar spine were conventionally adopted to describe cervical spine fractures (Magerl et al. 1994). The most modern systems are the Subaxial Cervical Spine Injury Classification (SLIC) system and the AOSpine classification. However, there is currently no generally accepted classification system for subaxial cervical spine injuries. The Magerl classification is primarily based on the pathomorphological uniformity (Magerl et al. 1994). According to the SLIC system, the injury morphology is classified as follows: 0, no abnormality; 1, compression fracture; 2, burst fracture; 3, distraction injury; and 4, translation injury. The SLIC scoring system grades discoligamentous complex integrity as: 0, intact; 1, indeterminate; and 2, disrupted. Finally, neurological status is defined as: 0, intact; 1, nerve root injury; 2, complete spinal cord injury; 3, incomplete spinal cord injury; and +1, persistent cord compression (Dvorak et al. 2007) (Table 7.3). An increasing score within each category is intended to reflect

increasingly severe injury. Injuries which score 5 or more points on SLIC scale are all treated surgically, whereas those scoring 3 or less are treated nonsurgically. Conservative treatment with a Philadelphia collar is recommended for patients with a total score of 1–3 (Momin et al. 2022). A score of 4 is considered equivocal. The AOSpine Classification Systems (subaxial and thoracolumbar) were developed to improve morphology-based classification systems with the goal of facilitating communication in clinical and research settings (Mushlin et al. 2019; Vaccaro et al. 2016). The classification system describes injuries based on four criteria: (1) morphology of the fracture, (2) neurological status, (3) clinical modifiers, and (4) facet joint injury (only valid for cervical subaxial classification). Injuries are described by their level, followed by the morphologic type of the primary injury. The secondary injuries and modifiers are placed in parentheses (facet injury, neurologic status, and case-specific modifiers) (Schnake et al. 2017; Vaccaro et al. 2016).

The principal movements of the subaxial spine are flexion and extension. The vertebral artery enters the transverse foramen at C6 in 90% of the population and travels up the subaxial cervical spine (Aebi 2010). The cervical spines can be functionally divided into anterior and posterior columns (Panjabi et al. 1975). The anterior column consists of the anterior longitudinal ligament, the vertebral body or intervertebral disc, and the posterior longitudinal ligament. The posterior column consists of the structures located posterior to the posterior longitudinal ligament: the facet joints, the vertebral arch, and the spinous processes with the interspinous ligament. This concept is useful to describe the lower cervical spine injury mechanism. Based on this, Allen and colleagues developed a comprehensive classification system in 1982 (Allen et al. 1982). This system consists of six major injury types based on the association of specific morphological fracture patterns with specific direction of force exerted to the cervical spinal column: compressive flexion, vertical compression, distractive flexion, compressive extension, distractive extension, and lateral flexion. The usefulness of such a system is that the injury of a particular patten acts in a biologically predictable fashion to allow for a more accurate treatment plan. In thoracolumbar spine injuries, a three-column concept of spine injury was originally proposed. This concept can also be applied to the subaxial cervical spine (Sundgren et al. 2007) (Table 7.4).

Table 7.4 Column theory of spine construction and stability

Two-column theory (Holdsworth)	Three-column theory (Denis)
Anterior column Anterior vertebral body Anterior longitudinal ligament Anterior annulus fibrosus	Same
	Middle column Posterior longitudinal ligament Posterior annulus fibrosus Posterior vertebral body wall
Posterior bone-ligament complex Posterior laminar arch Supraspinous ligament Infraspinous ligament Posterior lateral capsule Ligamentum flavum	Same

Disruption of any two indicates instability

7.4.1 Compression Injuries

7.4.1.1 Flexion-Compression Injuries

This injury is the result of caudally and anteriorly directed major injury vector. Flexion-compression injuries range from minor wedging of the anterior superior vertebral body end plate to severe collapse and retropulsion of the vertebral body with facet joint distraction and posterior ligamen-

tous disruption. Compressive fractures without facet fracture or subluxation are usually stable injuries. Higher stages of injury involve increased ventral osseous and dorsal ligamentous injury and may be unstable. Treatment of more unstable injuries depends on the neurological status of the patient. Neurologically intact injuries can be treated with a halo vest. If the lesion is unstable after 3 months of injury, surgical fusion should be considered (Stauffer 1986).

7.4.1.2 Extension-Compression Injuries

The major injury vector is axial compression with the spine in extension, resulting in unilateral or bilateral fractures of posterior structures including laminae, pedicles, or facet joints.

7.4.1.3 Vertical Compression Injuries

The main injury vector is directed caudally and causes mainly anterior column disruption. Compressive failure of the entire vertebral body results in a typical burst fracture caused by an axial loading mechanism. Bone fragments are often displaced posteriorly into the spinal canal. If there is component of extension, there may be associated with vertebral arch fracture.

7.4.2 Distraction Injuries

7.4.2.1 Flexion-Distraction Injuries

This type of injuries are the most common subtype of subaxial cervical fractures. The common features of this group is the tension-shear failure of the posterior column, usually the ligamentous complex. Typically there is little bony injury with exception of a minor compression failure of the caudal vertebral segment. However, there is severe ligamentous damage affecting the dorsal facet capsule complex, ligamentum flavum, and interspinous ligaments, as well as injury to the posterior longitudinal ligament and intervertebral disc. A significant number of patients with this injury also have an associated closed head injury. The major vector is the distraction with a minor injury vector of flexion. The injuries of distraction flexion result from hypertension sprain to bilateral facet dislocations.

7.4.2.2 Extension-Distraction Injuries

This injury has a major injury vector of axial distraction with the spine postured in extension. This injury typically manifests in the anterior splaying or fish-mouthing of the intervertebral disc space associated with the anterior longitudinal ligament disruption. The presence of a ventral avulsion fracture resulting from an avulsion of the anterior longitudinal ligament may provide a clue to this injury type. Distractive extension injuries are commonly associated with neurologic impairment. The most common associated neurological injury is a central cord syndrome. The bony ligamentous injury is usually stable and will heal with immobilization.

7.4.3 Lateral Flexion

This group of injuries has a major injury vector of axial compression, but is offset laterally to lateral bending. Lateral flexion injuries are secondary to asymmetrical compressive loading resulting in unilateral vertebral body compression failure and ipsilateral dorsal arch fracture. Lateral flexion injuries are very rare injuries and may be associated with a unilateral traction injury to the brachial plexus.

7.5 Spinous Process Fracture (Clay-Shoveler's Fracture)

The name of this cervical spine fracture is derived from an injury occurring in Australian clay miners in which the head and neck are abruptly pulled into hyperflexion when they attempt to throw a shovel full of clay from the mine floor. The clay-shoveler's fracture is an oblique fracture of the base of the spinous process of the C6, C7, or T1. This avulsion fracture is caused by abrupt forced flexion of the head and upper cervical spines combined with a heavy upper body and lower neck muscular contraction, which results in overstretching or controlling action of the supraspinous and interspinous ligaments. This fracture is stable because the posterior ligamentous structures are not damaged. The clay-

shoveler's fracture is usually mimicked by unfused apophyses that have a smooth and well-corticated margins.

7.6 Fractures of the Thoracolumbar Spines

Thoracolumbar injuries generally result from high-energy trauma, including motor vehicle collisions and gunshot wounds. However, low-energy trauma is the leading cause of thoracolumbar injuries in the elderly as osteoporosis makes this population vulnerable to injuries from falls. There are three biomechanical zones in the thoracolumbar spine. The T1–T8 region is relatively rigid and is fixed by the rib cage. The region from T9 to L2 that serves as a transition between immobile and mobile regions is the most trauma-vulnerable thoracolumbar spine. From L3 to the sacrum, the spine is very mobile and prone to injury (Anand et al. 2006).

Several classification systems have been proposed. Holdsworth categorized thoracolumbar fractures according to the structural integrity of the vertebral column (Holdsworth 1970). The two-column biomechanical concept of the spine, which emphasizes the anterior column and the posterior ligamentous complex, was subsequently modified by Denis with a third column and the middle column (Denis 1983). This biomechanical model of the spine includes the anterior column (anterior vertebral body, anterior longitudinal ligament, and anterior annulus fibrosus), the middle column (posterior vertebral body, posterior longitudinal ligament, and posterior annulus fibrosus), and the posterior column (posterior elements and posterior spinal ligaments) (Magerl et al. 1994). Injury to any two of the three columns creates an unstable spine. Denis described and classified each fracture type according to the status of each of the three columns (Anand et al. 2006) (Table 7.5). The classification systems most frequently used today for thoracolumbar injury are the Denis three-column system, the Margerl System, the Thoracolumbar Injury Classification System (TLICS), and, most recently, the AOSpine Thoracolumbar Spine Injury Classification System (Momin et al. 2022). The AOSpine system is based on fracture morphology, with more severe injuries progressing from type A to type C with subtypes 1–3 within each type of injury (Fig. 7.9).

Table 7.5 Denis three-column fracture classification

Fracture type	Injured column
1 Compression fracture	Anterior column compression
2 Burst fracture Type A: fracture of both endplates Type B: fracture of the upper endplate Type C: fracture of the lower endplate Type D: burst fracture with rotation Type E: lateral burst fracture	Anterior and middle column injury
3 Seat-belt type injuries Type A: one-level damage Type B: two-level damage	Middle and posterior column injuries
4 Fracture-dislocation injuries Type A: flexion-rotation type Type B: shear type Type C: flexion-distraction type	Anterior, middle, and posterior column injuries

The classification and description of thoracolumbar spine fractures below are based on the Denis three-column classification system. Denis describes four major types of thoracolumbar fractures: compression fracture, burst fracture, seatbelt-type injuries, and fracture-dislocations.

7.6.1 Compression Fractures

The anterior column fails under axial load during anterior flexion of the spinal column. The height of the anterior vertebral body on a lateral film is lost, but the height of the posterior vertebral body that forms the middle column is maintained. There is no disruption of the posterior ligaments,

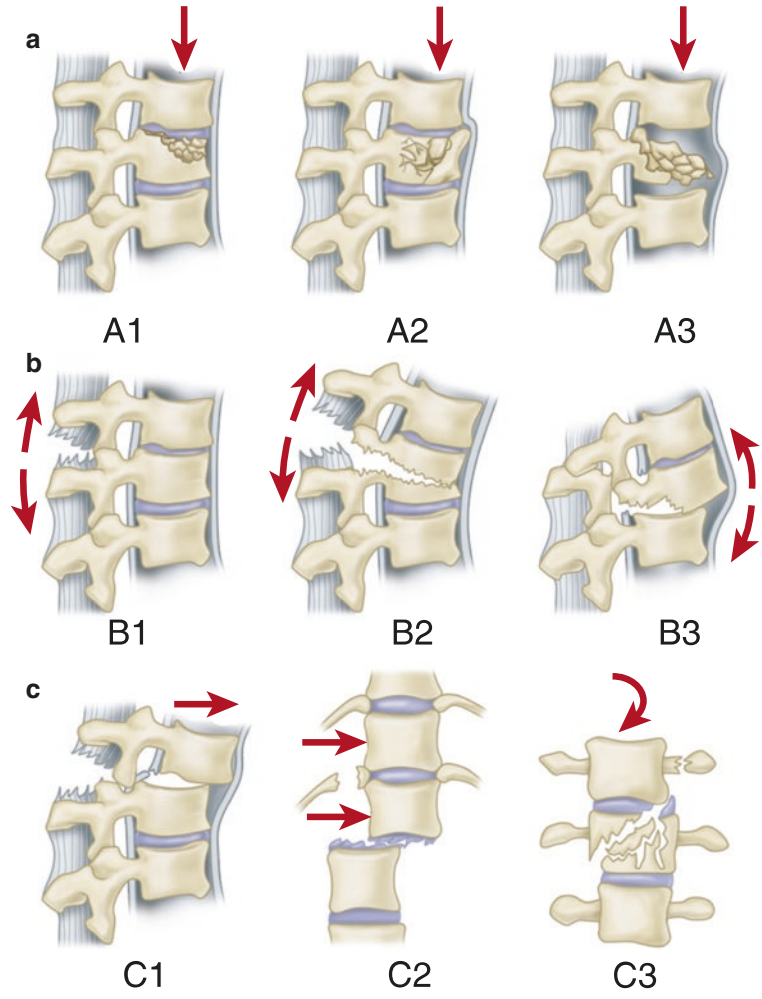

Fig. 7.9 AOSpine classification of spinal injuries. (**a**) Compression injuries: A1, impaction; A2, split; A3, burst. (**b**) Distraction injuries: B1, posterior ligamentous; B2, posterior osseous; B3, anterior through disc. (**c**) Torsion injuries: C1, type A with torsion; C2, type B with torsion; C3, torsion shear

and there is no increase in the distance between the spinous processes on the lateral X-ray.

7.6.2 Burst Fractures

These injuries result from axial loading of the spinal column with little or no spinal flexion. Both the anterior column and middle column fail under compression, the vertebral body bursts, usually propelling bone fragments posteriorly into the spinal canal. Posterior column is intact. The spinal canal is often compromised to varying degrees by the posteriorly displaced bone with or without neurological deficits. Correlation between the degree or canal stenosis has not been well established.

7.6.3 Flexion-Distraction (Seatbelt) Injuries

Holdsworth did not include this fracture type in the classification. This injury, also known as a Chance fracture, most often occurs by an automobile passenger restrained by a seatbelt (Fig. 7.10). Ecchymoses are common in the abdomen and there is a combination of intra-abdominal injury and spinal fracture, the so-called seatbelt syndrome. In seatbelt-type injuries, both the posterior and middle columns will distract from the tensile forces produced by flexion, and although the anterior column may compress under these forces. These fractures usually occur in the upper lumbar spine near the transition between the relatively mobile

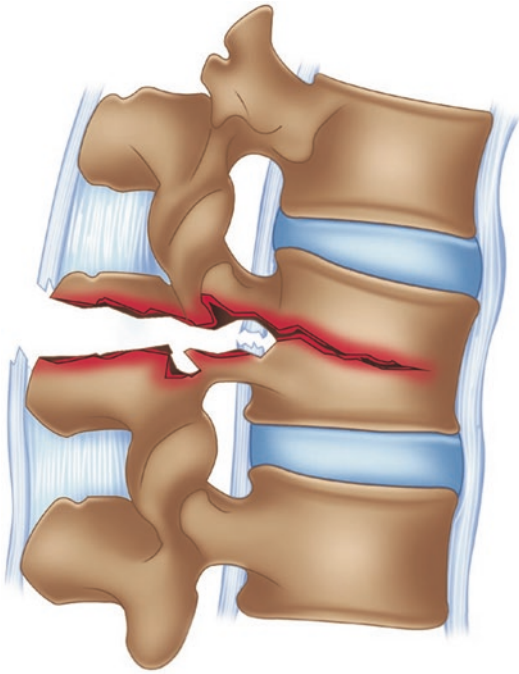

Fig. 7.10 Chance fracture. Horizontal split occurs through the spinous process, lamina, and vertebral body

lumbar spine and relatively inflexible thoracic spine stabilized by the thoracic cage. This injury may be osseous, passing through the vertebral body and posterior elements. Bony injuries are believed to be more stable than their soft tissue counterparts and are less likely to require surgical stabilization. Plain X-rays show little displacement but often show a fracture line that passes through the vertebral body and spinous process (Zhang et al. 2013).

7.6.4 Fracture-Dislocations

The presence of any significant anterior-posterior or lateral translation between adjacent vertebral bodies suggests fracture-dislocation. These are the most unstable thoracolumbar fractures and the most often associated with neurological injuries in 75% of cases. 52% of neurologically injured fracture-dislocation patients show complete paraplegia (Denis 1984). Biomechanically, it is characterized by failure of all three columns under compression, tension, rotation, shearing, or combinations, resulting in subluxation or dislocation.

References

Aebi M. Surgical treatment of upper, middle and lower cervical injuries and non-unions by anterior procedures. Eur Spine J. 2010;19(Suppl 1):S33–9.

Allen BL, Ferguson RL, Lehmann TR, et al. A mechanistic classification of closed, indirect fractures and dislocations of the lower cervical spine. Spine. 1982;7:1–27.

Anand N, Vaccaro AR, Kim MR, et al. Evolution of thoracolumbar trauma classification systems: assessing the conflict between mechanism and morphology of injury. Top Spinal Cord Inj Rehabil. 2006;12:70–8.

Anderson LD, D'Alonzo RT. Fractures of the odontoid process of the axis. J Bone Joint Surg. 1974;56-A:60–4.

Anderson PA, Montesano PX. Morphology and treatment of occipital condyle fracture. Spine. 1988;13:731–6.

Breig A, el-Nadi AF. Biomechanics of the cervical spinal cord. Relief of contact pressure on and overstretching of the spinal cord. Acta Radiol Diagn (Stockh). 1966;4:602–24.

Breig A, Turnbull I, Hassler O. Effects of mechanical stresses on the spinal cord in cervical spondylosis. A study on fresh cadaver material. J Neurosurg. 1966;25:45–56.

Denis F. The three-column spine and its significance in the classification of acute thoracolumbar spine injuries. Spine. 1983;8:817–31.

Denis F. Spinal instability as defined by the three-column spine concept in acute spinal trauma. Clin Orthop Relat Res. 1984;189:65–76.

Dvorak MF, Fisher CG, Fehlings MG, et al. The surgical approach to subaxial cervical spine injuries: an evidence-based algorithm based on the SLIC classification system. Spine (Phila Pa 1976). 2007;32:2620–9.

Fielding JW, Cochran GVB, Lansing JF III. Tears of the transverse ligament of the atlas: a clinical and biomechanical study. J Bone Joint Surg. 1974;56-A:1683–7.

Hadley MN, Dickman CA, Browner CM, et al. Acute traumatic atlas fractures: management and long-term outcome. Neurosurgery. 1988;23:31–5.

Holdsworth F. Fractures, dislocations and fracture-dislocation of the spine. J Bone Joint Surg. 1970;52-A:1534–51.

Holtz A, Levi R. Spinal cord injury. Oxford: Oxford University Press; 2010.

Jackson RS, Banit DM, Rhyne AL, et al. Upper cervical spine injuries. J Am Acad Orthop Surg. 2002;10:271–80.

Karlstrom G, Olerud S. Internal fixation of fractures and dislocations in the cervical spine. Orthpedics. 1987;51:496–9.

Magerl F, Aebi M, Gertzbem S, et al. A comprehensive classification of the thoracic and lumbar injuries. Eur Spine J. 1994;3:184–201.

Menezes AH, Traynelis VC. Anatomy and biomechanics of normal craniovertebral junction (a) and biomechanics of stabilization (b). Childs Nerv Syst. 2008;24:1091–100.

Momin E, Parmar V, Resnick DK. Subaxial cervical spine injuries. In: Steinmetz MP, Berven SH, Benzel EV, editors. Benzel's spine surgery. 5th ed. Philadelphia: Elsevier; 2022.

Mushlin H, Kole MJ, Chryssikos T, et al. AOSpine subaxial cervical spine injury classification system: the relationship between injury morphology, admission injury severity, and long-term neurologic outcome. World Neurosurg. 2019;130:e368–e74.

Panjabi MM, White AA III, Johnson RM. Cervical spine mechanics as a function of ligament transection. J Bone Joint Surg. 1975;57-A:582–5.

Ryan MD, Henderson JJ. The epidemiology of fractures and fracture-dislocations of the cervical spine. Injury. 1992;23:38–40.

Schnake KJ, Schroeder GD, Vaccaro AR, et al. AOSpine classification systems (subaxial, thoracolumbar). J Orthop Trauma. 2017;31(Suppl 4):S14–23.

Shedid D, Benzel EC. Cervical spondylosis anatomy: pathophysiology and biomechanics. Neurosurgery. 2007;60:S7–13.

Spence KF Jr, Decker J, Sell KW. Bursting atlantal fracture associated with rupture of the transverse ligament. J Bone Joint Surg. 1970;52-A:543–8.

Stauffer ES. Management of spine fractures C3-C7. Orthopaedic Clin North Am. 1986;17:45–53.

Steinmetz MP, Benzel EC. Benzel's spine surgery. 4th ed. Philadelphia: Elsevier; 2017.

Sundgren PC, Philipp M, Maly PV. Spinal trauma. Neuroimaging Clin N Am. 2007;17:73–85.

Sweeney PJ. Clinical evaluation of cervical radiculopathy and myelopathy. Neuroimaging Clin N Am. 1995;5:321–7.

Vaccaro AR, Koerner JD, Radcliff KE, et al. AOSpine subaxial cervical spine injury classification system. Eur Spine J. 2016;25:2173–84.

White AA 3rd, Punjabi M. Update on the evaluation of instability of the lower lumbar spine. Instr Course Lect. 1987;36:513–20.

White A, Southwick W, Punjabi M. Clinical instability in the lower cervical spine: a review of past and current concepts. Spine. 1976;1:15–27.

Wilberger JE, editor. Spinal cord injuries in children. New York: Futura Publishing Company; 1986.

Williams KD. Fractures, dislocations, and fracture-dislocations of the spine. In: Azar FM, Beaty JH, editors. Campbell's operative orthopaedics. 14th ed. Philadelphia: Elsevier; 2021.

Zhang S, Wadhwa R, Haydel J, et al. Spine and spinal cord trauma: diagnosis and management. Neurol Clin. 2013;31:183–206.

Recommended Additional Reading

American Spinal Injury Association. International standards for neurological classification of spinal cord injury. Revised 2019. Richmond: American Spinal Injury Association; 2019.

Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.

Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. Wolters Kluwer: New Delhi; 2015.

Eagler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker Inc.; 1998.

Garfin SR, Eismont FJ, Bell GR, et al. Rothman-Simeone and Herkowitz's the spine. 7th ed. Philadelphia: Elsevier; 2018.

Holtz A, Levi R. Spinal cord injury. Oxford: Oxford University Press; 2010.

Noback CR, Strominger NL, Demarest RJ, et al. The human nervous system: structure and function. 6th ed. Totowa: Humana Press; 2005.

Vaccaro AR, Fehlings MG, Dvorak MF, editors. Spine and spinal cord trauma. Evidence-based management. New York: Thieme Medical Publishers; 2011.

Wilberger JE, editor. Spinal cord injuries in children. New York: Futura Publishing Company; 1986.

8 Imaging Studies of Spinal Cord Injuries

The most critical tasks in spinal cord injury management are early detection of the spinal cord injuries, prevention of neurologic deterioration, optimization of initial medical management, correct interpretation of all the diagnostic evaluations, and provision of the most appropriate care (Williams 2021). Imaging plays an important role in assessing acute and chronic spinal cord injuries or lesions. The use of appropriate imaging technology is an important part of the diagnosis and management of spinal cord injuries. For an effective imaging study, the normal anatomy and characteristics of each imaging modality are relevant as a basis for understanding pathologic alteration. If a patient is seriously injured, damage to the spinal column or spinal cord should be suspected. The trauma of the spine or spinal cord should be considered with the expected injury mechanism. The treating physician should perform appropriate imaging as soon as it is done safely. As in other areas of medicine, imaging is based on history and physical examination (Laker and Concannon 2011). The mechanism of injury combined with the proposed clinical examination will determine the initial evaluation of the spinal column. The physician is equipped with both plain X-rays and computed tomography (CT) scans, which can be used to evaluate the bony spine, and these tools should be used to rule in or rule out spinal column injury (Hadley and Walters 2013). The purpose of imaging the bony spine with X-rays is to provide a quick overview of the regional bony anatomy and to guide additional imaging studies, such as CT or magnetic resonance imaging (MRI). Table 8.1 shows the imaging characteristics of various spinal structures in CT and MRI (Klein 2015).

For the purpose of clinical imaging, the choice of the imaging method and the value of the information provided are highly dependent on the clinical stage of care. For example, in the acute stage, immediately after hospitalization, the most urgent information is to determine whether or not there has been damage to the spine and spinal cord, and X-ray and CT are widely used. Injuries that involve the thoracic, lumbar, or sacral areas of the spine can generally be diagnosed using CT, which has been established as the diagnostic imaging modality of choice in these areas. It is usually obtained as part of the primary work-up by the trauma surgeons or the physicians in the emergency department. Additional MRI examination in these areas or use of other modalities is generally not necessary, although there are circumstances in which obtaining an MRI is appropriate (Williams 2021). However, depending on the type or mechanism of the suspected injury, MRI can also be of great value. Because of the information that can be provided for the neural tissue of the spinal cord itself, MRI may be of considerable value during recovery and evaluation of the effects of injuries or for the planning of surgical interventions or rehabilitation strategies (Fehlings et al. 1999).

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Table 8.1 Imaging modalities, sequences, and appearance of various spinal structures

Imaging modalities and sequences	Lipid	CSF/Edema	Bone	Spinal cord/nerve	White matter	Gray matter
CT (Hounsfield units)	−70 to −30	0–15	>1000	20–45	20–30	35–45
T1-weighted	Hyperintense	Hypointense	Hypointense	Intermediate	Brighter	Darker
T2-weighted	Less hyperintense	Hyperintense	Hypointense	Intermediate	Darker	Brighter
T1-postcontrast	Normal enhancement of vascular structures, abnormal enhancement at sites of blood–brain barrier disruption and hypervascularity (tumor, infection, inflammation, demyelination)					
Short-tau inversion recovery (STIR)	Hypointense	Hyperintense	Hypointense	Intermediate	Darker	Brighter
Diffusion-weighted imaging (DWI)	Reduced diffusivity (DWI hyperintense, apparent diffusion coefficient hypointense) at foci of cytotoxic edema (acute infarction) or hypercellularity (abscesses and some tumors); enhanced diffusivity (DWI hyperintense, apparent diffusion coefficient hyperintense) at foci of vasogenic edema, sclerosis, gliosis					

Modified from Klein (2015), with permission

8.1 Guidelines of Imaging Studies of Spine and Spinal Cord Injuries

Guidelines are developed to identify low-risk standards when cervical spine imaging is not indicated. The guidelines include the National Emergency X-radiography Utilization Study (NEXUS) criteria and the Canadian C-spine Rule (CCR) (Stiell et al. 2003). The NEXUS criteria include the absence of all of the following five conditions: midline cervical tenderness, altered level of consciousness or intoxication, abnormal neurologic findings, or painful distraction injuries (Table 8.2). Patients who meet all NEXUS criteria are classified as low-risk patients. Patients who are not alert or who do not meet the NEXUS criteria for other reasons must undergo a radiographic evaluation. The CCR was developed by evaluating several criteria in a multicenter collaborative study of medical centers in Canada and can be applied to alert and stable trauma patients with higher sensitivity and specificity than NEXUS (Stiell et al. 2003) (Table 8.3). The CCR may be followed to determine which trauma patients who are awake and alert (as indicated by a score of 15 on the Glasgow Coma Scale) need additional imaging studies. The CCR is based on three clinical questions derived from 25 positive and negative clinical predictor variables associated with spine injury. First, patients who are considered to be at high risk due to their age, dangerous mechanism of injury, or the presence of paresthesias must undergo radiography. Second, patients with any one of five low-risk characteristics can perform an active range of motion assessment. Third, patients who are able to actively rotate their neck 45 degrees to the left and right regardless of pain do not require radiography (Stiell et al. 2001). The American College of Radiology's (ACR) specific recommendations on imaging of the spine should be applied to patients who do not fall into the low-risk category based on the CCR and the NEXUS (Daffner and Hackney 2007). Table 8.3 summarizes the criteria for high-risk of spine injury. A cervical spine "clearance" protocol for obtunded patients recommends that cervical CT is performed at the

Table 8.2 National Emergency X-Radiography Utilization Study (NEXUS) low-risk criteria

Criteria	Comment
No posterior midline cervical spine tenderness	Midline posterior tenderness is deemed to be present if the patient reports pain on palpation of the posterior midline neck from the nuchal ridge to the prominence of the T1 vertebra, or if the patient evinces pain with direct palpation of any cervical spinous process
A normal level of alertness	An altered level of alertness can include any of the following: a Glasgow Coma Scale score of 14 or less; disorientation to person, place, time, or events; inability to remember three objects at 5 min; a delayed or inappropriate response to external stimuli; or other findings.
No evidence of intoxication	Patients should be considered intoxicated if they have either of the following: a recent history provided by the patient or an observer of intoxication or intoxicant ingestion or evidence of intoxication on physical examination such as an odor of alcohol, slurred speech, ataxia, dysmetria, or other cerebellar findings or any behavior consistent with intoxication. Patients may also be considered to be intoxicated if tests of body fluids are positive for alcohol above 0.08 mg/dL or other drugs that affect the level of alertness
No focal neurologic deficit	A focal neurologic deficit is any focal neurologic finding on motor or sensory examination
No painful distracting injuries	No precise definition of painful distracting injury is possible. This category includes any condition thought by the clinician to be producing pain sufficient to distract the patient from a second cervical injury. Such injuries may include, but are not limited to, any long bone fracture; visceral injury requiring surgical consultation; large laceration; degloving injury; crush injury; large burns; or any other injury causing acute functional impairment. Physicians may also classify any injury as distracting if it is thought to have the potential to impair the patient's ability to appreciate other injuries

Cervical spine imaging is unnecessary if a patient meets all five criteria
From Stiell et al. (2003)

Table 8.3 Canadian C-Spine Rule (CCR) for alert and stable trauma patients

Criteria or assessment	Definitions
There are no high-risk factors that mandate radiography	High-risk factors include any of the following: • Age 65 years or older • Dangerous mechanism of injury Fall from height >3 ft (5 stairs) Axial loading injury Driving, high-speed motor vehicle crash (>100 km/h [60 mph]), rollover or ejection Motorized recreational vehicle or bicycle collision • Paresthesias in the extremities
There is a low-risk factor that allows safe assessment of neck range of motion	Low-risk factor includes any of the following: • Simple rear-end motor vehicle collision excludes being pushed into oncoming traffic, being hit by a bus or a large truck, a rollover, and being hit by a high-speed vehicle • Sitting up in the emergency dept. • Ambulatory at any time following injury • Delayed onset of neck pain • Advance of midline cervical spine tenderness
The patient is able to actively rotate their neck	Can rotate neck 45° to the right and to the left

Cervical spine imaging is unnecessary if patients meet all three criteria

same time as cranial scan. If this is normal, the patient is left with the cervical collar in place for the first 24 h. After this time, if the patient is still in coma, a limited MRI examination consisting of fast spin-echo T1- and T2-weighted and short-tau inversion recovery (STIR) sagittal images of the cervical region should be performed. If the MR examination is normal, surgeons are advised that it is safe to remove the cervical collar (Daffner 2011).

Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injury by the American Association of Neurological Surgeons and the Congress of Neurological Surgeons Joint Guidelines Committee, updated in 2013, recommended radiographic evaluation of asymptomatic and symptomatic patients (Hadley and Walters 2013). Radiographic evaluation of the cervical spine is not recommended for asymptomatic patients who do not have neck pain or tenderness, who has a normal neurological examination, who is without an injury detracting from an accurate evaluation, and who is able to complete a functional range of motion examination, in the awake state. It is advisable to stop cervical immobilization for these patients without cervical spinal imaging. In the awake symptomatic patient, high-quality CT imaging of the cervical spine is recommended (Hadley and Walters 2013). If high-quality CT imaging is available, routine 3-view cervical spine radiographs (anteroposterior, lateral, and odontoid views) are not recommended. If high-quality CT imaging is not available, a 3-view cervical spine series is recommended. If it is necessary to further define areas that are suspicious or not well visualized on the plain cervical X-rays, this must be supplemented with CT if available. For the obtunded or unavailable patients, high-quality CT imaging is recommended as the initial imaging modality of choice. Routine 3-view cervical spine radiographs are not recommended if CT imaging is available (Walters et al. 2013). Similar imaging criteria can be applied to patients with thoracic and lumbar spine injuries (Hadley and Walters 2013).

Controversy persists over the optimal diagnostic imaging protocol for trauma patients with respect to the spine. A protocol proposed by Williams (2021) is depicted in Fig. 8.1.

8.2 Imaging Modalities

8.2.1 Plain Radiographs

Plain spine radiography has some advantages over more advanced imaging studies because it is inexpensive and easy to perform, and it exposes less radiation compared to CT scans. However, plain X-rays are insensitive to many disorders of the spine and spinal cord, and these disorders

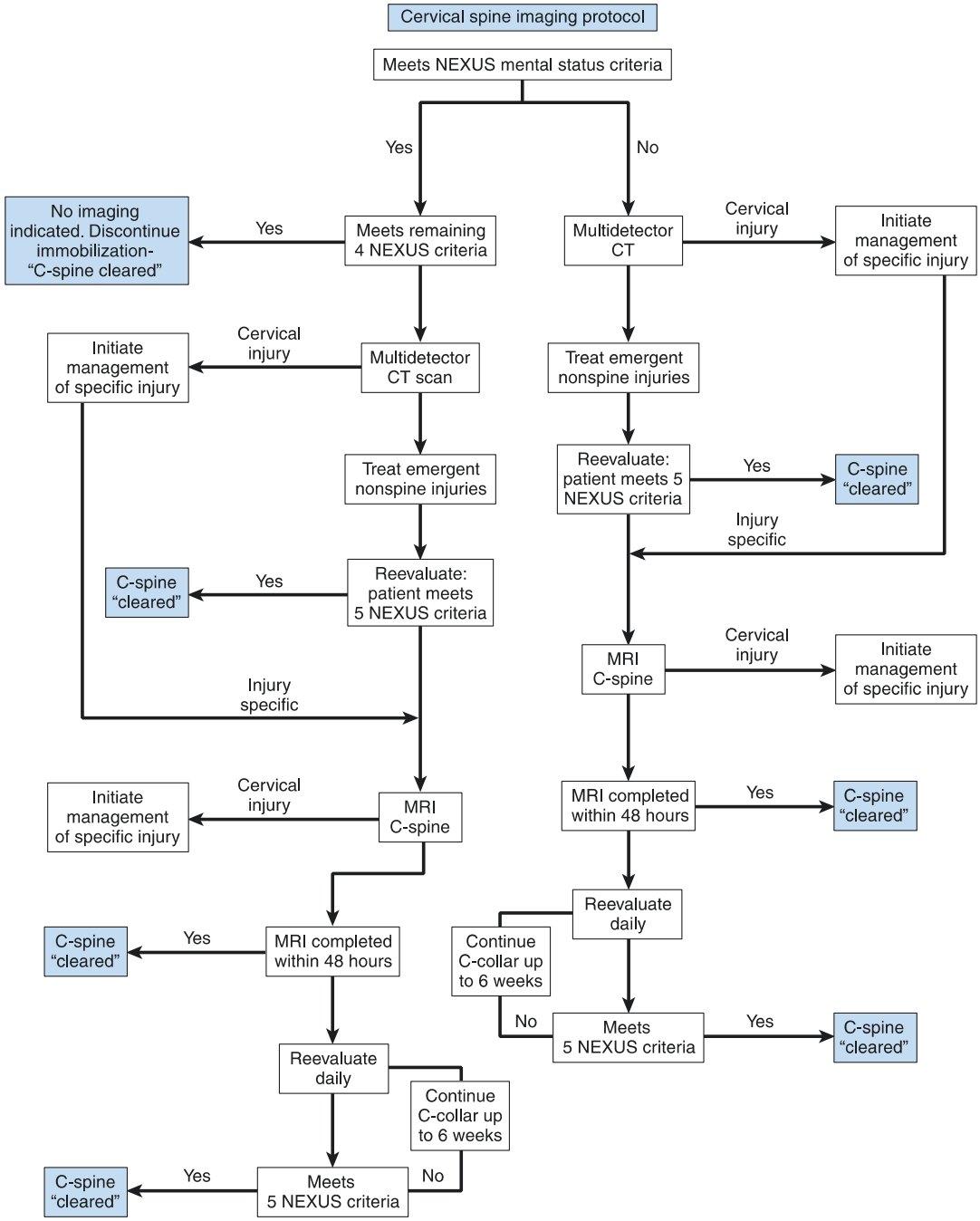

Fig. 8.1 A protocol of cervical spine diagnostic imaging in patients with no spinal cord injury. From Williams (2021), with permission

may require confirmation by advanced imaging studies. The medical and trauma history should inform the clinician when further work-up and imaging are required. If a fracture in the cervical spine is detected, an accompanying fracture in the thoracic or lumbar spine should be considered, and an imaging of the entire spine should be performed.

In general, anteroposterior, lateral, and open-mouth odontoid views are obtained for the cervical spine. The four contour lines of the cervical spine should be examined for continuity in the lateral view. These lines include the anterior vertebral body line, the posterior vertebral body line, the spinolaminar line, and the spinous process line (Fig. 8.2). A swimmer's view can be added if the lateral view does not adequately visualize the C7-T1 junction to prevent the humeral heads from obscuring the spine (Fig. 8.3). Anterior or posterior translation of vertebral bodies greater than 3.5 mm in the subaxial cervical spines represents instability. A 50% shift of one vertebral body over another adjacent vertebral body suggests bilateral facet dislocations.

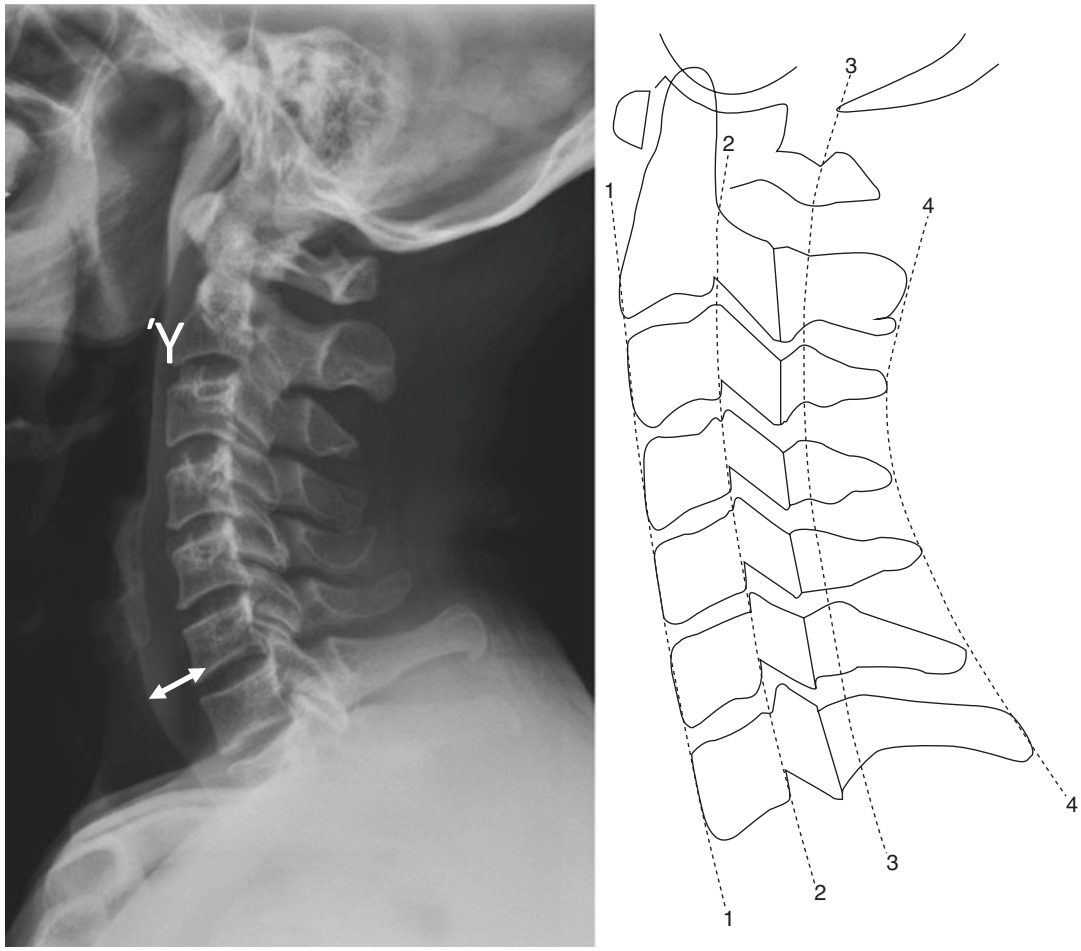

Fig. 8.2 Normal four imaginary lines in the lateral cervical spine. (1) Anterior vertebral body line, (2) posterior vertebral body line, (3) spinolaminar line, and (4) spinous process line. Note, the width of the prevertebral soft tissue in adults should be less than 7 mm at the level of C2 (asterisk) and 22 mm at C6 (arrow)

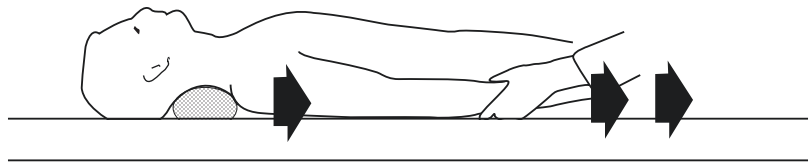

Fig. 8.3 Swimmer's view. To overcome superimposition of the shoulders on the lower cervical spine in the lateral projection by traction on arms and shoulders

The open-mouth odontoid view is needed if there is a history of trauma. The open-mouth view facilitates visualization of the atlantoaxial (C1–2) articulation and provides additional views for examining the occipital condyles, lateral masses of C1 and C2, and the dens. Patients should be alert and cooperative in performing the open-mouth view. Atlantodens interval greater than 3 mm in adults and greater than 5 mm in children in the upper cervical spines suggests atlantoaxial instability due to ligamentous failure. Flexion and extension views should be obtained in an active patient in a pain-free range of motion. They should never be taken in the obtunded patient, as this increases the risk of further injury.

Thoracolumbar spine injury and stability can be assessed by Denis three-column concept. Findings for instability of the thoracolumbar spine include displacement of the vertebral body more than 2 mm indicating possible ligamentous disruption, widening of the interspinous space, widening of the facet joints, disruption of the posterior vertebral body line, or loss of vertebral body height over 50%.

8.2.2 Magnetic Resonance Imaging

X-ray-based imaging studies, including CT, provide detailed information about anatomical changes of high-density materials such as bone and cartilage following traumatic injuries. MRI enables the evaluation of bony details, marrow signals, malalignments, stenosis, and radicular lesions. MRI provides information about changes in soft tissues such as gray matter and white matter in the spinal cord and vascular changes (Kaji and Hockberger 2007). The details of changes in tissue structure at the cellular level can also be obtained through changes in magnetization relaxation times, magnetization transfer, and changes in water self-diffusion (Krings et al. 2007).

MRI has a very important role in the spine and spinal cord injury imaging, but is often performed several hours after injury. It is typically not the initial imaging study performed after spine trauma because of relative insensitivity in detection and detail of fractures since cortical bone appears dark, the difficulty of patient monitoring during the procedure, and longer imaging time than plain radiographs or CT (Klein 2015). Because MRI is most effective for evaluating soft tissue injury by showing either discontinuity of anatomic structures such as the ligamentum flavum and annulus fibrosus or hemorrhage and edema associated with tissue disruption, the timing of the study is very important. If the MRI is performed within the first 48 h after injury, the sensitivity for hemorrhage and edema is optimal (Williams 2021).

MRI can be used to characterize the cause and severity of myelopathy and to guide surgical intervention (Lammertse et al. 2007). Abnormality of MRI in the spinal cord sometimes occurs in negative bony imaging of the spinal column (SCIWORA) (Goldberg and Kershan 2010). It is important to pay attention to the possibility, especially in children and adolescents. MRI is recommended for patients who are unconscious or obtunded, or no abnormality in CT and radiographic examinations, but who are suspected of having injuries or persistent neck pain or tenderness (Goldberg and Kershan 2010). In contrast to most other imaging methods, MRI is able to take images in any desired orientation. This is particularly advantageous for spinal imaging, where a sagittal view of the spinal column is often more informative than a series of axial slices produced by most other imaging modalities. Furthermore, unlike CT, in which the minimum slice thickness is determined by the size of the X-ray detectors, there is no intrinsic limit on the spatial resolution that can be achieved in any given direction. Another major advantage of MRI is the absence of ionizing radiation, which is used in other methods such as X-rays and CT (Hattingen et al. 2015) (Table 8.4).

MRI utilizes the interaction between the magnetic spin property of hydrogen protons in biological tissue. Differences in the density of hydrogen protons within tissues and in relaxation times of protons (hydrogen atoms) between different tissues produce different signal intensities and provide tissue contrast in the images. The rate of return to the equilibrium of excited protons is called the relaxation time (Klein 2015). T1 is defined as the relaxation

time in which the protons return to the equilibrium state. T2 is defined as the spin–spin relaxation time, or the relaxation time compared with adjacent protons. Proton-density, T1 recovery, and T2 decay of the tissue are three parameters determining the images. The latter two are time constants. The terms T1 and T2 represent time constants for proton relaxation. The two relaxation rates, T1 and T2, affect the signal intensity of the image. Structures containing more water, such as cerebrospinal fluid and edema, have long T1 and T2 relaxation rates and lead to relatively low-signal intensity (dark) on T1-weighted images (T1W) and higher signal intensity (white) on T2-weighted images (T2W). The relationships between TR, TE, and the image contrast obtained are summarized in Fig. 8.4. Structures with little water contents such as air or cortical bone appear dark on both T1W and T2W (Table 8.5). The signal intensity in the spinal cord is intermediate in both T1W and T2W, but the signal intensity in T2W is relatively low,

Table 8.4 High-risk criteria for spine injury Modified from Stiell et al. (2003)

High-risk criteria
Altered mental status (Glasgow Coma Scale <15)
Multiple fracture
Drowning or diving accident
Significant head or facial injury
Age >65 years
Fall of >1 m
Axial load to head
High-speed motor vehicle crash
Motor vehicle crash with large vehicle
Motor vehicle crash with rollover, ejection
Pedestrian struck by vehicle
Crash from motorized recreational vehicle
Paresthesias in extremities
Rigid spinal disease
Ankylosing spondylitis
Diffuse idiopathic skeletal hyperostosis

Table 8.5 Tissue brightness on T1 and T2 sequences

Sequence	Bright	Dark
T1-weighted image	Adipose tissue	Air, infection, inflammation, tumor, calcification, blood (acute or chronic), CSF
T2-weighted image	Edema, infection, inflammation, subacute blood (methemoglobin), CSF	Air, calcification, fibrous tissue, hemosiderin, melanin, flow void, protein-rich fluid

Acute, 1–3 days; subacute, 3–7 days; chronic, >14 days
Modified from Laker and Concannon 2011, with permission

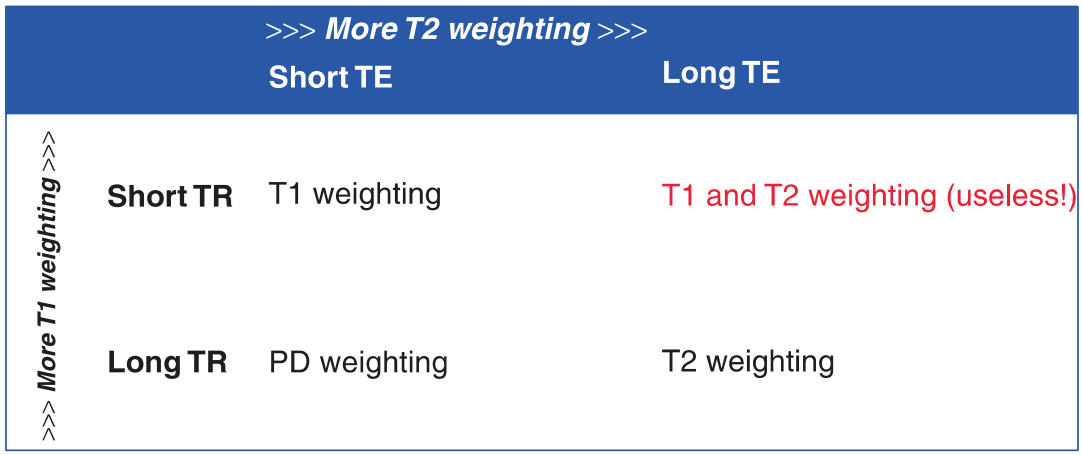

Fig. 8.4 Relationships between TR, TE, and the resulting image contrast. Note a short TR and a long TE result in combined T1 and T2 weighting which tend to cancel each other out. Conversely a tissue with a short T1 often has a short T2, giving a high signal from T1 weighting but a low signal from T2 weighting. Therefore, the resulting images have low signal and very little contrast. PD, proton-density. From Hattingen et al. (eds) 2015, with permission

surrounded by high-intensity CSF (Klein 2015). Gadolinium is the most commonly used contrast material in MRI and causes significant prolongation of T1 relaxation times (Laker and Concannon 2011). Magnetization can be recovered before the MR signal is measured by changing the repetition time (TR) to create a T1W. To create a T2W, magnetization is allowed to decay before measuring the MR signal by changing the echo time (TE) (Moseley et al. 2009). Gradient echo sequences with a long TE are said to have T2* weighting. T2* weighting is ideal for identifying hemorrhage.

The process of developing the fMRI and diffusion tensor imaging (DTI) methods of the spinal cord has resulted in methodological advances that contribute to the improvement in all MRI methods for imaging the spinal cord (Battal et al. 2011; Ducreux et al. 2007; Eppenberger et al. 2014). Diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) are based on the diffusion properties of water molecules. Fraction anisotropy (FA) value is significantly decreased, while mean diffusivity (MD) is increased at the level of spinal cord injury (D'souza et al. 2017). Short-tau inversion recovery (STIR) imaging is a technique to suppress fat to improve visualization of adjacent edema and other abnormalities on MRI (Dionello et al. 2013).

8.2.2.1 MRI of Spinal Cord Pathology

MRI signal abnormalities in the spinal cord may indicate the cause of the acute neurological deficit and signs of prognosis (Flanders et al. 1990). Acute fractures are represented by the decreased signal in T1W against the background of the high signal of marrow fat and by a bright signal on T2W if fat suppression is used. Findings in the acute phase include identification of extrinsic spinal cord compression by bone, intervertebral disk, and epidural hematoma, and intrinsic spinal cord pathology, including cord swelling, edema, and hemorrhage (Flanders et al. 1990, 1996). A spectrum of spinal cord pathology ranges from minimal cord edema (bright T2W) to cord hemorrhage (bright or dark T2W and possibly dark T1W depending on the stage of hemoglobin) (Fig. 8.5) Acute hemorrhage within the spinal cord is seen as a hypointense signal in T2W. The signal intensity of hemorrhage in T1W and T2W varies according to the stage of hemoglobin breakdown, which converts from deoxyhemoglobin in the acute stage to methemoglobin in the next few days and hemosiderin after 2 weeks. Myelomalacia and posttraumatic syrinx or cysts are subacute and chronic findings, respectively (Yoshioka et al. 2006) (Table 8.6).

MRI depends on the presence of MR-active nuclei in tissue. Hydrogen is abundant in the human body and has a large magnetic moment,

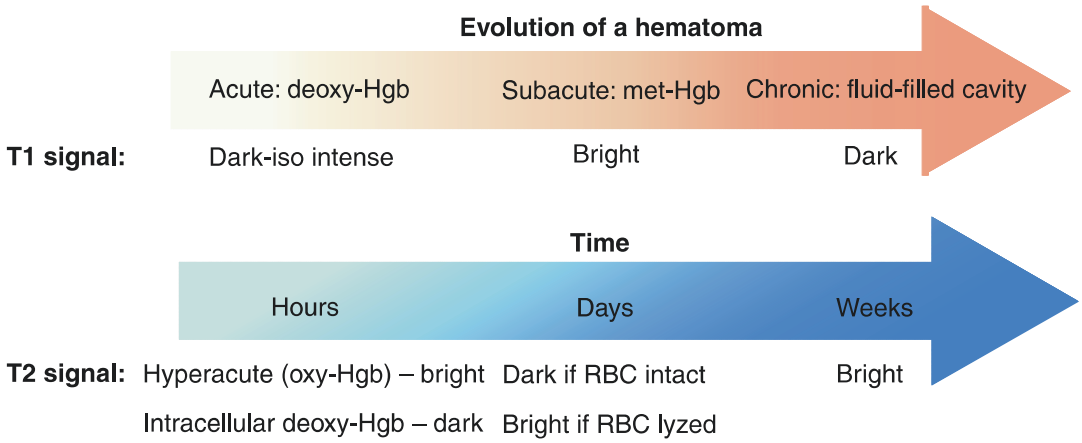

Fig. 8.5 Magnetic resonance characteristics of hemoglobin breakdown. Evolution of a hematoma (red arrow) over time (blue arrow). From Fehlings (ed) (2013)

Table 8.6 MRI findings according to the pathology and duration after spinal cord injuries

Pathology	MRI findings
Acute	
External compression of the spinal cord	• Evidence of spinal cord compression • Compression by bone, extruded intervertebral disk, epidural hematoma
Bone fracture	• Low-signal intensity on T1WI in bony fragments
Ligament injury	• High-signal intensity on T2WI • Fat-suppression MR sequences
Spinal cord swelling	• Smooth enlarged cord contour
Edema	• High-signal intensity on T2WI • Low-signal intensity on T1WI
Hemorrhage	• Low-signal intensity on T2WI for acute hemorrhage, surrounded by high intensity by edema • Signal intensity based on hemoglobin breakdown stage
Subacute	
Myelomalacia	• High intensity on T2WI and intermediate signal intensity between cord and CSF on T1WI • Similar signal intensity to edema
Chronic	
Posttraumatic syrinx formation	• Isointense with CSF
Atrophy of spinal cord	• Decreased AP diameter: <7mm in cervical and <6mm in the thoracic spinal cord

so hydrogen is used for clinical MRI. MR images, especially T1- and T2-weighted images, are routinely used in clinical practice when a spinal cord injury or disease is suspected. MRI is routinely used when it is available in patients with neurological deficits following a vertebral injury (Klein 2015; Yoshioka et al. 2005). This is useful for evaluating compression of the spinal cord by prolapsed disk or bony fragments. Its greatest benefit seems to be in the evaluation of the spinal cord itself (Quencer et al. 1992). The usefulness of MRI in determining the extent of the skeletal injury is limited to its inability to adequately visualize the cortical bone.

The MRI characteristics of the acutely injured cord reflect the clinical symptoms. If the injury is mild and there is a transient neurological dysfunction, the spinal cord may appear normal. As the injury and neurological deficits increase, MRI may indicate edema and hemorrhage in the spinal cord (Quencer and Bunge 1996). Long TR images are the most sensitive to showing spinal cord edema, which appears to be a region of high-signal intensity in the spinal cord. The areas of evolution from hypointensity to hyperintensity are typical of hemorrhage. The presence of hemorrhage is associated with a poor prognosis. Contrast media can be used in MRI of the spine. Gadolinium chelate is a paramagnetic substance that has a positive effect on magnetic susceptibility. This leads to an increase or brightening of the signal on T1WI. The use of contrast agent in MR of the spine improves the detection of postsurgical epidural fibrosis, epidural abscess, and intramedullary and extramedullary tumor (Nijenhuis et al. 2006). Due to the intact blood–nerve barrier, the intrathecal nerve roots are normally not enhanced after admission of intravenous contrast agents. In contrast, the dorsal root ganglion shows strong enhancement due to the lack of the barrier (Hattingen et al. 2015).

8.2.2.2 Recommended Imaging Protocols

Spine MR protocols should include T1-weighted and T2-weighted sequences in the axial and sagittal planes. Coronal planes are useful in assessing scoliosis and diseases of the cervicothoracic and lumbosacral plexus, which follow the course of the lateral paravertebral muscles. T2-weighted short-tau inversion recovery (STIR) sequences should be added if there are any questions about edema. Since the spinal cord has a cross-sectional diameter of only 10–14 mm, a high-resolution MRI is required to visualize small spinal cord lesions (Hattingen et al. 2015). Suggested protocols for spinal MR imaging based on clinical symptoms are shown in Table 8.7.

Table 8.7 Proposed MR imaging sequences based on clinical symptoms

Sequencetype					
Clinical question	T2-weighted FSE	T1-weighted spin echo	T2*-weighted multi-echo (e.g. MEDIC, MERGE)	T2-weighted STIR	Other sequences
Radiculopathy	Sagittal	Sagittal	Axial (caveat: stenosis of intervertebral foramina is overestimated)	Sagittal; coronal to see nerval plexus	Oblique 2D or 3D T2-weighted images with reformats perpendicular to neural foramina
	Axial	Axial			
Myelopathy	Sagittal	Sagittal	Axial (caveat: bony stenosis of spinal canal is overestimated)	Coronal to see scoliosis	3D T2-weighted myelography
	Axial	Axial			
	Coronal to see scoliosis	Coronal to see scoliosis			
Myelitis	Sagittal	Sagittal with and without contrast agent	Axial	Sagittal	
	Axial	Axial with contrast agent		Coronal to see adjacent tissue changes	
Spinal cord injury	Sagittal	Sagittal	Axial to see haemorrhage	Sagittal	
	Axial	Axial		Coronal to see adjacent tissue changes	
Vascular myelopathy	Sagittal	Sagittal with and without contrast agent			Diffusion weighted imaging and time-resolved contrast-enhanced angiography; 3D T1-weighted sequence with fat saturation; 3D T2-weighted imaging
		Axial with contrast agent			
Intradural tumour	Sagittal	Sagittal with and without contrast agent	Axial to see haemorrhage		Diffusion weighted imaging and diffusion tensor imaging
	Axial	Axial with contrast agent			
Extradural tumour	Sagittal	Sagittal with and without contrast agent		Sagittal	
		Axial with contrast agent		Coronal to see adjacent tumour spread	

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8.3 Cervical Spine Imaging Study

Cervical spine imaging is based on the criteria of the Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injury by the American Association of Neurological Surgeons and the Congress of Neurological Surgeons Joint Guidelines Committee, updated in 2013, in the awake asymptomatic or symptomatic patient, and in the obtunded or unavailable patient. High-quality CT imaging of the cervical spine is recommended as the initial choice of imaging studies. If high-quality CT imaging is not available, a 3-view cervical spine series (anteroposterior, lateral, and open-mouth odontoid views) is recommended. This should be supplemented with CT. Oblique view as initial imaging is not recommended (Klein 2015). Combining the cervical CT scan with the head, chest, abdomen, and pelvic examinations, which are often ordered for these patients, has resulted in a lower cost than if the cervical study is performed separately.

At a minimum, a thorough clinical examination must be completed, and a radiograph of the lateral cervical spine must be ordered. The lateral view of the 3-view cervical spine series is generally most useful. Other views, including flexion-extension films, are typically of little value for detection injuries and should not be routinely obtained for an initial assessment of trauma (Insko et al. 2002). Approximately 5% of patients with a spine injury have second lesions. If spinal cord injury cannot be ruled out with standard films, further examinations such as flexion-extension views, CT scans, or MRI studies should be completed. Cervical spine X-rays are useful for minor trauma with a normal neurological examination with neck pain. People who have lower consciousness after high-speed car accidents and who voluntarily move their upper extremities but do not move the lower extremities are more appropriately imaged with a spine CT scan. In patients with neurologic injuries, CT alone misses a small number of clinically significant injuries and therefore recommends MRI.

Plain radiographs visualize the bones of the spine. They can provide limited information about large soft tissue masses that occur inside the spinal canal or form the vertebral column. The standard radiographic projections of each of the regions are anteroposterior and lateral. In the cervical and lumbar regions, oblique projections visualize the neural foramina and pars interarticularis. Lateral radiographs of the cervical and lumbar spine in flexion and extension after careful study of radiographs with standard projections can give information on instability of the spine or the degree of movement. Anteroposterior and lateral views may show loss of vertebral disk space height, facet arthropathy, spondylolisthesis, malalignment, fracture, and congenital osseous abnormalities. Oblique views are often ordered to evaluate the foramen, but this is highly dependent on patient positioning. Flexion-extension views may be added to evaluate for instability, particularly if a spondylolisthesis is found on lateral views. Greater than 3.5 mm of translational displacement or 20° of angular motion is significant and indicates instability (White et al. 1975).

If C7 and T1 are not adequately assessed on the true lateral projections, the lateral swimmer's view may be performed to visualize the cervicothoracic junction. The swimmer's view is done by placing a patient with one arm completely abducted over the head and slightly depressing the shoulder when attempting to visualize the entire cervical spine to the level of the upper end plate of T1 (Klein 2015) (Fig. 8.3). However, posture for this view may exacerbate the instability of the injured spine and CT should be performed instead if there is a high clinical suspicion of injury to the area. Because of the severe paraspinal muscle spasm associated with a spinal injury, flexion-extension radiographs immediately after injury may not exhibit instability (Insko et al. 2002). Short-term immobilization and follow-up radiographs, including dynamic lateral radiographs, should be obtained in patients with persistent axial pain or new-onset neurological deficit. Dynamic flexion-extension view is valuable during the follow-up period to assess potential ligamentous instability in injury recovery. There may be differences depending on the doctor, but the flexion-extension view of the acute and subacute phase should generally be avoided.

A high-quality lateral film, including the C7-T1 level, detects 70–90% of cervical fractures or dislocations. This should be the initial film obtained and should be examined in an orderly and methodical fashion. The occipitoatlantal articulation is checked first. Secondly, the atlantoaxial articulation is assessed using the atlantodental interval. It should not exceed 3 mm for adults and 5 mm for children. Prevertebral soft tissue shadows (anterior prevertebral soft tissue line) greater than 7 mm at C2 or 22 mm at C6 may indicate swelling and may be a clue to spinal trauma. Normal measures for many of the osseous relationships and soft tissue contours in the cervical spine using a lateral radiogram are summarized in Table 8.8. The lines drawn along the anterior vertebral bodies, the posterior vertebral bodies, and the spinolaminar line and spinous process line are then evaluated for deviations or discontinuities (Fig. 8.2). The deviation of any of these lines may indicate subluxation or dislocation. The intervertebral disk spaces, cervical facet joints, and interspinous spaces are well visualized on the lateral view. The cervical facet joints should be parallel to each other (Klein 2015). Finally, the integrity of each individual segment is evaluated (Table 8.9).

Table 8.8 Normal measurements of the cervical spine parameters in the lateral film

Parameters	Adults	Children
Predental space (anterior atlantodens interval	<3 mm	<4–5 mm
C2–C3 pseudosubluxation (physiologic benign pseudosubluxation)	<3 mm	<4–5 mm
Prevertebral (retropharyngeal) space	<7 mm at C2	½ to 2/3 vertebral body distance anteroposteriorly
	<5 mm at C3–C4	
	<22 mm at C6	<14 mm at C5
Angulation of two adjacent vertebrae	<11°	<11°
Basion-dens interval	<12 mm	
Spinal cord dimension	>13 mm	Adult size by 6 years of age

Table 8.9 Observation points in the cervical lateral film

Observation points
All seven cervical vertebral bodies
Alignment of four imaginary lines • Anterior vertebral body line • Posterior vertebral body line • Spinolaminar line • Spinous process line
Atlantodens interval
Intervertebral angulation
Presence of fractures
Fanning of spinous processes
Prevertebral soft tissue, <5 mm at C3
Findings of cervical spine instability • Atlantodens interval: >3 mm in adults, >5 mm in children • Anterior or posterior translation of vertebral bodies >3.5 mm • Angulation between adjacent vertebrae >11° • Flexion tear-drop fracture

The next film obtained is the anteroposterior view. The anteroposterior view helps to assess parts of the cervical spine that are not adequately evaluated in the lateral film. The cervical spines from C3 to the cervicothoracic junction can be visualized on the anteroposterior view. On this view, the interspinous distances must be symmetrical and the spinous processes must be carefully examined for rotational malalignment. Anteroposterior imaging of the normal spine should show the spinous processes positioned in the midline at each level. The uncovertebral joints (C3–C6) should be symmetric and vertically aligned at all levels. The vertebral bodies should be equal to height and have a smooth cortical surface (Klein 2015).

The third film to be obtained is an open-mouth odontoid view to examine the C1–C2 region. The open-mouth odontoid view shows the atlantoaxial articulation. The occipital condyles, the lateral masses of C1, the dens, and the lateral masses of C2 should be assessed. In this view, the lateral masses of the C1 should be aligned over the lateral masses of C2. Lateral displacement may indicate a burst fracture of C1. From this view, most fractures of the odontoid process are visualized. The sensitivity of this series of films is estimated at 93%, with an accuracy of 84% (Holliman et al. 1991; Streitwieser et al. 1983). However, a

single view is less sensitive and less accurate. The sensitivity of the plain film evaluation can be increased by adding supine oblique views. Oblique films are obtained without moving the patient's head and are taken by tilting the tube 30 degrees from horizontal.

Flexion-extension films may be useful for detecting occult ligamentous instability that is concealed by initial muscle spasm. If indicated, these films should be made so that the patient is positioned himself under supervision but without the assistance of the clinician. Under no circumstances should the patient's head be passively moved for this study. They are not indicated if an unstable lesion is diagnosed with plain films. If the spine is unstable, the risk of worsening of the spinal cord compromise and a high incidence of muscle spasms or guarding limiting adequate neck movement are limitations of flexion-extension radiographs to assess stability in the acute phase. Once neck muscle spasm in the neck has subsided and the patient controls neck movement cooperatively, dynamic flexion-extension radiographs are taken to evaluate the stability of the cervical spine. Flexion-extension radiograph is not recommended in obtunded patients (Klein 2015).

Plain or planar CT is useful for more accurately describing detected occult injuries, as well as known injuries. Plain CT is suitable for visualizing the spinal column (Platzer et al. 2006). The contents of the spinal canal are relatively difficult to see, but epidural fat helps to demarcate the thecal sac. Axial CT imaging can define a lesion of the vertebral body or posterior elements, encroachment on the spinal canal (Klein 2015). Sagittal and coronal reconstructions of the spinal column can improve information about the mechanism of injuries. Planar tomography may be a superior diagnostic modality in fractures of dens, subluxation of vertebral bodies, atlantooccipital dislocation, and in some cases, fractures of the lateral mass and articular processes. The disadvantages of CT imaging of the cervical spine include the delivery of a higher radiation dose with a 50% increase in mean radiation dose to the cervical spine in pediatric patients for helical CT compared with conventional radiography (Adelgais et al. 2004). A tenfold increase in radiation dose to the skin and a 14-fold increase in dose to the thyroid were reported when a CT scan of the cervical spine was compared with a five-view X-ray series (Kaji and Hockberger 2007; Rybicki et al. 2002).

Another important consideration of cervical spine injury is the possibility of carotid or vertebral artery injury or dissection, estimated at an incidence of 0.1–0.4% (Martin and Eldrup-Jorgensen 1991). The diagnosis of blunt carotid artery injury should be suspected in patients with neck hyperextension injuries or with cervical spine fractures and patients with neurological deficits not considered intracranial trauma (Martin and Eldrup-Jorgensen 1991).

8.4 Thoracic and Lumbar Spine Imaging Study

Although not well defined, similar considerations with cervical spine imaging should be applied to the initial imaging of thoracolumbar spine injuries. Approximately 25% of patients with one vertebral injury have another at a noncontiguous site (cervical–thoracic, cervical–lumbar, thoracic–lumbar, multilevel same segment) (Daffner 2011). If plain films are taken as the initial imaging study, the films should include anteroposterior and lateral views. If the oblique view is not absolutely indicated, it is usually not included in the acute setting.

When examining plain X-rays of the thoracic and lumbar spine, the mechanism of injury should be considered along with the assessment of alignment, bony integrity, and joint space disruption. The anteroposterior and lateral projections should be displayed at the same time with a reference point to identify the exact level. Each level should be examined for instability. The following list provides some features to check for spinal instability (Daffner et al. 1990; Fehlings 2013).

- Displacement >2 mm by all or a major portion of a vertebra
- Widening of the interlaminar or interspinous space. Increase >2 mm at contiguous levels
- Wide facet joints. Widening, malalignment, or loss of contact between contiguous facets
- Disrupted posterior vertebral body line. Any fracture, rotation, displacement, angulation, or absence of the posterior margin of the vertebral body
- Wide vertebral canal. Increase >2 mm in the interpedicular distance at contiguous levels

8.5 Imaging for Ankylosing Spondylitis or Diffuse Idiopathic Skeletal Hyperostosis (DISH)

The spinal cord may be compressed anteriorly by the ossification of posterior longitudinal ligament and compressed posteriorly by hypertrophic calcification of the ligamentum flavum in patients with ankylosing spondylitis. In addition, facet joints and uncovertebral joint hypertrophy can cause spinal cord compression. Patients with long-standing ankylosing spondylitis are predisposed to fractures of the spine. Horizontal fractures occur through the ossified intervertebral disk space and/or endplate and the posterior elements in the thoracic and lumbar spine. Biomechanically, these fractures resemble the seatbelt type of injury in that flexion and extension axes of the ankylosed spine are shifted away from their normal location in the center of the nucleus pulposus (Graham and Van Peteghem 1989). Patients can sustain serious spinal injury even after minor trauma (Bhatia and Bowen 2007).

Swallowing disorders can be caused by diffuse idiopathic skeletal hyperostosis (DISH), which is caused by the formation of osteophytes in the anterior part of the cervical spine and hypertrophic anterior longitudinal ligament. Patients with ankylosing spondylitis or DISH are at increased risk of vertebral fractures, but fractures cannot be initially displaced and can lead to delayed spinal cord injury. CT or MRI is strongly recommended in patients with midline tenderness, even if plain X-rays are negative.

References

Adelgais KM, Grossman DC, Langer SG, et al. Use of helical computed tomography for imaging the pediatric cervical spine. Acad Emerg Med. 2004;11:228–36.

Battal B, Kocaoglu M, Bulakbasi N, et al. Cerebrospinal fluid flow imaging by using phase-contrast MR technique. Br J Radiol. 2011;84:758–65.

Bhatia RG, Bowen BC. Thoracolumbar spine trauma. In: Goethem V, van den Hauwe L, Parizel PM, editors. Spinal imaging: diagnostic imaging of the spine and spinal cord. Heidelberg: Springer; 2007.

Daffner RH. Imaging of vertebral trauma I: indications and controversies. In: Daffner RH, editor. Imaging of vertebral trauma. 3rd ed. Cambridge: Cambridge University Press; 2011.

Daffner RH, Hackney DB. ACR appropriateness criteria on suspected spine trauma. J Am Coll Radiol. 2007;4:762–75.

Daffner RH, Deeb ZL, Golderberg AL, et al. The radiologic assessment of post-traumatic vertebral stability. Skelet Radiol. 1990;19:103–8.

Dionello R, Lopez de Heredia L, Hughes RJ, et al. Review: indications for interventional radiology in the management of patients with spinal cord injuries. Top Spinal Cord Inj Rehabil. 2013;19:211–21.

D'souza MM, Choudhary A, Poonia M, et al. Diffusion tensor MR imaging in spinal cord injury. Injury. 2017;48:880–4.

Ducreux D, Fillard P, Facon D, et al. Diffusion tensor magnetic resonance imaging and fiber tracking in spinal cord lesions: current and future indications. Neuroimaging Clin N Am. 2007;17:137–47.

Eppenberger P, Andreisek G, Chhabra A. Magnetic resonance neurography: diffusion tensor imaging and future directions. Neuroimaging Clin N Am. 2014;24:245–56.

Fehlings MG, editor. Critical care in spinal cord injury. London: Future Medicine; 2013.

Fehlings MG, Rao SC, Tator CH, et al. The optimal radiologic method for assessing spinal canal compromise and cord compression in patients with cervical spinal cord injury. Part II: results of a multicenter study. Spine (Phila Pa 1976). 1999;24:605–13.

Flanders AE, Schaefer DM, Doan HT, et al. Acute cervical spine trauma: correlation of MR imaging findings with degree of neurologic deficit. Radiology. 1990;177:25–33.

Flanders AE, Spettell CM, Tartaglino LM, et al. Forecasting motor recovery after cervical spinal cord injury: value of MR imaging. Radiology. 1996;201:649–55.

Goldberg AL, Kershan SM. Advances in imaging of vertebral and spinal cord injury. J Spinal Cord Med. 2010;33:105–16.

Graham B, Van Peteghem PK. Fractures of the spine in ankylosing spondylitis. Diagnosis, treatment, and complications. Spine (Phila Pa 1976). 1989;14:803–7.

Hadley MN, Walters BC. Introduction to the guidelines for the management of acute cervical spine and spinal cord injuries. Neursurgery. 2013;72(Suppl 2):5–16.
Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.
Holliman CJ, Mayer JS, Cook RT, et al. Is the anteroposterior cervical spine radiograph necessary in initial trauma screening? Am J Emerg Med. 1991;9:421–5.
Insko EK, Vicente H, Gracias VH, et al. Utility of flexion and extension radiographs of the cervical spine in the acute evaluation of blunt trauma. J Trauma. 2002;53:426–9.
Kaji A, Hockberger R. Imaging of spinal cord injuries. Emerg Med Clin N Am. 2007;25:735–50.
Klein JP. A practical approach to spinal imaging. Continuum (Minneap Minn). 2015;21:36–51.
Krings T, Lasjaunias PL, Hans FJ, et al. Imaging in spinal vascular disease. Neuroimaging Clin N Am. 2007;17:57–72.
Laker SR, Concannon LG. Radiologic evaluation of the neck: a review of radiography, ultrasonography, computed tomography, magnetic resonance imaging, and other imaging modalities for neck pain. Phys Med Rehabil Clin N Am. 2011;22:411–28.
Lammertse D, Dungan D, Dreisbach J, et al. Neuroimaging in traumatic spinal cord injury: an evidence-based review for clinical practice and research. J Spinal Cord Med. 2007;30:205–14.
Martin RF, Eldrup-Jorgensen J. Blunt trauma to the carotid arteries. J Vasc Surg. 1991;14:789–93.
Moseley ME, Liu C, Rodriguez S, et al. Advances in magnetic resonance neuroimaging. Neurol Clin. 2009;27:1–19.
Nijenhuis RJ, Mull M, Wilmink JT, et al. MR angiography of the great anterior radiculomedullary artery (Adamkiewicz artery) validated by digital subtraction angiography. AJNR Am J Neuroradiol. 2006;27:1565–72.
Platzer P, Jaindl M, Thalhammer G, et al. Clearing the cervical spine in critically injured patients: a comprehensive C-spine protocol to avoid unnecessary delays in diagnosis. Eur Spine J. 2006;15:1801–10.
Quencer RM, Bunge RP. The injured spinal cord: imaging, histopathologic clinical correlates, and basic science approaches to enhancing neural function after spinal cord injury. Spine. 1996;21:2064–6.
Quencer RM, Bunge RP, Egnor M, et al. Acute traumatic central cord syndrome: MRI-pathological correlations. Neuroradiology. 1992;34:85–94.
Rybicki F, Nawfel RD, Judy PF, et al. Skin and thyroid dosimetry in cervical spine screening: two methods for evaluation and a comparison between a helical CT and radiographic trauma series. AJR Am J Roentgenol. 2002;179:933–7.
Stiell IG, Wells GA, Vandemheen KL, et al. The Canadian C-spine rule for radiography in alert and stable trauma patients. JAMA. 2001;286:1841–8.
Stiell IG, Clement CM, McKnight RD, et al. The Canadian C-spine rule versus the NEXUS low-risk criteria in patients with trauma. N Engl J Med. 2003;349:2510–8.
Streitwieser DR, Knopp R, Wales LR, et al. Accuracy of standard radiographic views in detecting cervical spine fractures. Ann Emerg Med. 1983;12:538–42.
Walters BC, Hadley MN, Hurlbert RJ, et al. American Association of Neurological Surgeons; Congress of Neurological Surgeons. Guidelines for the management of acute cervical spine and spinal cord injuries: 2013 update. Neurosurgery. 2013;60(Suppl 1):82–91.
White AA 3rd, Johnson RM, Panjabi MM, et al. Biomechanical analysis of clinical stability in the cervical spine. Clin Orthop Relat Res. 1975;109:85–96.
Williams KD. Fractures, dislocations, and fracture-dislocations of the spine. In: Azar FM, Beaty JH, editors. Campbell's operative orthopaedics. 14th ed. Philadelphia: Elsevier; 2021.
Yoshioka K, Niinuma H, Kawakami T, et al. Three-dimensional demonstration of the artery of Adamkiewicz with contrast-enhanced magnetic resonance angiography. Ann Thorac Surg. 2005;79:1785.
Yoshioka K, Niinuma H, Ehara S, et al. MR angiography and CT angiography of the artery of Adamkiewicz: state of the art. Radiographics. 2006;26:563–73.

Recommended Additional Reading

American Spinal Injury Association. International standards for neurological classification of spinal cord injury. Revised 2019. American Spinal Injury Association: Atlanta; 2019.
Azar FM, Beaty JH, editors. Campbell's operative orthopaedics. 14th ed. Philadelphia: Elsevier; 2021.
Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Cohen-Adad J, Wheeler-Kingshott CAM, editors. Quantitative MRI of the spinal cord. New York: Elsevier; 2014.
Crossman A, Neary D. Neuroanatomy: an illustrated colour test. 5th ed. Philadelphia: Elsevier; 2015.
Daffner RH, editor. Imaging of vertebral trauma. 3rd ed. Cambridge: Cambridge University Press; 2011.
Durrant DH, True JM. Myelopathy, radiculopathy, and peripheral entrapment syndromes. Boca Raton: CRC Press; 2002.
Fehlings MG, editor. Critical care in spinal cord injury. London: Future Medicine; 2013.
Fehlings MG, Vccaro AR, Roakye M, et al., editors. Essentials of spinal cord injury: basic research to clinical practice. New York: Thieme; 2013.
Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.
Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.
Passias PG, editor. Cervical myelopathy. Philadelphia: Jaypee Brothers Medical Publishers (P) Ltd; 2016.

9 Commonly Used Laboratory Tests in the Management of Spinal Cord Injuries

Laboratory testing can be used to diagnose a specific condition, monitor disease progression, or confirm diagnoses that can help the physician narrow down the differential diagnosis. Laboratory tests are tools for gaining additional information about the patient. By themselves, these tests are not therapeutic; however, when combined with a thorough medical history and physical examination, these tests can confirm a diagnosis or provide valuable information about a patient's condition and response to therapy that is not apparent from the medical history and physical examination alone. Physicians involved in the evaluation and treatment of spinal cord injuries and disorders should be familiar with the patient's disability and changed condition, as well as with special diagnostic tools and diagnostic tests required for general medical management. The diagnostic process required in the process of diagnosing and treating various medical issues related to spinal cord injuries, including laboratory tests, is very important in order to solve the medical problems early and not delay rehabilitation. In particular, spinal cord physicians are commonly treated with associated medical problems, including bladder and bowel dysfunction, electrolyte changes, endocrinologic changes, wound care or pressure injury management, autonomic dysfunction, sexual problems, etc. In addition, since the life expectancy of people with spinal cord injuries is increased and the prevalence of metabolic disorders such as obesity, hypertension, and diabetes is higher than in the general population, it is necessary to be familiar with appropriate diagnostic tests related to these diseases. Laboratory tests applicable to physicians involving in spinal cord medicine include simple blood tests that are used to assess complete blood cell counts (CBC), electrolyte disorders, liver or kidney functions. Specific laboratory tests, including urine analysis and urine culture/sensitivity, inflammatory markers, nutrition markers, bone turnover markers, coagulation markers, metabolites, arterial blood gas, lipids, and cardiac tests, are applicable to certain medical problems.

This chapter describes the basic laboratory tests, as well as their clinical implications and applications, required to diagnose various medical complications and assess pathological processes among the diagnostic tools related to medical problems in spinal cord injuries/disorders.

9.1 Factors to Be Considered in Appropriate Laboratory Testing

As much as possible, coordinate patient activities with test schedules to avoid conflicts with meal times and administration of medications, treatments, or other diagnostic tests and travel times. NPO (Latin, *non* per os; nothing by

H.-Y. Ko, *Management and Rehabilitation of Spinal Cord Injuries*,
https://doi.org/10.1007/978-981-19-0228-4_9

mouth) status is maintained when necessary, and medications should be administered in a timely manner. Most normal blood test values are determined by measuring fasting samples. Certain factors can affect test results. For example, patient's posture is important when measuring plasma volume, as this value is 12–15% higher in a person who has been supine for several hours. Changing from the supine position to a standing position can change the values as follows: increased hemoglobin (Hb), red blood cell (RBC) count, hematocrit (Hct), calcium (Ca), potassium (K), phosphorus (P), aspartate aminotransferase (AST), phosphatases, total protein, albumin, cholesterol, and triglycerides. Moving from an upright position to a supine position results in increased hematocrit, calcium, total protein, and cholesterol. A tourniquet that is applied for longer than 1 minute leads to laboratory value increases in protein (5%), iron (6.7%), AST (9.3%), and cholesterol (5%) and decreases in K^+ (6%) and creatinine (2% to 3%). Age, gender, race, environment, posture, diurnal, and other cyclic variations, foods, beverages, fasting or postprandial state, drugs, and exercise can all influence the derived values (Fischbach and Dunning III 2015).

Many professional organizations are changing the values of clinical laboratory data from conventional units to Système International (SI) units. Many data is currently reported in both ways. For example, SI concentrations are written as amount per volume (moles or millimoles per liter) rather than as mass per volume (grams, milligrams, milliequivalents per deciliter, milliliters, or liter). Numerical values can differ or be the same between systems. For example, chloride is the same in both systems: 95–105 mEq/L (conventional unit) and 95–105 mmol/L (SI unit). Clinical laboratory data can be reported in conventional units, SI units, or both. Examples of conversion of data from the two systems are included in Table 9.1. To convert SI units to conventional U.S. units, *divide* by the conversion factor; to convert conventional US units to SI units, *multiply* by the factor. For example, to convert a digoxin level (drug management) of 0.6 nmol/L (SI units), *divide* by the factor 1.281 to get conventional units of 0.5 ng/dL. To convert a Ca^{2+} (electrolyte) value of 8.6 mg/dL (conventional units), *multiply* by the factor 0.2495 to get the SI units of 2.15 mmol/L (Fischbach and Dunning III 2015).

9.2 Commonly Used Laboratory Tests in Spinal Cord Injuries

9.2.1 Simple Blood Tests

9.2.1.1 Complete Blood Cell Counts

The CBC is one of the most frequently ordered laboratory procedures. The CBC is a basic blood test and a group of tests that evaluate the composition and concentration of the cellular components of blood: red blood cells (RBCs), white blood cells (WBCs), and platelets. The RBC parameters consist of the RBC count, hemoglobin (Hb), hematocrit (Hct), red blood cell distribution width (RDW), and three RBC indices such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). The WBC parameters are the WBC, neutrophil, lymphocyte, eosinophil, and basophil counts. The platelet parameters are the platelet count, platelet distribution width (PDW), mean platelet volume (MPV), and plateletcrit (Nah et al. 2018). The CBC is often a routine blood test and is used to assess anemia, infection, fever, weakness, and blood disorders. Table 9.2 shows the normal values of the CBC test. In addition to the normal values, critical values for hemoglobin <5.0 g/dL (heart failure and death) or hemoglobin >20.0 g/dL (hemoconcentration and clogging of capillaries), hematocrit <15% (cardiac failure and death), platelet count <30,000/μL (tendency for spontaneous bleeding, prolonged bleeding time, and petechiae), WBC count <2500/μL or >30,000/μL are specified.

Table 9.1 Examples of conversion between conventional units and SI units

Component	System	Present reference intervals	Present unit	Conversion factor	SI reference intervals	SI unit symbol
Alanine aminotransferase (ALT)	Serum	5–40	U/L	1.00	5–40	U/L
Albumin	Serum	3.9–5.0	g/dL	10	39–50	g/L
Alkaline phosphatase	Serum	35–110	U/L	0.01667	0.6–1.8	μkat/L
Aspartate aminotransferase (AST)	Serum	5–40	U/L	0.01667	0.08–0.67	μkat/L
Bilirubin	Serum					
Direct		0–0.2	mg/dL	17.10	0–4	μmol/L
Total		0.1–1.2	mg/dL	17.10	2–20	μmol/L
Calcium	Serum	8.6–10.3	mg/dL	0.2495	2.15–2.57	mmol/L
Carbon dioxide, total	Serum	22–30	mEq/L	1.00	22–30	mmol/L
Chloride	Serum	98–108	mEq/L	1.00	98–108	mmol/L
Cholesterol	Serum					
Age <29 year		<200	mg/dL	0.02586	<5.15	mmol/L
30–39 year		<225	mg/dL	0.02586	<5.80	mmol/L
40–49 year		<245	mg/dL	0.02586	<6.35	mmol/L
>50 year		<265	mg/dL	0.02586	<6.85	mmol/L
Complete blood count	Blood					
Hematocrit						
Men		42–52	%	0.01	0.42–0.52	1
Women		37–47	%	0.01	0.37–0.47	1
Red cell count	Blood					
Men		$4.6–6.2 \times 10^6$	/mm^3	10^6	$4.6–6.2 \times 10^{12}$/L	
Women		$4.2–5.4 \times 10^6$	/mm^3	10^6	$4.2–5.4 \times 10^{12}$/L	
White cell count		$4.5–11.0 \times 10^3$	/mm^3	10^6	$4.5–11.0 \times 10^9$/L	
Platelet count		$150–300 \times 10^3$	/mm^3	10^6	$150–300 \times 10^9$/L	
Cortisol	Serum					
8 AM		5–25	μ/dL	27.59	140–690	nmol/L
8 PM		3–13	μg/dL	27.59	80–360	nmol/L
Cortisol	Urine	20–90	ng/24 h	2.759	55–250	nmol/24 hr
Creatine kinase	Serum					
High CK group (black men)		50–250	U/L	1.00	50–520	U/L
Intermediate CK group (nonblack men, black women)		35–345	U/L	1.00	35–345	U/L
Low CK group (nonblack women)		25–145	U/L	1.00	25–145	U/L
Creatinine kinase isoenzyme, MB fraction	Serum	>5	%	0.01	>0.05	1
Creatinine	Serum	0.4–1.3	mg/dL	88.40	35–115	μmol/L
Men		0.7–1.3	mg/dL	88.40	62–115	μmol/L
Women		0.4–1.1	mg/dL	88.40	35–97	μmol/L
Digoxin, therapeutic	Serum	0.5–2.0	ng/mL	1.281	0.6–2.6	nmol/L
Erythrocyte indices	Blood					

(continued)

Table 9.1 (continued)

Component	System	Present reference intervals	Present unit	Conversion factor	SI reference intervals	SI unit symbol
Mean corpuscular volume (MCV)		80–100	microns^3	1.00	80–100	fL
Mean corpuscular hemoglobin (MCH)		27–31	pg	1.00	27–31	pg
Mean corpuscular hemoglobin concentration (MCHC)		32–36	%	0.01	0.32–0.36	1
Ferritin	Serum					
Men		29–438	ng/mL	1.00	29–438	µg/L
Women		9–219	ng/mL	1.00	9–219	µg/L
Folate	Serum	2.5–20.0	ng/mL	2.266	6–46	nmol/L
Follicle-stimulating hormone (FSH)	Serum					
Children		≤12	mlU/mL	1.00	≤12	IU/L
Men		2.0–10.0	mlU/mL	1.00	2.0–10.0	IU/L
Women, follicular		3.2–9.0	mlU/mL	1.00	3.2–9.0	IU/L
Women, midcycle		3.2–9.0	mlU/mL	1.00	3.2–9.0	IU/L
Women, luteal		2.0–6.2	mlU/mL	1.00	2.0–6.2	IU/L
Gases, arterial	Blood					
PO_2		80–95	mm Hg	0.1333	10.7–12.7	kPa
PCO_2		37–43	mm Hg	0.1333	4.9–5.7	kPa
Glucose	Serum	62–110	mg/dL	0.05551	3.4–6.1	mmol/L
Iron	Serum	50–160	µg/dL	0.1791	9–29	µmol/L
Iron-binding capacity	Serum					
Total iron-binding capacity		230–410	µg/dL	0.1791	41–73	µmol/L
Saturation		15–55	%	0.01	0.15–0.55	1
Lactate dehydrogenase	Serum	120–300	U/L	1.00	120–300	U/L
Luteinizing hormone	Serum					
Men		4.9–15.0	mlU/mL	1.00	4.9–15.0	IU/L
Women, follicular		5.0–25	mIU/mL	1.00	5.0–25	IU/L
Women, luteal		3.1–13	mlU/mL	1.00	3.1–13	IU/L
Magnesium	Serum	1.2–1.9	mEq/L	0.4114	0.50–0.78	mmol/L
Osmolality	Serum	278–300	m0sm/kg	1.00	278–300	mmol/kg
Osmolality	Urine	None defined	m0sm/kg	1.00	None defined	mmol/kg
Phenobarbital, therapeutic	Serum	15–40	µg/ml	4.306	65–175	µmol/L
Phenytoin, therapeutic	Serum	10–20	µg/mL	3.964	40–80	µmol/L
Phosphate (phosphorus, inorganic)	Serum	2.3–4.1	mg/dL	0.3229	0.75–1.35	mmol/L
Potassium	Serum	3.7–5.1	mEq/L g/mL	1.00	3.7–5.1	mmol/L
Protein, total	Serum	6.5–8.3	g/dL	10.0	65–83	g/L
Sodium	Serum	134–142	mEq/L	1.00	134–142	mmol/L
Theophylline, therapeutic	Serum	5–20	µg/mL	5.550	28–110	µmol/L
Thyroid-stimulating hormone (TSH)	Serum	0–5	µlU/mL	1.00	0–5	mIU/L
Thyroxine	Serum	4.5–13.2	µg/dL	12.87	58–170	nmol/L
T_3-uptake ratio	Serum	0.88–1.19	1	1.00	0.88–1.19	1
Triiodothyronine (T_3)	Serum	70–235	ng/mL	0.01536	1.1–3.6	nmol/L

Table 9.1 (continued)

Component	System	Present reference intervals	Present unit	Conversion factor	SI reference intervals	SI unit symbol
Triglycerides	Serum	50–200	mg/dL	0.01129	0.55–2.25	mmol/L
Urate (urie acid)	Serum					
Men		2.9–8.5	mg/dL	59.48	170–510	μmol/L
Women		2.2–6.5	mg/dL	59.48	130–390	μmol/L
Urea nitrogen	Serum	6–25	mg/dL	0.3570	2.1–8.9	mmol/L
Vitamin B_{12}	Serum	250–1000	pg/mL	0.7378	180–740	pmol/L

Table 9.2 The normal values of the CBC test

RBC parameters		WBC parameters		Platelet parameters	
RBC count	4.0–6.2 × $10^6/\mu$L (male) 3.5–5.0 × $10^6/\mu$L (female)	WBC count	4500–11,000/ μL	Platelet count	150–400 × $10^3/\mu$L
Hemoglobin	14.0–18.0 g/dL (male) 12–16 g/dL (female)	Neutrophils (segmented neutrophils)	54–62%	MPV	6.4–11 μm^3 (fL)
Hematocrit	39–51% (male) 35–47% (female)	Eosinophils	1–3%	PDW	10.0–17.9%
MCV	82–93 μm^3	Lymphocyte	25–35%	Plateletcrit	0.15–0.62%
MCH	26–34 pg	Basophils	<0.75%		
MCHC	31–38%	Monocytes	3–7%		
RDW	11.5–14.5%				

RBC, red blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width; WBC, white blood cell; MPV, mean platelet volume; PDW, platelet distribution width

RBC Parameters

RBC Count

The RBC (erythrocyte) count (4.6–6.2 × $10^6/\mu$L for male, 4.2–5.4 × $10^6/\mu$L for female) determines the total number of erythrocytes in a sample of blood. Most anemias are associated with low RBC count, hemoglobin, and hematocrit. Common causes are excessive bleeding; a deficiency of iron, vitamin B12, or folic acid; destruction of red cells by antibodies or mechanical trauma; bone marrow malignancy and fibrosis; and structurally abnormal hemoglobin. The RBC count is also decreased due to excessive IV fluids, cancer, and kidney diseases. An elevated RBC count can be caused by dehydration, hypoxia, and polycythemia vera.

Hemoglobin

Hemoglobin (14–18 g/dL for male, 12–16 g/dL for female) is the protein in RBC that transports oxygen from the lungs throughout the body' tissues. Hemoglobin also plays an important role in maintaining the shape of the RBCs. In their natural shape, RBCs are round with narrow centers that resemble donut with no hole in the middle. An abnormal hemoglobin structure can therefore disrupt the shape of RBCs and impair their function and flow through the blood vessels.

RBC Indices

The three main RBC indices are used to determine the average size and hemoglobin level of the RBCs, and they help determine the cause of anemia. The three RBC indices are as follows: mean corpuscular volume (MCV, 80–100 μm^3), the average size of the erythrocytes; mean corpuscular hemoglobin (MCH, 27–31 pg), the average amount of hemoglobin inside an erythrocyte; and mean corpuscular hemoglobin concentration (MCHC, 32–36%), the average

concentration of hemoglobin in the erythrocytes. Normal-sized RBC is termed normocytic. If the MCV is below normal, the RBCs are smaller than normal and are referred to as microcytic. If the MCV is elevated, the RBCs are larger than normal and are called macrocytic.

Hematocrit

The hematocrit (39–51% for male, 35–47% for female) is a test that measures the percentage of blood volume that consists of the RBCs, i.e., the packed red cell volume. A decrease in the number or size of RBCs also decreases space requirement, resulting in a lower hematocrit. An increase in the number or size of RBCs increases the space they occupy, resulting in a higher hematocrit.

WBC Parameters

The WBC (leukocyte, 4500–11,000/μL) count is an important part of the CBC. A differential determines the percentage of two main subpopulations, the granulocyte cells and the mononuclear cells. Granulocytes include neutrophils (segmented neutrophils, 54–62%), eosinophils (1–3%), and basophils (<0.75%). Mononuclear cells include lymphocytes (25–35%) and monocytes (3–7%).

An elevated WBC count occurs in infection, allergy, systemic illness, inflammation, tissue injuries, and leukemia. A low WBC count may occur in some viral infections, immune deficiency states, and bone marrow failure. The WBC count provides clues about certain illnesses and helps physicians monitor a patient's recovery from others.

Platelet

Platelets (thrombocyte) (150–300 × $10^3/\mu$L) aid the coagulation process by adhering to the injured blood vessel walls, where they form the initial platelet plug. A low platelet count may occur in patients with AIDS, viral infections, lymphoma, and lupus erythematosus. A decreased platelet count is also a cause of thrombocytopenia, and can be due to aplastic anemia, leukemia, lymphoma, or bone marrow fibrosis. A low platelet count can occur due to increased destruction. This can result from antibody production, which is often induced by heparin. A mean platelet volume (MPV, 6.4–11 μm^3) measures the average size of platelets. MPV is closely related to a platelet count. Increased MPV is observed in cardiovascular diseases, cerebral stroke, respiratory diseases, chronic renal failure, etc. Abnormally low MPV values correlate with thrombocytopenia (Korniluk et al. 2019). Platelet distribution width (PDW, 10.0–17.9%) reflects variation of platelet size distribution (Farias et al. 2010).

9.2.1.2 Electrolyte Tests

The electrolyte tests are used to identify an imbalance in electrolyte, fluid, or pH. An electrolyte test includes measuring sodium, potassium, chloride, and bicarbonate. These ions are measured to evaluate renal, endocrine, and acid-base function. They are components of both renal function and comprehensive profiles of metabolic biochemistry. Electrolyte concentrations are also evaluated to assist in the study of conditions that cause dehydration, fatigue, cognition deterioration, lung disease, or heart problems.

Other important electrolytes routinely measured in serum or plasma include calcium and phosphorus. These are measured together because they are both affected by bone and parathyroid diseases. Magnesium is another electrolyte that is routinely measured. If there is an imbalance in a single electrolyte such as sodium or potassium, a retest can be used to monitor the imbalance until it is resolved. If there is an acid-base imbalance, blood gases may be ordered that measure the oxygen, carbon dioxide, and pH in the arterial blood.

Importance of electrolyte imbalance lies in part in the serious consequences that result from relatively small changes that can cause diseases or abnormal conditions. For example, the reference range for potassium is 3.7–5.1 mmol/L (mEq/L). Potassium is often a STAT test because values below 3.0 mmol/L are associated with arrhythmia, tachycardia, and cardiac arrest, and values above 6.0 mmol/L are associated with bradycardia and heart failure. Abnormal potassium cannot be treated without reference to bicarbonate, which is a measure of the buffering capacity of the plasma. Sodium bicarbonate and dissolved

carbon dioxide work together to resist changes in blood pH. For example, a high level of plasma bicarbonate indicates a condition called metabolic alkalosis which leads to high blood pH. This can cause hydrogen ions to shift from the cells to the extracellular fluid in exchange for potassium. As potassium moves into the cells, the plasma concentration decreases.

Sodium

Sodium (134–142 mEq/L) is the main extracellular cation. The sodium levels rise directly related to the osmotic pressure of the plasma. Sodium is responsible for almost half of the osmolality of the plasma and therefore plays a main role in maintaining the normal distribution of water and the somatic pressure in the extracellular fluid component. Since water often follows sodium by diffusion, the loss of sodium leads to dehydration and the retention of sodium leads to edema. Hyponatremia can be caused by extrarenal sodium loss (e.g., diarrhea, vomiting, blood loss, excessive sweating, fluid sequestration in third space) or renal sodium loss (e.g., osmotic diuresis, adrenal insufficiency, salt-wasting nephropathy), excessive water drinking, excessive diuretic therapy, and inappropriate secretion of antidiuretic hormone (SIADH). Conditions with hypernatremia do so without promoting an equivalent gain in water. Such conditions include pure water loss (e.g., unreplaced insensible loss, hypodipsia, diabetes insipidus) or hypotonic fluid loss (e.g., vomiting, diarrhea, nasogastric drainage, use of osmotic cathartic agents, loop diuretics).

Potassium

Potassium (3.7–5.1 mEq/L) is the electrolyte used to identify renal failure. Like sodium, potassium is filtered freely by the kidney. In the distal tubule of the kidney, however, sodium is absorbed, and potassium is excreted. Common causes of low serum potassium are vomiting, diarrhea, alkalosis, excessive use of thiazide diuretics, excessive intravenous fluid administration, and SIADH. Hyperkalemia is also commonly caused by diabetes insidious, hemolytic anemia, digitalis toxicity, and Addison's disease. Hyperkalemia is the most significant and life-threatening complication in renal failure. Potassium levels <3.0 mEq/L are associated with marked neuromuscular symptoms and indicate a critical degree of intracellular depletion. Potassium levels <2.5 mEq/L may be life threatening.

Calcium and Phosphorus

Calcium (8.6–10.3 mg/L) and phosphorus (2.3–4.1 mg/dL) are measured together, as both are likely to be abnormal in bone and parathyroid diseases. Parathyroid hormone causes resorption of these minerals from bone. However, it promotes intestinal absorption and renal reabsorption of calcium and renal excretion of phosphorus. In hyperparathyroidism, serum calcium is increased, and phosphorus is reduced. In hypothyroidism and renal disease, serum calcium is low, but phosphorus is high.

Magnesium

Serum magnesium levels (1.2–1.9 mEq/L) may be increased by hemolytic anemia, renal failure, hyperparathyroidism, magnesium-based antacids, and Addison's disease. Serum magnesium is also decreased in diarrhea, hypoparathyroidism, pancreatitis, Cushing's disease, and with excessive diuretic use. Low magnesium can be caused by a number of antibiotics and other drugs and by the administration of intravenous solutions. Magnesium is needed for the secretion of parathyroid hormone, and therefore, a low serum magnesium can induce hypocalcemia.

9.2.1.3 Liver and Kidney Functions

Liver Function Test

The liver function test refers to a group of serologic tests that evaluate various aspects of liver function. Laboratory tests for total protein, albumin, ammonia, and cholesterol are markers for the synthetic function of the liver. Tests for cholesterol, bilirubin, and alkaline phosphatase (ALP) are measurements of the excretory function of the liver. The enzymes alanine aminotransferase (ALT, formerly SGPT), aspartate aminotransferase (AST, formerly SGOT),

gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH), and virus tests are markers for liver damage.

Serum Transaminases

ALT (5–40 U/L for male, 4–35 U/L for female) is present in tissues other than the liver, and its concentration in the liver is far higher than in any other tissue. ALT is very sensitive to necrotic or inflammatory liver damage. A remarkable increase in serum AST level (5–40 U/L for male, 7–34 U/L for female) occurs in acute viral hepatitis, acute drug-induced liver damage, and ischemic hepatitis. The level of the increase does not correlate with the extent of liver cell necrosis and therefore has no predictive prognostic value. AST is not as specific for liver disease as ALT, which is increased in myocardial infarction, pancreatitis, muscle diseases, and many other conditions (Chopra and Griffin 1985).

Alkaline Phosphatase

The serum alkaline phosphatase (30–115 U/L) activity originates from liver, bone, intestine, and placenta. In normal children with active bone growth, influx of enzyme from osteoid tissue can lead to threefold elevation in alkaline phosphatase values above the normal value (Chopra and Griffin 1985). Sustained elevation of serum alkaline phosphatase and phosphorus levels reflects osteoblastic activity (Kim et al. 1990). Alkaline phosphatase levels are not correlated with degree of bone activity or maturation of heterotopic ossification and thus cannot be used to assess maturity of the ectopic bone or predict recurrence. Higher values last an average 5 months. Elevation of serum creatinine phosphokinase may be a more reliable predictor of heterotopic ossification (Sherman et al. 2003; Singh et al. 2003).

Lactate Dehydrogenase

LDH (120–300 U/L) is found in almost all cells in the body, including liver, myocardium, skeletal muscle, brain, kidney, and RBCs. Different forms of the isoenzymes exist in different tissues. An elevated serum LDH value is a nonspecific finding. The hepatic origin isoenzymes are LDH4 and LDH5, which are also derived from the skeletal muscles (Chopra and Griffin 1985).

Bilirubin

The normal value for total bilirubin (0.1–1.2 mg/dL) is less than 1 mg/dL. Two fractions, a conjugated or direct fraction (0–0.2 mg/dL) and an unconjugated or indirect fraction, are obtained fairly routinely. It is useful to classify hyperbilirubinemia into conjugated and unconjugated categories. Unconjugated bilirubin is formed in the reticuloendothelial (RE) cells of the spleen. Direct bilirubin is formed only by the liver, and therefore, is specific for hepatic or biliary disease. Its concentration in the blood is very low and, therefore, even slight increases are significant. Direct bilirubin is not sensitive to all forms of liver disease and is not always elevated in the earliest stages of disease; therefore, ALT is needed to exclude a diagnosis. Patients are considered to have conjugated hyperbilirubinemia if more than 50% of the elevated total bilirubin level is conjugated, and classified as having unconjugated hyperbilirubinemia if more than 80% of the total bilirubin level is unconjugated or indirect.

Blood Ammonia

Ammonia (<50 μmol/L) is generated by bacterial degradation of nitrous contents (dietary protein, blood) in the intestine. Ammonia levels are also useful in diagnosing and treating hepatic encephalopathy, a serious brain disorder caused by the accumulated toxins that result from liver disease and liver failure. Although ammonia levels of the blood and cerebrospinal fluid are elevated in most patients with hepatic coma, there is a poor correlation between blood ammonia levels and the degree of hepatic encephalopathy. The correlation is better with arterial ammonia than with venous ammonia, which can be increased by muscular exercise, seizure activity, or even clenching the fist.

9.2.1.4 Kidney Function Test

Blood tests for the kidney function include measurements and calculations: BUN, creatinine, uric acid, carbon dioxide, glucose, calcium, chloride, phosphorus, potassium, sodium, BUN-to creatinine ratio (calculated), and estimated glomerular filtration rate (GFR) (calculated). The urine tests, except routine urinalysis, include cre-

atinine clearance, urea clearance, urine osmolality, urine protein, and urine sodium.

Blood Tests for Kidney Function

Blood Urea Nitrogen

Blood urea nitrogen (BUN) (6–25 mg/dL) is a byproduct of food protein metabolism. This waste product is then filtered from the blood and excreted in the urine by the kidneys. The BUN test measures the amount of nitrogen contained in the urea. High BUN levels can indicate kidney dysfunction, but because BUN is also affected by protein intake and liver function, the test is usually done together with a blood creatinine, a more specific indicator of kidney function.

Creatinine

A waste product that comes from a byproduct of muscle energy metabolism is filtered from the blood by the kidneys and excreted into the urine. Production of creatinine (≤1.3 mg/dL) depends on a person's muscle mass, with very little fluctuation. An elevated blood creatinine level is a more sensitive indicator of impaired kidney function than the BUN. Blood creatinine levels in the blood vary depending on age, race, and body size. BUN is often ordered with creatinine for comparison. The BUN/creatinine ratio is also a useful indicator of kidney disease. The ratio should be between 10:1 and 20:1.

Cystatin C

The glomerular filtration rate (GFR) is a calculation that determines how well the blood is filtered by the kidneys. This is a way to measure remaining kidney function. GFR is crucial for the diagnosis, staging, and prognosis of chronic kidney disease (CKD). In addition, low GFR is also a strong predictor of cardiovascular disease, frailty, increased risk of hospitalizations, and early mortality. The GFR is estimated in a laboratory setting using readily available information such as age, sex, race, and measurement of serum creatinine as the biomarker of filtration. However, serum creatinine is an incomplete biomarker because it is known to be affected by diet, muscle mass, certain medications, rapidly changing kidney function, and active kidney secretion (Stevens et al. 2006; Tangri et al. 2011).

Cystatin C (0.5–1.0 mg/L) is an endogenous 13 kDa protein of the cystatin superfamily of cysteine protease inhibitors, is produced by all nucleated cells at a relatively constant rate and excreted almost exclusively by glomerular filtration, then almost completely reabsorbed and catabolized by proximal tubular epithelial cells. Cystatin C has been suggested as a potential alternative to serum creatinine because it potentially has fewer non-GFR determinants. A minor reduction in GFR leads to and increase in above normal cystatin C concentrations, even when serum creatinine is still within normal range. The use of serum cystatin C helps to avoid the limitations related to both diet and muscle mass that affect serum creatinine. Cystatin C may be more accurate than serum creatinine in estimating GFR, and is more strongly associated with all-cause mortality and cardiovascular events (Ferguson et al. 2003). Cystatin C generation is considered constant; therefore, serum levels are not influenced by variables other than kidney function (Tangri et al. 2011). Cystatin C as a marker for estimating GFR is independent of gender, age, muscle mass, and cirrhosis and does not need to be corrected for height or weight. It is superior to serum creatinine.

9.2.2 Urinalysis

A routine urinalysis is often the first test conducted if kidney problems are suspected. A small, randomly collected urine sample is examined physically for things like color, odor, appearance, and concentration (specific gravity); chemically for substances such a protein, glucose, and pH; and microscopically for the presence of cellular elements (RBCs, WBCs, and epithelial cells), bacteria, crystals, and casts.

9.2.2.1 Physical Tests

The physical tests measure the color, transparency, and specific gravity of a urine. The specific gravity of urine (1.003–1.030) is a measure of the concentration of dissolved solutes of the kidney

in order to concentrate the urine. The specific gravity varies with fluid and solute intake. It is increased (>1.035) in persons with diabetes mellitus and persons taking large amounts of medication. It is also increased after radiologic studies of the kidney owing to the excretion of X-ray contrast dye. A consistently low specific gravity (<1.003) is observed in persons with large amount fluid intake and diabetes insipidus. In renal failure, the specific gravity remains equal to that of blood plasma (1.008–1.010) regardless of changes in the patient's salt and water intake.

9.2.2.2 Biochemical Tests

Biochemical urine tests are available for measuring as follows: pH (4.6–8.0, average 6.0), protein (qualitative 0, 0–0.1 g/24 h), blood, leukocytes, glucose (qualitative 0, ≤0.3 g/24 h), ketones (qualitative 0), urobilinogen (0–4 mg/24 h), and nitrate. Some disease bacteria, including the lactose-positive *Enterobacteriaceae, Staphylococcus, Proteus, Salmonella,* and *Pseudomonas,* can reduce nitrate in urine to nitrite. A positive nitrite test indicates bacteriuria, or the presence of bacteria in the urine. Urobilinogen is a substance that is formed in the gastrointestinal tract by the bacterial reduction of conjugated bilirubin. Increased urobilinogen in urine occurs in prehepatic jaundice (hemolytic anemia), hepatitis, and other forms of hepatic necrosis that impair the blood circulation in the liver and surrounding organs. The urobilinogen test is helpful in differentiating these conditions from obstructive jaundice, which leads to a decreased production of urobilinogen. The presence of white blood cells in the urine usually means a urinary tract infection, such as cystitis, or kidney diseases, such as pyelonephritis or glomerulonephritis.

9.2.3 Infection/Inflammatory Markers

9.2.3.1 Erythrocyte Sedimentation Rate

The erythrocyte sedimentation rate (ESR) (0–13 mm in 1 h for male, 0–20 mm in 1 h for female) is the rate at which erythrocytes sediment over a period of 1 h. This is a common hematology test and a nonspecific measure of inflammation. To perform the test, anticoagulated blood was traditionally placed in an upright tube, known as a Westergren tube and the rate at which the erythrocytes fall was measured and reported in mm/h. Elevated ESR indicates nonspecific tissue inflammation, including infection, anemia, chronic disease, allergic reaction, malignancy, or in patients taking heparin). However, normal ESR tends to exclude active infection or active inflammatory disorders such as rheumatoid arthritis, SLE, acute rheumatic fever, arteritis, or polymyalgia rheumatica. ESR can be used to follow therapeutic responses of chronic inflammation.

9.2.3.2 C-Reactive Protein

C-reactive protein (CRP) (0.8 mg/dL) is an acute-phase reactant serum protein that is produced by the liver in response to inflammation. A high level of CRP in the blood is an inflammation marker. It can be caused by a variety of diseases, from infection to cancer. CRP levels rise rapidly in the presence of infection or inflammation, then fall as the inflammation subsides. Thus, it is usually used to monitor the progress of infection during antibiotic treatment. The major advantage of CRP over ESR test is that it can be performed on freeze-stored serum. High CRP levels can also indicate inflammation in the arteries of the heart, which can mean a higher risk of heart attack. However, the CRP test is an extremely nonspecific test, and CRP levels can be elevated in any inflammatory condition.

9.2.4 Coagulation Markers

9.2.4.1 Prothrombin Time and International Normalized Ratio

The prothrombin time (PT) (8.3–10.8 s) evaluates the integrity of the extrinsic and common pathways of plasma-mediated hemostasis. It measures the time, in seconds, for clot formation to occur after mixing a sample of patient plasma with tissue factor (thromboplastin) and calcium. It is sensitive to fibrinogen deficiencies and fac-

tors II, V, VII, or X. Since three of these factors have vitamin K-dependent synthesis (factors II, VII, and X), the PT assay was used to monitor anticoagulation with vitamin K antagonists such as warfarin. Given the importance of monitoring PT results for long-term warfarin therapy, the international normalized ratio (INR) was introduced to normalize PT results among different laboratories. The INR (0.9–1.2) is calculated as INR = (patient PT/standard PT), in which the standard PT represents the geometric mean of multiple normal samples from the testing laboratory (Panigrahi and Liu 2020).

9.2.4.2 Activated Partial Thromboplastin Time

The activated partial thromboplastin time (aPTT) (21–33 s) evaluates the integrity of the intrinsic and common pathways of plasma-mediated hemostasis. It measures the time, in seconds, for clot formation to occur after a sample of patient's plasma has been mixed with phospholipid, calcium, and an activator of the intrinsic pathway of coagulation (e.g., celite, kaolin, silica, or ellagic acid). The aPTT is more sensitive to deficiencies in factors VIII and IX than other factors in the intrinsic and common pathways. There is no reference standard reagent for the aPTT analogous to the INR for PT, individual institutions have to define their own normal ranges and aPTT values cannot be compared between laboratories (Panigrahi and Liu 2020).

9.2.4.3 Fibrinogen

Fibrinogen (200–375 mg/dL for male, 200–430 mg/dL for female) is a substrate for three major enzymes: thrombin, plasmin, and factor XIIIa. Due to various functional interactions, it plays a crucial role in hemostasis. Fibrinogen is the soluble precursor to insoluble fibrin, and it also supports platelet aggregation. The fibrin clot also activates the fibrinolytic system. The balance between coagulation and fibrinolysis thus determines the clinical manifestations (Mosesson 2005; Hasegawa et al. 2018). During tissue and vascular injury, it is enzymatically converted to fibrin by thrombin and then to a fibrin-based blood clot.

9.2.4.4 D-dimer

D-dimer ($\leq$0.25 μg/mL) is a soluble fibrin degradation product that is released into the blood when a clot is lysed by plasmin through the fibrinolytic mechanism. That is, D-dimers are produced during the polymerization of fibrinogen when it forms fibrin. D-dimer is an indirect marker of fibrinolysis and fibrin turnover; this molecule exhibits unique properties as a biological marker of hemostatic abnormalities as well as an indicator of intravascular thrombosis. D-dimer has been extensively investigated for excluding the diagnosis of venous thromboembolism and is used routinely for this indication (Hasegawa et al. 2018; Johnson et al. 2019). D-dimer levels may be used to predict the likelihood of DVT development in patients with spinal cord injuries. D-dimer is detectable at levels greater than 0.5 μg/mL of fibrinogen equivalent units in nearly all patients with venous thromboembolism. In general, it is sensitive test but it lacks specificity for the diagnosis of DVT and is therefore only useful if it is negative because plasma levels of D-dimer are increased in a variety of inflammatory and prothrombotic conditions associated with activation of coagulation, such as infection, surgery, and trauma. According to a study, the optimal timing for screening test by D-dimer is 2 weeks after traumatic cervical spinal cord injuries, and optimal threshold level for D-dimer for diagnosing DVT is 16 μg/dL (0.16 μg/mL) (Masuda et al. 2015). A positive D-dimer is 0.5 μg/mL or greater. Since this is a screening test, a positive D-dimer is a positive screen. There is not necessary a critical level for a D-dimer (Ghazanfar and Thomsen 2018; Lim et al. 2018). Combined examination of D-dimer and ultrasound screening in patients with acute spinal cord injuries improves the detection of venous thrombosis, including pulmonary embolism, compared to D-dimer screening alone (Kumagai et al. 2020).

False negatives and false positives can occur. Due to the occurrence of false-negative results, a D-dimer should only be used in the setting of low suspicion for DVT or pulmonary embolism and also known as venous thromboembolism. There are various physiologic states or diseases that can

cause patients to have an elevated D-dimer in the absence of pulmonary embolism, DVT, or disseminated intravascular coagulation (DIC). These include pregnancy, malignancy, cigarette smoking, trauma, or infection or sepsis. In addition, elderly patients, immobilized patients, patients with autoimmune diseases, or patients who have recently had surgery may have an elevated D-dimer (Bounds and Kok 2021).

9.2.5 Arterial Blood Gas

Arterial blood gas (ABG) analysis is an essential part of diagnosing and managing a patient's ventilation, oxygenation status, and acid-base balance. Therefore, common indications include diagnosis and assessment of respiratory disorders, assessment of oxygenation and guide oxygen therapy, assessment of metabolic disturbance. An ABG test measures the acidity (pH) and the levels of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) in the arterial blood.

9.2.5.1 pH

The pH value (7.35–7.45) measures the acidity of the blood, reflecting the number of hydrogen ions (H^+). The pH of blood is usually between 7.34 and 7.45. Blood is slightly basic (alkaline).

9.2.5.2 Partial Pressure of Oxygen (PaO_2)

PaO_2 (75–100 mmHg) reflects the amount of oxygen gas dissolved in the blood. Less than expected PaO_2 indicates hypoxemia. This may be due to hypoventilation or a mismatch of ventilation and perfusion.

9.2.5.3 Partial Pressure of Carbon Dioxide ($PaCO_2$)

$PaCO_2$ (35–45 mmHg) is the amount of CO_2 dissolved in the blood. Acute changes in $PaCO_2$ will alter the pH. As a general rule, low pH with high $PaCO_2$ suggests respiratory acidosis, while low pH with low $PaCO_2$ suggests a metabolic acidosis.

9.2.5.4 Bicarbonate (HCO_3^-)

Bicarbonate (22–26 mEq/L) is a weak base that is regulated by the kidneys as part of acid-base homeostasis. Bicarbonate prevents the pH of the blood from becoming too acidic or too basic. Together with pH determination, bicarbonate measurements are used to diagnose and treat disorders associated with acid-base imbalance in the respiratory and metabolic systems. The bicarbonate content of serum or plasma is a significant indicator of electrolyte dispersion and anion deficit.

9.2.5.5 Base Excess

The metabolic component of the acid-base balance is reflected in the base excess. This is a calculated value derived from the blood pH and $PaCO_2$. It is defined as the amount of acid required to restore 1 l of blood to its normal pH at a $PaCO_2$ of 40 mmHg. The base excess (−2 to + 2 mmol/L) increases in metabolic alkalosis and decreases in metabolic acidosis, but its usefulness in interpreting blood gas results is controversial.

9.2.5.6 Anion Gap

The anion gap (<11 mEq/L, 3–11 mEq/L) helps in the diagnosis of metabolic acidosis. This difference between the concentrations of measured anions and cations increases with dehydration and decreases with hypoalbuminemia. The gap also widens as the concentration of unmeasured anions such as ketones and lactate increases.

9.2.5.7 Oxygen Saturation

Oxygen saturation (sO_2) (94–100%) measures the percentage of hemoglobin that is fully combined with O_2. It can be obtained non-invasively and continuously using a pulse oximeter.

9.2.6 Lipid Profile

A blood lipid profile usually includes total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides.

9.2.6.1 Total Cholesterol

Total cholesterol (<200 mg/dL) includes both LDL cholesterol and HDL cholesterol levels and provides a preview of the lipid panel. Because it measures both HDL and LDL cholesterol, total cholesterol itself can be misleading and is usually not used for treatment decisions.

9.2.6.2 HDL Cholesterol

HDL (40–60 mg/dL, desirable > 60 mg/dL) is considered good cholesterol and higher values protect against heart diseases.

9.2.6.3 LDL Cholesterol

LDL (optimal < 100 mg/dL) is considered bad cholesterol, and a higher level can clog blood vessels and increase the risk of heart disease and stroke. Desired LDL targets are personalized based on medical condition.

9.2.6.4 Triglycerides

Triglycerides (<150 mg/dL) are the main components of natural fats and oils found in the blood and stored in fat cells. Foods high in trans and saturated fats, simple carbohydrates, concentrated sweets, excessive calorie consumption and alcohol use can increase triglyceride levels.

9.2.7 Nutrition Markers

Serum visceral proteins such as albumin and prealbumin have traditionally been used as markers of nutritional status of patients. Prealbumin is often preferred over albumin these days because it has a shorter half-live and reflects faster in nutritional state (Bharadwaj et al. 2016). Additionally, the BMI, hemoglobin, total cholesterol, and total protein are assessed. Other nutrition markers such as urinary creatinine or 3-methylhistidine as indicators of muscle protein breakdown have not been widely used. Serum somatomedin C (insulin growth factor-1, IGF-1) is less affected by inflammation and falls during malnutrition (Keller 2019).

9.2.7.1 Serum Visceral Protein

Serum Albumin

Albumin (3.9–5.0 g/dL) is the most abundant protein in human serum, making up 55–65% of total plasma protein. Approximately 300–500 g of albumin is distributed in the body fluid, and the average adult liver synthesizes about 15 g per day, with 4% of the total albumin pool being degraded daily. Albumin has been used as an indicator of malnutrition in patients in clinically stable conditions for decades. Albumin has been criticized for its lack of specificity and long half-life (approximately 20 days) as a biomarker in nutritional evaluation. Serum albumin can be used as a biomarker for the differential diagnosis of unexplained weight loss (involuntary weight loss of more than 5 kg in the previous 6 months) due to a malignancy. Multivariate analysis showed that the strongest predictors of a neoplasm were age >80 years, white blood cell count >12,000/mm^3, and serum albumin <3.5 g/dL (Keller 2019).

Serum Prealbumin

Determining the level of prealbumin (18–40 mg/dL), a hepatic protein, is a sensitive and cost-effective method of assessing the severity of illness resulting from malnutrition in patients who are critically ill or have a chronic disease (Beck and Rosenthal 2002). Prealbumin, also named transthyretin, is a transport protein for thyroid hormone and is synthesized by the liver and partly catabolized by the kidneys. The use of prealbumin has been recommended as a nutritional marker, especially during refeeding and in the elderly (Ingenbleek 2019). The main advantage of prealbumin compared to albumin is its shorter half-life (2–3 days) (Table 9.3), making it a more favorable marker for acute changes of the nutritional status. Serum prealbumin concentrations below 10 mg/dL are associated with malnutrition (Table 9.4). Prealbumin was not influenced by intestinal protein losses in patients with protein-losing enteropathy (Keller 2019). Prealbumin levels may be increased in renal dysfunction, cor-

Table 9.3 Characteristics of serum visceral proteins

Protein	Half-life	Reference range
Albumin	20 days	3.5–4.8 g/dL
Prealbumin	2 days	16–35 mg/dL
Transferrin	10 days	0.16–0.36 g/dL
Retinol-binding protein	½ day	3–6 mg/dL
IGF-1	2 h	0.01–0.04 mg/dL

Modified from Spiekeman (1995)

Table 9.4 Prealbumin risk stratification

Prealbumin level	Risk level
<5.0 mg/dL (<50 mg/L)	Poor prognosis
5.0–10.9 mg/dL (50–109 mg/L)	Significant risk; aggressive nutritional support indicated
11.0–15.0 mg/dL (110–150 mg/L)	Increased risk; monitor status biweekly
15.0–35.0 mg/dL (150–350 mg/L)	Normal

Adapted from Bernstein et al. (1995)

ticosteroid therapy or dehydration, while it can be decreased in infection, physiological stress, liver dysfunction, and overhydration (Dellière and Cynober 2017). Zinc deficiency may lower prealbumin levels, but vitamin deficiencies do not (Bernstein et al. 1995).

An increase in the C-reactive protein/prealbumin ratio (≤0.24) in patients in the medical intensive care unit has been associated with mortality (Li et al. 2017). Routine measurement of prealbumin has been recommended as a useful nutritional and prognostic indicator in non-ICU patients without inflammation (Dellière and Cynober 2017; Keller 2019). In high-risk patients, prealbumin levels determined twice weekly during hospitalization can alert the physician to declining nutritional status, improve patient outcome, and shorten hospitalization (Beck and Rosenthal 2002). Patients with prealbumin levels below 15 mg/dL are advised to receive a consultation from the hospital's nutritional team (Bernstein et al. 1995) (Table 9.4).

Transferrin

It is controversial whether transferrin (160–360 mg/dL) is valuable as a measure of nutritional assessment. Transferrin is a transport for iron. It has a relatively long half-life (10 days) and has also been used as a marker of the nutritional status. It is affected by other factors such as iron status, liver disease, and inflammation. As with prealbumin, the level of transferrin increases with renal failure. Transferrin levels are elevated during iron deficiency, while decreased in iron overload conditions. Serum levels decrease with severe malnutrition, but it has been found that this marker is unreliable in assessing mild malnutrition and of fat-free mass in a group of elderly Italian patients (Sergi et al. 2006).

Retinol-Binding Protein

Retinol-binding protein (RBP) (3–6 mg/dL) is a low molecular weight protein with the physiological role of transporting retinol from the liver to target organs and represents the visceral protein with the shortest half-life (approximately 12 h) (Spiekeman 1995). RBP is more difficult to measure than the prealbumin and is affected by the vitamin A status. RBP measurements have not been widely used in nutrition assessment (Keller 2019).

9.2.7.2 Non-visceral Protein Markers

Serum Cholesterol

Some nutritional screening tools use total serum cholesterol (<200 mg/dL) as a parameter for malnutrition. However, the sensitivity and specificity for monitoring malnutrition is low.

Serum Insulin Growth Factor 1 (IGF-1)

IGF-1 (10–1000 ng/mL), formerly called somatomedin C, is a ubiquitous growth factor, and the circulating form is mainly produced by the liver. IGF-1 levels have wide normal range and variations by age, sex, and pubertal stage. Pituitary growth hormone stimulates its release. Its serum half-life is short (approx. 24 h) (Keller 2019). Fasting lowers plasma IGF-1 levels more than fourfold and IGF-1 levels increase during nutritional support. IGF-1 levels were a reliable index of protein-energy malnutrition in elderly patients in the post-surgery recovery period of hip fracture. However, this marker was also influenced by inflammation (Campillo et al. 2000). IGF-1 performed better than albumin or transferrin to

monitor protein and energy status during nutritional rehabilitation (Unterman et al. 1985).

Serum Zinc

Zinc (66–110 μg/dL) deficiency has been associated with taste and smell disorders, reduced immunity, and increased risk of pneumonia. Zinc deficiency is due to low intake of zinc-containing foods such as meat and reduced absorption due to intestinal malabsorption (Tuerk and Fazel 2009). With severe zinc deficiency, skin lesions, anemia, diarrhea, anorexia, decreased lymphocyte function, impaired visual function, and mental retardation may be observed. Several psychological functions were impaired in elderly subjects with zinc deficiency (Marcellini et al. 2006). Most serum zinc is bound to albumin. Therefore, albumin deficiency makes interpretation of serum zinc levels difficult (Keller 2019).

9.2.8 Metabolites

9.2.8.1 Glucose

Normally, blood glucose rises slightly after a meal and insulin is released by the beta cells of the pancreas into the blood in response. Insulin works glucose can get inside muscle, fat, and liver. After the body has used up the required energy, the remaining glucose is stored as glycogen in the liver and muscles for short-term storage and/or as triglycerides in the fat. After a person has not eaten for a few hours, the blood glucose level drops. The pancreas stops releasing insulin. If the blood glucose level drops too low between meals or after a strenuous workout, glucagon is excreted to induce the liver to break down stored glycogen to convert it into glucose, which increases blood glucose level. When the balance is disrupted and the glucose level in the blood rises, then the body tries to restore the balance.

Random Blood Sugar Test

A blood sample is taken at a random time. Regardless of when a person last ate, a random blood sugar level of 200 mg/dL (11.1 mmol/L) or higher indicates diabetes.

Fasting Blood Sugar Test

A blood sample is taken after an overnight fast of more than 8 h. A fasting blood sugar level of less than 100 mg/dL (5.6 mmol/L) is normal. A fasting blood sugar level of 100–125 mg/dL (5.6–6.9 mmol/L) is considered to be pre-diabetes. If it is 126 mg/dL (7 mmol/L) or higher in two separate tests, people have diabetes.

2-Hour Postprandial Glucose

This test is done to see how the body responds to sugar and starch after eating. As a person digests food in the stomach, blood glucose or blood sugar levels rise sharply. In response, the pancreas releases insulin to help move these sugars from the blood into the cells of muscles and other tissues that are to be used as fuel. Insulin and blood glucose levels should return to normal within 2 h of eating. If the blood glucose level stays high, the person may have diabetes. Normal results for the two-hour postprandial age-based test are: less than 140 mg/dL (7.8 mmol/L) for those who do not have diabetes; more than 180 mg/mL (10.0 mmol/L) for people with diabetes.

Hemoglobin A1C

Hemoglobin A1C (4.7–5.8%) test, which does not require fasting, shows the average blood sugar level over the past 3 months. It measures the percentage of blood sugar that is bound to hemoglobin, the oxygen-carrying protein in erythrocytes. The higher the blood sugar level, the more hemoglobin a person with bound sugar has. A HbA1C level of 6.5% or higher indicates diabetes. A HbA1C of less than 5.7% is considered normal.

Oral Glucose Intolerance Test

For this test, people fast overnight and the fasting blood sugar level is measured. Then he/she drinks a sugary-containing liquid and the blood sugar levels are tested periodically for the next 2 h. A blood sugar level of less than 140 mg/dL (7.8 mmol/L) is normal. A reading of more than 200 mg/dL (11.1 mmol/L) after 2 h indicates diabetes. A value between 140 and 199 mg/dL (7.8 mmol/L and 11.0 mmol/L) indicates pre-diabetes.

9.2.8.2 Lactate

Lactate (5–20 mg/dL) is a normal end product of glycolysis, with the highest level of production occurring in the muscles. This test measures the amount of lactate in the blood or less often in the cerebrospinal fluid (CSF). Normal blood lactate levels are 1.3 mmol/L. Lactate metabolism mainly occurs in the liver and kidney. Lactate can only be metabolized by the conversion to pyruvate. Therefore, blood lactate levels depend on pyruvate metabolism. A measurement of blood lactate should be part of the assessment of every critically ill patient unless the diagnosis is obvious and immediate intervention (surgery) is required, such as a ruptured aneurysm. Especially in the early stages of critical illness, elevated blood lactate levels indicate tissue hypoxia and inadequate compensation mechanisms.

9.2.8.3 Urea

The urea (10–35 g/specimen) test is useful for assessing protein intake and/or nitrogen balance. Urea is a low molecular weight substance that is freely filtered by glomeruli and the majority is excreted into the urine, although variable amounts are reabsorbed along the nephron. It is the main end product of protein metabolism. About 50% of the solute excretion in urine and 90–95% of total nitrogen excretion consist of urea under normal conditions. Factors that tend to increase urea excretion include increased glomerular filtration rate, increased dietary protein intake, protein catabolic conditions, and water diuretic states. Factors that reduce urea excretion include low protein intake and conditions that result in low urine output (e.g., dehydration).

9.3 Infrequently Used but Important Laboratory Tests in Spinal Cord Injuries

9.3.1 Cardiac Markers

Cardiac markers are used for the diagnosis and risk stratification of patients with chest pain and suspected acute coronary syndrome (ACS). Cardiac troponins, in particular, have become the cardiac markers of choice for patients with ACS. In fact, cardiac troponin is an essential cardiac marker in defining acute myocardial infarction (MI) in the consensus guidelines of the European Society of Cardiology (ESC) and the American College of Cardiology (ACC). These guidelines recommend measuring cardiac biomarkers when patients are presenting with suspected MI and that the only biomarker currently recommended for the diagnosis of acute MI is cardiac troponin due to its superior sensitivity and accuracy (Amsterdam et al. 2014; Roffi et al. 2016). For example, patients with elevated troponin levels but negative creatine kinase-MB (CK-MB) values who were previously diagnosed with unstable angina or minor myocardial injury are now classified as non-ST-segment elevation MI (NSTEMI), even in the absence of diagnostic electrocardiogram (ECG) changes (Roffi et al. 2016).

Classification of cardiac biomarkers is the following (Jacob and Khan 2018):

1. Biomarkers of myocardial injury:
   (a) Biomarkers of myocardial necrosis: CK-MB fraction, myoglobin, cardiac troponins.
   (b) Biomarkers of myocardial ischemia: Ischemia-modified albumin (IMA), heart-type fatty acid-binding protein (H-FABP).
2. Biomarkers of hemodynamic stress: Natriuretic peptides (NPs): atrial natriuretic peptide (ANP), N-terminal proBNP (NT-proBNP), B-type natriuretic peptide (BNP).
3. Inflammatory and prognostic markers: hs C-reactive protein (CRP), sCD40L, homocysteine.

The timing of appearance and resolution of serum/plasma cardiac markers in acute myocardial infarction is summarized in Table 9.5.

9.3.1.1 Cardiac Troponins

Troponins (TPT <0.01 ng/mL, TPI <0.04 ng/mL) are the contractile proteins in muscle cells that are present in the blood very early 3–9 h post-infarction. Cardiac-specific information

Table 9.5 The timing of appearance and resolution of serum/plasma cardiac markers in acute myocardial infarction

Cardiac marker	Appearance (hours)	Peak (hours)	Resolution (days)
Myoglobin	1–3	4–12	1
Troponin I	2–6	15–20	5–7
CK (total)	4–6	24	2–3
CK-MB	4–6	15–20	2–3
AST	6–8	24–48	3–4
LDH	12	24–48	10–14

has been identified, and troponin-I and troponin-T are commonly used among the three troponins (troponin-I, troponin-T, and high-sensitivity troponin) in the contractile component of the myocardium (Sharma et al. 2004). Both are highly specific and sensitive for myocardial damage, although troponin-T is known to increase in unstable angina. Troponin-I rises in 4–6 h, peaks at 12 h, and returns to baseline in 3–10 days, while troponin-T stays elevated for 12–48 h and returns to normal in 10 days (Jacob and Khan 2018).

9.3.1.2 Creatine Kinase and Creatine Kinase-MB

Creatine kinase (CK) (49–348 U/L for male, 38–206 U/L for female) is an enzyme that is found almost exclusively in skeletal muscle, heart muscle and in smaller amounts in the brain and lungs. Three isoenzymes, based on primary location, are identified by electrophoresis: brain and lungs CK-BB, heart CK-MB, and skeletal muscle CK-MM. The CK is important for intracellular storage and release of energy. The earliest biomarkers to increase is the muscle enzyme CK, or creatinine phosphokinase (CPK), which is present in the cytosol of the myocytes and released into the bloodstream primarily from the necrotic myocardium. The levels increase and decrease in a predictable time frame. Measuring the serum levels can help determine the extent and timing of the damage (van Leeuwen and Bladh 2015).

The CK-MB fraction (<4.4 ng/mL), which is more specific to the myocardium, quickly replaced the CK and is considered the gold standard. CK-MB produces almost 30% of the CK in the myocardium, and an increase of >5% of the total CK activity suggests damage to the cardiac muscle. CK-MB appears 4–6 h after onset of chest pain in the blood and peaks between 10 and 12 h after myocardial infarction. It has been the best cardiac marker for early detection for decades. The best detection time is between 6 and 48 h. Therefore, normal CK-MB can present if patient arrives late. CK-MB usually returns to normal in 72 h. Because there is a delay in increasing CK-MB levels after onset of chest pain, other potential markers such as myoglobin and troponin were assessed (Amsterdam et al. 2014; Roffi et al. 2016; Jacob and Khan 2018).

9.3.1.3 Myoglobin

The small heme protein, myoglobin (28–72 ng/mL for male, 25–58 ng/mL for female), that assists in oxygen transport in all muscle tissues increased within 1 h and rises faster than cardiac troponin or CK-MB, peaks in almost 8–10 h, and returns to normal within 24 h. Thus, it is a sensitive early indicators of cardiac damage, and although it is nonspecific for the myocardium, it has found use as an excellent negative predictor of myocardial injury. If no increase in serum myoglobin levels is observed in two samples every 2–4 h, AMI is practically excluded (Jacob and Khan 2018).

9.3.1.4 Homocysteine

Homocysteine ($\leq$13 μmol/L) is an intermediate amino acid and an independent risk factor for the development of atherosclerosis. About 5–7% of the general population has moderate hyperhomocysteinemia, which may be a result of vitamin deficiencies that can be successfully treated or genetic disorders. Hyperhomocysteinemia causes intimal thickening, disruption of the elastic lamina, smooth muscle hypertrophy, and platelet aggregation, and is therefore directly related with vascular injury. It is therefore a useful risk assessment marker requiring regular tests (Jacob and Khan 2018).

9.3.2 Bone Turnover Markers

Bone turnover markers are a series of protein or protein derivative biomarkers that released during bone remodeling by osteoblasts or osteoclasts (Brown 2016; Greenblatt et al. 2017). Three main types of bone cells are involved in the process of bone remodeling, namely osteoclasts, osteoblasts, and osteocytes. Osteoblasts lay down and mineralize new bone matrix, while osteoclasts are responsible for bone resorption. Osteocytes mainly act as mechanosensors (Hlaing and Compston 2014). Bone markers can be divided into formation and resorption markers.

9.3.2.1 Bone Formation Markers

Bone-Specific Alkaline Phosphatase

Alkaline phosphatase (ALP) (35–110 μg/L) is a membrane-bound enzyme and is found in almost all body tissues. There are four isoenzymes of ALP in the circulation: intestinal, placental, germ cells, and a nonspecific form. Total alkaline phosphatase is confounded by other sources, including liver, intestinal, and placental sources. The tissue nonspecific ALP gene encodes kidney, liver, and bone isoforms of ALP. Bone-specific ALP is produced by osteoblasts and its production correlates positively with bone formation rate as measured by histomorphometry (Hlaing and Compston 2014; Greenblatt et al. 2017; Jain and Camnacho 2018). Total and bone-specific alkaline phosphatase have the benefit of being more widely available than other bone turnover markers (Jain and Camnacho 2018).

Osteocalcin

Osteocalcin (9–43 ng/mL) is a small noncollagenous protein that is synthesized by osteoblasts. Its synthesis is stimulated by 1,25-dihydroxyvitamin D. Osteocalcin may also be released during bone resorption, though it has still been shown to correlate well with bone formation. Although it is a sensitive marker of bone formation, the use of osteocalcin measurements in clinical practice is limited by assay variability, sample instability and high biological variability (Hlaing and Compston 2014; Jain and Camnacho 2018).

Procollagen Type 1 Extension Peptides

Type 1 collagen is derived from its precursor, procollagen. The procollagen molecule contains amino- and carboxy-terminal extensions, which are removed enzymatically during extracellular processing, which leads to the production of type 1 collagen. This cleavage results in the release of procollagen type 1 N-terminal propeptide (P1NP, 22–87 μg/L) and procollagen type 1 C-terminal propeptide (P1CP) (Hlaing and Compston 2014; Jain and Camnacho 2018). PINP and PICP are propeptides on opposite ends of the major secretory protein product of osteoblasts, type I collagen.

9.3.2.2 Bone Resorption Markers

Tartrate-Resistant Acid Phosphatase

Tartrate-resistant acid phosphatase (TRACP) is a member of a heterogeneous group of lysosomal enzymes. There are two forms of TRACP in the circulation: TRACP5a and TRACP5b (Hlaing and Compston 2014; Jain and Camnacho 2018).

Collagen Cross-Link Molecules

Pyridinoline (PYD) and deoxypyridinoline (DPD) are molecules that mechanically stabilize collagen molecule by cross-linking between individual collagen peptides. PYD is found in cartilage, bone, ligaments, and blood vessels, whereas DPD is almost solely found in bone and dentin. Thus, DPD is a more specific and sensitive marker than PYD (Hlaing and Compston 2014; Jain and Camnacho 2018). These bone turnover markers are tested in urine as part of 24 h urine collections or as second morning voided urine collections with creatinine correction.

Cross-Linked Telopeptide of Collagen 1

Telopeptides of type 1 collagen are the most extensively studied and used bone resorption markers. There are two forms depending on the cross-link forming site with collagen: the N-terminal telopeptide (NTX) and C-terminal

telopeptide (CTX), which are released during collagen degradation (Hlaing and Compston 2014; Jain and Camnacho 2018). NTX is most commonly measured in the urine on a second morning voided urine or on a 24-h urine measurement. It does not vary with postprandial status as drastically as CTX but should still be measured fasting. CTX is the standard biomarker for bone resorption. It is a stable biomarker that rapidly decreases with antiresorptive therapy. Optimal serum measurement is performed after an overnight fast in the morning to blunt effects of diurnal variation and feeding (Jain and Camnacho 2018).

9.3.3 Hormonal Markers

9.3.3.1 Antidiuretic Hormone

Antidiuretic hormone (ADH, vasopressin, arginine vasopressin) (<1.5 pg/mL, higher at night) is a nonapeptide synthesized in the hypothalamus. ADH is an important hormone that is responsible for water, osmolar, and blood pressure homeostasis. Its function is vital in times of thirst, bleeding, the third spacing of fluid, and other scenarios where effective arterial blood flow decreases. Its efforts serve to maintain volume status as well as blood pressure to continue adequate tissue perfusion. Hyperosmolar states trigger the release most. ADH is stored in neurons within the hypothalamus. These neurons express osmoreceptors that respond to blood osmolarity and respond to changes of only 2 mOsm/L (Davies 1972). Therefore, slight increases in osmolarity lead to the secretion of ADH. ADH then acts primarily in the kidneys to increase water reabsorption and thus return the osmolarity to baseline.

ADH increases progressively during the night, peaking at midnight or 4 a.m. (George et al. 1975). No diurnal variation in urinary output and antidiuretic hormone secretion is observed in both paraplegic and tetraplegic patients, while antidiuretic hormone levels in the control group increase significantly at night. Lack of normal diurnal variation of antidiuretic hormone (ADH) may play a role in the nocturnal polyuria of tetraplegic patients, a phenomenon similar to that documented in enuretic children and the elderly (Asplund and Aberg 1991; Kilinc et al. 1999; Moon et al. 2004).

9.3.3.2 Cortisol and Adrenocorticotropic Hormone (ACTH)

The cortisol level (5–25 μg/dL at 8 a.m.; 3–13 μg/dL at 8 p.m.) is to help diagnose adrenocortical insufficiency such as Cushing's syndrome and Addison's disease. Cortisol is the main glucocorticoid secreted by the adrenal cortex. The results of ACTH and cortisol tests are evaluated together, since they each control the other's concentrations, i.e., any change in on causes a change in the other. Cortisol excess from any source is known as Cushing's syndrome. Cortisol excess that results from ACTH excess produced by the pituitary gland is known as Cushing's disease. Cortisol levels vary diurnally, with the peak values occurring between 6 and 8 a.m. and reaching the lowest levels between 8 p.m. and midnight in the evening, although bursts of cortisol excretion can occur at night. ACTH levels also exhibit a diurnal variation, peaking between 6 and 8 a.m. and reaching their lowest level between 6 and 11 p.m. (Provan 2018; van Leeuwen and Bladh 2015).

Specimens are usually collected at 8 a.m. and 4 p.m. The ACTH (cosyntropin) stimulated rapid test evaluates adrenal gland function directly and indirectly evaluates pituitary gland and hypothalamus function. Cosyntropin is a synthetic form of ACTH. A baseline cortisol level is recorded before the cosyntropin injection. Specimens are then collected at 30 and 60 min intervals. If the adrenal glands function is normal, the cortisol levels increase significantly after the administration of cosyntropin. The corticotropin-releasing hormone (CRH) stimulation test, like the dexamethasone suppression test (DST), works to differentiate Cushing's disease from conditions in which ACTH is secreted ectopically (van Leeuwen and Bladh 2015). The challenge tests are listed in Table 9.6.

Table 9.6 Challenge tests

Challenge tests	Baseline (conventional units)	Normal results (conventional units)
ACTH (cosyntropin)-stimulated rapid test	• 8 a.m. Birth–11 year: 10–340 μg/dL 12–18 year: 10–280 μg/dL Adult or older adult: 5–25 μg/dL • at 4 p.m. Birth–11 year: 10–330 μg/dL 12–18 year: 10–272 μg/dL Adult or older adult: 3–16 μg/dL	• 3- or 6-min response • Cortisol 18–20 μg/dL or incremental increase of 7 μg/dL over baseline value
Dexamethasone suppression overnight test		• Cortisol less than 1.8 μg/dL next day
Corticotropin-releasing hormone stimulated test		• Cortisol peaks at greater than 20 μg/dL within 3—60 min • ACTH increases twofold to fourfold within 30–60 min
Metyrapone stimulated overnight test		• Cortisol less than 3 μg/dL next day • ACTH greater than 75 pg/mL • 11-deoxycortisol greater than 7 μg/dL

References

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2014;23:e139–228.

Asplund R, Aberg H. Diurnal variation in the levels of antidiuretic hormone in the elderly. J Intern Med. 1991;229:131–4.

Beck FK, Rosenthal TC. Prealbumin: a marker for nutritional evaluation. Am Fam Physician. 2002;65:1575–8.

Bernstein L, Bachman TE, Meguid M, et al. Measurement of visceral protein status in assessing protein and energy malnutrition: standard of care. Prealbumin in nutritional care consensus group. Nutrition. 1995;11:169–71.

Bharadwaj S, Ginoya S, Tandon P, et al. Malnutrition: laboratory markers vs nutritional assessment. Gastroenterol Rep (Oxf). 2016;4:272–80.

Bounds EJ, Kok SJ. D Dimer. 2020 Aug 16. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.

Brown JP. Bone turnover markers: defining a therapeutic target. Clin Biochem. 2016;49:527–8.

Campillo B, Paillaud E, Bories PN, et al. Serum levels of insulin-like growth factor-1 in the three months following surgery for a hip fracture in elderly: relationship with nutritional status and inflammatory reaction. Clin Nutr. 2000;19:349–54.

Chopra S, Griffin PH. Laboratory tests and diagnostic procedures in evaluation of liver disease. Am J Med. 1985;79:221–30.

Davies AG. Antidiuretic and growth hormones. Br Med J. 1972;2:282–4.

Dellière S, Cynober L. Is transthyretin a good marker of nutritional status? Clin Nutr. 2017;36:364–70.

Farias MG, Schunck EG, Dal Bó S, et al. Definition of reference ranges for the platelet distribution width (PDW): a local need. Clin Chem Lab Med. 2010;48:255–7.

Ferguson TW, Komenda P, Tangri N. Cystain C as a biomarker for estimating glomerular filtration rate. Curries Opin Nephrol Hypertens. 2003;24:295–300.

Fischbach FT, Dunning MB III. A manual of laboratory and diagnostic tests. 9th ed. Philadelphia: Wolters Kluwer; 2015.

George CPL, Messerli FH, Genest J, et al. Diurnal variation of plasma vasopressin in man. J Clin Endocrinol Metab. 1975;41:332–8.

Ghazanfar MN, Thomsen SF. D-dimer as a potential blood biomarker for disease activity and treatment response in chronic urticaria: a focused review. Eur J Dermatol. 2018;28:731–5.

Greenblatt MB, Tsai JN, Wein MN. Bone turnover markers in the diagnosis and monitoring of metabolic bone disease. Clin Chem. 2017;63:464–74.

Hasegawa M, Wada H, Yamaguchi T, et al. The evaluation of D-dimer levels for the comparison of fibrinogen and fibrin units using different D-dimer kits to diagnosis VTE. Clin App Thromb Hemost. 2018;24:655–62.

Hlaing TT, Compston JE. Biochemical markers of bone turnover-uses and limitations. Ann Clin Biochem. 2014;51(Pt 2):189–202.

Ingenbleek Y. Plasma transthyretin as a biomarker of sarcopenia in elderly subjects. Nutrients. 2019;11:895.
Jacob R, Khan M. Cardiac biomarkers; what is and what can be. Indian J Cardiovsc Dis Women WINCARS. 2018;3:240–4.
Jain S, Camnacho P. Use of bone turnover marker in the management of osteoporosis. Curries Opin Endocrinol Diabetes Obes. 2018;25:366–72.
Johnson ED, Schell JC, Rodgers GM. The D-dimer assay. Am J Hematol. 2019;94:833–9.
Keller U. Nutritional laboratory markers in malnutrition. J Clin Med. 2019;8:775.
Kilinc S, Akman MN, Levendoglu F, et al. Diurnal variation of antidiuretic hormone and urinary output in spinal cord injury. Spinal Cord. 1999;37:332–5.
Kim SW, Charter RA, Chai CJ, et al. Serum alkaline phosphatase and inorganic phosphorus values in spinal cord injury patients with heterotopic ossification. Paraplegia. 1990;28:441–7.
Korniluk A, Koper-Lenkiewicz OM, Kamińska J, et al. Mean platelet volume (MPV): new perspectives for an old marker in the course and prognosis of inflammatory conditions. Mediators Inflamm. 2019;9213074.
Kumagai G, Wad K, Kudo H, et al. D-dimer monitoring combined with ultrasonography improves screening for asymptomatic venous thrombosis in acute spinal cord injury. J Spinal Cord Med. 2020;43:353–7.
Li L, Dai L, Wang X, et al. Predictive value of the C-reactive protein-to-prealbumin ratio in medical ICU patients. Biomark Med. 2017;11:329–37.
Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood Adv. 2018;2:3226–56.
Marcellini F, Giuli C, Papa R, et al. Zinc status, psychological and nutritional assessment in old people recruited in five European countries: Zincage study. Biogerontology. 2006;7:339–45.
Masuda M, Ueta T, Shiba K, et al. D-dimer screening for deep vein thrombosis in traumatic cervical spinal injuries. Spine J. 2015;15:2338–44.
Moon DG, Kin MH, Lee JG, et al. Antidiuretic hormone in elderly male patients with severe nocturia: a circadian study. BJU Int. 2004;94:571–5.
Mosesson MW. Fibrinogen and fibrin structure and functions. I Thromb Haemost. 2005;3:1894–904.
Nah EH, Kim S, Cho S, et al. Complete blood count reference intervals and patterns of changes across pediatric, adult, and geriatric ages in Korea. Ann Lab Med. 2018;38:503–11.
Panigrahi AK, Liu LL. Patient blood management: coagulation. In: Gropper MA, editor. Miller's anesthesia. 9th ed. Philadelphia: Elsevier; 2020.
Provan D, editor. Oxford handbook of clinical and laboratory investigation. 4th ed. Oxford: Oxford University Press; 2018.
Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267–315.
Sergi G, Coin A, Enzi G, et al. Role of visceral proteins in detecting malnutrition in the elderly. Eur J Clin Nutr. 2006;60:203–9.
Sharma S, Jackson PG, Makan J. Cardiac troponins. J Clin Pathol. 2004;57:1025–6.
Sherman AL, Williams J, Patrick L, et al. The value of serum creatine kinase in early diagnosis of heterotopic ossification. J Spinal Cord Med. 2003;26:227–31.
Singh RS, Craig MC, Katholi CR, et al. Predictive value of creatine phosphokinase and alkaline phosphatase in identification of heterotopic ossification in patients after spinal cord injury. Arch Phys Med Rehabil. 2003;84:1584–8.
Spiekeman A. Nutritional assessment (protein nutriture). Anal Chem. 1995;67:429–36.
Stevens LA, Coresh J, Greene T, et al. Assessing kidney function – measured and estimated glomerular filtration rate. N Engl J Med. 2006;354:2473–83.
Tangri N, Stevens LA, Schmid CH, et al. Changes in dietary protein intake has no effect on serum cystatin C levels independent of the glomerular filtration rate. Kidney Int. 2011;79:471–7.
Tuerk M, Fazel N. Zinc deficiency. Curr Opin Gastroenterol. 2009;25:136–43.
Unterman TG, Vazquez RM, Slas AJ, et al. Nutrition and somatomedin. XIII. Usefulness of somatomedin-C in nutritional assessment. Am J Med. 1985;78:228–34.
van Leeuwen AM, Bladh ML. Davis's comprehensive handbook of laboratory diagnostic tests with nursing implications. 6th ed. Philadelphia: F.A. Davis Company; 2015.

Recommended Additional Reading

Corbett JV. Laboratory tests and diagnostic procedures with nursing diagnoses. 7th ed. Upper Saddle River: Pearson Education, Inc.; 2008.
McPherson RA, Pincus MR, editors. Henry's clinical diagnosis and management by laboratory methods. 21st ed. Philadelphia: W. B. Saunders; 2007.
Provan D, editor. Oxford handbook of clinical and laboratory investigation. 4th ed. Oxford: Oxford University Press; 2018.
van Leeuwen AM, Bladh ML. Davis's comprehensive handbook of laboratory diagnostic tests with nursing implications. 6th ed. Philadelphia: F.A. Davis Company; 2015.
Williamson MA, Snyder LM, editors. Wallach's interpretation of diagnostic tests. Pathways to arriving at a clinical diagnosis. 10th ed. Philadelphia: Wolters Kluwer; 2015.

10 Pharmacokinetics and Pharmacotherapeutics in Spinal Cord Injuries

Spinal cord injuries cause problems in many human systems such as cardiovascular dysfunction, bladder, bowel, and sexual dysfunction, and psychological issues such as sleep disorder and depression as well as respiratory and extremity dysfunctions including pain and spasticity, heterotopic ossification related to the dysfunctional somatosensory system and musculoskeletal complications. In order to control these problems, drugs other than general rehabilitation are required for each dysfunction, and the importance of drug treatment and the frequency of clinical use are increasing. One of the most common tools used by physicians involved in treating people with spinal cord injuries is prescribing medication. Many medications used to treat people with spinal cord injuries aim to relieve the effects of spinal cord injuries or diseases such as pain, spasticity, neurogenic bladder, and neurogenic bowel. In addition, since the demand for rehabilitation intervention gradually increases from the acute phase of spinal cord injury, physiatrists involved in the treatment of spinal cord injury patients should have familiar and sufficient knowledge of medications that respond to various medical problems following spinal cord injuries. Understanding the basic drug mechanisms can help spinal cord injury physicians better understand a patient's response to the drug. In developing a treatment plan that includes drug therapy, prescribers consider many aspects in order to achieve the goal of safe, appropriate, and effective therapy. These include drug safety, the role and responsibilities of the physician, the step-by-step process of prescribing therapy and writing the prescription, and follow-up measures. It is particularly important to promote adherence to the therapeutic regimen and to keep up-to-date with the latest developments in drug therapy (Arcangelo and Wilbur 2017).

Many people with spinal cord injuries suffer from acute and chronic medical problems and are often given cardiovascular drugs, analgesics, gastrointestinal agents, and antibiotics. The use of multiple drugs predisposes such individuals to adverse drug reactions. Therefore, an understanding of key concepts in clinical pharmacology is critical to the successful use of drugs in patients with spinal cord injuries. Clinical pharmacology should deal with the pharmacodynamics and pharmacokinetics of the human body. However, this chapter explains the basic contents of pharmacokinetics which focus on the absorption, distribution, and elimination of drugs. This chapter reviews medications that are often used for conditions frequently managed in spinal cord injuries. However, this chapter does not describe all medications used to treat patients with spinal cord injuries, but rather explains the basic drug mechanism, pharmacokinetics, dosage, and side effects, including drug interactions, for commonly used medications requiring special attention. The emphasis will be on this chapter to describe the problems that are easily overlooked

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when using medications. As the description of the medication can be repeated in each subsequent chapter, it is hoped that the contents of the medication listed in this chapter will be useful for easy reference in practice.

10.1 Pharmacokinetics and Drug Metabolism

Pharmacokinetics is the study of how the body processes the drug in terms of absorption, distribution, and elimination. Pharmacodynamics refers to how the drug acts on the body, that is, how the drug induces its therapeutic or toxic effect at both a cellular and a systemic level. The purpose of pharmacokinetic processes is to get the drug to the site of action, where it can produce its pharmacodynamic effect. Pharmacokinetics can help the clinician determine the onset and duration of a drug's action, and what blood levels would produce therapeutic and toxic effects (Fig. 10.1). The goal of drug administration is to achieve a desired therapeutic effect with minimal adverse effects. Once a drug reaches its site of action, a cascade of cellular responses occurs that manifest as a desired effect of the drug. The molecular response of a drug is highly variable between individuals. This often explains the different responses to therapies in different individuals. In addition, the target receptor response can be altered by other factors, such as previous exposure to similar agonists or antagonists or up or down regulation of the receptors due to disease state or genetic variability (Cristian 2009). The selection of a drug formulation, dose, frequency of dose administration, and adverse events are based on the principles of pharmacokinetics: the processes of absorption, distribution, metabolism, and elimination (Bateman and Eddleston 2006; Corbett and Owens 2011; Fan and de Lannoy 2014).

10.1.1 Absorption

Absorption is the process of transferring the drug from site of administration to the blood. Routes of administration include enteral (oral, sublingual, and rectal) and parenteral (transdermal, inhalation, subcutaneous, intramuscular, and intravenous). Each of these routes will affect the amount of drug and the time it takes to reach the drug site. Drugs can be absorbed via passive

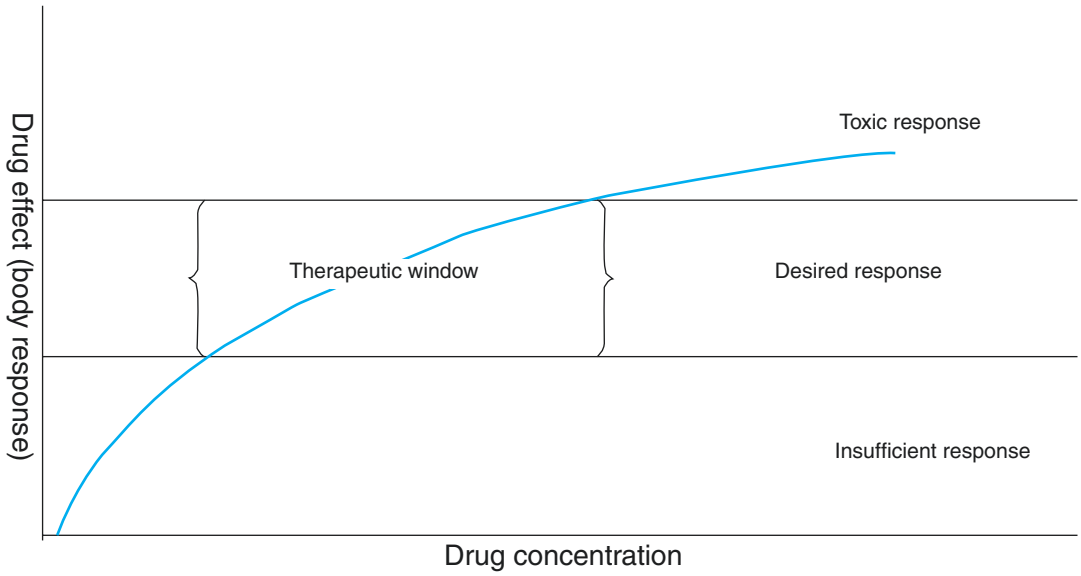

Fig. 10.1 Drug concentration versus drug effect. The concentration range within which the desired response occurs is the therapeutic window

diffusion, active diffusion, or pinocytosis. Most often, drugs are absorbed by passive diffusion (Corbett and Owens 2011). Orally administered drugs are absorbed from the intestine, usually in the upper small intestine, where the surface area is greatest. Due to insufficient absorption or metabolism in the intestinal wall or liver, all of an orally administered dose may not be able to enter the systemic circulation before the drug enters the systemic circulation. This metabolism before a drug reaches the systemic circulation is termed "first-pass metabolism." First-pass metabolism can be avoided by giving drugs by other routes (e.g., sublingual or dermal administration) (Bateman and Eddleston 2006). As a result of first-pass metabolism, some of the drugs will not enter the systemic circulation, which decreases the drug's bioavailability (Corbett and Owens 2011). The rate of drug absorption is determined by the concentration of the free drug or the rate of delivery from a sustained-release preparation. The fraction of oral dose that actually reaches the systemic circulation is known as "bioavailability." Bioavailability is expressed as a percentage (Bateman and Eddleston 2006). The absolute bioavailability of an oral drug is the oral bioavailability of that drug compared to the bioavailability of that drug after intravenous administration. The relative bioavailability is when the oral drug is compared to another route of administration or product.

The extent of absorption refers to the amount of drug that will ultimately be absorbed. The extent of absorption is more important in the treatment of chronic conditions for which drugs are administered regularly. The fate of a drug after absorption is called "disposition." Disposition includes distribution, metabolism, and elimination. The absorption and disposition processes can be separate and occur consecutively if they are actually all interrelated and many occur simultaneously (Posner 2015).

10.1.2 Distribution

The distribution phase is the initial phase after drug administration and the subsequent phase of decreasing drug concentration. Once drug molecules have started to enter the systemic circulation, they will be distributed to different tissues and may be bound (Posner 2015). The distribution of the drugs varies depending on several factors including the size of the drug molecule, affinity for aqueous and lipid tissues (water or lipid solubility), tissue permeability, systemic circulation, protein binding, pH, and blood flow to an area (Corbett and Owens 2011). Plasma protein binding refers to the proportion of total drug in the plasma that is bound to plasma proteins. Once a drug is in the systemic circulation, protein binding may be the most important factor, as the drug's response depends on the amount and activity of the free drug that is not bound to plasma proteins, rather than the total circulating plasma drug concentration. Albumin, the major protein that binds the acidic drugs, is the most common protein that binds to drugs in general (Corbett and Owens 2011). If the drug is mainly bound to plasma protein and remains in the vascular compartment, the concentration of bound and unbound drug together will be high and the distribution will be small (Posner 2015).

The volume of distribution describes the amount of drug in the body in relation to its plasma concentration. The volume of distribution is useful in calculating the loading dose. The loading dose of a drug is calculated by multiplying the volume of distribution by the desired drug concentration. The drug is first delivered to tissues with good blood circulation and then to areas with less blood flow (Cristian 2009). The drug equilibrates with the tissues according to the blood supply and its relative water solubility (hydrophilic) or lipid solubility (lipophilic). In general, the more lipophilic the drug, the more it gets into lipid-rich tissues and tends to accumulate there, including the brain. The less lipophilic the drug, the more remains in the plasma (Bateman and Eddleston 2006). Lipid-soluble drugs readily distribute into the fatty tissues, where they may be stored and even concentrated. However, water-soluble drugs tend to remain in the highly vascularized spaces of the skeletal muscle (Peterson 2017).

10.1.3 Metabolism

Medicines are eliminated predominantly through metabolism in the liver or through renal filtration or secretion. Drug metabolism refers to the process by which a drug is chemically converted to a metabolite. After oral administration, many drugs are absorbed from the small intestine and transported through the portal circulation to the liver, where they are metabolized by phase I and II reactions. The 2-step process of phase I and II reactions makes the drug molecule more water soluble, so the drug can be excreted via the kidneys (Corbett and Owens 2011). Most drugs are hydrophobic and therefore are not easily excreted by the kidneys. Biotransformation of hydrophobic parent drug into hydrophilic metabolites in the liver improves drug excretion by the kidneys. Phase I reactions through oxidations, reductions, or hydrolyses add a polar group to the parent compound to make it more polar. Cytochrome P450 of the phase I reaction is the most abundant enzyme and therefore the rate-limiting step of hepatic oxidation of the drug. The metabolites produced by phase I reactions are usually not polar enough for rapid elimination. In phase II reactions, endogenous substances such as sulfate, glucuronic acid, acetic acid, and glutathione transferase enzymes are added to form a highly polar conjugate. Sulfate, glucuronic acid, and glutathione transferase enzymes are important phase II enzymes. Such conjugation, usually in the liver with glucuronic acid (glucuronide) or sulfate, converts the drug into a highly polar compound that is easily excreted by the kidneys (Bateman and Eddleston 2006; Posner 2015). These phase I and II reactions are important in decreasing the biologic activity of a drug.

10.1.4 Elimination

Drugs can be eliminated through metabolism of the drug from an active form to an inactive form. Drugs can also be eliminated by excretion from the body. Therefore, elimination is a combination of the metabolism and excretion of drugs from the body (Peterson 2017). Drugs are primarily excreted from the biologic system through the kidneys, although some excretion occurs in saliva, feces, sweat, and through the mammary glands (Corbett and Owens 2011). Most drugs are eliminated by renal filtration or secretion by "first-order" (linear) kinetics. The rate at which it is eliminated is critical to the duration of drug action. The amount of drug that is eliminated is directly proportional to the plasma concentration. In general, the rate at which drugs are metabolized and excreted from the body is proportional to the blood concentration, and hence to the dose of drug administered. Such drugs are said to obey first-order kinetics (Bateman and Eddleston 2006). However, certain drugs follow an elimination of "zero-order" kinetics. These drugs have dose-dependent, nonlinear, saturation kinetics. Occasionally enzyme metabolism is saturable, i.e., the body cannot eliminate more than a certain amount of drug over a fixed period of time due to a limiting amount of metabolizing enzyme. Drugs like phenytoin and alcohol are said to conform zero-order (saturation) kinetics. In contrast to drugs that obey first-order kinetics, even a small increase in the dose of these drugs leads to a disproportionate increase in plasma concentration, which can precipitate toxicity (Bateman and Eddleston 2006).

Half-life is defined as the time in which the plasma concentration of a drug in the body will decrease by one-half. A drug can be considered to be completely eliminated after three to five half-lives. Many drugs exhibit a pharmacological action (pharmacodynamic) that is longer than the half-life because they produce secondary cellular changes that persist after the drug has gone. There may also be a delay in the onset of effect after the peak level in the blood (Bateman and Eddleston 2006). For most drugs, the therapeutic effects occur over a wide range of drug concentrations, while for some drugs, the therapeutic effects are within a narrow therapeutic concentra-

tion (Cristian 2009). Serious toxicity can develop outside of this narrow range of concentration. Changes in renal function are probably the most important clinical consideration in determining drug dosage levels. When deciding on initial doses for drugs that are eliminated by the kidneys, renal function should be assessed, usually via a serum creatinine concentration level and an estimated creatinine clearance (Corbett and Owens 2011).

10.2 Therapeutic Drug Monitoring

One of the most confusing aspects of pharmacology is the variety of names given to different drugs or even to the same compound. Drugs that are chemically and functionally similar often have generic names that share a common ending or suffix. The following listed in Table 10.1 are some drug classes that contain groups of drugs

Table 10.1 Common drug suffixes

Drug class	Suffix	Examples	Indication or effect
Angiotensin-converting enzyme (ACE) inhibitors	-pril	Captopril, enalapril	Antihypertensive, congestive heart failure
Barbiturates	-barbital	Phenobarbital, secobarbital	Sedative-hypnotic, antiseizure, anesthetic
Benzodiazepine	-epam or -olam	Diazepam, temazepam, alprazolam, triazolam	Sedative-hypnotic, antianxiety, antiseizure, anesthetic
Beta blockers	-olol	Propranolol, metoprolol	Antihypertensive, antianginal, antiarrhythmic, congestive heart failure
Bisphosphonates	-dronate	Alendronate, pamidronate	Osteoporosis
Bronchodilators (adrenergic)	-erol	Albuterol, pirbuterol	Bronchodilation
Bronchodilators (xanthine derivatives)	-phylline	Theophylline, aminophylline	Bronchodilation
Calcium channel blockers (dihydropyridine group)	-ipine	Nifedipine, nicardipine	Antihypertensive, antianginal
Cyclooxygenase type 2 (COX-2) inhibitors	-coxib	Celecoxib	Pain, inflammation
Glucocorticoids	-sone or -olone	Cortisone, dexamethasone, prednisone, prednisolone, triamcinolone	Anti-inflammatory, immunosuppressants
Histamine H2-receptor blockers	-idine	Cimetidine, ranitidine	Gastric ulcers
HMG-CoA reductase inhibitors (statins)	-statin	Pravastatin, simvastatin	Hyperlipidemia
Local anesthetics	-caine	Lidocaine, bupivicaine	Local anesthetic, antiarrhythmics
Low molecular-weight heparins	-parin	Dalteparin, enoxaparin	Anticoagulants
Oral antidiabetics (sulfonylurea group)	-amide	Chlorpropamide, tolbutamide	Antidiabetic (type II diabetes mellitus)
Penicillin antibiotics	-cillin	Penicillin, ampicillin, amoxicillin	Bacterial infections
Proton pump inhibitors	-prazole	Omeprazole, lansoprazole	Gastric ulcers
Tetracycline antibiotics	-cycline	Tetracycline, doxycycline	Bacterial infections
Various other antibacterials	-micin or -mycin	Streptomycin, gentamicin, erythromycin	Bacterial infections

Adapted from Ciccone (2007)

Table 10.2 Drugs with low therapeutic index

Effects	Drugs
Analgesics	Opioid narcotics
Antiepileptics	Carbamazepine, valproic acid, phenytoin
Psychiatric medications	Tricyclic antidepressants, monoamine oxidase inhibitors
Antispasmodics	Baclofen, tizanidine
Anticoagulation	Warfarin, heparin

that share a common suffix (Ciccone 2007). In clinical practice, there is no need to measure plasma concentrations of most drugs. The precise drug concentration is not critical when a drug has high bioavailability and concentrations are not very variable, the relationship between dose and plasma concentration is reasonably predictable, and there is a wide therapeutic index (Posner 2015). Drugs with a low therapeutic index whose relationship between dose and plasma concentration are not well established require therapeutic drug monitoring (Table 10.2). In general, therapeutic drug monitoring is measured without a set time while taking the drug (e.g., phenytoin and digoxin), but some drugs measure the peak plasma concentration (e.g., gentamicin) or just before taking the next dose (e.g., vancomycin) (Bateman and Eddleston 2006).

10.2.1 Patient Evaluation Before Medications

For the safety of drug treatment, it is very important to have a patient's medical history and be completed physical examination prior to prescribing any medication. Clinicians need to have information about the drugs they are currently taking, as well as information on drug interaction, allergy, and adverse effects of the drug being prescribed. Information about the patient's specific diet and the over-the-counter medications they are likely to be taking is also very important. Vital signs and cognitive function, overall cardiopulmonary and gastrointestinal functions, nutritional status, and degree of fluid intake should also be evaluated. Decrease in lean body mass, increase in adipose tissue, decrease in plasma protein, and decrease in renal function in the elderly can lead to a high drug concentration, which leads to unexpected side effects.

10.2.2 Drug Dose Determination

The desired drug effect should be defined when drug treatment is initiated. However, the onset of efficacy for some drugs may be delayed for weeks to months. Failure of drug effects may be due to drug interactions or noncompliance with the drugs. If a dose of drug does not produce its desired effect, then increasing the dose is justified only if toxicity is absent and the likelihood of serious toxicity is small. Altering the effects of the drug is usually achieved by changing the drug dose, but not the medication interval. However, this will only occur if increasing the dose does not result in a peak concentration that is toxic, and decreasing the dose does not result in a minimal level that falls below the minimum effective concentration. Alternatively, the dose can be changed by decreasing or increasing the frequency of the dose, but not the amount. In general, doses are given at intervals equal to the half-life of the drug. For most drugs, a change in the effect of the drug can be achieved by changing the amount or frequency of the dose. For drugs with a narrow therapeutic range, a small increase in dose can cause toxicity, while a small decrease in concentration can lead to a loss of efficacy. Therefore, changes in the dosage should not exceed 50% of the previous dose and dose change should not occur more frequently than every three to four half-lives.

10.2.3 Adverse Effects

An adverse effect of the drug is an undesirable effect produced by a drug at standard doses. The most common offenders include drugs with narrow therapeutic concentrations that are taken in combination with other drugs. An exaggerated response may be due to altered pharmacokinetic or pharmacodynamic properties of the patient. Changes in absorption, body composition, or

renal function can change the distribution and half-life of a drug. In addition, changes with age or genetic variability may explain altered pharmacodynamic changes in response to a drug. The suspicion of adverse drug reactions is very high in people with multiple illnesses and multiple medications. Any new symptoms in such individuals should be considered as a potential adverse effect of a medication.

The effectiveness of a drug can be severely impaired by poor tolerance. For example, an anticholinergic drug prescribed for an overactive bladder may be of little benefit because the dose is limited by undesired effects on dry mouth and constipation. The narrow therapeutic index not only limits the tolerable dose, but can also lead to poor adherence to the prescribed dosage regimen (Posner 2015).

Adverse drug reactions can be divided into the following types (Bateman and Eddleston 2006):

- A: Predictable, e.g., bradycardia by β-adrenoceptor antagonists.
- B: Bizarre, e.g., Steven-Johnson reaction by anti-epileptic drugs.
- C: Chronic effects occurring only with prolonged treatment, e.g., iatrogenic Cushing's syndrome by corticosteroids.
- D: Delayed effects occurring many years after treatment, e.g., second malignancies in effects treated with alkylating agents.
- E: End-of-treatment effects, which occur when drugs are stopped suddenly, e.g., myocardial infarction after acute withdrawal of β-adrenoceptor antagonists.
- F: Teratogenic effects on the developing fetus, particularly in the first trimester.

Type A and B adverse reactions are the most important clinically.

10.2.4 Medication Safety

For the safety of medication, clinicians require accurate knowledge of the drugs being prescribed and the interaction between the drugs they are taking. The medication error and associated adverse drug events can occur in any of the medicine use process: prescribing, dispensing, and administration. Particular attention should be paid to high-alert medications. The most common drugs occurring iatrogenic adverse drug events associated with medicine use process in the United States are aspirin, NSAIDs, opioids, digoxin, anticoagulants, diuretics, antimicrobials, glucocorticoids, antineoplastics, hypoglycemics, and insulin (Cohen 2007; Cristian 2009). Among these, anticoagulants, narcotics and opioids, insulin, and sedatives are classified as high-alert medications. Opioids and narcotics cause various gastrointestinal symptoms, including constipation, and central nervous system symptoms, regardless of dose. Warfarin has a variety of drug–drug interactions with other drugs as well as with fruits and foods (Holbrook et al. 2005; Ansel et al. 2008).

10.2.5 Drug–Drug Interactions

Treating a patient with several drugs at the same time, known as "polypharmacy" is extremely common. Drug–drug interaction is an undesirable drug effect when several drugs are taken together. Many are not of clinical importance, but others can have a profound impact on safety and efficacy, and some can be life threatening (Posner 2015). Interaction between drugs can lead to changes in their pharmacokinetics (pharmacokinetic interaction) or an increase or decrease in their biological effect (pharmacodynamic interaction). The effect of certain drugs is exaggerated or the desired effect is reduced by other drugs. Pharmacokinetic interactions usually involve changes in metabolism in the liver or excretion by the kidneys. In rare cases, protein-binding displacement leads to a change in distribution. In the case of pharmacodynamic interactions, different drugs act on different receptor systems and often produce an increased biological effect (Bateman and Eddleston 2006). The risk factors for drug–drug interaction are the use of drugs with a low therapeutic index, polypharmacy, and multisystem disease. The therapeutic index (therapeutic ratio) is the ratio between the toxic dose and the

therapeutic dose of a drug. The closer this ratio is to 1, the more difficult the drug is to use in clinical practice. Drug–drug interaction may occur throughout the process of drug absorption, distribution, and metabolism. In particular, when drugs that act on the central nervous system such as antispastic agents, antiepileptic agents, and antidepressants are taken together, side effects caused by drug–drug interactions such as somnolence and cognitive disorders are very common. In addition, care should be taken not to prescribe together tizanidine and drugs that inhibit cytochrome P450, such as fluoroquinolones, cimetidine, antiarrhythmics, and acyclovir (Cristian 2009) (Table 10.3).

10.2.6 Drug–Disease Interactions

Abnormal or disease states can alter pharmacokinetics of drugs. Some examples of changing in physiological effect are given in Table 10.4. Gastrointestinal disorders can affect drug absorption. Changes in mobility, pH, and contact surface area of the small bowel can affect drug absorption. Changes in body composition due to disease or abnormal metabolic conditions such as malnutrition, cachexia, and fluid overload can affect drug distribution of hydrophilic drugs, hydrophobic drugs, and highly protein-bound drugs. Diseases or abnormal conditions of the liver or kidney can alter metabolism and elimination of drugs.

10.3 Altered Pharmacokinetics in Spinal Cord Injuries

After spinal cord injury, a number of degenerative phenomena change metabolic and physiological functions. These changes persist during the acute, subacute, and in most cases chronic phases of the disease. Physiological and metabolic functions are altered in people with spinal cord injuries. Therefore, the basic pharmacokinetic and pharmacodynamic assumptions derived from able-bodied individuals do not apply. There is a significant need for accurate and precise

Table 10.3 Drug–drug interactions

Drug–Drug	Pharmacologic effect
• Baclofen + tricyclic antidepressant	Exacerbate depression, hypotension
• Baclofen + monoamine oxidase inhibitor	Exacerbate depression, hypotension
• Lamotrigine + phenytoin, phenobarbital, rifampin	Decrease lamotrigine serum levels by 40%
• Phenyotin + enteral nutrition	Decrease phenytoin levels
• Phenytoin + methyphenidate	Increase phenytoin levels
• Phenytoin + diazepam	Increase phenytoin levels
• Tizanidine + clonidine	Hypotension, syncope
• Tizanidine + ciprofloxacin	Increase tizanidine levels
• Tizanidine + vluvoxamine	Increase tizanidine levels
• Tizanidine + oral contraceptives	Increase tizanidine levels
• Dantrolene + calcium channel blockers	Hypotension, hyperkalemia
• Tramadol + carbamazepine	Reduce tramadol levels
• Tramadol + tricyclic antidepressant	Reduce seizure threshold
• Tramadol + selective serotonin reuptake inhibitors	Reduce seizure threshold, serotonin syndrome
• Tramadol + opioids	Reduce seizure threshold
• Tramadol + monoamine oxidase inhibitor	Reduce seizure threshold, serotonin syndrome
• Methylphenidate + guanethidine, clonidine	Hypotension
• Amantadine + anticholinergic agents	Dry mouth, urinary retention, constipation
• Amantadine + quinine or quinidine	Increase amantadine levels
• Amantadine + live attenuated influenza vaccine	May inhibit replication of live vaccine virus

From Cristian (2009)

Table 10.4 Drug–disease interactions

Drug–Disease	Physiologic effect
• Phenytoin–Diabetes	Increase glucose levels
• Phenytoin–Osteoporosis	Decrease vitamin D metabolism
• Phenytoin–Liver disease	Impaired phenytoin metabolism
• Baclofen–Chronic kidney disease	Impaired clearance
• Baclofen–Epilepsy	May reduce seizure threshold
• Tizanidine–Liver disease	Impaired clearance
• Tizanidine–Renal disease	Impaired clearance
• Tramadol–Seizure	May reduce seizure threshold
• Methylphenidate–Cardiomyopathy	Sudden cardiac death
• Methylphenidate–Hypertension	Increase blood pressure
• Methylphenidate–Epilepsy	Reduce seizure threshold
• Amantadine–Glaucoma	May precipitate attack of glaucoma
• Amantadine–Psychiatric disease	May exacerbate underlying psychiatric disorder, increase suicide risk
• Amantadine–Benign prostatic hyperplasia	Urinary retention
• Opioids–Constipation	Increase constipation
• NSAIDS–Chronic kidney disease	Worsen renal function, hyperkalemia

From Cristian (2009)

pharmacological schedules specifically designed for people with spinal cord injuries (Mestre et al. 2011).

10.3.1 Absorption

In patients with spinal cord injuries, the oral route can be disadvantageous due to impaired GI motility. Due to slowed peristalsis of the stomach, intestines, and colon, the rate of drug transport to its site of absorption and rate of absorption is reduced. Spinal cord injury usually decreases large intestine motility and therefore would be expected to increase the transit time of drugs through the large intestine. Since most drugs are extensively absorbed before the large intestine, spinal cord injury would not be expected to have any clinically significant effect on drug absorption.

Absorption in the GI tract is dependent on passive diffusion and is therefore preferred when the drug is in a non-ionized lipid-soluble form. This seemingly simplified process is made more difficult by an additional factor: the fluctuating pH of the GI tract. Weak acids do not exist in a protonated form in acidic environments (e.g., in the stomach) and diffuse easily. Weak bases ionize in the stomach, preventing its absorption, but do not ionize in a basic pH environment (e.g., in the intestine). Therefore, in individuals with spinal cord injuries, the absorption of basic drugs is prolonged, as a slowed gastric emptying delays the mobilization of the contents toward the alkaline environment of the intestine. This phenomenon is attributed to the effect of slower gastric emptying and GI motility, as the drugs take longer to reach their main absorption site (small intestine). The delayed absorption increases the time it takes for plasma concentration peaks to reach the therapeutic effect of these drugs. In patients with spinal cord injuries, orally administered drugs such as aspirin and paracetamol take longer to reach the maximum plasma concentration compared with uninjured controls. Other drugs commonly prescribed to patients with spinal cord injuries that have shown to be affected by delayed gastric emptying and decreased GI motility are theophylline, dantrolene, carbamazepine, and baclofen (Mestre et al. 2011). The absorption of these drugs is significantly reduced when administered orally. The solution to altered pharmacokinetics in orally administered drugs could be complementary dosing with metoclo-

pramide, a gastroprokinetics. The use of metoclopramide at an initial oral dose of 10 mg 30 min before taking the desired drug improves its absorption (Gilman et al. 1996).

Other routes of administration also have limitations for the physiology of patients with spinal cord injuries. In people with spinal cord injuries, there is an altered venous blood flow and limited microvasculature flushing of the dermis and muscles. In high cervical cord injury, poor pulmonary function makes the pulmonary route of drug administration inefficient (Mestre et al. 2011).

10.3.2 Distribution

As a drug enters the systemic blood flow, the molecules have to diffuse to the target tissue where they exert their effect. The distribution of drugs into the target tissue depends on a physicochemical process known as blood–tissue partitioning. These mechanisms occur because of the drug's ability to bind with plasma proteins and tissue macromolecules. Albumin is the main plasma protein and is responsible for transporting drugs through systemic blood flow. However, patients with spinal cord injuries often have hypoalbuminemia. Due to low albumin levels, drugs with high plasma protein binding such as naproxen have an increased distribution, while drugs with low plasma protein binding such as phenacetin, gentamicin, and amikacin will have a normal distribution.

10.3.3 Metabolism

Drug metabolism takes place mainly in the cytochrome P450 complex of the hepatocyte smooth endoplasmic reticulum. After spinal cord injury, hepatic microvascular blood flow is decreased, and hepatocyte gene expression and catecholamine metabolism are affected (Segal et al. 2000). These physiological alterations pose a disadvantageous outcome for high hepatic extraction drugs such as phenacetin, methylprednisolone, and cyclosporin A. These drugs present an increased bioavailability due to impaired hepatic metabolic clearance (Segal et al. 1998).

10.3.4 Elimination

The renal route of excretion is the most important and depends on glomerular filtration, active tubular secretion, and passive tubular reabsorption. The smallest decrease in renal function, as seen in the case of spinal cord injury, can develop into drug toxicity. Altered physiology in patients with spinal cord injury prolongs the half-life of most drugs due to slowed renal clearance. Examples of this phenomenon have been observed in amikacin, cefotiam, doxycycline, ketamine, diclofenac, vancomycin, and lorazepam (Mestre et al. 2011).

A spinal cord injury may also affect the hepatic clearance of a drug. If spinal cord injury altered hepatic blood flow, the kinetics of high extraction drugs such as propranolol and lidocaine can be significantly affected.

10.4 Medication Categories Commonly Prescribed in Spinal Cord Injuries

People with spinal cord injuries may experience decreased quality of life and daily functioning due to manifestations related to spinal cord injury such as neurogenic bladder and bowel, as well as secondary health conditions. Treatment of common conditions such as neurogenic bladder, autonomic dysreflexia, and pain requires the use of drugs such as anticholinergics, sympatholytics, anticonvulsants, and analgesics, which, in addition to the target organ, can also act on the autonomic and central nervous systems, as well as other organ systems (Hwang et al. 2015). Patients with spinal cord injuries often require long-term healthcare management for secondary complications such as spasticity, urinary tract infections, pain, and pressure injuries, and are also at increased risk of several chronic comorbidities such as diabetes and heart disease over the course of their lives. Treatment protocols for managing

chronic secondary complications after spinal cord injuries are designed to address pain, spasticity, bladder and bowel dysfunction, depression, anxiety, etc. (Kitzman et al. 2017).

10.4.1 Autonomic and Cardiovascular Drugs

Drugs that mimic and inhibit autonomic nerves are widely used in spinal cord medicine to treat cardiovascular, respiratory, urinary tract, and gastrointestinal complications. In addition, side effects and interactions associated with many drugs can be attributed to autonomic mechanisms. The influences of autonomic innervations that are important for clinical practice are summarized in Table 10.5. In most cases, both divisions innervate each target tissue, with two exceptions notable: the sympathetic nervous system has minimal influence on salivation and there is no parasympathetic innervation of the blood vessels. Sympathetic innervations stimulate the cardiovascular system, inhibit the gastrointestinal and urinary tracts, and dilate pupils and bronchioles. Parasympathetic innervations have the opposite effects (Becker 2012).

10.4.1.1 Medications for Orthostatic Hypotension

Orthostatic hypotension is an important medical problem that needs to be solved first in the rehabilitation process of patients with spinal cord injuries. This is because orthostatic hypotension affects the patient's normal postural changes and mobilities, as well as participation in activities of daily living, thereby delaying rehabilitation and reducing quality of life. Orthostatic hypotension is defined as a decrease in systolic blood pressure of at least 20 mmHg or a decrease in diastolic blood pressure of at least 10 mmHg for the first 3 min of the upright position or a head-up tilt on a tilt table. It does not matter whether symptoms develop. Drugs, like non-pharmacological management, aims to increase blood volume and reduce venous blood retention. Drugs with a sympathetic effect, either directly or indirectly, are used. Several drugs have been used to treat orthostatic hypotension, but their effects vary. The most experienced drugs for orthostatic hypotension associated with spinal cord injury are midodrine, fludrocortisone, ephedrine, and pseudoephedrine.

Table 10.5 Autonomic control of selected target tissues

Target	Sympathetic effect	Parasympathetic effect
Heart	Excitatory	Inhibitory
Vasculature	Constriction	Insignificant
Bronchioles	Dilatation	Constriction
Oral/airway secretion	Insignificant	Stimulation
Gastrointestinal and urinary motility	Inhibitory	Excitatory
Pupil (via iris)	Mydriasis	Miosis

From Becker (2012)

Midodrine

Midodrine is a prodrug that is converted to its active metabolite, desglymidodrine, in various tissues, including the liver. It is a selective α1-adrenoceptor agonist that increases arterial blood pressure while standing via arterial and venous vasoconstriction. Midodrine is well absorbed after oral administration. Plasma desglymidodrine concentrations are closely related to the increase in blood pressure. The duration of action is only 2–4 h and shows a very fast effect, which reaches the peak serum concentration at 30 min after oral administration. Due to its short half-life of 2–4 h, it can be used as a short-term vasopressor when upright during the day, with little worsening of nocturnal hypertension (Chisholm and Anpalahan 2017). Typical dosing is between 2.5 and 15 mg once to three times daily during waking hours. An example of a three-times-daily schedule would be dosing prior to getting out of bed, before lunch, and mid-afternoon (Figueroa et al. 2010; Gibbons et al. 2017).

Midodrine carries a risk of significant supine hypertension; it is therefore recommended that individuals not take midodrine within 5 h of bedtime. A high supine blood pressure observed shortly after midodrine administration should not

lead to a decrease or discontinuation of the drug dose, but managed by avoiding the supine posture (Gibbons et al. 2017; Wright et al. 1998). The most frequently reported side effects, apart from hypertension in the supine position (supine hypertension), were piloerection (13%), pruritus or paresthesia of the scalp (10–13%), and urinary retention (6%) (Lamarre-Cliche 2002). Midodrine is also contraindicated in patients with acute renal disease, urinary retention, pheochromocytoma, and thyrotoxicosis.

Fludrocortisone

Fludrocortisone has been used off-label for many years for the treatment of orthostatic hypotension in patients with spinal cord injuries. Fludrocortisone is a synthetic mineralocorticoid that is commonly used to treat orthostatic hypotension in patients with spinal cord injuries. It acts by increasing renal sodium and water reabsorption, thus expanding intravascular blood volume. The beneficial effects of fludrocortisone in orthostatic hypotension were believed to be via the mineralocorticoid activity of the drug, causing a positive change in sodium balance and plasma volume. Fludrocortisone increases the α1-adrenoceptor of the vascular response to norepinephrine, and it probably at least partly exerts its pressor effects via this mechanism when administered over a long period of time (Lamarre-Cliche 2002). It has an elimination half-life of 3.5 h, but its biological half-life is between 18 and 36 h. The onset of action occurs over 3–7 days. The salt and water retention induced by fludrocortisone can be transitory.

Fludrocortisone is typically given at 0.1–0.2 mg once daily with little benefit seen from increasing the dose beyond 0.3 mg/day (Gibbons et al. 2017). A dose over 0.3 mg/day is usually associated with hypokalemia and edema, with little clinical benefit. Most of the side effects are caused by the drug's mineralocorticoid activity and include supine hypertension, edema, congestive heart failure, and hypokalemia. Because fludrocortisone has a low glucocorticoid activity, it can, theoretically, induce Cushing's syndrome, especially when given at high dosages (Lamarre-Cliche 2002).

Droxidopa

Droxidopa is an orally administered norepinephrine prodrug that is converted to norepinephrine both in the central nervous system and in the peripheral tissues, including sympathetic peripheral nerve endings. The increase in circulating plasma level of norepinephrine peaks 6 h after administration of droxidopa and norepinephrine levels remains elevated for at least 46 h. It is believed that neural norepinephrine replenishment is the primary mechanism of action for improving standing blood pressure with droxidopa (Gibbons et al. 2017; Kaufmann 2008). Droxidopa was approved by the FDA for the treatment of orthostatic hypotension in 2014. However, the use of droxidopa for the treatment of orthostatic hypotension in patients with spinal cord injuries is not well established.

The starting dose of droxidopa is 100 mg three times a day and can be titrated up to 1800 mg per day during waking hours. A recommended dosing schedule would be at 8 AM, noon, and 4 PM (Gibbons et al. 2017). It is not recommended to take droxidopa, like other agents for treating orthostatic hypotension, within 5 h of bedtime to avoid the risk of supine hypertension (Chisholm and Anpalahan 2017). Side effects of droxidopa include headache, dizziness, nausea, fatigue, and supine hypertension. Caution is advised in patients with congestive heart failure and chronic renal failure (Gibbons et al. 2017).

10.4.1.2 Medications for Supine Hypertension

Supine hypertension is defined as systolic blood pressure ≥150 mmHg or diastolic blood pressure ≥90 mmHg while supine (Baker and Kimpinski 2017; Gibbons et al. 2017). The presence of supine hypertension complicates treatment of orthostatic hypotension or is associated with orthostatic hypotension in patients with spinal cord injuries. Clinicians should manage patients with significant supine hypertension with short-acting antihypertensive drugs (captopril, losartan, transdermal nitroglycerin, hydralazine) given at bedtime, not during daytime hours, and avoid fludrocortisone. Calcium channel blockers (nifedipine) are not recommended for the treatment of

Table 10.6 Recommended medications for treatment of supine hypertension related to orthostatic hypotension

Drugs	Mechanism of action	Recommended dose
Captopril	Angiotensin-converting enzyme inhibitor	25 mg qhs
Clonidine	Central α2-agonist	0.2 mg with evening meal
Losartan	Angiotensin II receptor antagonist	50 mg qhs
Nitroglycerine patch	Vasodilator	0.1 mg/h patch qhs (remove patch in AM)
Hydralazine	Peripheral smooth muscle relaxant	10–25 mg qhs

Modified from Gibbons et al. (2017)

supine hypertension. It decreases systolic blood pressure greatly and aggravates morning orthostatic hypotension (Vallelonga and Maule 2019).

Recommended medications for treatment of supine hypertension related to orthostatic hypotension are summarized in Table 10.6. For the description of each drug, refer to "Nitrates", "Direct vasodilators", "Angiotensin-converting enzyme inhibitors", and "Angiotensin II receptor blockers" below.

10.4.1.3 Medications for Autonomic Dysreflexia

Nitrates

Various preparations of nitrate (isosorbide denigrate, isosorbide mononitrate, nitroglycerin, and amyl nitrate) are marketed not only in a tablet, but also as an ointment, spay, sublingual form, etc., and are used as an emergency medication for coronary artery disease and angina, as well as a sudden increase in blood pressure due to autonomic dysreflexia in patients with spinal cord injuries. Care should be taken to prevent orthostatic hypotension and tachycardia in the morning due to nitrate intake in patients with spinal cord injuries.

Oral nitrates undergo first-pass hepatic inactivation via hydrolysis. Oral nitrates take their initial effect within 60 min and last 4–8 h. Sublingual administration of nitrates results in onset of effects within 1–2 min and a rapid decrease in effects. On the other hand, transdermal application, either by ointment or by patch, allows gradual absorption and prolonged release. They then have a slow onset of action, with peak effects occurring after 60–90 min and lasting 3–6 h. When using nitrate patches, peak effects are achieved after 1–2 h and can last for up to 24 h. It is important to note, however, that continued long-term use of nitrates may lead to the development of tolerance to them. This can be avoided by ensuring a nitrate-free interval for short periods of time by removing a nitrate patch every day at bedtime and applying a new one in the morning.

Nitrates, after being converted into nitrous oxide, relax the smooth muscle. It does this by stimulating intracellular synthesis of cyclic guanosine monophosphate (GMP), which leads to dephosphorylation of myosin and loss of smooth muscle contractility.

The most common side effects of nitrates are vascular headache, which result from dilatation of the cerebral vasculature and orthostatic hypotension. Any form of nitrate, including nitroglycerin ointment, is contraindicated in patients treated with phosphodiesterase type 5 inhibitors (PDE5I) such as sildenafil within the last 24–48 h.

Calcium Channel Blockers

Calcium channel blockers (amlodipine, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nimodipine, nisoldipine, verapamil) are often used for hypertension and angina and are prescribed as nifedipine for autonomic dysreflexia in patients with spinal cord injuries. Common side effects of calcium channel blockers are orthostatic hypotension, headache, and peripheral edema. The concomitant use of other antihypertensive and antiarrhythmic drugs should be done with caution. Grapefruit juice can increase the effects of calcium channel blockers (Stitik et al. 2010).

Calcium channel blockers block the entry of Ca^{2+} ions into the myocardial, sinoatrial and atrioventricular nodes, and vascular smooth muscle cells by binding to specific voltage-sensitive channels in the cell membrane. This leads to sev-

eral cardiovascular effects: reducing the strength of myocardial contraction and the arterial smooth muscle contraction of the coronary arteries and peripheral arterioles. This leads to an improved coronary blood flow and a reduced peripheral vascular resistance with lowering of systemic blood pressure. Consequently, the depolarization of the pacemaker cell is impaired, leading to slowing of cardiac conduction.

Common side effects of the calcium channel blocks are primarily due to vasodilatation resulting in dizziness, headache, orthostatic hypotension, edema, and tachycardia. Concomitant use with β-blockers sometimes results in hypotension, cardiac dysrhythmia, or congestive heart failure.

Direct Vasodilators

The effect of direct vasodilators such as hydralazine is blunted and modified by reflex responses to vasodilation. The direct arterial dilation triggers baroreceptor-mediated sympathetic activation, which leads to tachycardia and increased cardiac output and myocardial oxygen demand. This makes making it dangerous to use these agents alone in patients with known or suspected coronary artery disease.

Hydralazine is a typical direct arterial vasodilator that was introduced in the early 1950s. The antihypertensive effect of hydralazine is accompanied by reflex activation of the autonomic reflexes, which results in an increase in the heart rate and cardiac output. Intramuscular or intravenous administration of hydralazine is used in hypertensive crises due to autonomic dysreflexia. The dose requirements to achieve the therapeutic goal are unpredictable. The commonly used dose is 10–20 mg, which can be repeated if necessary. Although an effect on the blood pressure can be observed in a few minutes, a maximum decrease occurs between 15 and 75 min (Ram 2002).

10.4.2 Medications for Respiratory Dysfunction

Respiratory disorders and infections are common in patients with spinal cord injuries. Various drugs are used to treat these conditions. Selective β-2 adrenergic agonists are useful in treating reversible airway obstruction. Anticholinergics can be useful in relieving bronchoconstriction. Mucolytics and expectorants are useful to facilitate pulmonary toilet by improving the quality and expulsion of mucus.

10.4.2.1 Selective β-2 Adrenergic Agonists

Selective β-2 adrenergic agonists (albuterol, levalbuterol, pirbuterol, salmeterol, formoterol, arformoterol, indacaterol) affinity for β-2 adrenergic receptors in bronchiolar smooth muscles. These drugs are provided in short- or long-acting forms. Albuterol, levalbuterol, and pirbuterol are classified as short-acting β-2 agonists that are used as an immediate-onset bronchodilator for rescue therapy in the event of acute symptoms and shortness of breath. Salmeterol, formoterol, arformoterol, and indacaterol are classified as long-acting β-2 agonists, used for a delayed-onset bronchodilator for a continuous bronchodilator to prevent acute symptoms of shortness of breath.

These drugs can be administered orally, subcutaneously, or by inhalation. Inhaled β-2 agonist bronchodilators activate specific β-2 adrenergic receptors on the surface of smooth muscle cells. This increases the level of intracellular cyclic adenosine monophosphate and increases relaxation of the smooth muscles. The inhalation route is preferred because it allows the drug to be administered directly to the lungs and the onset of action is faster. Using this route also minimizes side effects such as increased heart rate and blood pressure that can occur when drugs are administered orally or subcutaneously.

10.4.2.2 Anticholinergics

Anticholinergic medications (Ipratropium bromide, tiotropium) relieve bronchoconstriction by antagonizing the muscarinic cholinergic receptors. Anticholinergics compete with acetylcholine for postganglionic muscarinic receptors and inhibit cholinergically mediated bronchomotor tone, which leads to bronchodilation. Ipratropium is used as a bronchodilator with β-2 agonist to

increase bronchodilator effect. Tiotropium is a delayed-onset anticholinergic drug used for continuous bronchodilation to prevent acute symptoms of shortness of breath. Side effects associated with anticholinergics include tachycardia, nervousness, paradoxical bronchospasm, dry mouth, nausea, and vomiting. These drugs should avoid combining with other anticholinergics such as antihistamines to potentiate dry mouth and sympathomimetics, which can potentiate tachycardia and nervousness (Carl et al. 2014).

10.4.2.3 Methylxanthines

Theophylline and aminophylline are xanthine derivatives with bronchodilator properties by relaxing the bronchial smooth muscles, improving the contractility of the diaphragm and having a mild anti-inflammatory effect. The improved diaphragmatic contractility is probably mediated by weak adenosine antagonism. Theophylline improves respiratory muscle functions and stimulates the respiratory center, thereby promoting bronchodilation and reducing inflammation. Theophylline is not effective in treating acute bronchospasm. It can also improve contractility of the diaphragm muscle. The addition of theophylline and the related product aminophylline may benefit when patients are inadequate to respond to inhaled bronchodilator therapy as a first-line agent. Because of the potential for toxicity associated with theophylline, it is now recommended that clinicians monitor patient serum levels and maintain levels between 5 and 10 mg/L (Carl et al. 2014).

Common side effects with methylxanthines include tachyarrhythmias, restlessness, insomnia, tremor, nausea, vomiting, gastroesophageal reflux, seizures, and peptic ulcer aggravation. Methylxanthines should be used with caution in patients with a history of tachyarrhythmia, peptic ulcer disease, seizure disorders, or hyperthyroidism.

10.4.2.4 Mucolytics

Mucolytics (acetylcysteine) reduce mucus viscosity by splitting mucoprotein disulfide bonds so it can be removed via coughing or suction.

10.4.2.5 Expectorants

The pharmacological mechanism of expectorants (guaifenesin, terpin hydrate) is not clearly known how they increase respiratory tract secretion production. Expectorants are used to thin air passages to make it easier to cough up mucus and clear airways.

10.4.3 Anticoagulants for Deep Venous Thrombosis and Pulmonary Embolism

Anticoagulants are mainly used to prevent clot formation such as deep venous thrombosis (DVT) and pulmonary embolism (PE). Patients who are at risk for developing thromboembolic phenomena often appear in the rehabilitative setting. This includes patients with spinal cord injuries, stroke, multiple trauma, and hip and knee replacements. Patients with a cerebral thromboembolic event, patients with proximal DVT, and pulmonary embolism are generally treated similarly.

10.4.3.1 Heparin

Anticoagulants can be divided into heparin and coumarin groups. The heparin group is administered parenterally and includes unfractionated heparin (UFH), low molecular weight heparin (LMWH), and heparinoids, including fondaparinux and danaparoid. Full-dose IV UFH had been the mainstay of initial treatment of acute thromboembolic events such as DVT, pulmonary embolus, as well as unstable angina and non-Q-wave myocardial infarction, and requires inpatient therapy. It is currently acceptable to initiate therapeutic anticoagulation utilizing subcutaneous LMWH or certain heparinoids in appropriate patients, even on an outpatient basis in those with DVT, and even possibly pulmonary embolism.

If anticoagulant patients are in physical and occupational therapy, it is advisable to include this information in the therapy prescription so that the therapist can take appropriate precautions to avoid falls and injuries. This also warns the therapist to closely monitor and report possi-

ble signs of bleeding, such as a newly swollen joint, as this may represent a hemarthrosis.

Heparin and its derivatives have reactions associated with thrombosis and the formation of stable clots. Low-dose UFH and LMWH mainly prevent the conversion of prothrombin to thrombin (factor II) by inactivating factor Xa. At higher doses, heparin can prevent conversion of fibrinogen to fibrin by inactivating thrombin and also prevents the stable formation of fibrin clots. After subcutaneous injection, the onset of activity is rapid, with peak plasma concentrations at approximately 4 h. The metabolism occurs in the liver and in the reticuloendothelial system. The effects and pharmacokinetics of warfarin are described again below.

Side effects of most concerns with anticoagulants are bleeding, most commonly presenting as bruising, petechiae, epistaxis, GI, or urinary tract bleeding. Extreme caution should be exercised in people at increased risk of bleeding, including people already taking antiplatelet agents. A potential problem specific to heparin is heparin-induced thrombocytopenia, which occurs either through a direct effect on platelets or through an immunologic response. It is therefore important to monitor CBCs, especially at the beginning, but also at regular intervals during treatment.

LMWH is derived from UFH by depolymerization and has a higher ratio of antifactor Xa to antifactor IIa activity than pure UFH. Therefore, the incidence of bleeding complications is lower than that of UFH. The molecular size of the two classes of heparin does not allow oral administration as they would not be readily absorbed from the GI tract. Therefore, they are administered either by deep subcutaneous injection or intravenously. Although it is necessary to monitor the activated partial thromboplastin time (aPTT) during full-dose IV UFH therapy, it is not necessary to do so during standard fixed low-dose therapy of UFH and LMWH therapy because this index is essentially unaffected. It is important to note, however, that full therapeutic doses of LMWH can affect the aPTT.

They are used for prophylaxis depending on diagnosis or until the risk of thromboembolism has decreased. In acute DVT or PE, they are given in therapeutic doses in combination with warfarin, which is initiated within the first 3 days. Once a therapeutic INR is reached, usually within 5–7 days, heparin is discontinued while warfarin therapy is continued for a varying period of time depending on the underlying condition.

The dosages for the subcutaneous administration of heparin and heparin derivatives are shown in Table 10.7.

10.4.3.2 Warfarin

Warfarin is a racemic compound of two optically active isomers with a more potent S-enantiomer and a less potent R-enantiomer (Wells et al. 1994;

Table 10.7 Dosage of heparin and heparin derivatives

Type	Drug	Typical dosage (subcutaneous)
UFH	Heparin sodium	DVT prophylaxis, 5000 U q8-12h
LMWH	Enoxaparin (Lovenox)	DVT prophylaxis: 30 mg q12h DVT/PE treatment: 1 mg/kg q12h or 1.5 mg/kg qd
	Dalteparin (Fragmin)	DVT prophylaxis: 5000 U qd DVT/PE treatment: 200 U/kg qd
	Tinzaparin (Innohep)	DVT prophylaxis: 3500–4500 U qd DVT/PE treatment: 175 anti-Xa U/kg qd until therapeutic anticoagulation with warfarin
Heparinoids	Fondaparinux (Arixtra) Synthetic factor Xa inhibitor	DVT prophylaxis: 2.5 mg qd DVT/PE treatment: 5 mg qd (<50 kg), 7.5 mg qd (50–100 kg), 10 mg (>100 kg)
	Desirudin (Iprivask) Selective thrombin inhibitor	DVT prophylaxis: 15 mg q12h

UFH, unfractionated heparin; LMWH, low molecular weight heparin; DVT, deep venous thrombosis; PE, pulmonary embolism

Modified from Stitik et al. (2010)

Holbrook et al. 2005). The S-enantiomer is approximately 5 times more potent than the R-enantiomer. The principal mode of action of warfarin is based on the antagonism of the endogenous synthesis of coagulation factors dependent on vitamin K. Warfarin exerts its effect by lowering active vitamin K available for the activation of clotting factors II, VII, IX, and X (Holbrook et al. 2005). The required dosage of warfarin is very variable, and regular monitoring of the international normalized ratio (INR; ratio of prothrombin time to control) is necessary to ensure that coagulation status remains stable.

It is also important to educate patients so that they are aware of the various factors that can affect their therapy. Because warfarin has a narrow therapeutic index, it is of critical importance to identify factors that may result in either loss of efficacy with a consequent thrombotic or embolic event, or toxicity manifested as bleeding (Greenblatt and von Moltke 2005). A relatively rare but potentially dangerous adverse effect associated with the use of warfarin is skin necrosis, which can develop in susceptible people such as those with protein C deficiency, as local thrombosis usually occurs within the first few days after starting warfarin. Co-administration of heparin during the first 5–7 days of anticoagulation will reduce the risk of this reaction.

Warfarin interferes with vitamin K, by inhibiting the synthesis of hepatic coagulation factors II, VII, IX, and X. Its effect is detectable once the baseline level of these already circulating factors begins to be depleted by metabolic degradation. After oral administration, the maximum plasma concentration is between 1 and 9 h. Almost all drugs (97%) are bound to plasma albumin. The initial effect is noticeable within 24 h, but the maximum effect occurs between 3 and 4 days and lasts for 4–5 days. It is metabolized in the liver and has a half-life of approximately 2.5 days.

The number of reports of interactions between warfarin and drugs or foods is increasing, confirming both the widespread use of anticoagulants and their use with concomitant medications. Although the true mechanisms of drug interactions almost always remain unknown, there are several pharmacokinetic and pharmacodynamic factors that could affect the effect of warfarin (Holbrook et al. 2005). Although an understanding of a drug's pharmacology will help predict the potential for interaction with warfarin, clinical reality is far from certain. Regular monitoring of INR remains the best protection against major harm due to these pharmacokinetic and pharmacodynamic interactions. The most difficult drug groups to treat are those that self-potentiate bleeding: other anticoagulants such as heparin; antiplatelet agents such as acetylsalicylic acid, clopidogrel, dipyridamole, sulfinpyrazone, and ticlopidine; all NSAIDs including COX-2 selective NSAIDs. The risk of bleeding is greater when taken with warfarin, and INR monitoring will not help. All of these drugs should be avoided in combination with warfarin unless they have been shown to offer a benefit that outweighs the risk of bleeding, such as in artificial heart valves (Holbrook et al. 2005).

Many drugs and foods interact with warfarin, including antibiotics, drugs that affect the central nervous system, and cardiac medications. Warfarin's anticoagulant effect is potentiated by antibiotics (ciprofloxacin, cotrimoxazole, erythromycin, fluconazole, isoniazid, metronidazole, and miconazole), cardiac drugs (diltiazem, fenofibrate, amiodarone, clofibrate, propafenone, propranolol, and sulfinpyrazole), phenylbutazone, NSAIDs including piroxicam, alcohol (only with liver disease), sertraline, entacapone, cimetidine, omeprazole, and foods, such as fish oil, mango, grapefruit, and cranberry juice. Warfarin's anticoagulant effect was inhibited by some antibiotics (griseofulvin, rifampin, ribavirin, and nafcillin), drugs active on the central nervous system (barbiturates, carbamazepine, haloperidol, and chlordiazepoxide), adrenocorticoids, cholestyramine, sucralfate, foods high in vitamin K (parsley, cilantro, dill, cabbage, broccoli, lettuces, and other leafy greens except peas and green beans), large amounts of avocado, ginseng, and sushi containing seaweed (Wells et al. 1994; Holbrook et al. 2005) (Table 10.8). When patients are given drugs that interact with warfarin, an alternative drug with less potential to interact with warfarin should be considered, such as rabeprazole instead of omeprazole and acetamino-

Table 10.8 Clinically significant interactions with warfarin by drug group

Interaction	Antibiotics	Cardiovascular	Anti-inflammatory, analgesics	Central nervous system	Gastrointestinal	Foods, miscellaneous
Potentiation	Ciprofloxacin, cotrimoxazole, erythromycin, fluconazole, isoniazid, metronidazole, miconazole, amoxicillin, tetracycline, chloramphenicol	Amiodarone, diltiazem, clofibrate, propafenone, propranolol, sulfinpyrazone, acetylsalicylic acid, simvastatin, fenofibrate	Phenylbutazone, piroxicam, acetaminophen, acetylsalicylic acid, celecoxib, rofecoxib, indomethacin, tramadol	Alcohol (if concomitant liver disease), citalopram, entacapone, sertraline, phenytoin (biphasic with later inhibition)	Cimetidine, omeprazole	Fish oil, mango, grapefruit, cranberry juice, anabolic steroid
Inhibition	Griseofulvin, nafcillin, rifampin, cyclosporine	Cholestyramine, vitamin K	Sulfasalazine	Barbiturates, carbamazepine, chlordiazepoxide	Sucralfate	High vitamin K content foods, enteral feeds, large amounts of avocado, soy milk, sushi containing seaweed, ginseng, multivitamin supplement, chelation therapy, influenza vaccine
No effect	Enoxacin, vancomycin, cefamandole, cefazolin	Atenolol, bumetanide, felodipine, metoprolol, moricizine, heparin, furosemide	Diflunisal, ketorolac, naproxen, ibuprofen, methylprednisolone	Alcohol, fluoxetine, nitrazepam	Antacids, famotidine, nizatidine, psyllium, ranitidine	Green tea, vitamin E, tobacco

Modified from Wells et al. (1994) and Holbrook et al. (2005)

phen instead of NSAIDs. A more frequent INR test during the 2 weeks after starting or stopping treatment with other medications is advisable (Holbrook et al. 2005).

Warfarin sodium (Coumadin) is the most commonly used oral anticoagulant. Dosing is individualized and based on monitoring its effectiveness through regular PT assessment. Because of the significant interlaboratory variability of the thromboplastin reagents used to perform these assessments, a common standardized scale, the INR, has been developed to provide more comparable control of efficacy regardless of the reagents used. An INR of 2.0–3.0 is generally recommended for both prophylaxis and treatment of thromboembolism. The usual starting dose of warfarin is 5–10 mg once a day. Larger loading doses should be avoided, in view of the increased risk of bleeding. It should be started with lower loading doses in the elderly or debilitated, or in those known to be sensitive to warfarin (Stitik et al. 2010). Oral anticoagulation is usually started at the time of heparin treatment, overlaps it for about 4–5 days so that the INR increases to 2.0–3.0, and then continues alone.

10.4.3.3 Direct Oral Anticoagulants

Treatment of the vast majority of patients with venous thromboembolism has been based on the use of heparins, either UFH or LMWH, followed by the oral vitamin K antagonists (warfarin) (Kearon et al. 2012). However, all of these compounds had some limitations, including parenteral administration of heparins and the need for routine coagulation monitoring and dose adjustments for warfarin (Ageno et al. 2012). Direct oral anticoagulants (DOACs) have been developed to overcome some of these limitations (Barnes et al. 2015). The DOACs have a favorable pharmacologic profile (e.g., rapid onset and short half-life) and a predictable anticoagulant response, which makes their use particularly attractive for both the acute phase treatment and for the long-term secondary prevention of venous thromboembolism. In the acute treatment of venous thromboembolism, their effectiveness was not inferior to that of standard treatment and was associated with less major bleeding complications (Riva and Ageno 2016).

The use of DOACs has steadily increased since their approval and are now recommended over warfarin for stroke prevention in nonvalvular atrial fibrillation and for treatment of venous thromboembolism (Rawal et al. 2019). However, studies on the use of DOAC to prevent and treat deep venous thrombosis in patients with spinal cord injuries have not been well conducted (Hamidi et al. 2019). As the use of DOAC increases, the number of major and minor bleeding events that require medical intervention will continue to increase. Until 2015, warfarin was the only oral anticoagulant to have any benefit with a specific reversal agent. Since then, idarucizumab has been approved for reversal of dabigatran in October 2015, and andexanet alfa recently received approval for the reversal of apixaban or rivaroxaban in 2018 in patients with life-threatening or uncontrolled bleeding events (Rawal et al. 2019).

The DOACs act on specific targets in the coagulation cascade. According to their specific target, they are classified as direct thrombin inhibitors (e.g., dabigatran) and direct factor Xa inhibitors (e.g., apixaban, rivaroxaban, and edoxaban) (Ageno et al. 2012). The onset of action ranges between 1 and 4 h, which allows their use in the acute phase treatment of venous thromboembolism, and the half-life ranges between 9 and 14 h, which allows the anticoagulant effect to disappear sufficiently quickly after discontinuation. Compared to warfarin, the DOACs also show less potential for food–drug and drug–drug interactions and less inter- and intra-subject variability in dose response. Therefore, they do not require INR monitoring (Ageno et al. 2012; Riva and Ageno 2016; Rawal et al. 2019). The pharmacologic properties of the DOACs are summarized in Table 10.9.

Dabigatran

Dabigatran binds to the active site of the thrombin molecule and therefore inactivates both free and fibrin-bound thrombin. In contrast, indirect inhibitors of thrombin and factor Xa (such as

Table 10.9 Summary of the pharmacologic properties of the direct oral anticoagulants

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Administration	Oral	Oral	Oral	Oral
	BID	OD	BID	OD
Oral bioavailability	~6.5%	66% (without food) >80% (with food)	50%	62%
Time to peak plasma concentration	0.5–2 h	2–4 h	1–3 h	1–2 h
Mean half-life	12–14 h	5–9 h (young adult) 11–13 h (elderly)	~12 h	10–14 h
Renal clearance	85%	66% (only half as inactive metabolite)	27%	35%
Plasma protein binding	35% (dialyzable)	~90%	87%	~55%
Cytochrome P450 metabolism	No	Yes	Yes	Minimal
P-gp transport	Yes	Yes	Yes	Yes

BID, bis in die (twice a day); OD, once daily
From Riva and Ageno (2016)

UFH or LMWH) do not inactivate fibrin-bound thrombin, which can further stimulate thrombus expansion. Dabigatran is a highly selective, reversible, and potent thrombin inhibitor and is available orally as the prodrug, dabigatran etexilate. Dabigatran has a low percentage of plasma protein binding of approximately 35%. Therefore, it can be removed by dialysis. Dabigatran has a low potential for drug–drug interactions and is mainly excreted renally (Eisert et al. 2010; Riva and Ageno 2016; Rose and Bar 2018). Dabigatran is not metabolized by the cytochrome P450 enzymes and does not interact with food. It is a substrate of the efflux transporter P-glycoprotein (P-gp), which is found in the intestine and kidneys. Therefore, strong inhibitors (e.g., quinidine, ketoconazole, amiodarone, and verapamil) may increase absorption of dabigatran and potent inducers (e.g., rifampin) may decrease absorption of dabigatran (Riva and Ageno 2016).

Peak plasma concentrations of dabigatran occur 1–2 h after ingestion of the prodrug. The half-life of dabigatran is 12–14 h. Dabigatran is given in a dosage of 150 mg bid for the treatment of venous thromboembolism after 5–10 days of parenteral anticoagulation and 150 mg bid to prevent the recurrence of venous thromboembolism. In patients with life-threatening bleeding or those requiring urgent surgery who are taking dabigatran, idarucizumab (Praxbind®) is the reversal drug for dabigatran (Crowther and Cuker 2019; Cuker et al. 2019).

Rivaroxaban, Apixaban, and Edoxaban

Rivaroxaban, apixaban, and edoxaban are direct inhibitors of the activated factor X (Xa), while the indirect inhibitors of thrombin and factor Xa require the cofactor antithrombin to inhibit factor Xa. They can bind not only free factor Xa, but also factor Xa within the prothrombinase complex directly (Riva and Ageno 2016; Rose and Bar 2018). The specific reversal agent for the factor Xa inhibitors is andexanet alfa (Crowther and Cuker 2019).

Rivaroxaban

Rivaroxaban is a substrate for both cytochrome P450 enzymes and P-gp transporters. Therefore, rivaroxaban increases the absorption of dabigatran by drugs of P-gp inhibitors such as quinidine, amiodarone, ketoconazole, itraconazole, lopinavir, and indinavir, and suppresses the absorption when used with P-dg inducers such as rifampin, carbamazepine, and phenytoin (Riva and Ageno 2016; Rose and Bar 2018). The bioavailability of rivaroxaban after oral administration is dose-dependent: 80–100% are reported for the 10 mg dose and 66% for the 20 mg dose in the

fasted state. Administration with food results in delayed absorption but increased peak concentrations and is therefore recommended for therapeutic dosages. One-third of the drug is excreted unchanged through the urine, while the other two-thirds are converted into inactive metabolites and half are eliminated renally and half through the fecal route (Perzborn et al. 2010).

For the treatment of venous thromboembolism, rivaroxaban is given at a dosage of 15 mg bid for 21 days, and then 20 mg once daily and 150 mg once daily to prevent the recurrence of venous thromboembolism.

Apixaban

Apixaban is a substrate of cytochrome P450 and P-gp. However, apixaban has several routes for elimination that can reduce the extent of a drug interaction. Conversely, apixaban does not significantly modulate the function of cytochrome P450 enzymes or P-gp transporter. The bioavailability of apixaban after oral administration is approximately 50%, and plasma protein binding in humans is 87% (Riva and Ageno 2016; Rose and Bar 2018). Apixaban is administered at a dosage of 10 mg bid for 7 days, followed by 5 mg bid for the treatment of venous thromboembolism and 2.5 mg bid after at least 6 months of treatment to prevent the recurrence of venous thromboembolism.

Edoxaban

Edoxaban is a substrate of the P-gp transporter, while only a very small percentage (approximately 4%) is metabolized by cytochrome P450. The bioavailability of edoxaban after oral administration is 62%. Edoxaban is converted into several metabolites, primarily through hydrolysis. However, more than 70% are excreted unchanged. Approximately 35% of edoxaban is excreted in the urine and 60% in the feces. Edoxaban is administered at a dose of 60 mg bid once a day after 5–10 days of parenteral anticoagulation and then reduced to 30 mg once daily for the treatment of venous thromboembolism (Riva and Ageno 2016; Rose and Bar 2018).

10.4.4 Medications for Neurogenic Lower Urinary Tract Dysfunction

Treatment of the neurogenic bladder for spinal cord injury aims to prevent complications of the upper urinary tract system by not reducing detrusor compliance and intermittent catheterizations. However, this section describes drugs such as antimuscarinics and β3-agonists to increase detrusor compliance of the neurogenic bladder.

10.4.4.1 Antimuscarinic Agents

Antimuscarinic anticholinergic medications are the most commonly prescribed drugs for overactive neurogenic bladder in patients with spinal cord injuries. There are many antimuscarinic preparations available for the treatment of overactive neurogenic bladder. These drugs block activity of acetylcholine at the muscarinic receptors and decrease detrusor muscle contraction. Even so, there are a number of differences between these drugs, but whether this makes one more appropriate than the other for an individual patient is not conclusive (Wein and Chapple 2012). Antimuscarinic anticholinergic medications improve urine storage, lengthen the time between catheterizations or voiding, and decrease urinary frequency, incontinence, and nocturia.

Muscarinic receptors are located in the urinary tract, but are also present in the brain (M1, M3, M4, and M5 receptor subtypes), salivary glands (M1 and M3 receptor subtypes), heart (M2 receptor subtype), gastrointestinal smooth muscle (M2 and M3 receptor subtypes), and eyes (M3 and M5 receptor subtypes). This widespread distribution of muscarinic receptors in the body explains the commonly observed side effects of these agents, including cognitive problems, dry mouth, tachycardia, constipation, and blurred vision (Wein and Chapple 2012). Contraindications include obstructive gastrointestinal disease, severe ulcerative colitis, reflux esophagitis, unstable cardiovascular status in acute hemorrhage, glaucoma, and myasthenia gravis.

Oxybutynin

Oxybutynin is the most commonly used anticholinergic treatment for bladder overactivity. It is a tertiary amine with M1 and M3 selectivity. Oxybutynin acts as a competitive antagonist of acetylcholine at the postganglionic muscarinic receptors, which leads to relaxation of the bladder smooth muscle. It is a tertiary amine that has potent anticholinergic, musculotropic, and intravesicular anesthetic effects.

Oxybutynin is rapidly absorbed and eliminated after ingestion, with a maximum plasma concentration and elimination half-life of less than 1 h. For adults, the usual dose is 5 mg two or three times a day. This can be increased to a maximum of 5 mg four times a day for clinical response if the side effects are tolerated. In the elderly, a dose of 2.5 mg twice a day is likely to be adequate. Oxybutynin is available as an ER (extended release) formulation, solution for intravesical instillation, and as a transdermal patch. In adults, the recommended starting dose of oxybutynin ER is one 5 mg tablet once daily. In order to achieve a maintenance dose that provides an optimal balance between efficacy and tolerability, after at least 1 week on 5 mg daily, the dose may be increased to 10 mg once daily, with subsequent incremental increases or decreases of 5 mg/day. There should be an interval of at least 1 week between dose changes and the total daily dose should not exceed 20 mg (Wein and Chapple 2012).

Fesoterodine (Toviaz)

Fesoterodine is a prodrug that is converted into 5-hydroxymethyl tolterodine (Corcos et al. 2015). Fesoterodine is a competitive, specific muscarinic receptor antagonist. It is hydrolyzed rapidly and extensively to the 5-hydroxymethyl derivative by nonspecific plasma esterases.

The most common side effects are dry mouth and constipation. Common adverse effects include dizziness, headache, dry eye, dry throat, abdominal pain, diarrhea, dyspepsia, nausea, dysuria, and insomnia. Fesoterodine is not recommended for use in children and adolescents under 18 years of age due to lack of data on safety and efficacy. The recommended starting dose for adults including the elderly is 4 mg once daily. Based on individual responses, the dose may be increased to 8 mg once daily (Wein and Chapple 2012). The maximum daily dose is 8 mg.

Tolterodine

Tolterodine is a tertiary amine with no selectivity for muscarinic receptors. It is easily metabolized by P450. Due to its low lipophilicity, there is some crossing of the blood-brain barrier (Corcos et al. 2015). Tolterodine is not recommended in patients receiving substances that are potent CYP3A4 inhibitors, such as erythromycin, clarithromycin, ketoconazole, itraconazole, and antiproteases because of the increased serum concentrations of tolterodine in poor CYP2D6 metabolizers and the risk of overdose. Tolterodine is currently not recommended for children (Wein and Chapple 2012).

The dosage for the IR (immediate release) formulation is 1–2 mg twice daily and for the ER 2–4 mg once daily.

Propiverine

Propiverine inhibits calcium influx and modulation of intracellular calcium in smooth muscle cells of the urinary bladder, which leads to musculotropic spasmolysis and an inhibition of the efferent connection of the pelvic nerve due to anticholinergic action (Wein and Chapple 2012).

The recommended standard dose for adults and the elderly is one 30 mg capsule once a day. Due to a lack of data, propiverine should not be used in children. The only very common side effect is dry mouth. Common side effects are abnormal vision and accommodation.

Solifenacin

Solifenacin is a competitive cholinergic receptor antagonist. Of the muscarinic, it mainly acts on the M3 receptor. It is metabolized by P450 and easily absorbed through the gastrointestinal epithelium (90% availability).

Solifenacin has less dry mouth compared to oxybutynin, but the most common side effects are dry mouth and constipation. Safety and effec-

tiveness in children have not yet been established. Therefore, solifenacin should not be used in children. The dosage is 5–10 mg once daily.

10.4.4.2 β3-Agonist (Mirabegron)

Mirabegron is a potent selective agonist of the β3-adrenoceptor receptor. By stimulating β3-adrenoceptors in the bladder, mirabegron probably leads to bladder relaxation and thus to improved urine storage, and reductions in bladder contraction. Mirabegron is recommended as an option to treat overactive bladder or neurogenic detrusor overactivity after spinal cord injuries when antimuscarinic drugs are intolerable, clinically ineffective, or contraindicated (NICE 2013; Wöllner and Pannek 2016). There is an improvement in urodynamic parameters (increased maximum cystometric capacity, decreased maximum detrusor pressure during storage phase, and improvement of the compliance) and clinical parameters by administering mirabegron in neurogenic overactive detrusor of patients with spinal cord injuries (Wöllner and Pannek 2016).

Oral mirabegron is readily absorbed, with peak plasma concentrations reaching 3–5 h. The recommended dosage is 50 mg orally once daily with or without food or after a meal. When administered once daily, steady-state concentrations of mirabegron are reached within 7 days and there is two- to threefold accumulation of the drug. Mirabegron is eliminated in the urine (55%) and feces (34%), with unchanged mirabegron accounting for 45%. Mirabegron has a terminal elimination half-life of approximately 50 h (Deeks 2018).

10.4.5 Medications for Neurogenic Bowel Dysfunction

Many patients with spinal cord injuries are able to develop a routine of regular bowel evacuation without the use of medications. People with spinal cord injuries have significant chronic GI problems that require medical attention and can cause problems, such as constipation, abdominal discomfort, autonomic dysreflexia, and incontinence.

10.4.5.1 Laxatives

Many laxatives are available, and their effects range from mild (bulk forming agents) to more aggressive (hyperosmolar agents). Laxatives can facilitate or restore regular bowel movements in constipated patients with spinal cord injuries. All laxatives are used on people with spinal cord injuries as part of bowel program.

Bulk Forming Agents

Bulk forming agents, such as psyllium, methylcellulose, and polycarbophil, contain natural fiber, which increases the water content of the feces and promotes bacterial floral growth. These agents should be taken with plenty of fluids. Fiber supplements are well tolerated with occasional bloating and are believed to keep stool soft when the diet does not contain enough fiber. They take 3–5 days for full effect and should be taken after meals for maximal mixing with food (Klein 1982; Schryvers and Nance 1999).

Stool Softeners

Stool softeners (docusate sodium and docusate calcium) increase absorption of stool water as they stimulate secretion of water, sodium, chloride, and potassium inhibits absorption of glucose and bicarbonate, and support the mixing of water and fat throughout the intestines. Stool softeners are given at the highest dose and then reduce the dose when the first bowel movement occurs. Docusate can increase the uptake of other medications and is therefore not recommended for long-term use (Schryvers and Nance 1999).

Hyperosmolar Agents

Hyperosmolar agents (magnesium citrate, magnesium hydroxide, and polyethylene glycol) cause water secretion into the colon and rectum, which leads to a loosening and facilitating the expulsion of feces. These agents act within 3 h of ingestion and require plenty of fluids. Therefore, patients with renal insufficiency, heart disease, and electrolyte imbalances should be taken with caution.

Colonic Stimulants

Colonic stimulants (bisacodyl, cascara sagrada, castor oil, sodium bisphosphanate, and senna) act on colonic and rectal sensory nerve endings when they contact with the mucosal membrane as irritant cathartics, and then increase peristalsis through parasympathetic reflexes. Biscodyl influences fluid and electrolyte absorption in the entire intestine. Cascara and senna act on the large intestine, so that a delayed effect of about 8 h occurs and can lead to urine discoloration. Castor oil induces intestinal hydrolysis to form a cathartic.

Osmotic Laxatives

Osmotic laxatives (lactulose) act by drawing fluid into the colon and are more suitable for long-term use because tolerance does not develop and there is no risk of organ damage. It increases stool volume by metabolizing it to nonabsorbable fatty acids in the colon, thereby improving stool consistency. Lactulose enemas generate a release of carbon dioxide and hydrogen, and thus break up impacted stool. Lactulose should not be used regularly because of side effects including diarrhea, floating, cramping, and electrolyte imbalance (Schryvers and Nance 1999).

Glycerin suppository, along with digital stimulation, stimulates the rectal stretch reflex and is often used in patients with spinal cord injuries to wean off bisacodyl suppositories when switching to digital stimulation. It usually works within 30 min. Therevac SB, "mini-enema" is a combination of docusate sodium 293 mg and glycerin 275 mg in a plastic ampule. It was developed to meet the needs of patients with spinal cord injuries and acts as a mucosal stimulant and stool softener, with a rapid onset of action within 15 min (Dunn and Galka 1994).

10.4.5.2 Medications Reducing Gastric Acid Secretion

These drugs are also used for idiopathic gastric and duodenal ulcers and gastroesophageal reflux diseases. They are also widely used to prevent stress ulcers in patients with spinal cord injuries.

H2 Blockers

H2 blockers (cimetidine, famotidine, nizatidine, ranitidine) block histamine2 receptors of gastric acid producing parietal cells. Because of the change in gastric fluid acidity due to H2 blockers. GI absorption of various drugs can be altered.

Proton Pump Inhibitors

Proton pump inhibitors (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole) decrease gastric acid secretion by inhibiting the parietal cell membrane enzyme, which actively transports hydrogen ions out of the cells. They are used for many indications including gastroesophageal reflux disease, gastritis, peptic ulcer disease, erosive esophagitis, and prevention/treatment of ulcers induced by NSAID or ASA use. These drugs are well tolerated, but sometimes nausea, diarrhea, headache, dizziness, and possible colonization of gastric bacteria due to the elevation of the pH of gastric fluid.

Prostaglandin Analog

Prostaglandin analog (misoprostol), which is used to reduce gastric secretion, acts on mucosal protection and decreases gastric acid secretion. The most common side effect of this drug is diarrhea. Prostaglandin analog should not be used in women of childbearing potential because of abortifacient properties due to smooth muscle contraction.

10.4.5.3 Medications for Improving GI Motility (Prokinetic Agents)

The two most common drugs used to improve GI motility are metaclopramide and cisapride. The use of the latter is limited due to many drug interactions and potentially fatal arrhythmia. These drugs enhance acetylcholine release and/or action at the myenteric plexus, thereby stimulating upper GI peristalsis. This leads to reflux reduction and gastric emptying. Metaclopramide is administered 10–15 mg orally 30 min before meals and sleep for gastroesophageal reflux and should be reduced to 5 mg in elderly patients.

10.4.5.4 Antidiarrheal Drugs

The two most common drugs used for diarrhea are loperamide and diphenoxylate or its principal metabolite difenoxin (Lomotil), combined with atropine (Motofen). Antidiarrheal medications are often used for short-term treatment of acute, nonspecific diarrhea and can also be used for chronic inflammatory bowel disease-associated diarrhea. However, they should be avoided if diarrhea is suspected to be due to obstructive jaundice, fecal impaction, or infection with toxin production. If diarrhea is not controlled within 48 h, further work-up is required.

Antidiarrheal drugs directly inhibit the peristalsis of the intestinal smooth muscle. Since antidiarrheal agents affect bowel motility, abdominal discomfort and nausea can occur. In addition, opioid-like side effects such as fatigue, drowsiness, or dry mouth can occur. Lomotil and Motofen are chemically related to the narcotic analgesic meperidine (Demerol) and are combined with atropine. Therefore, they may interact with MAO inhibitors and, when used with other CNS depressants, are likely to cause sedation.

10.4.6 Medications for Spasticity

Spasticity is characterized by an abnormal increase in muscle tone or muscle stiffness that is associated with pain and interferes with movement and posture. Treatment of spasticity after spinal cord injuries can be multifaceted. Pharmacotherapeutic strategies include oral or systemic drugs (Baclofen, dantrolene sodium, diazepam, tizanidine, clonidine), and agents such as botulinum toxins and alcohols for focal chemodenervation. Before deciding on pharmacotherapy, it must be emphasized that spasticity not contributing to decreased function, pain, or increased burden of care does not need to be suppressed. Aggravating factors such as bladder or bowel distension or other noxious stimuli should be identified and limited as much as possible before initiating treatment (Riedel and Marino 2018).

10.4.6.1 Baclofen

Baclofen is a synthetic agonist of the neurotransmitter gamma-aminobutyric acid (GABA). It binds to GABA-B receptors, which leads to an inhibition of calcium influx that would enable the release of excitatory neurotransmitters (Curtis et al. 1997). It is also believed to have postsynaptic effects at the GABA-B receptor through multiple pathways, reducing the activity of both the gamma motor neuron and intrafusal spindle muscles (Misgeld et al. 1995). Baclofen, therefore, inhibits monosynaptic and postsynaptic reflexes (Ito et al. 1982; Riedel and Marino 2018). Baclofen reduces the release of excitatory neurotransmitters in the spinal cord, thereby reducing spinal reflex action, clonus, and flexor spasm, and improving the range of motion of the joints. Baclofen has been studied most extensively in patients with spinal cord injuries and in patients with multiple sclerosis, and has been shown to reduce spasticity and painful flexor spasms in these populations. There is less evidence of benefit in patient with spasticity of cerebral origin. It has been used for more than 40 years and generally has a low incidence of drug tolerance and/or side effects (Riedel and Marino 2018).

Baclofen can be administered orally for mild to severe spasticity. Baclofen is well absorbed orally, but it is 30% protein bound and has low lipid solubility. It does not readily cross the blood–brain barrier into the CNS (Albright et al. 1993). Baclofen is mostly excreted through the kidneys and a small amount is metabolized by the liver. It has a short half-life of approximately 3.5 h (Riedel and Marino 2018).

Side effects of oral baclofen include drowsiness during the first week of drug use. This drowsiness typically disappears when the dosage is adjusted. Other side effects reported include muscle weakness, ataxia, orthostatic hypotension, fatigue, headache, nausea, and dizziness. Sudden withdrawal can lead to temporarily increased spasticity, rhabdomyolysis, disorientation, hallucination, and seizures. Intrathecal baclofen provides long-term delivery of the medication into the intrathecal space bypassing the

blood–brain barrier and offers improved bioavailability compared to oral baclofen. Intrathecal baclofen provides effective concentrations in the cerebrospinal fluid and reduces plasma baclofen concentrations 100-fold (Rietman and Geertzen 2007). This reduction in plasma baclofen concentrations leads to a reduction in the side effects associated with oral use. Common side effects of intrathecal baclofen include chronic constipation, hypotonia, drowsiness, headache, vomiting, and paresthesia. A pump failure or problems with the catheter can trigger withdrawal symptoms. Mild withdrawal symptoms can include pruritus, agitation, diaphoresis, and increased muscle tone. Symptoms can process to seizures, hallucinations, delirium, rhabdomyolysis, and death if baclofen is abruptly stopped (Peng et al. 1998; Rietman and Geertzen 2007). Early detection of a pump malfunction that leads to an overdose is important to prevent toxicity such as seizures, respiratory depression, decreased cardiac function, and coma (Boster et al. 2016).

10.4.6.2 Dantrolene

Dantrolene (dantrolene sodium) is a peripherally acting agent. By suppressing the release of calcium ions from the sarcoplasmic retinaculum, excitation and contraction are decoupled, which reduces muscle tone, clonus, and spasm associated with spasticity. This effect is more pronounced in fast contracting fibers and affects both intrafusal and extrafusal fibers, indicating a component of muscle spindle sensitivity modulation (Jami et al. 1983). Calcium is necessary for cross-bridging of the actin and myosin, which results in muscle contraction. Dantrolene is unique in that it acts at the skeletal muscle level while other agents act at the spinal cord level.

Dantrolene is mainly metabolized in the liver and has a half-life of approximately 15 h. During the first 7–10 days, dantrolene can cause drowsiness, dizziness, nausea, and diarrhea. Side effects can also include dysphagia. Because dantrolene acts peripherally at the muscle level, it has no adverse effects on the CNS. However, it can still be associated with fatigue and muscle weakness (Carl et al. 2014). Dantrolene has a US FDA black box warning for hepatotoxicity, with reactions occurring more frequently in higher doses (daily dosage of 300 mg or more) and in women over 35 years of age on estrogen supplementation (Utili et al. 1977). Dantrolene-associated liver damage is usually reversible if liver function tests are monitored and the drug is appropriately discontinued. Baseline liver function tests are required in patients before starting dantrolene, usually again after 1 month and then every 3 months during treatment (Riedel and Marino 2018).

10.4.6.3 Diazepam

Diazepam, a long-acting benzodiazepine, is one of the oldest medications for spasticity in patients with spinal cord injuries. It also has anxiolytic, hypnotic, sedative, anticonvulsant, skeletal muscle relaxant, and amnestic effects. Benzodiazepines, including diazepam, act indirectly through the GABA-A receptors. Diazepam increases binding of GABA to its receptor, reducing spinal reflexes. Although diazepam is as effective as baclofen, it induces more sedation, which limits its clinical use. Adverse effects are more pronounced in the first 2 weeks of treatment. Other adverse effects include impaired memory, decreased attention, ataxia, weakness, constipation, and urinary retention. Diazepam is not intended for long-term chronic use in the treatment of spasticity because its strong sedative effect causes drowsiness, decreased psychomotor performance, dizziness, reflex tachycardia, and potential for tolerance and physical dependence (Carl et al. 2014). Chronic use of benzodiazepines can lead to significant pharyngeal phase dysphagia, notably cricopharyngeal incoordination, hypopharyngeal incoordination, and aspiration (Carl et al. 2014; Dantas and Nobre Souza 1997; Moosavi et al. 2020).

Diazepam is metabolized by the liver and its half-life can be from 20 to 50 h, with active metabolites lasting up to 100 h (Riss et al. 2008).

10.4.6.4 Tizanidine

Tizanidine, a centrally acting α-2 adrenergic agonist, binds to central α-2 receptors and reduces excitatory input to alpha motor neurons, thus improving spasm and clonus. It is believed to act

presynaptically to attenuate the release of excitatory neurotransmitters at the spinal cord level and possibly through effects on interneurons and postsynaptic release of excitatory neurotransmitters (Coward 1994). Common side effects of tizanidine include xerostomia, sedation, muscle weakness, postural hypotension, and dizziness. The risk of severe muscle weakness is lower in patients using tizanidine than in patients using diazepam and baclofen. Tizanidine is metabolized in the liver and has a half-life of about 3 h (Riedel and Marino 2018).

10.4.6.5 Clonidine

Clonidine, a centrally acting selective α-2 adrenergic receptor agonist used in the management of hypertension, is effective in the treatment of spasticity associated with spinal cord injuries and traumatic brain injuries. It is available in oral form and as transdermal patch.

10.4.6.6 Botulinum Toxins

Botulinum toxins are produced by the Gram-positive aerobic bacteria C. botulinum. Several serotypes are produced, referred to as serotypes A through G, but two antigenically distinct serotypes of botulinum toxins are available on the market as types A and B. All serotypes act at the presynaptic terminal by blocking the release of acetylcholine into the synaptic cleft. Each botulinum toxin molecule consists of a heavy chain and a light chain. The heavy chain is responsible for the presynaptic binding of the toxin to receptors. The light chain is responsible for inhibiting the action of a specific protein that is responsible for acetylcholine release. For presynaptic vesicles containing acetylcholine to bind with the nerve terminal membrane and release their contents into the synaptic cleft, a complex set of proteins called SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) proteins is needed. SNARE proteins include SNAP-25 (synaptosome-associated protein-25), synaptobrevin, and syntaxin (Riedel and Marino 2018).

Botulinum toxin serotype A (onabotulinum toxin A, abobotulinum toxin A, incobotulinum toxin A) is a metalloprotease that proteolytically cleaves SNAP-25 at nerve endings to inhibit fusion of the synaptic vesicle with the presynaptic membrane of the axon terminal and thus ultimately relaxes the muscle. Serotype B (rimabotulinum toxin B) inhibits synaptobrevin. Thus, by injecting botulinum toxin into certain muscles, local muscular hyperactivity can be reduced without affecting other muscles, thereby improving function and preventing deformities, which is why its use in focal spasticity would be indicated (Palazón-García et al. 2019). Compared with the serotype A, the serotype B causes more intense anticholinergic effects such as dry mouth, dysphagia, and voiding difficulties (Carl et al. 2014; Ozcakir and Sivrioglu 2007). It is estimated that botulinum toxin reaches the neuromuscular junction within 12 h and that an effect occurs in 4–7 days, with the duration of the effect varying from 3 to 6 months.

10.4.7 Pain Medications

Although pain in patients with spinal cord injuries is classified as nociceptive or neuropathic, patients often experience mixed pain. The optimal medication for neuropathic pain is unclear, although a better understanding of the pathophysiology of neuropathic pain suggests that nonopioid agents such as anticonvulsants and antidepressants should be more effective than opioids or nonsteroidal anti-inflammatory drugs (NSAIDs). When anticonvulsants are used to treat neuropathic pain, they are commonly referred to as membrane-stabilizing drugs.

10.4.7.1 Gabapentin

Gabapentin is the first-line treatment for neuropathic pain. It has a very favorable side effect profile and reputation for minimal drug interactions. There is no evidence of its effectiveness in acutely painful conditions. It has been used to treat spasticity in patients with spinal cord injuries. It was originally thought to inhibit gamma-aminobutyric acid (GABA) receptors because of its structural similarity to GABA, a major CNS excitatory neurotransmitter. Gabapentin has been considered as a calcium channel blocker and hip-

pocampal CA1 neural enhancer. There is evidence that it may increase the excitatory threshold of the interneuron pool for polysynaptic reflexes. It does not bind to plasma protein, is not metabolized, and is excreted by the kidneys at the rate of creatinine clearance.

CNS depressions like somnolence, dizziness, fatigue, and ataxia are the main side effects. Side effects are usually temporary with resolution in 2 weeks. Rare side effects have been reported, including leukopenia, thrombocytopenia, increased BUN, rash, and nonlethal EKG abnormalities that required discontinuation. Given the rarity of serious adverse events, routine laboratory monitoring and monitoring of serum gabapentin levels are not required. Cimetidine minimally reduces renal gabapentin excretion and Maalox reduces gabapentin bioavailability by 20%. However, these drug interactions are clinically insignificant.

The reported dose for the relief of neuropathic pain is between 900 and 2400 mg per day, divided tid. A maximum daily dose of 3600 mg was well tolerated in a small number of patients for a short duration. At the start of therapy, a bedtime dose of 300 mg on the first day, then bid dose on the second day, and a subsequent tid dosage can be used to help patients adjust to the CNS depressive effects.

10.4.7.2 Pregabalin

A second analog of GABA, pregabalin, is also a first-line drug for neuropathic pain in patients with spinal cord injury. Pregabalin is used to treat pain due to fibromyalgia and anxiety disorders. Pregabalin is a calcium channel blocker. However, it is also believed that there are other mechanisms of action, including modulating the release of various neurotransmitters such as glutamate, noradrenaline, and substance P to produce their net inhibitory effects on neurons. Pregabalin does not bind to plasma proteins and almost the entire dose is excreted unchanged in the urine, with elimination following first-order kinetics.

Dizziness, somnolence, and dry mouth have been reported commonly. Complaints of headache, weight gain, edema, blurred vision, and difficulty with concentration have also been reported. Pregabalin is classified as a Schedule V controlled substance because it causes euphoria in selected people. Pregabalin has no known drug interactions.

Pregabalin is available as capsules in the following strengths: 25, 50, 75, 100, 150, 200, 225, and 300 mg. It is generally started at 50 mg tid for 1 week then increased to a maximum of 1000 mg tid.

10.4.7.3 Carbamazepine

Carbamazepine has also been extensively studied in neuropathic pain. Traditional belief is that carbamazepine is particularly effective for neuropathic pain. The relative lack of CNS side effects compared to other anticonvulsants offers an obvious advantage in terms of functional activities. The potential hematologic toxicity, the need for regular blood tests, baseline and periodic eye examinations, and numerous medication interactions make carbamazepine a less attractive choice. Carbamazepine binds and prolongs the inactivation of voltage-dependent sodium channels. The number of action potentials is consequently reduced. Due to its high lipid solubility, it is slowly absorbed into the body after oral administration and is highly protein bound. It induces the hepatic CYP450 enzymes and this increases the metabolism of several drugs, including its own.

Carbamazepine can often lead to hematologic side effects. CBC, LFTs, BUN and urinalysis, reticulocyte count, and serum iron levels are recommended prior to initiation of carbamazepine. CBC and LFTs should be checked regularly and discontinuation of medication should be considered if toxicity is suspected. A variety of toxicities can occur with carbamazepine, including leukopenia and thrombocytopenia, aplastic anemia and agranulocytosis, hepatotoxicity, skin reactions such as Steven-Johnson syndrome and toxic epidermal necrolysis, and, to a lesser extent, renal dysfunction.

Carbamazepine interacts with many drugs (Table 10.10). In addition, it should not be administered to people with TCA hypersensitivity due to possible cross-reactivity, or not be used within 2 weeks of an MAOI.

Table 10.10 Potential drug–drug interactions with carbamazepine

Interaction	Decreased serum level	Increased serum level
Medications whose serum levels are affected by carbamazepine	Acetaminophen, alprazolam, amitriptyline, bupropion, buspirone, clonazepam, cyclosporine, diazepam, dicumarol, doxycycline, glucocorticosteroids, haloperidol, lorazepam, methadone, midazolam, nortriptyline, contraceptives, phenytoin, risperidone, theophylline, tramadol, trazodone, valproate, warfarin	Clomipramine, phenytoin, primidone
Medications that affect serum carbamazepine levels	Cisplatin, doxorubicin HCL, felbamate, methsuximide, phenobarbital, phenytoin, primidone, rifampin, theophylline	Acetazolamide, azole antifungals, calcium channel blockers, cimetidine, clarithromycin, danazol, erythromycin, fluoxetine, grapefruit juice, isoniazid, nicotinamide, protease inhibitors, quinine, valproate

Modified from Stitik et al. (2010)

Carbamazepine is usually used at 100 mg bid first and then gradually increased to a maximum of 400 mg tid. Given the potential for hematologic toxicity, the maintenance dose should be reduced to the minimum effective level.

10.4.7.4 Valproic Acid

Valproic acid is being studied for use in neuropathic pain, postherpetic neuralgia, and polyneuropathy, but there is little evidence of effectiveness. Valproic acid, a lipid-soluble compound, is rapidly absorbed and is firmly bound to protein. Valproic acid is metabolized in the liver via oxidation and glucuronidation pathways. Active metabolites and a small, unchanged portion are then eliminated via the kidneys.

Nausea, tremors, drowsiness, and weight gain are common side effects. More serious complications are hepatotoxicity in children, pancreatitis, and prolonged bleeding time. Frequent monitoring of the previous parameters is recommended. It is believed that rare cases of valproic acid-induced encephalopathy are caused by an inhibition of ammonia metabolism. Valproic acid inhibits the metabolism of phenytoin, carbamazepine, and lamotrigine as it inhibits the oxidation and glucuronidation pathways. It also decreases the clearance of amitriptyline and nortriptyline.

Valproic acid is initiated at 250 mg/day and then titrated to a maximum dose of 1000 mg bid.

10.4.7.5 Opioid Analgesics

Narcotic analgesics are often referred to as opioid or opiate analgesics because some are derived from opium. Opiate analgesics are considered a second-line treatment for neuropathic pain after spinal cord injuries. More common side effects of opioid analgesics are nausea, vomiting, constipation, sedation, euphoria, tolerance, and physical/psychological dependence. Since all pure opioid agonists have equianalgesic doses with each other, the selection of a specific agent is based on the desired route of administration, duration of action, and side effect.

This class of medication mimics the effects of endogenous opioids produced by the body: endorphins, enkephalins, and dynorphins. All opioids bind to three primary receptor types with varying degrees of affinity: mu (μ), kappa (κ), and delta (δ). Each type of receptor has a unique CNS distribution and leads to different physiologic reactions via variable biochemical pathways (Friedman and Nabong 2020). Opioid analgesics can be categorized based on their affinity for a receptor and their intrinsic activity (i.e., amount of receptor stimulation they can produce). Morphine and methadone are full agonists because they have a high affinity for receptors and cause strong analgesia. Partial agonists such as codeine have lower affinity and are therefore less effective than full agonists. Pentazocine is an example of a mixed agonist/antagonist that

can activate unoccupied opioid receptors and block occupied ones. Antagonists (e.g., naloxone) are effective in reversing the effect of a full opioid agonist.

Slightly basic opioids are generally well absorbed in the small intestine. Short-acting agents show maximal effects between 30 and 60 min after administration and have a duration of approximately 4 h. Long-acting or SR agents achieve peak effects within 2–24 h and last for 12–72 h. The first value correlates with oral administration and the second value correlated with transdermal application. Hepatic conjugation is the primary pathway for most opioids, but metabolism can also occur in the kidneys, lungs, and CNS. Active and inactive metabolites are excreted in the urine and/or bile.

Opioid analgesics can be administered orally, intramuscularly, intravenously, subcutaneously, intraspinally, intranasally (as naloxone), rectally (as hydromorphone), transdermally (as fentanyl patches), and transmucosally (as fentanyl buccal tablets). Short-acting agents can be used to treat acute pain syndromes and episodes of breakthrough pain. Long-acting agents are generally more convenient for patients with chronic illness, and their sustained effects often help prevent pain-related nocturnal awakenings. The required oral doses are higher than the parenteral doses due to the first-pass effect after oral administration. Treatment of neuropathic pain usually required higher doses than nociceptive pain. Patients in need of chronic opioid therapy are often started with a short-acting agent that is titrated over several weeks for adequate analgesia and then switched to an equivalent dose of the long-acting agent.

The WHO recommends that all opioid therapies follow a fixed interval dosing schedule and not be given as needed. This strategy helps maintain stable serum drug levels and minimizes side effects that occur during peak levels and breakthrough pain at troughs. A person is considered tolerant of opioid therapy if they are taking more than 60 mg oral morphine per day, more than 26 μg transdermal fentanyl per hour, more than 30 mg oxycodone per day, more than 8 mg hydromorphone per day, or an equivalent dose of another opioid for more than 1 week (de Leon-Casasola 2002).

The most obvious and emergent adverse event associated with opioids is an overdose: acute opioid toxicity, which results in either impaired functional ability and a subsequent fall or other trauma or respiratory suppression and risk of death or hypoxic injury. Concomitant prescription of opioids with benzodiazepines or sedative-hypnotics increases risk of overdose. Opioids exert their gastroenterological effects via kappa receptors in the stomach and small bowel and by mu receptors in the small bowel and colon (Friedman and Nabong 2020). Constipation is principally mediated by mu receptors. Stimulation of mu receptors causes tonic, non-propulsive contractions in the small bowel and colon, increased absorption of colonic fluid, and dryness of the stool (Dorn et al. 2014; Friedman and Nabong 2020). Constipation is almost universal to some extent in all patients who use opioids, can affect quality of life, and is associated with significant health care utilization. The American Gastroenterological Association's guidelines on management of opioid-induced constipation (Crockett et al. 2019) make a strong recommendation for the use of laxatives as a first-line agent for opioid-induced constipation. Laxatives include stool softeners such as docusate sodium, osmotic diuretics such as polyethylene glycol, and stimulants such as senna and bisacodyl (Friedman and Nabong 2020).

Tramadol HCL

Tramadol is a centrally acting synthetic analgesic and a unique drug in that it is not classified as a controlled substance, although its μ-receptor binding affinity is similar to codeine. Tramadol has an additional mechanism of action that is very similar to many antidepressants. Due to the dural mechanism, tramadol can be an effective analgesic for both nociceptive and neuropathic pain (Ebell 2007). Ultracet contains 37.5 mg of tramadol and 325 mg of acetaminophen. Its advantages are synergistic analgesia and reduced dose-dependent side effects.

Tramadol has two complementary analgesic mechanisms, including a weak activation of μ-receptors and a modification of the pain impulse transmission via a weak inhibition of the reuptake of norepinephrine and serotonin. This compound can therefore be thought of as both a synthetic opioid and a tricyclic antidepressant. Tramadol has high bioavailability. After oral administration, one-fifth of the drug is protein bound and undergoes extensive first-pass hepatic metabolism. The onset of analgesia can be seen within 1 h and a mean peak plasma concentration is reached within 1.5–2 h. The half-life of tramadol is 6 h. All metabolites and the unchanged portion are excreted renally.

The most common side effects are nausea, drowsiness, and constipation. The frequency of the side effects is lower than that of traditional opioids. Respiratory depression and pruritus are possible side effects associated with all opioids, but tramadol has a much lower risk of both incidents. Seizures are a rare but significant side effect of tramadol. Care should be taken when prescribing tramadol to patients with epilepsy, a history of seizures, or risk factors for seizures. SSRIs or TCAs should not be prescribed with tramadol as they may further lower the seizure threshold. CNS depressants and MAOIs should be avoided as they present a risk of hypertensive crisis. It should also be noted that carbamazepine markedly induces the metabolism of tramadol, so double the usual dose of tramadol may be required.

The usual dose range for tramadol is 50–100 mg every 4–6 h. The maximum recommended dose is 400 mg daily. Dosing adjustments are recommended for patients over 75 years of age (<300 mg/day), with a creatinine clearance less than 30 mL/min (every 12 h with a maximum daily dose of 200 mg), and a history of liver dysfunction. Patients with non-acute pain start with 50 mg per day, increased by one 50 mg dose every 3 days until the maximum daily dose is reached. Patients with acute pain can be treated with an initial dose of 50 mg, followed by another dose of 25–50 mg if adequate analgesia is not achieved within the first hour.

Oxycodone

Oxycodone is a morphine derivative that is available in generic short-acting form, short-acting IR form (OxyIR), controlled-release form (OxyContin), and in several combination analgesic products. OxyContin has high oral availability due to its minimal first-pass metabolism. Easy access has led to widespread abuse in the United States in the past.

A relatively short half-life enables OxyContin to reach a steady state within a short period of time and thus to achieve its full analgesic potential within a day or two after starting treatment. An additional advantage is that, unlike MS Contin, the absorption is independent of the pH. This enables patients to take the opioid with or without food. The liver largely metabolizes oxycodone to oxymorphone. Compared to morphine, oxycodone causes less nausea and vomiting, but more constipation.

Fentanyl TD (Duragesic)

Fentanyl is a strong (>80 times of morphine), short-acting opioid. A TD delivery system for fentanyl is possible because it has a low molecular weight and is highly lipophilic, which allows the drug to be absorbed through the skin and then distributed throughout the body. The average duration of the fentanyl patch is 72 h. The benefits of fentanyl TD include a lower incidence of constipation, nausea, and drowsiness. The patch cannot be used in acute pain syndromes because the initial absorption is delayed by 17–48 h.

Codeine

Codeine is a natural opioid found in opium and can be used as an analgesic, cough suppressant, or antidiarrheal agent. Codeine has less than one-seventh of the analgesic effectiveness of morphine and is often used in combination with acetaminophen or with NSAIDs to treat mild-to-moderate pain. It has a low potential for respiratory depression and a low potential for abuse. Codeine has high oral bioavailability because its phenyl ring protects the molecule from first-pass metabolism. After administration, codeine is demethylated into morphine, and active or inac-

tive metabolite, norcodeine. These metabolites are then conjugated hepatically and most are excreted by the kidneys.

The possible side effects of codeine are typical of narcotic analgesics in general. Codeine is considered dangerous if taken in high doses or for an extended period of time during pregnancy.

10.4.7.6 Antidepressants

Antidepressants are used off-label to treat neuropathic pain and chronic nonmalignant pain syndrome. With a comprehensive systemic review, antidepressants, including TCAs, venlafaxine, and SSRIs, are effective for a variety of neuropathic pain (Saarto and Wiffen 2010). Not only do these agents treat the psychiatric component of chronic pain, but they have been shown to have independent analgesic effects. The analgesic effect of TCAs on neuropathic pain has been widely studied. The secondary amine TCAs, nortriptyline, and desipramine are preferred over the tertiary amine TCAs, amitriptyline, as they have been shown to be equally effective and have fewer side effects such as drowsiness. Serotonin-norepinephrine reuptake inhibitors (SNRIs) appear to replace SSRIs for neuropathic pain. Venlafaxine (Effexor) and duloxetine (Cymbalta) are two SNRIs that have been studied in the treatment of pain due to postherpetic neuralgia and diabetic neuropathy. Venlafaxine has been shown to be as effective as imipramine in the treatment of polyneuropathy. Trazodone is not chemically related to any other antidepressants. It is rarely used for depression but is more commonly used as a hypnotic.

TCAs increase aminergic transmission by inhibiting the reuptake of serotonin and norepinephrine at presynaptic nerve-ending terminals to varying degrees. As a result, TCAs elevate pain thresholds in depressed and nondepressed patients. Analgesic doses are usually lower than those used for primary depression. TCAs are rapidly absorbed and bind to plasma albumin. The metabolism initially involves demethylation of tertiary amine to secondary amine, followed by hydroxylation, glucuronidation, and eventually renal excretion as inactive metabolites.

SSRIs selectively inhibit serotonin reuptake with less effect on NE reuptake. This selectivity offers the advantage of a superior side effect profile. Paroxetine and sertraline are the most commonly used agents in this class and both have chemical structures that are unique among the SSRIs as well as other antidepressants. In general, SSRIs are well absorbed by the oral route and then undergo hepatic metabolism followed by renal excretion.

Trazodone may act by inhibiting serotonin reuptake and by the mixed effects of serotonin agonist-antagonist. This combined mechanism of action is somewhat similar to that of tramadol. Although it is extensively metabolized in the liver, it has variable clearance that can lead to accumulation in some patients. SNRIs act as NE reuptake inhibitors through α2-adrenergic receptor blockade, serotonin reuptake inhibitors, and bind to opioid receptors.

Antidepressant is generally associated with a high incidence of sexual dysfunction. Antidepressants that inhibit serotonin reuptake can cause serotonin syndrome, a hyperexcitable state of nervousness and insomnia. Because SSRIs have a relatively specific effect on serotonin reuptake without a significant effect on NE reuptake, their side effect profile is generally superior to TCAs, especially with respect to cardiovascular issues, and they are much safer in cases of overdose. However, abrupt stopping of the SSRI has been reported to cause SSRI withdrawal syndrome in some individuals. This syndrome includes dizziness, light-headedness, insomnia, fatigue, anxiety/agitation, nausea, headache, and sensory disturbance.

Side effects of TCAs are mainly anticholinergic including dry mouth, blurred vision, tachycardia, constipation, aggravation of glaucoma, and urinary retention. They also cause antihistamine side effects such as sedation, so they are often prescribed as a single bedtime dose, and weight gain is related to the increased appetite for carbohydrates. Cognitive and behavioral changes such as agitation and memory impairment occur at plasma TCA concentrations greater than 0.450 μg/mL. Many TCAs are fatal at concentra-

tions greater than 1 μg/mL. Nortriptyline is generally considered superior to all TCAs because it is more effective and has a comparatively wide therapeutic range (Gillman 2007). TCAs also exert some quinidine-like cardiac effects, including prolongation of atrioventricular conduction time. Elderly and otherwise medically fragile patients should be started on nortriptyline rather than amitriptyline for the reason noted above and because side effects such as orthostatic hypotension and significant morning sedation, which can potentially affect rehabilitation.

Trazodone can be quite sedating and has other mild anticholinergic effects, but these are less common than those of TCAs. It also exhibits α-adrenergic blocking properties that can cause penile or clitoral priapism. Trazodone can increase serum digoxin and phenytoin levels and either increase or decrease prothrombin times in patients on warfarin. The most common side effects of venlafaxine are from increased serotonin levels such as irritability, insomnia, and sexual dysfunction as well as nausea and constipation.

TCAs, SSRIs, and bupropion should not be used in patients taking monoamine oxidase inhibitors (MAOIs) and should be used with caution in patients who have not had MAOIs for at least 2 weeks. The only exception to this rule is nortriptyline, which can be safely combined with MAOIs or sertraline (Gillman 2007). Concomitant use of other TCAs or SSRIs and MAOIs can lead to hyperpyretic crises, seizures, and death. TCAs should also be used with caution in patients taking other anticholinergic medications, neuroleptics, or CNS depressants.

10.4.8 Medications for Hypertension and Coronary Heart Disease

Patients with spinal cord injuries are at high risk of hypertension and coronary heart disease for the rest of their lives. Long-term drug treatment is indicated and beneficial in most patients with systemic hypertension. There is overwhelming evidence to suggest that antihypertensive drugs can protect against complications of hypertension. While non-pharmacological options should be implemented in all patients, the vast majority will require pharmacological treatment to achieve the desired blood pressure levels. Antihypertensive drugs are most effective in combination with dietary restriction of sodium and caloric intake, weight loss, increased physical fitness, and adherence to other lifestyle modifications.

While it is common to start treatment with a single drug, an appropriate combination of drugs is often required to effectively control blood pressure. Although diuretics and β-blockers are effective and well tolerated, other classes of drugs are being increasingly used as the first choice for the treatment of hypertension. Each class of antihypertensive drugs has advantages and some disadvantages (Ram 2002). The initial selection of either a diuretic, angiotensin-converting enzyme (ACE) inhibitor, calcium channel blocker, or angiotensin II receptor blocker (ARB) is appropriate depending on physician experience and patient acceptance (Chobanian 2017). The drug dosages must be properly titrated to achieve the target blood pressure levels, and combination therapy should be used optimally if necessary. Most current definitions refer to hypertension in the general population as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. A diastolic goal lower than 90 mmHg has been considered appropriate for most adults of the general population, but the systolic blood pressure goal has been more controversial (Chobanian 2017). However, there is no definition of arterial hypertension or the treatment goal for patients with spinal cord injuries. The selection of drugs for hypertension in patients with spinal cord injuries should be made in consideration of various factors such as neurological level of injury, autonomic dysreflexia, orthostatic hypotension, and neurogenic bladder caused by spinal cord injury. The dosage and frequency of administration of antihypertensive drugs commonly used for the treatment of systemic hypertension in patients with spinal cord injuries are summarized in Table 10.11.

Table 10.11 Antihypertensive drugs commonly used in patients with spinal cord injuries

Class		Drug	Therapeutic dose (mg)	Frequency of administration (times/day)
Angiotensin-converting enzyme inhibitors		Benazepril	20–40	1
		Captopril	75–200	2–3
		Enalapril	5–40	1–2
		Fosinopril	10–40	1
		Lisinopril	10–40	1
		Moexipril	7.5–30	1–2
		Perindopril	4–16	1
		Quinapril	10–80	1
		Ramipril	2.5–20	1
		Trandolapril	1–4	1
Angiotensin II receptor blockers		Candesartan	8–32	1
		Eprosartan	400–800	1
		Irbesartan	150–300	1
		Losartan	50–100	1–2
		Telmisartan	40–80	1
		Valsartan	80–320	1
Beta-blockers (beta1-selective)		Acebutolol	20–1200	1
		Atenolol	25–100	2
		Bisoprolol	2.5–20	1
		Metoprolol	50–200	1–2
		Nadolol	20–240	1
		Pindolol	10–60	1
		Propranolol	40–240	2–3
Calcium channel blockers	Dihydropyridines	Amiodipine	2.5–10	1
		Felodipine	2.5–10	1
		Isradipine	2.5–10	1–2
		Nicardipine	60–120	1–2
		Nifedipine	30–120	1–2
		Nosoldipine	20–140	1–2
	Benzothiazepines	Diltiazem	180–480	1–2
	Phenylalkylamines	Verapamil	120–480	1–2

10.4.8.1 Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are commonly used in patients with hypertension and coronary heart disease. One advantage of this class of drugs is the relative absence of cardiovascular side effects compared to other drugs. They have a protective effect on the kidneys in diabetics and are useful in reducing the risk of a recurrent stroke (Stitik et al. 2010).

ACE inhibitors (benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, and trandolapril) prevent the conversion of angiotensin I to angiotensin II by inhibiting ACE activity, a potent vasoconstrictor and adrenal stimulator (Tsioufis and Thomopoulos 2017). The overall effect is a reduction in systemic vascular resistance with a subsequent drop in blood pressure and an improvement in cardiac output. In addition, ACE inhibitors also prevent the breakdown of bradykinin and thereby potentiate its vasodilatory and other effects. Most ACE inhibitors are mainly excreted by the kidney, with the exception of fosinopril which is excreted both by the kidney and liver (Ram 2002).

ACE inhibitors relieve vasoconstriction by inhibiting the formation of angiotensin II. Angiotensin inhibition decreases aldosterone production, which leads to natriuresis and potas-

sium retention. Plasma aldosterone levels may return to baseline during long-term therapy with ACE inhibitors. While ACE inhibitors continue to be widely used in the treatment of hypertension, they are also beneficial in renal protection and in the treatment of congestive heart failure. It is known that ACE inhibitors improve insulin sensitivity. The renal and metabolic effects of ACE inhibitors make them a superior choice for patients with diabetes mellitus (Ram 2002). Currently, ACE inhibitors are used and recommended as initial monotherapy in patients with hypertension with comorbid conditions. At the optimal dosage, various ACE inhibitors have similar antihypertensive effects, but with variable duration of action (Ram 2002; Tsioufis and Thomopoulos 2017).

Drugs in this class are well tolerated with rare serious side effects. The originally reported side effects of ACE inhibitors such as neutropenia or renal dysfunction are rather unusual in clinical practice. Cough (dry, hacking, nonproductive) is the most common side effect of ACE inhibitors. Bronchospasm is uncommon. ACE inhibitor-induced cough occurs in 15–39% of recipients (Dicpinigaitis 2006; Luque and Ortiz Vazquez 1999). Cough is associated with all drugs in this class. ACE inhibitor-induced cough is not dose dependent (Dicpinigaitis 2006). It is believed that elevated bradykinin levels are a causative factor in the development of ACE inhibitor-induced cough (Ram 2002; Stitik et al. 2010; Tsioufis and Thomopoulos 2017). Hyperkalemia can occur when drugs that increase serum potassium level, such as potassium-sparing diuretics, with ACE inhibitors and ARBs. Because of its fetal toxicity, pregnancy is an absolute contraindication for therapy with ACE inhibitors (Ram 2002; Tsioufis and Thomopoulos 2017).

10.4.8.2 Angiotensin II Receptor Blockers

ARBs (candsartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, and valsartan) represent an important therapeutic advance in interrupting renin–angiotensin cascade to lower the blood pressure. ARBs selectively block the binding of angiotensin II to specific angiotensin receptors on the blood vessel, the heart, the adrenal cortex, and possibly other tissues, causing an increase in the circulating levels of angiotensin (Ram 2002; Tsioufis and Thomopoulos 2017). The consequences of angiotensin receptor antagonism are reversal of vasoconstriction, myocardial and vascular hypertrophy, and inhibition of aldosterone secretion effects, which are observed with ACE inhibitors. In contrast to ACE inhibitors, angiotensin receptor antagonists do not interfere with bradykinin metabolism. As the antihypertensive effects of ARBs and ACE inhibitors are similar, it is unclear whether the lack of bradykinin potentiation with ARBs is a disadvantage (Ram 2002).

All currently available ARBs are effective in the treatment of hypertension as monotherapy as well as in combination with diuretics. They differ in their duration of action and receptor binding properties. Side effects of ARBs are usually mild and rare. Drugs of this class are well absorbed by the GI tract and are well tolerated. Like ACE inhibitors, ARBs also decrease proteinuria in patients with impaired renal function. It has been suggested that ARBs cause less hyperkalemia than ACE inhibitors. Unlike ACE inhibitors, ARBs induce a lower incidence of dry coughs. As with ACE inhibitors, ARBs should be avoided during pregnancy (Ram 2002).

10.4.8.3 β-Blockers

β-Blockers have been used for hypertension, angina pectoris, and arrhythmias since the early 1970s. In addition, β-blockers are also used for migraine headaches, thyrotoxicosis, tremors, and for treatment of anxiety and aggression. These drugs bind to β-1 and β-2 adrenergic receptors with varying affinities. Those with a predominant β-1 receptor affinity are referred to as β-1 selective or cardioselective, as this receptor is primarily cardiac. Therefore, the therapeutic effect is to reduce heart rate and myocardial contractility, which helps reduce the myocardial oxygen demand in coronary artery diseases, leads to a decrease in blood pressure. There are β-blockers that are not selective because they have essentially equal affinities for both β-1 and β-2 receptors. There are also β-2 selective compounds.

However, they are not clinically relevant because blocking β-2 receptors, which are mainly located in bronchiolar smooth muscles, causes bronchoconstriction (Ram 2002; Stitik et al. 2010).

In general, β-blockers are classified as β-1 selective drugs (acebutolol, atenolol, betaxolol, bisoprolol, and metoprolol) and β-nonselective drugs (carteolol, carvedilol, labetalol, nadolol, penbutolol, pindolol, propranolol, sotalol, and timolol). Both the β-1 selective and the nonselective β-blockers are equally effective in the treatment of hypertension. There is no absolutely cardioselective β-blocker and all β-blockers are nonselective at high dosages. Although β-blockers lower the cardiac output acutely, their long-term action in the management of hypertension is most likely mediated by a decrease in peripheral vascular resistance.

β-Blockers are used as monotherapy or in combination with other drugs, especially diuretics, in the treatment of hypertension. Side effects of β-blockers can largely be attributed to their pharmacological effects (i.e., β-adrenoceptor blockade). Therefore, they can cause adverse events such as insomnia, depression, and nightmares in some patients, but not in a predictable manner. Orthostatic hypotension, bradycardia, and chronic COPD, asthma or CHF can be exacerbated by β-blockers (Stitik et al. 2010). β-blockers can cause some degree of fatigue, decrease exercise performance, and worsen vasospasm symptoms. Abrupt discontinuation of β-blockers may worsen angina due to increased sensitivity to catecholamines, resulting in rebound hypertension. Therefore, β-blockers should be tapered gradually. β-Blockers can negatively affect carbohydrate metabolism (Ram 2002).

10.4.8.4 Calcium Channel Blockers (See also section "Calcium Channel Blockers")

Calcium channel blockers were originally developed to treat angina pectoris or cardiac arrhythmias, but are now popular antihypertensive drugs. From a pharmacological perspective, calcium channel blockers are classified into dihydropyridines (e.g., amlodipine, felodipine, isradipine, nicardipine, nifedipine), benzothiazepines (diltiazem), and phenylalkylamines (verapamil). Dihydropyridines promote cardiac contractility and increase AV conduction; on the other hand, diltiazem and verapamil depress myocardial contractility and slow down AV conduction. The vasodilatory effects of calcium channel blockers are predominantly mediated by the blockade of L-type calcium channels. Nifedipine capsules that lead to a rapid hemodynamic effect exemplify short-acting dihydropyridines; long-acting slow-release dihydropyridines are exemplified by amlodipine, felodipine, and the tablet formulation of nifedipine. Nifedipine capsules (orally or sublingually) produce a rapid fall in blood pressure and may cause tachycardia.

Calcium channel blockers are effective as monotherapy or in combination with other antihypertensive drugs. Dihydropyridines appear to be more effective than diltiazem or verapamil in the treatment of hypertension. β-Blockers can be safely combined with dihydropyridines but can produce additive bradycardia and cardiodepression when combined with diltiazem or verapamil. Long-acting preparations are available for all calcium channel antagonists. Salt-sensitive patients respond easily to calcium channel antagonists. It is known that calcium channel antagonists tend to exert a moderate natriuretic effect. This effect is best expressed on a high-salt diet that would cause a greater fall in blood pressure. The effect of calcium channel antagonists on renal function continues to be examined closely.

10.4.9 Medications for Depression

Symptoms associated with depression include sadness, hopelessness, loss of ability to experience pleasure, apathy, social withdrawal, guilty feeling, sleep and appetite disturbances, fatigue, decreased libido, psychomotor retardation, and cognitive impairment. Depression is the largest nonfatal burden and accounts for about 12% of all years with a disability (Ustün et al. 2004).

Depression has been associated with an imbalance in the levels and activity of the neurotransmitters serotonin, norepinephrine, and dopamine.

Table 10.12 Specificity of serotonin versus norepinephrine reuptake blockade of the heterocyclics

Serotonin only	Serotonin and norepinephrine equally	Norepinephrine only
Trazodone (Desyrel)	Doxepin (Sinequan)	Maprotiline (Ludiomil)
Fluoxetine (Prozac)	Imipramine (Tofranil)	Despramine(Norpramin)
Paroxetine (Paxil)	Venlafaxine (Effexor)	Nortriptyline (Pamelor)
Sertraline (Zoloft)	Bupropion (Wellbutrin)	
Nefazodone (Serzone)	Amoxapine (Asendin)	
Fluvoxamine (Luvox)	Clomipramine (Anafranil)	
Citalopram (Celexa)	Amitriptyline (Elavil)	
	Mirtazapine (Remeron)	

Adopted from Polantin and Gajraj (2002)

Antidepressants rebalance the levels and activities of one or more of these neurotransmitters by decreasing neurotransmitter metabolism and increasing neurotransmitter levels, causing higher amounts to act at the receptor site in the synapse or act as a substitute neurotransmitter and actively bind to these receptors thereby enhancing activity. The amines most critically involved in depression are serotonin and norepinephrine, and the heterocyclic vary in their specificity for one or both of these amines (Polantin and Gajraj 2002) (Table 10.12). Serotonin is associated with mood and anxiety. Serotonin also affects sleep, cognition, sensory perception, memory, temperature regulation, motor activity, sexual behavior, hormone secretion, and appetite. Norepinephrine is also associated with mood and is one of the neurotransmitters targeted by antidepressants. Dopamine is particularly important in regulating movement, cognition, and emotional response (Carl et al. 2014). Antidepressants can improve depressive symptoms, but they can have side effects and interactions with other drugs that can alter cognition and communication. The most common side effects under treatment with antidepressants are dry mouth, dizziness, nausea, headache, and constipation followed by palpitations, sweating, and drowsiness (Riediger et al. 2017; Trindade et al. 1998). The risk of suicidal thinking and behavior associated with antidepressants is highest during the first few months of therapy or when the dosage is increased or decreased.

The use of antidepressants and the resulting costs have increased in recent years, partly due to the introduction of new drugs, including selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs). Antidepressants are classified into four categories based on mechanism of action: SSRIs, SNRIs, tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs). SSRI and SNRI have been preferred over the older TCA and MAOI because their side effects and drug interaction profiles are improved. Antidepressant therapy should be started at low doses and titrated every 1–3 days until a usually effective dose is achieved. This dose should be maintained for at least 4 weeks in order to assess the therapeutic effect of the drug. Most antidepressants have long half-lives, typically 12–36 h. Therefore, they are often only given once daily. Some antidepressants such as venlafaxine have a short half-life and are given more than once daily. Venlafaxine is also available in slow-release formulations for once-daily administration.

10.4.9.1 Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly used agents in the treatment of depression. They are also useful in treating obsessive-compulsive disorder, generalized anxiety disorder, panic disorder, and posttraumatic stress disorder. SSRIs selectively block the reuptake of serotonin, thereby improving the availability of these neurotransmitters at the level of the presynaptic neuron. Blocking reuptake of serotonin leads to increased serotonins in the synaptic cleft. The blocking effects of norepi-

nephrine and dopamine uptake by SSRIs are weak. The four most commonly used SSRIs are fluoxetine, paroxetine, sertraline, and fluvoxamine. Fluoxetine has the longest half-life of 2–3 days and its active metabolite has a half-life of 7–9 days. The half-lives of the other SSRIs are much shorter at approximately 20 h. The peak effect of the SSRIs is in the range of 4–8 h.

Common central nervous system effects include headache, insomnia, drowsiness, anxiety, nervousness, and tremor. Common GI side effects include nausea, diarrhea, anorexia, and dyspepsia. Sexual dysfunction, including erectile dysfunction, is relatively common. SSRI drugs should not be mixed with each other or with highly serotoninergic drugs such as clomipramine or trazodone because of the risk of serotonin syndrome.

10.4.9.2 Selective Serotonin and Norepinephrine Reuptake Inhibitors

Selective serotonin and norepinephrine reuptake inhibitors (SNRIs) block reuptake of serotonin and norepinephrine and weakly block reuptake of dopamine. SNRIs include bupropion, duloxetine, and mirtazapine.

10.4.9.3 Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) block reuptake of serotonin or norepinephrine, thereby improving the availability of these neurotransmitters at the level of the presynaptic neuron. Blocking reuptake leads to increased neurotransmitters in the synaptic cleft. TCAs include amitriptyline, nortriptyline, imipramine, amoxapine, clomipramine, doxepin, trimipramine, desipramine, maprotiline, and protriptyline. Some TCAs with strong sedative properties, such as dosepin, amitriptyline, or trazodone, are used at bedtime to help with depression-associated insomnia. These are also beneficial in patients with agitation and anxiety (Teasell et al. 1999).

Peak plasma concentrations of TCAs are usually reached 2–8 h after a dose. There is up to a 30-fold variation in the range of absorption of amitriptyline and other TCAs between different individuals. Some patients cannot tolerate a minimal dose of 10 mg per day, while others can tolerate up to 300 mg per day. Amitriptyline has a relatively long half-life and is therefore slow onset of action. It is best to administer at night, ideally 2–4 h before bedtime, so as not to prolong the sedative effect into the next day (Teasell et al. 1999).

Many TCAs have strong anticholinergic effects that can increase sedation, altered cognition, constipation, urinary hesitancy, blurred vision, and the risk of falls. Their use is not recommended in the elderly.

10.4.9.4 Monoamine Oxidase Inhibitors

Monoamine Oxidase Inhibitors (MAOIs) block the metabolism of catecholamines to inactive products. They include phenelzine, tranylcypromine, and isocarboxazid. The use of MAOIs to treat depression is limited because of their serious toxicity related to drug and food interactions. Therefore, these are generally not considered to be first-line medications for treating depression.

10.4.10 Medications for Anxiety

Anxiety affects the cognitive functions of attention and perception. The anxious patient also tends to focus on the negative aspects of the symptoms, which leads to rumination. Anxiety can also influence affect processing, problem solving, and anxiety regulation. Medications used to treat anxiety can also alter cognition. Benzodiazepines often have amnesic side effects, which include difficulty in processing new information and storing the information in memory, as well as consolidating information in memory. Chronic therapy with benzodiazepines can be associated with deficits in sustained attention and visuospatial impairment that are insidious and not recognized by the patient (Carl et al. 2014; Iverson et al. 2009). Prudent use of antianxiety medications can benefit rehabilitation for patients with spinal cord injuries because the patient may be more relaxed and cooperative.

10.4.10.1 Benzodiazepines

Benzodiazepines (alprazolam, clonazepam, diazepam, and lorazepam) are the drugs most commonly used to treat generalized anxiety disorder. These drugs may have anxiolytic, muscle relaxant, anticonvulsant, hypnotic, and sedative effects. Benzodiazepines such as diazepam are not beneficial in the treatment of posttraumatic stress disorder and may actually make symptoms of depression worse. Antidepressants are commonly used to treat posttraumatic stress disorder (Carl et al. 2014). The prescribing physician selects a benzodiazepine based on the rate of drug absorption, onset of action, duration of action, side effects, and drug interactions. The prescriber should initiate the benzodiazepine at a low dose and titrate it slowly to an effective dose. Prolonged treatment with benzodiazepines is associated with increased risk of accidents and psychomotor retardation, and cognitive decline and is not recommended (Carl et al. 2014; Ghaemi et al. 2001).

The most common side effects of benzodiazepines are sedation, dizziness, weakness, and unsteadiness. Side effects of benzodiazepine including sedation, ataxia, weakness, drowsiness, balance problems, slowed thought, difficulty concentrating, and reduced visual accommodation may affect participation in rehabilitation sessions. Chronic use of benzodiazepine can cause significant pharyngeal phase dysphagia, including cricopharyngeal incoordination, hypopharyngeal incoordination, and aspiration. Pharyngeal dysphagia can be reduced by discontinuing the medication (Dantas and Nobre Souza 1997). In patients with chronic obstructive pulmonary disease or dementia, anxiety should be treated with SSRIs or buspirone to avoid negative effects on respiratory function or cognitive awareness associated with benzodiazepines. Suddenly stopping benzodiazepines can lead to symptoms of mild-to-moderate withdrawal, including nightmares, restlessness, rebound anxiety, and insomnia. Symptoms of severe withdrawal include psychosis, seizures, and death (Carl et al. 2014).

10.4.10.2 Azapiron

Azapiron (buspirone), a nonbenzodiazepine antianxiety medication, acts as a partial serotonin receptor agonist and has antidepressant and anxiolytic effects. It also has weak actions on the dopamine receptors. Since it does not affect the central nervous system neurotransmitter GABA, it causes minimal sedation. The side effects are also minimal and can include drowsiness, dry mouth, dizziness, fatigue, headache, and insomnia. It can be used in the long-term management of anxiety disorders and is not associated with the development of tolerance or addiction.

10.4.10.3 Tricyclic Antidepressants (Amitriptyline, Clomipramine, and Imipramine)

Amitriptyline is used to treat posttraumatic stress disorder. Clomipramine is used to treat obsessive-compulsive disorder. Imipramine is used to treat panic disorder, generalized anxiety disorder, and posttraumatic stress disorder.

10.4.10.4 Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Antidepressants including SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) and SNRIs (venlafaxine) are most commonly used for posttraumatic stress disorder in patients with spinal cord injuries.

10.4.11 Medication for Sleep Disorder

Diagnostic criteria for insomnia include difficulty getting to sleep or staying asleep and results in daytime dysfunction in a patient who has an adequate opportunity to sleep (Sateia 2014). It is short term if symptoms occur for less than 3 months and chronic if symptoms occur at least 3 nights per week for 3 months or longer (Dopheide 2020; Sateia 2014). Sleep is divided

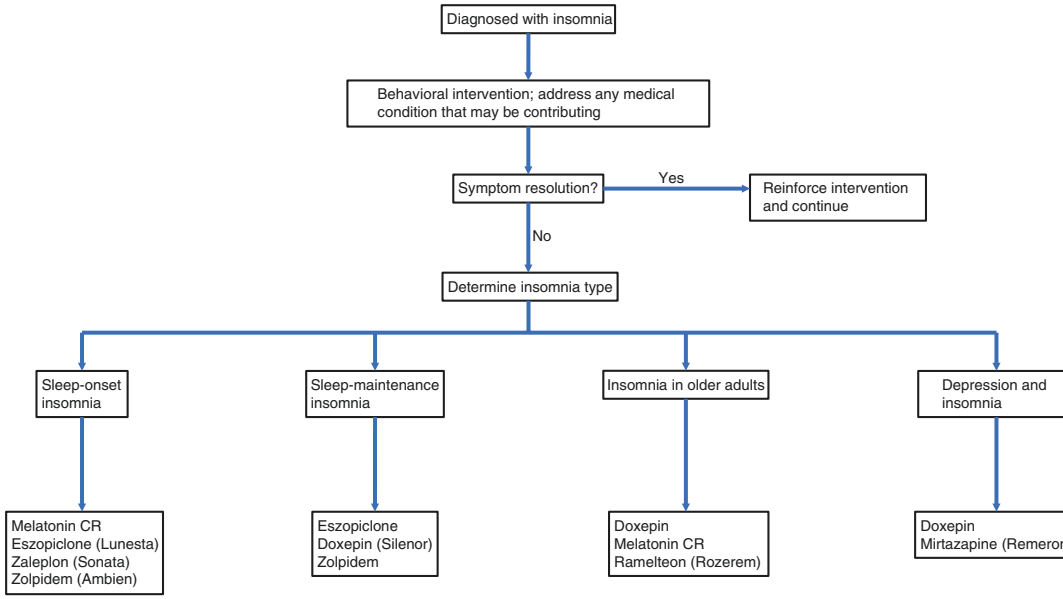

Fig. 10.2 Recommended algorithm for treatment of insomnia. Adapted from Matheson and Hainer (2017)

into five progressive stages: stage W (wakefulness), stage N1 (relaxed wakefulness), stage N2 (light sleep), stage N3 (deep or slow-wave sleep), and stage R (REM sleep or dreaming). Stage N1–N3 are phases of non-REM sleep in which cortical activity is low, while the brain is highly active during REM sleep (Dopheide 2020).

Sleep disorders are common in patients with spinal cord injuries. Daytime somnolence and poor concentration due to lack of sleep can seriously affect rehabilitation. Cognitive behavioral therapy for insomnia (CBT-I) is recommended as the initial intervention, followed by reassessment for pharmacotherapy in patients who have not responded to behavioral therapy (Dopheide 2020; Fine 2020). Therefore, the treatment of sleep disorders with hypnotics is very important for the overall management in the rehabilitation of patients with spinal cord injuries. There are two goals of pharmacotherapy. The first goal is to improve sleep quality and quantity, and the second goal is to improve insomnia-related daytime impairment. The selection of drugs depends on the onset and duration to the sleep defect. Hypnotics can be divided into two general categories: benzodiazepines and nonbenzodiazepines (chloral hydrate, eszopiclone, ramelteon, zaleplon, zolpidem) (Ciccone 2016). These agents are used to promote sleep, especially in relatively acute or short-term situations when sleep has been disturbed by illness, injury, or other factors. Figure 10.2 is an algorithm based on the type of insomnia when pharmacologic intervention is required.

10.4.11.1 Benzodiazepines

Benzodiazepines (estazolam, flurazepam, lorazepam, quazepam, temazepam, and triazolam) are a family of compounds that share the same basic chemical structure and pharmacological effects. Although the more well-known drugs of this family have been used for treatment of anxiety (e.g., diazepam), several benzodiazepines are specifically indicated for promoting sleep. Prolonged use can also cause tolerance and physical dependence.

Benzodiazepines do not bind selectively to a specific receptor (GABA–benzodiazepine receptor complex), which is located at certain inhibitory synapses in the reticular formation of the CNS. Benzodiazepines work by increasing the inhibitory effects on CNS synapses that use the neurotransmitter gamma-aminobutyric acid (GABA), which is the primary neurotransmitter that acts to inhibit presynaptic and postsynaptic neurons throughout the brain and spinal cord. In other words, benzodiazepines improve relaxation

and sleep by increasing the effect of the endogenous inhibitory neurotransmitter (GABA) in the brain. They are well absorbed, subject to very little first-pass metabolism, are mainly metabolized by the liver, are excreted with short half-lives, and their metabolites do not accumulate. Daytime drowsiness, headache, and fatigue are the most common side effects of using benzodiazepine at bedtime. Dependence and rebound insomnia can develop, especially if used regularly for more than a few weeks. These drugs should be used with caution in patients taking other CNS depressants.

10.4.11.2 Nonbenzodiazepines

Several nonbenzodiazepines (zolpidem, zaleplon, and eszopiclone) have been developed as sedative-hypnotics. These drugs are chemically different from benzodiazepines. They preferentially bind to the α1 subunit of the GABA type A receptor complex, which is one reason suggested for their selective hypnotic effect, but do not have anticonvulsant, anxiolytic, and muscle relaxant properties seen with benzodiazepines. These GABA type A drugs appear to be as effective as the benzodiazepines in promoting sleep. The drugs also seem to have a lower risk of producing certain side effects and causing problems when discontinued. These drugs likewise tend to have a shorter duration of action than traditional benzodiazepines, thus decreasing the chance of residual or "hangover" effects the next day. They are rapidly absorbed and have a mean half-life of 2½ h. It does not accumulate when used for a short period of time, so it is less likely to cause daytime sedation.

Zolpidem is the most commonly prescribed hypnotic in the nonbenzodiazepine category. Zolpidem and zaleplon have been reported to cause parasomnia-like episodes, including sleep eating, sleep walking, and sleep driving. Concomitant use with alcohol and administration at higher doses may lead to a higher risk of developing parasomnia behavior (Fine 2020).

10.4.11.3 Sedative Antidepressants

Although antidepressants are widely used for their sedative effects, only the tricyclic antidepressant doxepin (Silenor) has been approved by the FDA for the treatment of insomnia characterized by difficulties with sleep maintenance (Matheson and Hainer 2017). Doxepin is a tricyclic antidepressant medication. It was first approved by the FDA for the treatment of depression in the 1960s. After extensive scientific studies showed that it was also effective in treating sleep disorders, the FDA approved doxepin for the treatment of insomnia in 2010. In addition to depression and insomnia, doxepin is also used to treat certain anxiety disorders. Doxepin causes drowsiness by affecting the histamine receptors, which play a major role in managing the sleep–wake cycle. In particular, doxepin is an antagonist of the H1 receptor, which is responsible for mediating wakefulness and arousal. By binding to the H1 receptor, doxepin limits the effects of histamine, causing drowsiness and promoting sleep. Doxepin at doses of 3 and 6 mg improves sleep efficiency and total sleep time, and a 6 mg dose improves sleep latency (Roth et al. 2007).

Several other antidepressants are also used off-label to treat insomnia, especially trazodone, which is typically prescribed in doses of 50–100 mg at bedtime. However, the evidence for trazodone is weak, and should not be considered as first-line therapy (Roth et al. 2007). It has been postulated that the sedative effects of trazodone are mediated via α-adrenergic and mild histamine H1 blocking actions (Fine 2020). In addition to trazodone, mirtazapine, amitriptyline, and nortriptyline are used off-label to treat insomnia. These drugs have anticholinergic effects and should not be used in patients with glaucoma or difficulty with urinary retention.

10.4.11.4 Melatonin Agonists

Melatonin has a key role in regulating the sleep–wake cycle, and disruption of the timing of melatonin release or decreased melatonin production can contribute to insomnia. Ramelteon (Rozerem) is a FDA-approved melatonin agonist for insomnia related to sleep latency (Matheson and Hainer 2017).

10.4.12 Antibacterial Drugs

Antibacterial and other antimicrobial drugs must be selectively toxic to infectious microorganisms without excessive damage to human cells. These

mechanisms include (1) inhibition of bacterial cell wall synthesis and function, (2) inhibition of bacterial protein synthesis, and (3) inhibition of bacterial DNA/RNA function (Ciccone 2007).

10.4.12.1 Inhibition of Bacterial Cell Wall Synthesis and Function

Penicillin, cephalosporins, and several other commonly used drugs exert antibacterial effects by inhibiting the synthesis of bacterial cell walls. These drugs are selectively toxic because the bacterial cell walls are very different from the mammalian cell wall. The membrane that surrounds most bacterial cells (except *Mycoplasma*) is a relatively rigid and firm structure. The increased rigidity of bacterial cell walls is caused by the presence of protein–polysaccharide structures known as *peptidoglycans*. Drugs that cause inadequate production of peptidoglycans or other structural components within the cell wall can produce a selective bactericidal effect (Ciccone 2007). Table 10.13 shows agents that exert their primary antibacterial effects by impairing the synthesis and function of bacterial cell membrane.

Table 10.13 Drugs inhibiting bacterial cell wall synthesis and function

Penicillins	Cefotetan (Cefotan)
Natural penicillins	Cefoxitin (Mefoxin)
Penicillin G (Bicillin, Wycillin, many others)	Cefprozil (Cefzil)
Penicillin V (Beepen-VK, V-Cillin K, others)	Cefuroxime (Ceftin, Kefurox, Zinacef)
Penicillinase-resistant penicillins	Third-generation cephalosporins
Cloxacillin (Cloxapen, Tegopen)	Cefdinir (Omnicef)
Dicloxacillin (Dycill, Dynapen, Pathocil)	Cefditoren (Spectracef)
Methicillin (Staphcillin)	Cefoperazone (Cefobid)
Nafcillin (Nafcil, Unipen, others)	Cefotaxime (Claforan)
Oxacillin (Bactocill, Prostaphlin)	Cefpodoxime (Vantin)
Aminopenicillins	Ceftazidime (Fortaz, Tazidime, others)
Amoxicillin (Amoxil, Polymox, others)	Ceftibuten (Cedax)
Ampicillin (Omnipen, Polycillin, others)	Ceftizoxime (Cefizox)
Bacampicillin (Spectrobid)	Ceftriaxone (Rocephin)
Extended-spectrum penicillins	Fourth-generation cephalosporins
Carbenicillin (Geocillin, Geopen, Pyopen)	Cefepime (Maxipime)
Mezlocillin (Mezlan)	*Other agents*
Piperacillin (Pipracil)	
Ticarcillin (Ticar)	Aztreonam (Azactam)
Cephalosporins	Bacitracin (Bacitracin ointment)
	Colistin (Coly-Mycin S)
First-generation cephalosporins	Cycloserine (Seromycin)
Cefadroxil (Duricef)	Imipenem/cilastatin (Primaxin)
Cefazolin (Ancef, Kefzol)	Meropenem (Merrem I.V.)
Cephalexin (Keflex, others)	Polymyxin B (generic)
Cephalothin (Keflin)	Vancomycin (Vancocin)
Cephapirin (Cefadyl)	*Penicillin and Beta-lactamase Combinations*
Cephradine (Velosef)	
Second-generation cephalosporins	Ampicillin and clavulanate (Augmentin)
Cefaclor (Ceclor)	Ampicillin and sulbactam (Unasyn)
Cefamandole (Mandol)	Piperacillin and tazobactam (Zosyn)
Cefonicid (Monocid)	Ticarcillin and clavulanate (Timentin)

Adapted from Ciccone (2007)

Table 10.14 Drugs inhibiting bacterial protein synthesis

Aminoglycosides	Erythromycins	Tetracyclines	Other agents
Amikacin (Amikin)	Erythromycin (ERYC, E-Mycin, others)	Demeclocycline (Declomycin)	Chloramphenicol (Chloromycetin)
Gentamicin (Garamycin)	Erythromycin estolate (llosone)	Doxycycline (Monodox, Vibramycin, others)	Clindamycin (Cleocin)
Kanamycin (Kantrex)	Erythromycin ethylsuccinate (E.E.S., EryPed, others)	Minocycline (Minocin)	Ethionamide (Trecator-SC)
Neomycin (generic)	Erythromycin gluceptate (llotycin)	Oxytetracyline (Terramycin)	Lincomycin (Lincocin, Lincorex)
Netilmicin (Netromycin)	Erythromycin lactobionate (Erythrocin)	Tetracycline (Achromycin V, others)	Linezolid (Zyvox)
Streptomycin (generic)	Erythromycin stearate (Erythrocin, Erythrocot, others)		Quinupristin and Dalfopristin (Synercid)
Tobramycin (Nebcin)			Telithromycin (Ketek) Tigecycline (Jygacil)

Adapted from Ciccone (2007)

10.4.12.2 Inhibition of Bacterial Protein Synthesis

A fairly large and well-known group of antibacterial agents works by inhibiting or impairing the synthesis of these bacterial proteins. Drugs with such antibacterial effects include aminoglycosides (e.g., gentamicin and streptomycin), erythromycin, tetracyclines, and several other agents. Antibacterial drugs that work by this mechanism have a much higher affinity for bacterial ribosomes than human ribosomes, and thus have relative specificity in the treatment of bacterial infections (Ciccone 2007). Table 10.14 shows the drugs that exert their primary antibacterial effects by inhibiting protein synthesis.

10.4.12.3 Inhibition of Bacterial DNA/RNA Synthesis and Function

Failure to produce normal DNA and RNA prevents bacteria from mediating continued growth and reproduction. Drugs that exert antibacterial activity by directly or indirectly interfering with the structure, synthesis, and function of DNA and RNA of susceptible bacteria include fluoroquinolones, sulfonamides, and several other agents (Ciccone 2007). Table 10.15 lists the agents that exert their primary antibacterial effects by impairing the synthesis and replication of bacterial DNA and RNA.

Table 10.15 Drugs inhibiting bacterial DNA/RNA synthesis and function

Fluoroquinolones
Ciprofloxacin (Cipro)
Enoxacin (Penetrex)
Gatifloxacin (Tequin)
Levofloxacin (Levaquin)
Lomefloxacin (Maxaquin)
Moxifloxacin (Avelox)
Norfloxacin (Noroxin)
Ofloxacin (Floxin)
Sparfloxacin (Zagam)
Sulfonamides
Sulfadiazine (Silvadene)
Sulfamethizole (Thiosulfil Forte)
Sulfamethoxazole (Gantanol, Urobak)
Sulfisoxazole (Gantrisin)
Others
Aminosalicylic acid (Tubasal)
Clofazimine (Lamprene)
Dapsone (Avlosulfon)
Ethambutol (Myambutol)
Metronidazole (Flagyl, Protostat, others)
Mupirocin (Bactroban)
Rifabutin (Mycobutin)
Rifampin (Rifadin, Rimactane)
Rifapentine (Priftin)
Trimethoprim (Proloprim, Trimpex)

Adapted from Ciccone (2007)

10.5 Polypharmacy in Spinal Cord Injuries

The definitions for polypharmacy are numerous and the criteria vary from study to study. Some researchers have defined polypharmacy as the long-term use of two or more medications, others as taking two or three or at least three medications, or four to five medications daily (Linjakumpu et al. 2002). Polypharmacy is usually defined as the concomitant use of five or more different types of medications and is associated with negative health outcomes in the elderly and individuals with chronic diseases (Kitzman et al. 2017; Linjakumpu et al. 2002). The use of multiple medications is common in treating complications following spinal cord injury. Patients with spinal cord injuries often require long-term health management for secondary complications and are at increased risk for several chronic comorbidities such as diabetes and heart disease over the course of their lives.

The complexity of treatment regimens following spinal cord injuries increased the risk of drug-related problems, including adverse drug effects and medication errors resulting from drug–drug, drug–disease, or drug–nutrient interactions (Kitzman et al. 2017). Numerous negative health consequences are associated with polypharmacy, including increased risk of falls, adverse drug events, hospitalization, mortality, declines in functional status, and impaired cognition (Hand et al. 2018). The most common medication-related problems are untreated conditions, ineffective medications, adverse drug effects, and underusing and overdosing (Patel et al. 2017). Polypharmacy often has overlapping pharmacological mechanisms or targets, which increases the risk of drug-related problems. The most common medical problems in patients with spinal cord injuries are depression/anxiety, osteoporosis/osteopenia, hypertension, dyslipidemia, and osteoarthritis. The most common complaints are pain and bowel/bladder problems (Patel et al. 2017). Patients with spinal cord injuries most often use products to treat pain, constipation, muscle spasm, hypertension, and depression (Patel et al. 2017). The classes of drugs most commonly used to treat secondary complications in the spinal cord injury population as high-risk combinations based on their potential for overlapping effects are: sedative-hypnotic, nonbarbiturates, antianxiety, serotonin system agents (SSRIs and SNRIs), analgesics-narcotics, anticonvulsants, skeletal muscle relaxants, and tricyclic antidepressants. People with spinal cord injuries are often prescribed five or more drugs, take drugs at high risk, and have a higher incidence of drug-related problems. Polypharmacy that prescribed at least five medications concomitantly was 56% (Kitzman et al. 2017).

In a study that investigated the status of polypharmacy in adults who had sustained spinal cord injury during childhood, the prevalence of polypharmacy was 30.8% and the majority of which were taking five or six concomitant medications. The most commonly used drugs were muscle relaxants (50.3%), bladder medications (48.5%), bowel agents (41.5%), analgesics (26.4%), and antidepressants (16.9%). The drugs these patients are taking could be classified into 29 categories as shown in Table 10.16 (Hwang et al. 2015).

Table 10.16 Medications taken by participants

Category	Examples
Allergy	Antihistamines
Analgesics	Acetaminophen, NSAIDs, anticonvulsants, narcotics/opioids, etc.
Antibiotics	Nitrofurantoin, trimethoprim-sulfoxazole, fluoroquinolones, etc.
Anticholesterol	Fibrates, statins
Antidepressants	Tricyclic antidepressants, serotonergics, etc.
Antihypertensives	Diuretics, calcium-channl blockers, β-blockers, α-blockers, etc.
Antihypotensives	Fludrocortisone, midodrine

Table 10.16 (continued)

Category	Examples
Antithrombotics	Warfarin, heparin, etc.
Antipsychotics	Risperidone, olanzapine, etc.
Anxiolytics	Benzodiazepines, buspirones, etc.
Aspirin	–
Bladder	Anticholinergics/antimuscarinics
Bone	Bisphosphonates
Bowel agents	Bisacodyl, docusate, senna, etc.
Bronchodilators	Albuterol, ipratropium bromide, cromolyn sodium, etc.
Contraceptives	–
Diabetes	Insulin, sulfonylureas, biguanides
Iron supplements	–
Mood stabilizers	Lithium
Muscle relaxants	Baclofen, tizanidine, dantrolene, etc.
Psychostimulants	Methylphenidate
Sexual function	Sildenafil, tadalafil, etc.
Sleep-aids	Melatonin, zolpidem, diphenhydramine, etc.
Steroids	Prednisone, dexamethasone, etc.
Substance abuse	Disulfiram
Thyroid agents	Levothyroxine
Upper gastrointestinal	Proton-pump inhibitors, H_2-blockers, antacids
Vitamins	–
Other supplements	Calcium, homeopathic medications

From Hwang et al. (2015)

References

Ageno W, Gallus AS, Wittkowsky A, et al. American College of Chest Physicians. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e44S–88S.

Albright AL, Barron WB, Fasick MP, et al. Continuous intrathecal baclofen infusion for spasticity of cerebral origin. JAMA. 1993;270:2475–7.

Ansel J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonists: American college of chest physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133:160–98.

Arcangelo VP, Wilbur VF. Issues for the practitioners in drug therapy. In: Arcangelo VP, Peterson AM, Wilbur VF, Reinhold JA, editors. Pharmacotherapeutics for advanced practice. A practical approach. 4th ed. Philadelphia: Wolters Kluwer; 2017.

Baker J, Kimpinski K. Management of supine hypertension complicating neurogenic orthostatic hypotension. CNS Drugs. 2017;31:653–63.

Barnes GD, Ageno W, Ansell J, et al. Subcommittee on the control of anticoagulation of the international society on thrombosis and haemostasis. Recommendation on the nomenclature for oral anticoagulants: communication from the SSC of the ISTH. J Thromb Haemost. 2015;13:1154–6.

Bateman DN, Eddleston M. Clinical pharmacology: the basics. Surgery. 2006;24:291–6.

Becker DE. Basic and clinical pharmacology of autonomic drugs. Anesth Prog. 2012;59:159–69.

Boster AL, Adair RL, Gooch JL, et al. Best practices for intrathecal baclofen therapy: dosing and long-term management. Neuromodulation. 2016;19:623–31.

Carl LL, Gallo JA, Johnson PR. Practical pharmacology in rehabilitation: effect of medication on therapy. 1st ed. Champaign: Human Kinetics, Inc.; 2014.

Chisholm P, Anpalahan M. Orthostatic hypotension: pathophysiology, assessment, treatment and the paradox of supine hypertension. Intern Med J. 2017;47:370–9.

Chobanian AV. Guidelines for the management of hypertension. Med Clin North Am. 2017;101:219–27.

Ciccone C. Pharmacology in rehabilitation. 4th ed. Philadelphia: F. A. Davis Company; 2007.

Ciccone C. Pharmacology in rehabilitation. 5th ed. Philadelphia: F. A. Davis Company; 2016.

Cohen MR. Medication errors. 2nd ed. Washington, DC: American Pharmacists Association; 2007.

Corbett RW, Owens LW. Introductory pharmacology for clinical practice. J Midwifery Womens Health. 2011;56:190–7.

Corcos J, MacDiarmid S, Heesakkers J, editors. Overactive bladder. Practical management. West Sussex: Wiley; 2015.

Coward DM. Tizanidine: neuropharmacology and mechanism of action. Neurology. 1994;44:S6–10. discussion S10-1

Cristian A, editor. Medical management of adults with neurologic disabilities. 1st ed. New York: Demos Medical Publishing; 2009.

Crockett SD, Greer KB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute clinical guidelines committee. American Gastroenterological Association Institute guideline on the medical management of opioid-induced constipation. Gastroenterology. 2019;156:218–26.

Crowther M, Cuker A. How can we reverse bleeding in patients on direct oral anticoagulants? Kardiol Pol. 2019;77:3–11.

Cuker A, Burnett A, Triller D, et al. Reversal of direct oral anticoagulants: guidance from the anticoagulation forum. Am J Hematol. 2019;94:697–709.

Curtis DR, Gynther BD, Lacey G, et al. Baclofen: reduction of presynaptic calcium influx in the cat spinal cord in vivo. Exp Brain Res. 1997;113:520–33.

Dantas RO, Nobre Souza MA. Dysphagia induced by chronic ingestion of benzodiazepine. Am J Gastroenterol. 1997;92:1194–6.

de Leon-Casasola OA. Cellular mechanisms of opioid tolerance and the clinical approach to the opioid tolerant patient in the post-operative period. Best Pract Res Clin Anaesthesiol. 2002;16:521–5.

Deeks ED. Mirabegron: a review in overactive bladder syndrome. Drugs. 2018;78:833–44.

Dicpinigaitis PV. Angiotensin-converting enzyme inhibitor-induced cough: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1 Suppl):169S–73S.

Dopheide JA. Insomnia overview: epidemiology, pathophysiology, diagnosis and monitoring, and nonpharmacologic therapy. Am J Manag Care. 2020;26(4 Suppl):S76–84.

Dorn S, Lembo A, Cremonini F. Opioid-induced bowel dysfunction: epidemiology, pathophysiology, diagnosis, and initial therapeutic approach. Am J Gastroenterol Suppl. 2014;2:31–7.

Dunn KL, Galka ML. A comparison of the effectiveness of Therevac SB and bisacodyl suppositories in SCI patients' bowel programs. Rehabil Nurs. 1994;19:334–8.

Ebell M. Tramadol relieves neuropathic pain. Am Fam Physician. 2007;75:1335–6.

Eisert WG, Hauel N, Stangier J, et al. Dabigatran: an oral novel potent reversible nonpeptide inhibitor of thrombin. Arterioscler Thromb Vasc Biol. 2010;30:1885–9.

Fan J, de Lannoy IAM. Pharmacokinetics. Biochem Pharmacol. 2014;87:93–120.

Figueroa JJ, Basford JR, et al. Preventing and treating orthostatic hypotension: as easy as A, B, C Cleve. Clin J Med. 2010;77:298–306.

Fine L. Pharmacologic approach to insomnia. Phys Med Rehabil Clin N Am. 2020;31:255–64.

Friedman A, Nabong L. Opioids: pharmacology, physiology, and clinical implications in pain medicine. Phys Med Rehabil Clin N Am. 2020;31:289–303.

Ghaemi SN, Lenox MS, Baldessarini RJ. Effectiveness and safety of long-term antidepressant treatment in bipolar disorder. J Clin Psychiatry. 2001;62:565–9.

Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. J Neurol. 2017;264:1567–82.

Gillman PK. Tricyclic antidepressant pharmacology and therapeutic drug interactions updated. Br J Pharmacol. 2007;151:737–48.

Gilman TM, Segal JL, Brunnemann SR. Metoclopramide increases the bioavailability of dantrolene in spinal cord injury. J Clin Pharmacol. 1996;36:64–71.

Greenblatt DJ, von Moltke LL. Interaction of warfarin with drugs, natural substances, and foods. J Clin Pharmacol. 2005;45:127–32.

Hamidi M, Zeeshan M, Kulvatunyou N, et al. Operative spinal trauma: Thromboprophylaxis with low molecular weight heparin or a direct oral anticoagulant. J Thromb Haemost. 2019;17:925–33.

Hand BN, Krause JS, Simpson KN. Polypharmacy and adverse drug events among propensity score matched privately insured persons with and without spinal cord injury. Spinal Cord. 2018;56:591–7.

Holbrook AM, Pereira JA, Labiris R, et al. Systemic overview of warfarin and its drug and food interactions. Arch Intern Med. 2005;165:1095–106.

Hwang M, Zebracki K, Vogel LC. Medication profile and polypharmacy in adults with pediatric-onset spinal cord injury. Spinal Cord. 2015;53:673–8.

Ito T, Furukawa K, Karasawa T, et al. Effects of chlorpromazine, imipramine and baclofen on the spinal polysynaptic reflex in acute, chronic and 6-hydroxydopamine-treated spinal rats. Jpn J Pharmacol. 1982;32:1125–33.

Iverson LL, Iverson SD, Bloom FE et al. Introduction to neuropsychopharmacology. Oxford: Oxford University Press, Inc.; 2009.

Jami L, Murthy KS, Petit J, et al. Action of dantrolene sodium on single motor units of cat muscle in vivo. Brain Res. 1983;261:285–94.

Kaufmann H. L-dihydroxyphenylserine (Droxidopa): a new therapy for neurogenic orthostatic hypotension: the U.S. experience. Clin Auton Res. 2008;18(Suppl 1):19–24.

Kearon C, Akl EA, Comerota AJ, et al. American College of Chest Physicians. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e419S–94S.

Kitzman P, Cecil D, Kolpek JH. The risks of polypharmacy following spinal cord injury. J Spinal Cord Med. 2017;40:147–53.

Klein H. Constipation and fecal impaction. Med Clin North Am. 1982;66:1135–41.

Lamarre-Cliche M. Drug treatment of orthostatic hypotension because of autonomic failure or neurocardiogenic syncope. Am J Cardiovasc Drugs. 2002;2:23–35.

Linjakumpu T, Hartikainen S, Klaukka T, et al. Use of medications and polypharmacy are increasing among the elderly. J Clin Epidemiol. 2002;55:809–17.

Luque CA, Vazquez OM. Treatment of ACE inhibitor-induced cough. Pharmacotherapy. 1999;19:804–10.
Matheson E, Hainer BL. Insomnia: pharmacologic therapy. Am Fam Physician. 2017;96:29–35.
Mestre H, Alkon T, Salazar S, et al. Spinal cord injury sequelae alter drug pharmacokinetics: an overview. Spinal Cord. 2011;49:955–60.
Misgeld U, Bijak M, Jarolimek W. A physiological role for GABAB receptors and the effects of baclofen in the mammalian central nervous system. Prog Neurobiol. 1995;46:423–62.
Moosavi S, Woo M, Jacob DA, et al. Anticholinergic, anti-depressant and other medication use is associated with clinically relevant oesophageal manometric abnormalities. Aliment Pharmacol Ther. 2020;51:1130–8.
National Institute for Health and Care Excellence (NICE). Mirabegron for treating symptoms of overactive bladder. Technology appraisal guidance 2013. http://www.nice.org.uk. Accessed 13 Jan 2021.
Ozcakir S, Sivrioglu K. Botulinum toxin in poststroke spasticity. Clin Med Res. 2007;5:132–8.
Palazón-García R, Alcobendas-Maestro M, Esclarin-de Ruz A, et al. Treatment of spasticity in spinal cord injury with botulinum toxin. J Spinal Cord Med. 2019;42:281–7.
Patel T, Milligan J, Lee J. Medication-related problems in individuals with spinal cord injury in a primary care-based clinic. J Spinal Cord Med. 2017;40:54–61.
Peng CT, Ger J, Yang CC, Tsai WJ, et al. Prolonged severe withdrawal symptoms after acute-on-chronic baclofen overdose. J Toxicol Clin Toxicol. 1998;36:359–63.
Perzborn E, Roehrig S, Straub A, et al. Rivaroxaban: a new oral factor Xa inhibitor. Arterioscler Thromb Vasc Biol. 2010;30:376–81.
Peterson AM. Pharmacokinetic basis of therapeutics and pharmacodynamic principle. In: Arcangelo VP, Peterson AM, Wilbur VF, Reinhold JA, editors. Pharmacotherapeutics for advanced practice. A practical approach. 4th ed. Philadelphia: Wolters Kluwer; 2017.
Polantin PB, Gajraj NM. Integration of pharmacotherapy with psychological treatment of chronic pain. In: Turk DC, Gatchel RJ, editors. Psychological approaches to pain management: a practitioner's handbook. 2nd ed. New York: Guilford Press; 2002.
Posner J. Clinical pharmacology-the basics. Surgery. 2015;33:104–11.
Ram CV. Antihypertensive drugs: an overview. Am J Cardiovasc Drugs. 2002;2:77–89.
Rawal A, Ardeshna D, Minhas S, et al. Current status of oral anticoagulant reversal strategies: a review. Ann Transl Med. 2019;7:411.
Riedel P, Marino MH. Pharmacologic treatment tools: systemic medications and toxins, opportunities, and pitfalls. Phys Med Rehabil Clin N Am. 2018;29:501–17.
Riediger C, Schuster T, Barlinn K, et al. Adverse effects of antidepressants for chronic pain: a systematic review and meta-analysis. Front Neurol. 2017;8:307.
Rietman JS, Geertzen JH. Efficacy of intrathecal baclofen delivery in the management of severe spasticity in upper motor neuron syndrome. Acta Neurochir Suppl. 2007;97(Pt 1):205–11.
Riss J, Cloyd J, Gates J, et al. Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. Acta Neurol Scand. 2008;118:69–86.
Riva N, Ageno W. Use of the direct oral anticoagulants for the treatment of venous thromboembolism. Hematol Oncol Clin North Am. 2016;30:1035–51.
Rose DK, Bar B. Direct oral anticoagulant agents: pharmacologic profile, indications, coagulation monitoring, and reversal agents. J Stroke Cerebrovasc Dis. 2018;27:2049–58.
Roth T, Rogowski R, Hull S, et al. Efficacy and safety of doxepin 1 mg, 3 mg, and 6 mg in adults with primary insomnia. Sleep. 2007;30:1555–61.
Saarto T, Wiffen PJ. Antidepressants for neuropathic pain: a Cochrane review. J Neurol Neurosurg Psychiatry. 2010;81:1372–3.
Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014;146:1387–94.
Schryvers O, Nance PW. Urinary and gastrointestinal systems medications. Phys Med Rehabil Clin N Am. 1999;10:473–92.
Segal JL, Maltby BF, Langdorf MI, et al. Methylprednisolone disposition kinetics in patients with acute spinal cord injury. Pharmacotherapy. 1998;18:16–22.
Segal JL, Brunnemann SR, Castañeda-Hernández G, et al. Altered hepatocyte gene expression in a rat model of chronic spinal cord injury. J Clin Pharmacol. 2000;40:1045–65.
Stitik TP, Klecz R, Greenwald BD, et al. Pharmacotherapy of disability. In: Frontera WR, Gans BM, Walsh NE, et al., editors. DeLisa's physical medicine and rehabilitation. 5th ed. Philadelphia: Wolters Kluwer; 2010.
Teasell RW, Merskey H, Deshpande S. Antidepressants in rehabilitation. Phys Med Rehabil Clin N Am. 1999;10:237–53.
Trindade E, Menon D, et al. Adverse effects associated with selective serotonin reuptake inhibitors and tricyclic antidepressants: a meta-analysis. CMAJ. 1998;159:1245–52.
Tsioufis C, Thomopoulos C. Combination drug treatment in hypertension. Pharmacol Res. 2017;125:266–71.
Ustün TB, Ayuso-Mateos JL, Chatterji S, et al. Global burden of depressive disorders in the year 2000. Br J Psychiatry. 2004;184:386–92.
Utili R, Boitnott JK, Zimmerman HJ. Dantrolene-associated hepatic injury. Incidence and character. Gastroenterology. 1977;72(4 Pt 1):610–6.
Vallelonga F, Maule S. Diagnostic and therapeutical management of supine hypertension in autonomic failure: a review of the literature. J Hypertens. 2019;37:1102–11.
Wein AJ, Chapple C. Overactive bladder in clinical practice. London: Springer; 2012.

Wells PS, Holbrook AM, Crowther NR, et al. Interactions of warfarin with drugs and food. Ann Intern Med. 1994;121:676–83.

Wöllner J, Pannek J. Initial experience with the treatment of neurogenic detrusor overactivity with a new β-3 agonist (mirabegron) in patients with spinal cord injury. Spinal Cord. 2016;54:78–82.

Wright RA, Kaufmann HC, Perera R, et al. A double-blind, dose-response study of midodrine in neurogenic orthostatic hypotension. Neurology. 1998;51:120–4.

Recommended Additional Reading

Arcangelo VP, Peterson AM, Wilbur VF, Reinhold JA, editors. Pharmacotherapeutics for advanced practice. A practical approach. 4th ed. Philadelphia: Wolters Kluwer; 2017.

Carl LL, Gallo JA, Johnson PR. Practical pharmacology in rehabilitation: effect of medication on therapy. 1st ed. Champaign: Human Kinetics, Inc.; 2014.

Ciccone C. Pharmacology in rehabilitation. 5th ed. Philadelphia: F. A. Davis Company; 2016.

Ciccone C. Pharmacology in rehabilitation. 5th ed. Philadelphia: F. A. Davis Company; 2007.

Corcos J, et al. editors. Overactive bladder. Practical management. West Sussex: Wiley; 2015.

Cristian A, editor. Medical management of adults with neurologic disabilities. 1st ed. New York: Demos Medical Publishing; 2009.

Ebenezer IS. Neuropsychopharmacology and therapeutics. 1st ed. West Sussex: Wiley; 2015.

Iverson LL, Iverson SD, Bloom FE, et al. Introduction to neuropsychopharmacology. Oxford: Oxford University Press, Inc.; 2009.

Lader M, Cardinali DP, Pandi-Perumal SR, editors. Sleep and sleep disorders: a neuropsychopharmacological approach. New York: Springer; 2006.

Polantin PB, Gajraj NM. Integration of pharmacotherapy with psychological treatment of chronic pain. In: Turk DC, Gatchel RJ, editors. Psychological approaches to pain management: a practitioner's handbook. 2nd ed. New York: The Guilford Press; 2002.

Satzung BG, Masters SB, Trevor AJ, editors. Basic and clinical pharmacology. 11st ed. New York: McGraw-Hill; 2009.

Stitik TP, Klecz R, Greenwald BD, et al. Pharmacotherapy of disability. In: Frontera WR, Gans BM, Walsh NE, et al., editors. DeLisa's physical medicine and rehabilitation. 5th ed. Philadelphia: Wolters Kluwer; 2010.

Localization and Characterization of Spinal Cord Lesions

11

For persons with minor or intermittent symptom that suggests a spinal cord lesion or similar symptoms nearby, a quick screening or neurologic mini-examination may be initially adequate. The results of such a screening examination determine the subject of further more detailed subsequent examination, the localization of the lesion site, and the specifying spinal cord injury/lesion. There are several ways to conduct a screening examination. The elements of an initial screening neurological examination are listed in Table 11.1. In screening examination of motor function, sensory function, and coordination in the upper and lower extremities can be performed in a single, multi-faceted maneuver. In most clinical situations where screening examination is appropriate, the primary concern is to detect a lesion involving the corticospinal tract (Campbell 1992).

Table 11.1 Elements of an initial screening neurological examination suggesting a spinal cord lesion

Examination list
1. Cognition and communication during conversation with physician
2. Muscle strength, tone, and bulk proximally and distally in all extremities
3. Pain or temperature, vibration medially and laterally in all extremities
4. Proprioception and coordination
5. Segmental reflexes: deep tendon reflexes, superficial reflexes, and pathological reflexes
6. Cranial nerves examinations

Among the various symptoms when brain damage is ruled out and it is not a cauda equina lesion, pathological reflexes such as Babinski's sign, finger jerk, and Hoffman's sign and spasticity accompanied by hyperactive deep tendon reflexes depending on the injured area are the most characteristic neurological symptom suggesting a spinal cord injury. Clinical problems in the acute phase focus mainly on motor, sensory, and autonomic function and early prediction of outcome. A thorough neurological examination is performed and recorded. This should be repeated at appropriate intervals to detect changes in neurological status. The neurological level of injury by definition, motor, and sensory, is determined. The presence and absence of muscle strength, reflexes, and sharp/dull and light touch senses must be accurately documented. Accurate neurological assessment including motor strength, sensory functions, superficial reflexes, deep tendon reflexes, and pathological reflexes, as well as functional assessment are needed to understand specific neurological/functional impairments and rehabilitation programs for individual disabilities and rehabilitation goals. Clues can be obtained by the speed of onset of the neurological problems and the relative components of motor, sensory, and autonomic symptoms and signs (Bican et al. 2013).

Almost half of the patients with spinal injuries have significant associated injuries, many of

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which are life-threatening. The most common associated injuries are injuries to the head, chest, and long bones. Ten percent have three or more such injuries (Saboe et al. 1991). Hypotension at first presentation may be the result of neurogenic shock, but its classic presentation in conjunction with bradycardia is relatively rare. Therefore, the presentation of shock requires evaluation for significant blood loss. The clinical sign and symptoms of a traumatic brain injury may also have another cause. Vertebral injuries can also cause vertebral artery occlusion and cause similar symptoms. The acute onset and severe weakness associated with ischemia, bleeding, or injury have very different signs than later, with spinal shock and hyporeflexia. The gradual onset of weakness caused by slow onset myelopathy suggests an upper motor neuron lesion weakness with hyperreflexia, with no apparent spinal shock or hyporeflexia. The distribution of weakness between upper and lower motor neuron lesions may differ, but an accurate distinction is a need when there are differences in the distribution of weakness and reflexes (Table 11.2). Sensory changes are also common in spinal cord lesions that affect both the long tracts and the segment function. The distribution of abnormal sensations can help determine the location of the lesion and the nature of the problem. An altered sensation in a specific dermatomal distribution thus implies radiculopathy, while a generalized sensory disturbance with a sensory level indicates a spinal cord injury or myelopathy. Brown-Séquard syndrome often presents mixed sensory and motor symptoms, including both motor weakness and sensory disturbances of the affected segments and long tracts. This results in contralateral spinothalamic and ipsilateral dorsal column loss and upper motor neuron lesion below it.

Table 11.2 General neurological signs to localize the lesion to the spinal cord

Is the neurological signs localizable to the spinal cord?
Signs strongly suggestive of spinal cord
Suspended band of sensory loss
Sensory level on the torso
Spinal tract crossed findings, e.g., pyramidal on one side and contralateral spinothalamic
Dissociated sensory loss conforming to cord syndromes, e.g., syringomyelia and anterior cord syndrome
Root plus long tract signs, e.g., spondylotic myelopathy and sarcoidosis
Isolated tractopathy, e.g., anterior horn, posterior column, and spinothalamic tract
Lhermitte's sign
Acute urinary retention
Signs consistent with, but not diagnostic of spinal cord
Bilateral symmetric sensory loss with no hyperreflexia, e.g., polyneuropathy
Paraplegia without sensory signs, e.g., parasagittal lesion of the brain
Generalized hyporeflexia, e.g., polyneuropathy
Unilateral or bilateral upper motor neuron lesion signs, e.g., lesions of the brain or brainstem
Ascending sensory loss, e.g., AIDP or CIDP
Exertional worsening of symptoms, e.g., vascular disease of the leg(s), MS, or lumbar stenosis
Signs not suggestive of spinal cord
Monoplegia of an arm
Cranial nerve deficits, except V
Pure lower motor neuron lesion signs
Paratonia, e.g., frontal lobe lesion
Stiffness rather than spasticity, e.g., Parkinson's disease
Dysarthria, dysphagia, brisk jaw reflex, e.g., brainstem lesion or ALS
Weakness with normal sensation and reflexes, e.g., myasthenia gravis
Proximal muscle weakness, e.g., myopathy

Modified from Bican et al. (2013), with permission

11.1 Clinicoanatomical Considerations

Knowing the structure and function of the various levels of motor control, the relationships between the motor systems, and changes in motor activity that occur in disease helps to understand motor system disorders. Various descending suprasegmental motor systems modulate the activity that occurs at the segmental level. The pyramidal (corticospinal) system arises from the primary motor cortex in the precentral gyrus. The corticospinal system is the primary suprasegmental motor control mechanism. The function of the corticospinal system is modulated and adjusted by the activity of the extrapyramidal and cerebellar systems. Centers in the brainstem that give rise to the vestibulospinal, rubrospinal, and related pathways are important for postural

mechanisms and standing and righting reflexes (Campbell 1992). Classical clinical examination of motor function of the spinal cord injury/disease is mainly related to the examination of the pyramidal tract, except for the cauda equina lesion, which is included as a spinal cord injury in the ISNCSCI. Other motor tracts of the extrapyramidal system are associated with more proximal automatic movements. The relationship between descending tracts and motor function is a very complex issue. The most typical sign of spinal cord injury is weakness, and a level of spinal cord injury may be exhibited by the decrease or increase of reflex activities due to spinal cord injury. Whether certain types of damage occur on the descending pathway is clinically less important, as the spinal cord is too small to distinguish the pathways involved accurately.

The various pathways that are affected by an intramedullary injury or extramedullary pressure lead to classical clinical findings, for example, posterior cord syndromes with loss of position and movement sensation as well as lateral and central cord damage associated with loss of pain and temperature sensation. Weakness resulting from intramedullary tumors may typically spread from proximal to distal in the extremities due to lamination of the corticospinal tract. Dissociated sensory loss, preservation of dorsal column function with loss of spinothalamic function, is considered characteristic of intramedullary lesions. However, extramedullary tumors have been reported to cause this sensory pattern. In degenerative cervical myelopathy, sensory abnormalities in the lower extremities tend to affect the sensation of vibration more than the position sense, and pain and temperature are usually not affected unless the spinal damage is advanced. Lhermitte's sign also is often reported.

There is a discrepancy between the skeletal level of injury and the neurological level. For example, a patient with a C6 burst fracture can show that the C7 motor level is spared. This is because the motor neuron pool for the myotome is cephalad to the corresponding vertebral body. The motor neuron pool is one segment cephalad to the corresponding vertebral body in the cervical spine, two segments higher in the thoracic spine and three segments higher in the lumbar spine.

11.2 Neurological Classification of Spinal Cord Injury

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) is the most commonly used assessment of impairment resulting from spinal cord injury, including cauda equina lesion. The ISNCSCI clarifies patients based on clinical examination rather than radiological or anatomical abnormalities. Key elements include bilateral assessment of 10 key muscles and 28 dermatomes. Rectal examinations, including rectal sensation and voluntary anal contraction, are also evaluated. In addition to the elements of the ISNCSCI examination, general medical and neurological examinations including mental status, cranial nerves, and muscle stretch/superficial/pathological reflexes should be performed.

Key muscle functions are assessed in the supine position. Each key muscle is assigned a score from 0 to 5. The motor level is defined as the most caudal segment with normal motor function. The motor level should be at least the lowest key muscle with grade 3 strength, and all cephalad segmental muscles should have grade 5 strength. Left and right motor levels can be obtained. The motor score is the sum of the individual motor strength grades from each key muscle. The value is between 0 and 100.

With 28 dermatomes, light touch and pinprick on both sides are evaluated. For each segment, a score of 0 (absent), 1 (impaired), 2 (normal), and NT (not testable) is determined for each modality. The sensory score is the sum of the dermatomal sensory scores of each modality, ranging from 0 to 112. The sensory level is defined as the highest level with normal sensory function. Anal examination, including the sensory function of perianal mucocutaneous junction, deep anal pressure, and voluntary anal contraction, is an essential element of the ISNCSCI.

The neurological level of injury is defined as the highest level of the left and right motor and sensory levels. The zone of partial preservation refers to the segment of partially preserved dermatomes and myotomes caudal to the neurological level of injury. The zone of partial preservation of motor and sensory can be evaluated in complete and incomplete lesions. For more details on the ISNCSCI, see Chap. 13.

11.3 Upper Motor Neuron and Lower Motor Neuron Lesion

It is important to understand the concept of upper and lower motor neuron injury/lesion. In the acute phase of spinal cord injury due to spinal shock, it is sometimes difficult to clinically differentiate between upper and lower motor neuron lesions in an acute phase of spinal cord injury due to spinal shock (Ko et al. 1999). Weakness can occur with injuries of the lower motor neuron type or upper motor neuron lesion type. The location of the upper motor neuron lesion weakness does not always correspond to the expected pattern. The supply of the upper motor neuron begins in the prefrontal motor cortex, runs through the internal capsule and the brainstem, and projects into the spinal cord. The supply of the lower motor neuron (motor unit) begins in the anterior horn cells of the spinal cord and includes the spinal nerve roots, the plexus, the peripheral nerves, the neuromuscular junction, and muscle fibers (Fig. 11.1). Most of the lesions in the cervical and thoracic cord cause predominantly upper motor neuron type injuries. However, at the level of the injury and the adjacent segments of the lesion epicenter, lower motor neuron type injury resulting from a compromise of the nerve roots and/or the anterior horn cells may be combined. Therefore, most types of spinal cord injuries related to vertebral body fractures or pathological lesions can occur in certain localized lower motor neuron lesions around the neurological level of the injury or lesion.

Upper motor neuron lesions are associated with upper motor neuron lesions findings such as spastic weakness, hyperreactive muscle stretch reflexes (deep tendon reflexes), clonus, Babinski

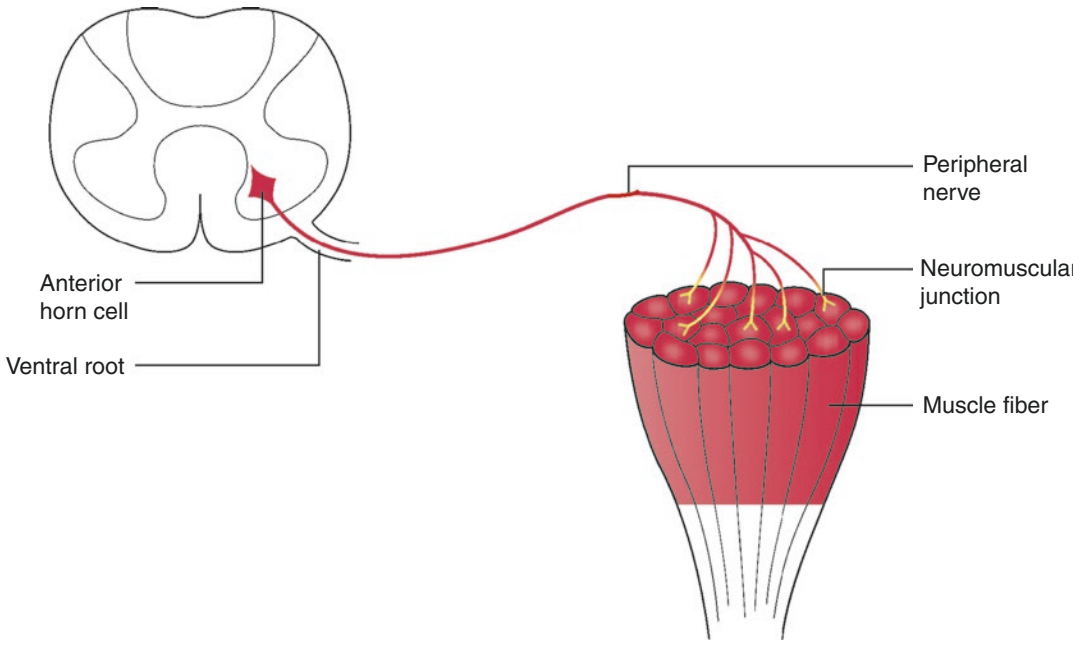

Fig. 11.1 The motor unit

sign, and detrusor overactivity and/or detrusor-sphincter dyssynergia. The results of the lower motor neuron lesion are characterized by flaccid weakness, hyporeflexia, and significant muscle atrophy (Table 11.3). The terminal segments of the spinal cord, the conus medullaris, is located approximately at the level of the vertebral body L1 to L2. The lesions at the upper lumbar vertebral bodies may show a mixture of upper and lower motor neuron lesion lesions. The injuries below the L2 vertebral body may cause lower motor neuron type injury.

Table 11.3 Differentiation of the clinical features of upper motor neuron vs. lower motor neuron lesion

Feature	Upper motor neuron lesion	Lower motor neuron lesion
Site of the lesion	Cerebral hemispheres, cerebellum, brainstem, spinal cord	Anterior horn cells or ventral horn of the gray matter, nerve roots, peripheral nerves, neuromuscular junction, muscles
Type of paralysis	Spastic paralysis or rigidity	Flaccid paralysis
Muscle tone	Spasticity, rigidity	hypotonia
Topographical pattern of weakness	Tetraplegia, hemiplegia, diplegia, paraplegia	Proximal in myopathy, distal in neuropathy
Atrophy	No or disuse atrophy	Severe atrophy
Deep tendon reflex	Hyperreactive	Absent or hyporeactive
Superficial reflex	Absent or present, controversial	Present, controversial
Pathological reflex	Positive including Babinski, ankle clonus, and/or Hoffman sign and finger jerk	Absent and/or flexor plantar reflex
Fasciculation	Absent	Present
EMG	Normal nerve conduction, decreased interference pattern and firing rate	Abnormal nerve conduction, Large-sized motor unit action potential, Abnormal spontaneous activities including fasciculation potentials

11.4 Neurological Signs and Symptoms Associated with Spinal Cord Lesion

The first thing of the physician examining a patient with suspected spinal cord injury is to determine whether there is a spinal cord disease or injury, and if so, assess the site of the injury and the extent of the injury. When the occurrence of various neurological symptoms, including motor weakness, is clearly related to trauma associated with a vertebral fracture, the determination of a spinal cord injury can be straightforward. However, if the motor or sensory abnormalities or gait disturbances appear gradually, whether these symptoms are due to abnormalities in the brain, brainstem, spinal cord, nerve roots, peripheral nerves, or muscles, that is, whether it is an upper motor neuron lesion or a lower motor neuron lesion should be distinguished. Based on the evaluation of these symptoms, the anatomical location causing the symptoms is determined. Although this assessment process can be assisted by MRI and neurophysiological tools, the localization of specific lesions is performed by assessing not only various motor/sensory functions, but also superficial reflexes, deep tendon reflexes, pathological reflexes, and autonomic symptoms, which are segmented. Of course, the neurological assessment of spinal cord injury is based on The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI, eighth ed., Revised 2019). Still, it is accompanied by the assessment of various neurological symptoms mentioned above. Clinical classification after 72 h after spinal cord injury can predict long-term neurological and functional outcomes and thus establish a rehabilitation plan accordingly (Brown et al. 1991).

11.4.1 Muscle Bulk

Visual inspection of the muscle bulk, contour, and symmetry is part of a careful neurological assessment. Acute spinal cord injury does not result in these abnormalities. To assess muscle bulk, careful inspection of the major muscle groups is performed. Atrophy can be the result of a lower motor neuron lesion. Weakness does not necessarily correspond with the degree of atrophy. In cases of monoradiculopathy associated with vertebral fracture, atrophy is not prominent since most muscles receive innervation from multiple nerve roots. In cases of chronic radiculopathy, e.g., cervical spondylosis, atrophy may precede weakness, whereas weakness may precede atrophy in cases of acute radiculopathy.

11.4.2 Muscle Tone

Muscle tone is a compilation of many components. Muscle tone is necessary for maintaining skeletal posture. Hypertonicity or hypotonicity is a manifestation of tone abnormality. Spasticity and rigidity refer to common forms of increased muscle tone (hypertonicity) due to upper motor neuron lesions. In spasticity, the increased muscle tone is due to an exaggeration of the stretch reflex. If the muscle is slowly stretched, the increased tone may not be found.

11.4.3 Muscle Strength

Weakness can cause loss of strength, speed, rapidity, or agility of movement and may reduce the range of motion or amplitude before applying force to the formal strength testing. When examining muscle strength, voluntary or active muscle contraction is assessed rather than reflex contraction. There are many factors that complicate strength testing. Experience gained from examining a large number of patients may help reinforce the examiner's impression of loss of strength, especially if the impairment is mild. Muscle weakness should be distinguished from loss of range of motion for other reasons and contracture of antagonists. Passive movements to assess the range of motion are sometimes necessary to distinguish whether movement restriction is due to weakness, pain, muscle spasm, or fibrous or bony changes. Limitation of movement due to severe weakness can ultimately result in contractures and deformities.

Quantitative measurements and recordings of exam results help diagnose and assess progressing or recovery of weakness. In manual muscle testing, the strength of each muscle is tested on a scale and assessed quantitatively. Strength is most commonly evaluated using the five-level MRC (Medical Research Council) scale developed in the UK in World War II to evaluate patients with peripheral nerve injuries. The MRC scale has been widely used for the evaluation of strength. However, the scale is heavily weighted for the evaluation of very weak muscles. In a severe peripheral nerve injury, an improvement from grade 0 (no contraction) to grade 1 (a flicker) is highly significant, as it signals the onset of reinnervation (Compston 2010; Medical Research Council 1943) (Table 11.4). In clinical practice, the MRC scale is often expanded to include subgrades, such as 5− and 4+. The MRC

Table 11.4 Grading of muscle strength

Grade	Description (British Medical Research Council)	Description (ISNCSCI)
0	No contraction	Total paralysis
1	Flicker or trace of contraction	Palpable or visible contraction
2	Active movement, with gravity eliminated	Active movement, full range of motion (ROM) with gravity eliminated
3	Active movement against gravity	Active movement, full ROM against gravity
4	Active movement against gravity and resistance	Active movement, full ROM against gravity, and moderate resistance in a muscle-specific position
5	Normal power	Normal active movement, full ROM against gravity and full resistance in a functional muscle position expected from an otherwise unimpaired person

finally saw the need to include grades 4−, 4, and 4+, which are used to indicate movement against slight, moderate, and strong resistance, respectively (Medical Research Council 1943). The currently used muscle strength grading system can be a modified description based on the MRC scale.

11.4.4 Reflexes

The presence or absence of superficial reflexes, deep tendon reflexes, and pathological reflexes, and changes in reaction depend on the site of the spinal cord injury and whether the injury is the upper motor neuron lesion or the lower motor neuron lesion. Reflex activity is very important in determining the presence or absence of the reflex arcs in the corresponding spinal cord segments. The muscle stretch, reflex is tested as part of all neurological examination.

The stretch reflex is a monosynaptic reflex in which a sensory afferent neuron synapses directly with a motor efferent neuron in the anterior horn of the gray matter. The sensory afferents (group la) are stimulated when the muscle spindle is stretched, as occurs with percussion of a deep tendon. Superficial reflexes are those reflexes that respond to stimulation of the skin or mucous membranes. The most commonly tested superficial reflexes in the patient suspected to have spine cord lesion are the superficial abdominal, anal, cremasteric, and Babinski reflexes.

11.4.4.1 Superficial and Deep Tendon Reflexes

All deep tendon and superficial reflexes including superficial abdominal reflex, cremasteric reflex, plantar reflex (van Munster et al. 2012), bulbocavernosus (bulbospongiosus) reflex, superficial anal reflex, and dartos reflex, should be carefully evaluated (Table 11.5). By assessing the reflexes of the rectus abdominis, the T7–T12 reflex arcs can be assessed and the bulbocavernosus reflex is suitable for assessing the integrity of S2–S4 reflex arc (Vodusek 2003). The bulbocavernosus reflex is a well-known segmental polysynaptic reflex with crossover in the sacral spinal cord, that is useful for gaining information about the state of the sacral spinal cord segments. When present, it is indicative of intact spinal reflex arcs (S2–S4 spinal segments) with afferent and efferent nerves through the pudendal nerve (Yang and Bradley 1999). The bulbocavernosus reflex is an important segmental spinal reflex concerned with the induction of bulbocavernosus muscle contraction (Yang and Bradley 2000) (Fig. 11.2). The bulbocavernosus reflex is performed by applying pressure to the glans penis or clitoris, or by pulling on the Foley catheter. A normal response involves contraction of the external anal sphincter (Spector et al. 2008).

The superficial abdominal reflexes are tested by stimulating the abdominal wall on one side with a blind or sharp object and observing for the contraction of the ipsilateral abdominal muscles. The normal response is contraction of the abdominal muscles resulting in a deviation of the umbilicus or linea alba to the ipsilateral side. The upper abdominal or supraumbilical reflex is innervated by nerve roots T7–T9. The umbilical reflex is innervated by nerve roots T9–T11 and the lower abdominal or infraumbilical is innervated by the lower thoracic and upper lumbar roots. The cremasteric reflex is triggered by stimulating the skin of the upper, inner thigh from proximal to distal and observing the ipsilateral elevation of the testicle as a result of contraction of the cremasteric muscle (Fig. 11.3). The nerve roots that innervate the reflex are L1 and L2 via the ilioinguinal and genitofemoral nerves. The cremasteric reflex may be absent in elderly man or if they have a varicocele, epididymitis, or other urological diseases (Nelson et al. 2003). The cutaneous anal reflex is the contraction of the external anal sphincter when the perianal tissues are stimulated. This reflex is innervated by nerve roots S2–S4 via the inferior hemorrhoidal nerve (Byrne et al. 2000). The dartos reflex is a somatoautonomic reflex that depends on the sympathetic segment T11–L2. The dartos reflex produces unilateral elevation of the testis with vermicular contraction of the scrotal skin and penile retraction. Intact dartos reflex arc reflects the integrity of the afferent and efferent branches of the genitofemoral nerve (T11–L2) (Soler et al. 2017; Yilmaz

Table 11.5 Segmental levels of the superficial, deep tendon, and pathologic reflexes

Name	Method	Response	Level
Scapulohumeral reflex	Tapping lateral edge of the scapular spine or acromion	Humeral abduction or scapular elevation	C1–C4
Biceps reflex	Tapping biceps tendon at the elbow	Contraction of biceps	C5
Brachioradialis reflex	Tapping brachioradialis tendon at the wrist	Contraction of brachioradialis	C6
Triceps reflex	Tapping of triceps tendon	Contraction of triceps	C7
Finger jerk (Tromner reflex)	Flipping distal phalanx of the middle finger	Brisk flexion of the fingers and/or thumb	C8 (pyramidal tract)
Hoffman sign	Flicking downward upon the middle fingernail	Brisk flexion of the fingers and/or thumb	C8–T1 (pyramidal tract)
Abdominal reflex	Stroking beneath coastal margins and above inguinal ligaments	Contraction of abdominal muscles	T7–T12
Dartos reflex	Touch or local cold on the scrotum	Slow, writhing, vermicular contraction of scrotal skin and penis retraction	T11(12)–L2 Sympathetically mediated scrotal reflex
Cremasteric reflex	Stroking medial upper thigh	Ipsilateral elevation of testicle	L1–L2
Adductor reflex	Tapping adductor longus	Hip adduction	L2–L3
Knee jerk	Tapping patella tendon	Knee extension	L3–L4
Oppenheim sign	Stroking tibia crest	Extension of toes	L4–L5
Gluteal reflex	Stroking skin of buttock	Contraction of glutei	S2–S3
Ankle jerk	Tapping Achilles tendon	flexion of ankle	S1
Plantar reflex	Stroking sole	Flexion of toes	S1
	Stroking sole	Extension of toes (Babinski)	S1 (pyramidal tract)
Chaddock sign	Stroking lateral foot dorsum	Extension of toes	S1 (pyramidal tract)
Superficial anal reflex	Stroking or pricking of perianal region	Contraction of external anal sphincter, winking anus	S2–S4
Bulbocaveronosus (bulbospongiosus) reflex	Pinching or squeezing glans penis or clitoris	Contraction of external anal sphincter	S3–S4

Modified from Vinken and Bruyn (1976)

et al. 2006) (Fig. 11.4). The anocutaneous reflex (anal reflex) is used to assess S2-S4 and involves contraction of the external anal sphincter in response to stimulation of the perianal skin.

If an increase in tone or reflex is noted, care should be taken not to confuse reflex spasm with voluntary contraction. It is important not to move the examiner's finger when testing the anal sphincter contraction. To test the bulbocavernosus reflex, use the examiner's finger in the rectum and use the other hand to quickly squeeze the patient's glans penis. In a female, the examiner can prick the clitoris with a cotton swab. The reflex is present when the examiner feels a brief contraction of the anal sphincter around the finger. If the patient has a Foley catheter, the catheter can be quickly pulled to trigger the reflex. The examiner can feel the balloon of the catheter pressing on the inserted finger as the catheter is pulled, and the examiner should not confuse this with contraction of the anal sphincter. The presence of the bulbocavernosus reflex indicates that the reflex arc of the sacral segments, at least conus medullaris, is preserved.

The combination of hypoactive reflexes at a segmental level and hyperactive reflexes caudal to this level is commonly found in patients with spinal cord injuries. The deep tendon reflexes usually examined include the scapulohumeral, biceps, triceps, brachioradialis, knee jerk, and ankle jerk. The scapulohumeral reflex (Shimizu reflex) is elicited by tapping of the lateral edge of the scapular spine or the acromion in a caudal direction, with the reaction of humeral abduction

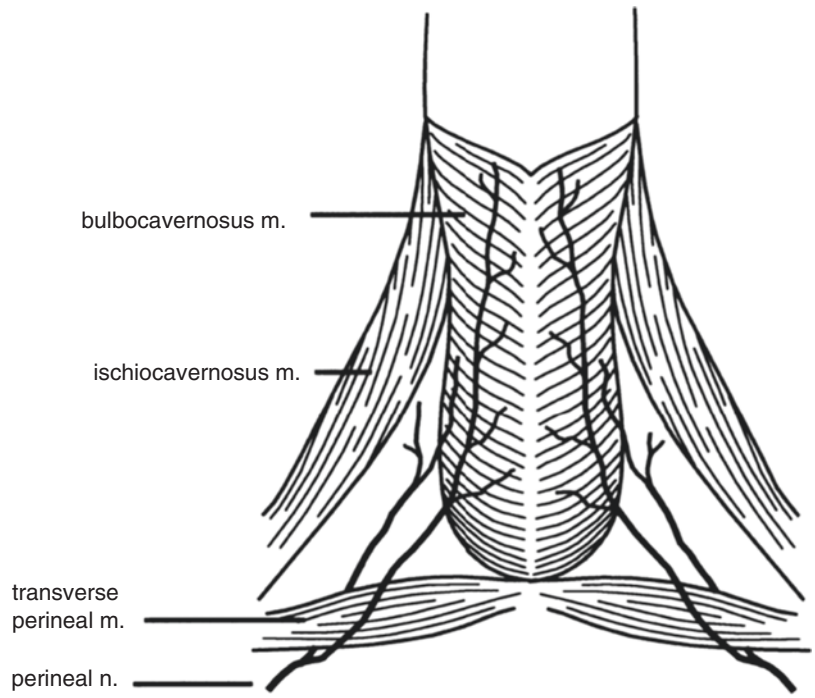

Fig. 11.2 The bulbocavernosus muscle and its innervation by the perineal nerve. The muscle is bilateral and attaches along the median raphe of the bulbus urethra. The nerve trunk originates dorsolateral to the muscle and branches across the ventral surface of the muscle. From Yang and Bradley (1999), with permission

and scapular elevation. The major muscles participating in the scapulohumeral reflex are the upper trapezius, the levator scapulae, and the deltoid (Rumi and Yoon 2004; Shimizu et al. 1993). It is believed that the reflex center of the scapulohumeral reflex is between C1 and C4 (Fig. 11.5). This reflex can be used to assess high cervical cord lesions cephalad to C4. While patients with severe spinal cord injuries during the acute period are generally flaccid and do not have deep tendon reflexes, those with incomplete injuries may be quite spastic. These patients may have an exaggerated triple flexion response when stroking the plantar surface of the foot. This reflex response can be confused with the voluntary withdrawal of a noxious stimulus. The presence of a crossed adductor response to patellar tendon taps in the acute injury period (up to 20 days) is highly predictive of motor incomplete injury (Calancie et al. 2004). The Jendrassik maneuver can accentuate the reflexes of the lower extremities and requires the patient to pull interlocked fingers apart while testing the reflex. Clenching the teeth or pressing down on the examination table with the thighs can accentuate the reflexes of the upper extremity.

Patients with lower thoracic injuries may have Beevor's sign, which is not a pathological reflex; it is a sign resulting from an imbalance in muscle strength between the upper and lower abdominal muscles. This is an upward deviation of the umbilicus, when patients contract their abdominal muscles as in a sit-up, and is due to relatively weaker lower abdominal muscles compared with upper abdominal muscles. A positive Beevor's sign represents an imbalance in muscle innervation above and below the umbilicus. A positive Beevor's sign indicates the neurological level of injury of motor at the T8 to T11 (T10) region (Pearce 2005). Beevor's sign is not specific for spinal cord lesion or upper motor neuron lesion, it is also seen with other diseases causing lower abdominal weakness such as facioscapulohumeral muscular dystrophy or amyotrophic lateral sclerosis (Cho and Bhattacharyya 2018).

11.4.4.2 Pathological Reflexes

Most pathological reflexes are related to disease affecting the corticospinal tract and associated pathways. The names of the reflexes and triggering methods are very confusing. Many of the responses are merely variations in the method

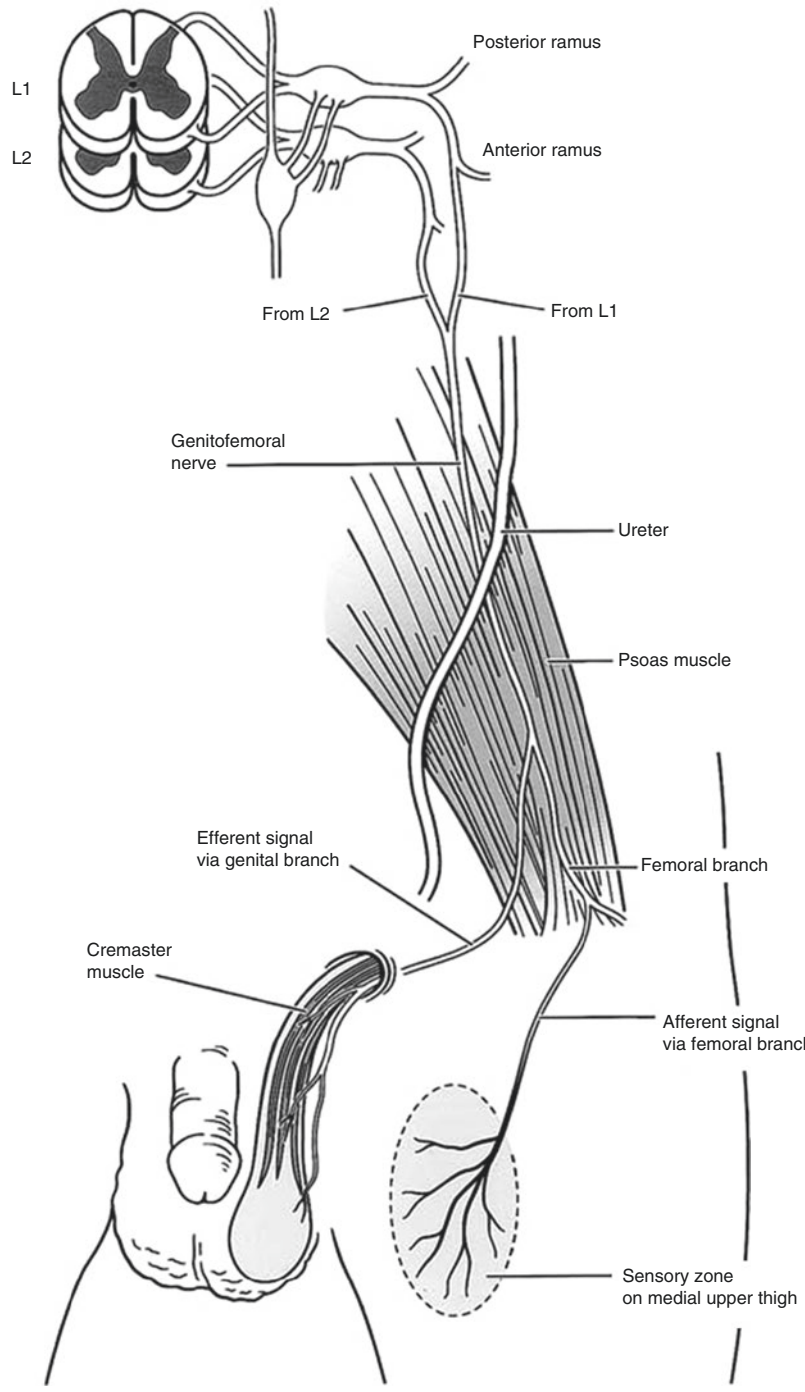

Fig. 11.3 Schematic representation of the innervation relevant to the cremasteric reflex. The stimulus is transmitted from the medial thigh via the cutaneous nerves and the femoral branch of the genitofemoral nerve to the nuclei at L1 and L2. The response is transmitted from the nuclei to the cremasteric muscle via the genital branch of the genitofemoral nerve. From Nelson et al. (2003), with permission

of eliciting the same responses, or modification of the same reflex. Among the pathological reflexes, it is important to examine Hoffman's sign, Babinski sign, and ankle conus. Although the presence of a Babinski sign indicates corticospinal tract injury, the absence of a Babinski sign does not exclude corticospinal tract dysfunction (Cho and Bhattacharyya 2018).

The Hoffmann sign is a commonly used physical examination maneuver taught as an indicator

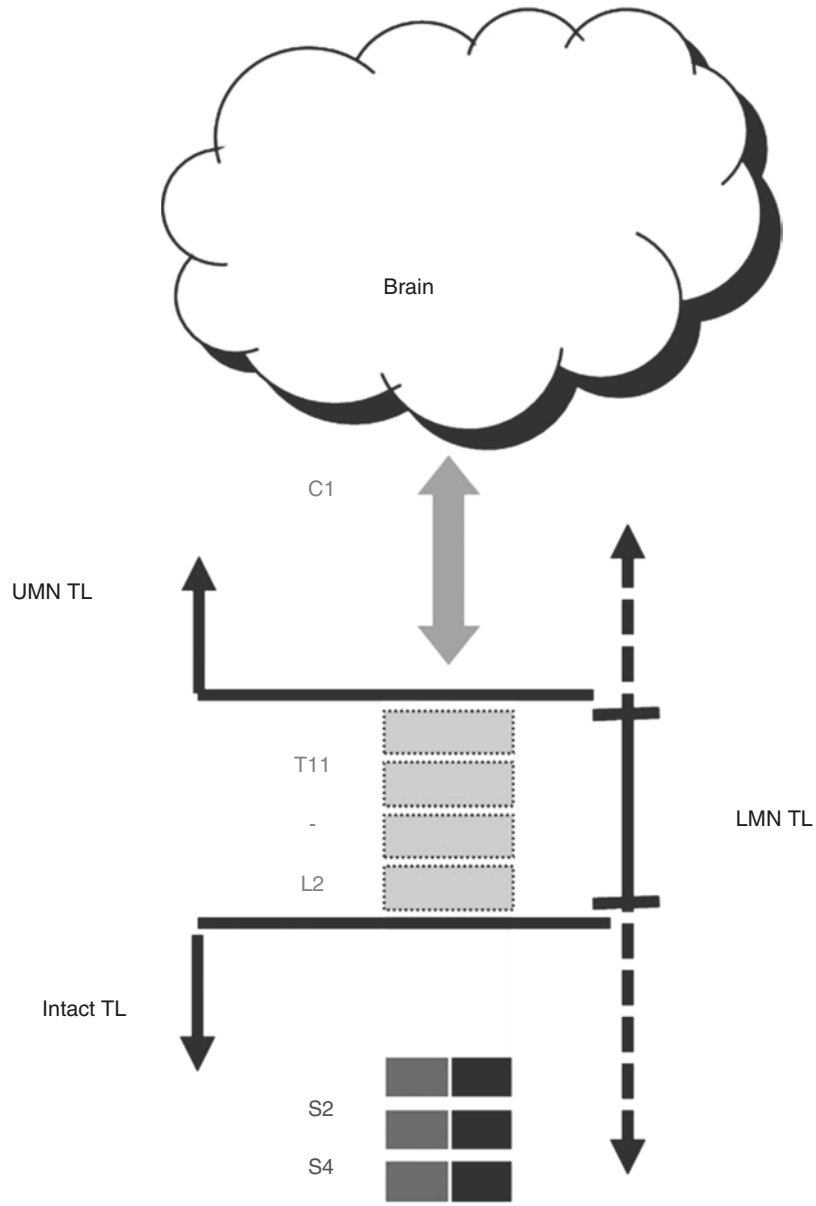

Fig. 11.4 Schematic representation of the groups according to the level of the lesion and integrity of the T11–L2 segment. UMN, upper motor neuron; LMN, lower motor neuron; TL, thoracolumbar. From Soler et al. (2017), with permission

of upper motor neuron lesion and is attributed to a nineteenth-century German neurologist, Johann Hoffmann (Fogarty et al. 2018). The Hoffmann sign is one of finger flexion reflexes and is often used in clinical practice as a finding for an upper motor neuron lesion. It is triggered by flicking downward upon the nail of the middle finger. A positive sign is indicated by involuntary flexion of the neighboring fingers and/or thumb (Houten and Noce 2008). The Hoffmann sign is assumed that positive sign involved injury to the proximal segment of C8–T1. The Hoffmann sign can also occur in asymptomatic people with an estimated prevalence of about 2% (Malanga et al. 2003). The finger jerk (Tromner reflex) is triggered by the examiner supporting the patient's completely relaxed hand with extension of the metacarpophalangeal joint flexion of the proximal interphalangeal joint of the middle finger and briskly flips the patient's distal phalanx of the

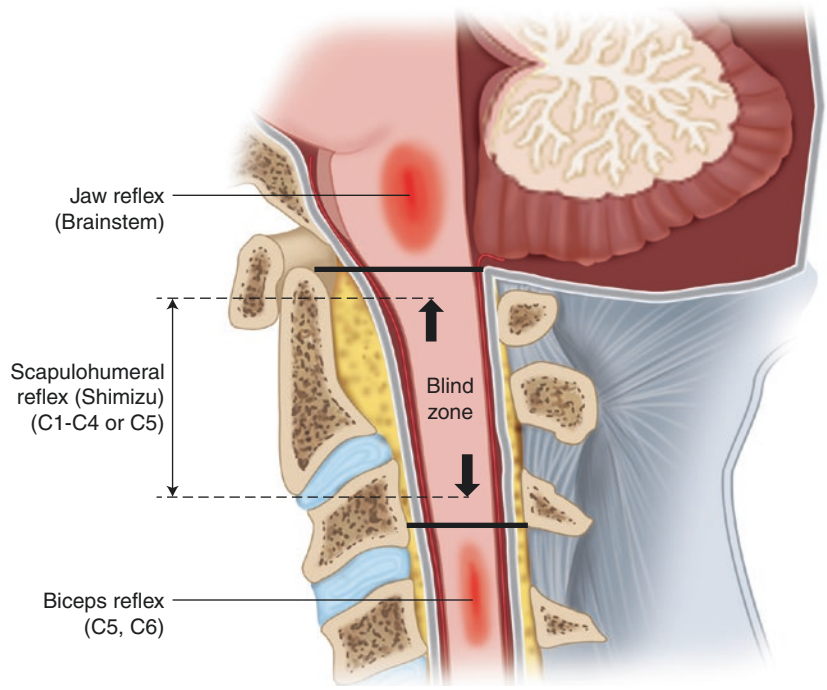

Fig. 11.5 Neurological lesions of the high cervical cord are difficult to isolate by reflexes or signs, unless the clinician evaluates the scapulohumeral reflex (Shimizu reflex). Adapted from Durrant and True (2002), which was originally modified from Shimizu et al. (1993)

middle finger upward, as though to flip a handful of water high into the air. The finger jerk is mediated by mainly the C8 nerve root. A positive response is noted by the resulting contraction of the flexor digitorum profundus at the index or long finger and the flexor pollicis longus (Rumi and Yoon 2004). This is physically seen as a rapid flexion response of the thumb, index, and/or long fingers simultaneously. A positive Hoffmann's or finger jerk suggests a corticospinal lesion at or above the C5 or C6 level, but an isolated Hoffmann's or finger jerk in the absence of other myelopathic signs or symptoms does not confirm a spinal cord lesion. The examiner should always attempt to correlate with additional long tract signs, diagnostic imaging, and laboratory work (Durrant and True 2002). The dynamic Hoffman's test can help to elicit upper motor neuron lesion signs in patients with a negative static Hoffmann sign, thereby increasing the sensitivity of the clinical neurological examination that helps clinically in the diagnosis of early spondylotic myelopathy or congenital cervical narrowing. The dynamic Hoffmanns sign is the Hoffmann sign, which is checked with the head in neutral and during multiple active full flexion to extension as tolerated by the patient (Denno and Meadows 1991).

Babinski sign must be part of the general withdrawal reflex synergy released by a lesion of supraspinal pathways projecting onto the interneuronal zone of the lumbosacral cord (van Gijn 1975, 1978). The mechanisms of the Babinski sign are explained as follows: The Babinski sign could be released by a dysfunction of the pyramidal tract fibers that project onto the interneuronal zone, at least in the interneurons that subserve the flexion reflex synergy, of which the Babinski sign is part. Alternatively, the Babinski sign could result from interference with pyramidal fibers projecting directly on motor neurons (van Gijn 1978). The effector organ of the Babinski sign is the extensor hallucinate longus (Soler et al. 2017). A positive Babinski sign represents the

loss of upper motor neuronal suppression of this spinal reflex. If Babinski sign is absent in upper motor neuron lesion, it is thought to be due to a disruption of the segmental reflex pathways caused by the common peroneal nerve or deep perineal nerve neuropathy resulting from a pressure injury, or by the unexcitability of spinal motor neurons due to spinal shock (van Gijn 1996a, b). Babinski sign can include dorsiflexion of the great toe alone or in combination with ankle dorsiflexion and hip flexion (triple response). The Babinski sign is determined by the first movement of the great toe; when this movement is definite continuing stimulus is unnecessary. The same reflex can be elicited by stroking the lateral side of the foot (Chaddock's sign), stroking pressure along the tibia crest (Oppenheim's sign), or squeezing the gastrocnemius (Gordon's sign). The Chaddock is probably the most reliable second choice. It is performed by the same stimulus as that used for the Babinski sign applied along the lateral surface of the foot beginning near the heel and extending up to the fifth toe. The stimulus is a slow deep pressure. The examiner may evoke Oppenheim's sign by dragging his knuckles slowly and firmly down the tibia crest from the knee to ankle. An advantage of Chaddock method is a lower chance of eliciting a withdrawal response. Pseudo-Babinski responses may occur in the absence of corticospinal tract disease. Plantar hyperesthesia can lead to an exaggerated response. With a true Babinski sign, there is palpable tonic or clonic contraction of the hamstring muscles. This does not occur in the presence of a pseudo-Babinski sign (Durrant and True 2002).

Certain pathological reflexes may appear in the acute period. One of them is the delayed plantar response, which can occur within hours of spinal cord injury. The delayed plantar response requires a strong stimulus and is triggered by stroking with a blunt instrument upward from the heel toward the toes along the lateral sole of the foot and continuing medially across the metatarsal heads. The response is a slow flexion and relaxation of the toes starting about 0.5 s after the stimulus. The delayed plantar response is present in almost all individuals with complete spinal cord injury, lasting for weeks, and although it can be observed in persons with incomplete injuries, usually transient and rarely lasts more than 7 days in patients with incomplete spinal cord injury (Ko et al. 1999).

A clonus response is a series of abnormal rhythmic involuntary contractions following the brisk passive stretching of a muscle or tendon. Most commonly seen on the ankle after a quick stretch of the gastrocnemius, clonus may also be seen on the patella after stretching the quadriceps and on the wrist or fingers after rapid passive extension. Occasionally, a clonus may occur with slight foot stimulation or with slight stretching of the gastrocnemius when resting the foot. Varying degrees of clonus may occur. Clonus may be sustained or may not be sustained. Sustained clonus is often associated with more severe impairment of the corticospinal tract. A transient unsustained clonus may not always be secondary to disease of the central nervous system (Durrant and True 2002).

11.4.4.3 Other Signs and Tests

The Romberg test is one of the classical tests of proprioceptive sensory loss. This is a test for postural instability that only becomes apparent following closure of the eyes. It is essentially dependent on the integrity of the proprioceptive pathways transmitted through the dorsal columns of the spinal cord. With a disorder of the posterior column of the spinal cord, patients exhibit typical sensory ataxia when there is a lack of visual feedback and compensation for their placement and posture. Truncal ataxia and minor cerebellar signs may be mimicked by the presence of lower motor neuron lesion type weakness, loss of proprioceptive function, or damage of the Clarke's column (the nucleus dorsalis) located at the base of the posterior horns of gray matter, extending from T1 to L2 (L4). When nystagmus occurs in association with cervical cord disease, such as syringomyelia, craniovertebral anomalies, or a tumor, the disease has affected structures rostral to the foramen magnum, particularly in Chiari malformation. Patchy demyelination of the dorsal columns can lead to Lhermitte's phenomenon, with flexion or hyperextension of the neck

accompanied by an electric shock-like sensation with radiation down the back, into the legs, into the arms, or occasionally in the sternum or upwards to the head (Critchley and Eisen 1997). The Lhermitte's sign often occurs in focal traumatic or demyelinating disorders of the spinal cord. Neoplastic disease affecting the spinal cord may also contribute to a Lhermitte's sign. The mechanical stretching of the irritated spinal cord and thecal membranes facilitates axonal discharge and ephaptic transmission. Cervical flexion in combination with a Valsalva maneuver or a supine straight leg raise can help elicit a "slump maneuver" Lhermitte's sign (Durrant and True 2002).

11.4.5 Sensory Assessment

Knowledge of the dermatomal map is crucial for recognizing and localizing spinal cord lesions. Each area of skin may be innervated by several adjacent dorsal root ganglia. Basically, the standard of sensory evaluation in patients with spinal cord injuries is to test for pinprick and light touch on the key areas of the dermatome suggested by the ISNCSCI. Test for vibration or proprioception is optional. Severe proprioception impairment can lead to ataxic gait (sensory ataxia) and Romberg's sign. Sensory dissociation is a term that refers to preservation of the sense of vibration and position and impairment of the perception of pain and temperature. Sometimes a term of sensory dissociation can be used in small-sized syrinx or central cord syndrome, when the senses of the lateral spinothalamic tract (pain and temperature) are impaired or absent and the senses of the anterior spinothalamic tract (light touch and light pressure) are preserved.

Some important features of dermatomal segmentation are as follows: there is no C1 dermatome; on the trunk, the C4 and T2 dermatomes are contiguous; the thumb, middle finger, and fifth finger are innervated by C6, C7, and C8, respectively; the nipple is at the level of T4; the umbilicus is at the level of T10; in the posterior axial line of the leg (medial thigh), the lumbar and sacral dermatomes are contiguous (Byrne et al. 2000). In the embryo, the great toe and tibia lie along the preaxial border, while the little toe and fibula lie along the postaxial border. At the end of the embryonic period (8th week), medial rotation of the lower limb reverses the preaxial and postaxial borders, creating a spiral arrangement of the dermatomes in the lower limb. Therefore, the great toe and tibia are medial, and the little toe and fibula are lateral. Thus, the tibial border is the original preaxial border and the fibular border is the postaxial border of the lower limb. The great toe is supplied by nerves from a more rostral dermatome (L4) rather than the little toe (S1).

References

Bican O, Minagar A, Pruitt AA. The spinal cord: a review of functional neuroanatomy. Neurol Clin. 2013;31:1–18.

Brown PJ, Marino RJ, Herbison GJ, et al. The 72-hour examination as a predictor of recovery in motor complete quadriplegia. Arch Phys Med Rehabil. 1991;72:546–8.

Byrne TN, Bezel EC, Waxman SG. Disease of the spine and spinal cord. Oxford: Oxford University Press; 2000.

Calancie B, Molano MR, Broton JG. Tendon reflexes for predicting movement recovery after acute spinal cord injury in humans. Clin Neurophysiol. 2004;115:2350–63.

Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Cho TA, Bhattacharyya S. Approach to myelopathy. Continuum (Minneap Minn). 2018;24(2, Spinal Cord Disorders):386–406.

Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: nerve injuries research committee. His Majesty's stationery office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 Figures. Brain. 2010;133:2838–44.

Critchley E, Eisen A. Introduction. In: Critchley E, Eisen A, editors. Spinal cord disease. Basic science, diagnosis and mangement. London: Springer; 1997.

Denno JJ, Meadows GR. Early diagnosis of cervical spondylotic myelopathy. A useful clinical sign. Spine (Phila Pa 1976). 1991;(16):1353–5.

Durrant DH, True JM. Myelopathy, radiculopathy, and peripheral entrapment syndromes. Boca Raton: CRC Press; 2002.

Fogarty A, Lenza E, Gupta G, et al. A systematic review of the utility of the Hoffmann sign for the diagnosis of degenerative cervical myelopathy. Spine (Phila Pa 1976). 2018;(43):1664–9.
Houten JK, Noce LA. Clinical correlations of cervical myelopathy and the Hoffmann sign. J Neurosurg Spine. 2008;9:237–42.
Ko HY, Ditunno JF, Graziani V, et al. The pattern of reflex recovery during spinal shock. Spinal Cord. 1999;37:402–9.
Malanga GA, Landes P, Nadler SF. Provocative tests in cervical spine examination: historical basis and scientific analyses. Pain Physician. 2003;6:199–205.
Medical Research Council (Nerve injuries committee). Aids to the examination of the peripheral nervous system. Memorandum No. 45 (superseding War Memorandum No. 7). London: Her Majesty's Stationery Office; 1943.
Nelson CP, Williams JF, Bloom DA. The cremasteric reflex: a useful but imperfect sign in testicular torsion. J Pediatr Surg. 2003;38:1248–9.
Pearce JM. Beevor's sign. Eur Neurol. 2005;53:208–9.
Rumi MM, Yoon ST. Cervical myelopathy. History and physical examination. Semin Spine Surgery. 2004;16:234–40.
Saboe LA, Reid DL, Davis LA, et al. Spinal trauma and associated injuries. J Trauma. 1991;31:43–8.
Shimizu T, Shimada H, Shirakura K. Scapulohumeral reflex. Spine. 1993;18:2182–90.
Soler JM, Previnaire JG, Amarenco G. Dartos reflex as autonomic assessment in persons with spinal cord injury. Spinal Cord Ser Cases. 2017;3:17097.
Spector LR, Madigan L, Rhyne A, et al. Cauda equina syndrome. J Am Acad Orthop Surg. 2008;16:471–9.
van Munster CE, Weinstein HC, Uitdehaag BM, et al. The plantar reflex: additional value of stroking the lateral border of the foot to provoke an upgoing toe sign and the influence of experience. J Neurol. 2012;259:2424–8.
van Gijn JV. Babinski response: stimulus and effector. J Neurol Neurosurg Psychiatry. 1975;38:180–6.
van Gijn J. The Babinski sign and the pyramidal syndrome. J Neurol Neurosurg Psychiatry. 1978;41:865–73.
van Gijn J. The Babinski sign: the first hundred years. J Neurol. 1996a;243:675–83.
van Gijn J. Should the Babinski sign be part of the routine neurologic examination? Neurology. 1996b;66:1607–9.
Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part I, Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976.
Vodusek DB. Bulbocavernous reflex revisited. Neurourol Urodyn. 2003;22:681–2.
Yang CC, Bradley WE. Somatic innervation of the human bulbocavernosus muscle. Clin Neurophysiol. 1999;110:412–8.
Yang CC, Bradley WE. Reflex innervation of the bulbocavernosus muscle. BJU Int. 2000;85:857–63.
Yilmaz U, Yang CC, Berger RE. Dartos reflex: a sympathetically mediated scrotal reflex. Muscle Nerve. 2006;33:363–8.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.
Alpert JN. The neurologic diagnosis. A practical bedside approach. 2nd ed. Cham: Springer; 2019.
American Spinal Injury Association. International standards for neurological classification of spinal cord injury. 8th ed. Revised 2019. Atlanta: American Spinal Injury Association; 2019.
Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.
Crossman A, Neary D. Neuroanatomy: an illustrated colour test. 5th ed. Philadelphia: Elsevier; 2015.
Fulton JF, Keller AD. The sign of Babinski: a study of the evolution of cortical dominance in primates. Springfield: Charles C Thomas; 1932.
Hislop HJ, Avers D, Brown M. Daniels and Worthingham's muscle testing. 9th ed. St. Louis: Elesvier; 2014.
Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia: Elsevier; 2016.
Passias PG, editor. Cervical myelopathy. Philadelphia: Jaypee Brothers Medical Publishers (P) Ltd; 2016.
Patten J. Neurological differential diagnosis. 2nd ed. London: Springer; 1996.
Windle WF. The spinal cord and its reaction to traumatic injury. In: Bousquet WF, Palmer RF, editors. Modern pharmacology-toxicology: a series of monographs and textbooks. New York: Marcel Dekker; 1980.

12 Current Epidemiology of Spinal Cord Injuries

Knowledge of the incidence and prevalence of spinal cord injuries is very important for health care planning. However, there are great variations in the quality of information about the incidence and prevalence of traumatic or nontraumatic spinal cord injuries. Most epidemiological data on the incidence and prevalence provide an extrapolation based on the numbers collected in some clinical centers or based on assumptions about the mean life expectancy of individuals after spinal cord injury. There is also insufficient information whether patients with cauda equina or conus medullaris lesions are classified as spinal cord injury and included in the epidemiological data analysis or not. Most of the epidemiological data describe spinal cord injury due to traumatic injuries. However, it is necessary to include nontraumatic spinal cord injuries with increasing aging population. A global epidemiology study of traumatic spinal cord injuries reported wide ranges across different regions of the world, with an annual incidence rate ranging from 2 to 290 cases per million population and a prevalence varying from 236 to 4200 per million population (Lee et al. 2014).

Data on epidemiology of traumatic spinal cord injury for the United States come mainly from the National Spinal Cord Injury Statistical Center (NSCISC), 14 model systems, and 5 follow-up centers. The NSCISC database contains about 13% of new spinal cord injury cases in the United States. With regard to gender, men are by far more affected by traumatic spinal cord injury. In case of nontraumatic spinal cord injury, the proportion of female is nearly equal to males. The incidence of spinal cord injury in the United States is between 30 and 50 per million per year, with approximately 10,000–12,000 new injuries each year. These numbers do not reflect patients who died at the scene of the accident or before arriving at the hospital (Jain et al. 2015). Motor vehicle accidents are the leading cause of spinal cord injury (38.6%), followed by falls (32.2%), violence (mainly gunshot wound) (14.0%), sports/recreation activities (7.8%), and medical/surgical complications (4.2%) based on data collected since 2015. A recent estimate shows that the annual incidence of spinal cord injury is approximately 54 per million people in the United States, or about 17,810 new cases each year. Spinal cord injury mainly affects young adults between the ages of 16 and 30; the average age at injury has increased from 29 years in the 1970s to 43 years since 2015, of whom 78% are men, 44.6% are single, and 67.3% are employed (NSCISC 2021b). It is estimated that more than 294,000 people with spinal cord injury live in the United States (Lasfargues et al. 1995; NSCISC 2021b).

Unfortunately, there is no global registry for collecting epidemiological data on spinal cord injury. Also, even in industrialized countries, there is often no national registry for spinal cord injuries. Census estimation of the percent-

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age of people with spinal cord injury in the general population is very rare. According to the World Health Organization (WHO) report, 15% of the world's population are affected by disability and less than 0.1% of the population have spinal cord injury (World Health Organization (WHO) 2013).

12.1 Incidence and Prevalence: Traumatic Spinal Cord Injuries

Although the incidence of spinal cord injuries appears to be stable overall, its prevalence is increasing. The global incidence of traumatic spinal cord injuries is estimated to be 23/million in 2007 (Fitzharris et al. 2014). The global prevalence of traumatic spinal cord injury is estimated at 1000/million people (Cripps et al. 2011; Singh et al. 2014). The data is only a rough estimate as valid data is only available in some countries. Therefore, this number should be treated with care. Numbers vary greatly in different parts of the world. The mean incidence of spinal cord injury in developing countries is estimated to be 25.5/million/year with a range between 2.1 and 130.7/million/year. In North America, the incidence of traumatic spinal cord injury is more than twice (40 per million) compared with Western Europe (16 per million) and Australia (15 per million) (Lee et al. 2014) (Figs. 12.1 and 12.2). The estimate of the incidence and prevalence of traumatic spinal cord injuries in Australia of June 30, 2011, was 21.0–32.3 per million per year and 490–886 per million, respectively (New et al. 2015).

According to Dr. Leigh et al. at the National Traffic Injury Rehabilitation Hospital in South Korea, the incidence of traumatic spinal cord injuries in 2018 based on data from three insurance systems covering more than 98% of the total population of South Korea, namely the National Health Insurance (41.26 per million), National Workers' Compensation (5.86 per million), and Automobile Insurance (11.85 per million) is 58.97/million/year (personal communication with Dr. Leigh Nov. 2021). In Japan, the annual inci-

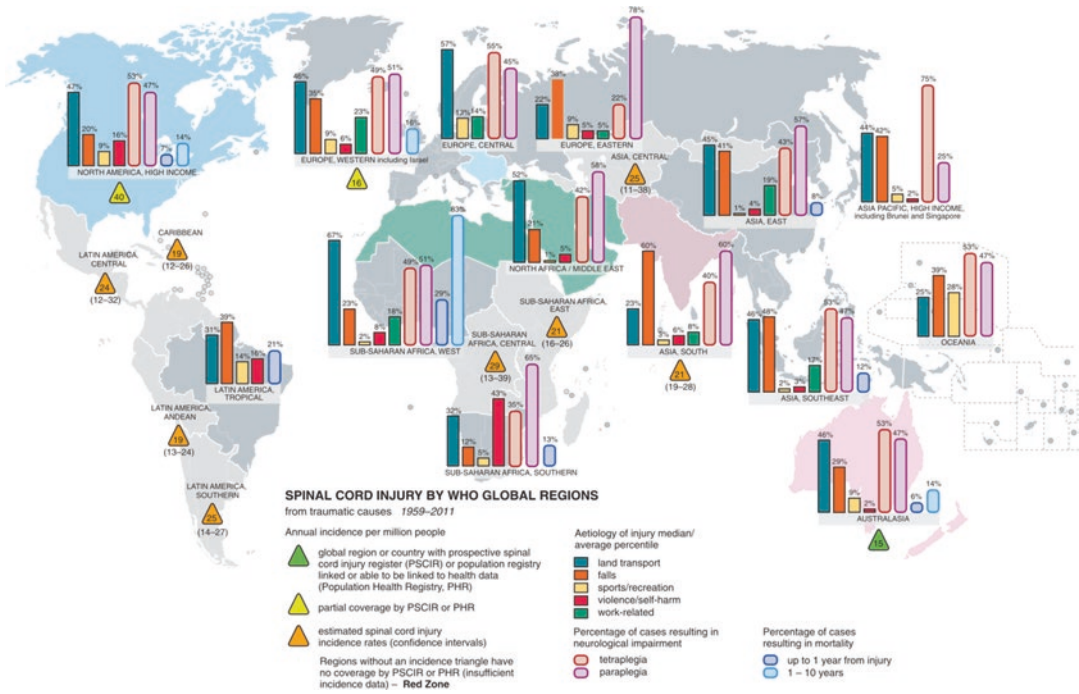

Fig. 12.1 Spinal cord injury by WHO Global Regions from traumatic causes 1959–2011. From Lee et al. (2014), with permission

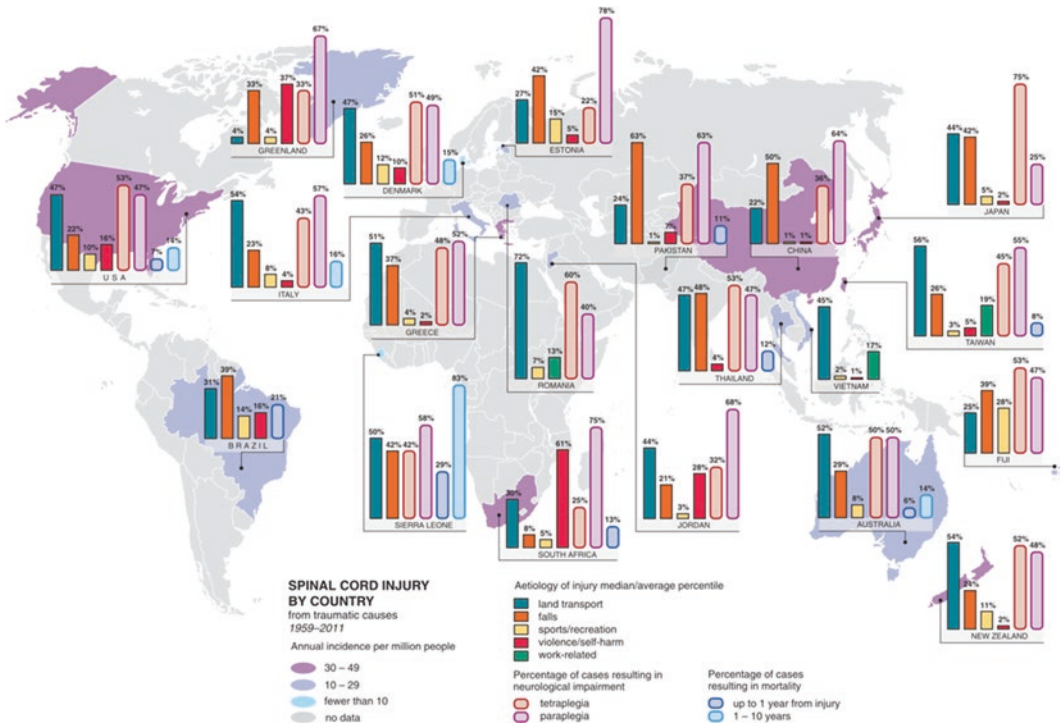

Fig. 12.2 Spinal cord injury by country from traumatic causes 1959–2011. From Lee et al. (2014), with permission

dence of traumatic spinal cord injury, excluding AIS E, was reported to be 49 per million, and the median age was 70.0 years, which is considered to reflect the characteristics of Japan, a super-aged society (Miyakoshi et al. 2021). The incidence of traumatic spinal cord injuries in China showed 66.5 per million in 2018 (Hao et al. 2021).

Worldwide incidence of spinal cord injury is estimated to be 40 and 83 cases per million population per year, with annual estimates of approximately 250,000–500,000 (Wyndaele and Wyndaele 2006). The worldwide incidence of only traumatic spinal cord injury is estimated to be between 10.4 and 83/million/year (Razdan et al. 1994), but these numbers should be interpreted with caution. There are many differences in the incidence of spinal cord injuries as they vary widely depending on various factors. Patients with traumatic spinal cord injury who die at the scene of the accident or die on the way to an emergency room are generally not included in the statistical data analysis. The mortality rate after admission to a hospital is between 4.4% and 16.7%, which is significantly less mortality rates than on site and before arrival at the hospital (Jain et al. 2015). This also applies to patients with terminally ill malignancies associated with spinal cord injury. These facts lead to a systematic bias to the overall incidence of spinal cord injury, resulting in a lower estimate. Technical limitations and a systematic bias may exist in data collection in different countries. Therefore, only a rough estimates are provided.

The number of people living with traumatic spinal cord injury in the United States is estimated at about 273,000, ranging from 238,000 to 332,000. The prevalence of spinal cord injury is the highest in the United States and the lowest in France and Finland (Singh et al. 2014). More than 236 per million have been reported in many parts of the world, but prevalence data is missing from some of the major global populations. An annual incidence of new traumatic spinal cord injuries has increased significantly over the age 55. The proportion of tetraplegia and of incomplete injuries also increased.

12.2 Incidence and Prevalence: Nontraumatic Spinal Cord Injuries

There are few reports of epidemiologic studies on nontraumatic spinal cord injury compared to traumatic spinal cord injury. In Western developed countries, the proportion of nontraumatic spinal cord injuries has increased steadily over the past decade, as demographic changes due to the rapid increase in the elderly population have a profound effect on the cause of spinal cord injury. The incidence of nontraumatic spinal cord injury varies from 12 to 76 per million population (New et al. 2014; Nijendijk et al. 2014; Noonan et al. 2012; O'Connor 2015). Global maps of epidemiological findings of nontraumatic spinal cord injuries (1959–2011) are presented by WHO global regions (Fig. 12.3) and countries (Fig. 12.4), which were produced to compile global data summarizing the epidemiology of nontraumatic spinal cord injuries with a focus on incidence, prevalence, level of injury, etiology, and survival (New et al. 2014). The average age-adjusted incidence rate of nontraumatic spinal cord injury in Victoria, Australia, between 2000 and 2006 was 26.3 cases per million per year for adults and 0.7 cases per million per year for those under 15 years. Nontraumatic spinal cord injury is closely related to age and is more common than traumatic spinal cord injury (New and Sundararajan 2008). The median age of onset of nontraumatic spinal cord injury in Australia is 67 years ranged 52–77 (New et al. 2011). The prevalence of nontraumatic spinal cord injury in Victoria, Australia, in June 2010 was 367.2 per million (New et al. 2013). In the Norwegian Spinal Cord Injury Registry, the average age of people with nontraumatic spinal cord injury was 55 years and 59% were male. The incidence of nontraumatic spinal cord injury was 7.7–10.4 per million per year, which is lower than the incidence of traumatic spinal cord injury. People with nontraumatic spinal cord injury were older, less severely injured, and their length of hospital stay was shorter than people with traumatic spinal cord injury (Halvorsen et al. 2019).

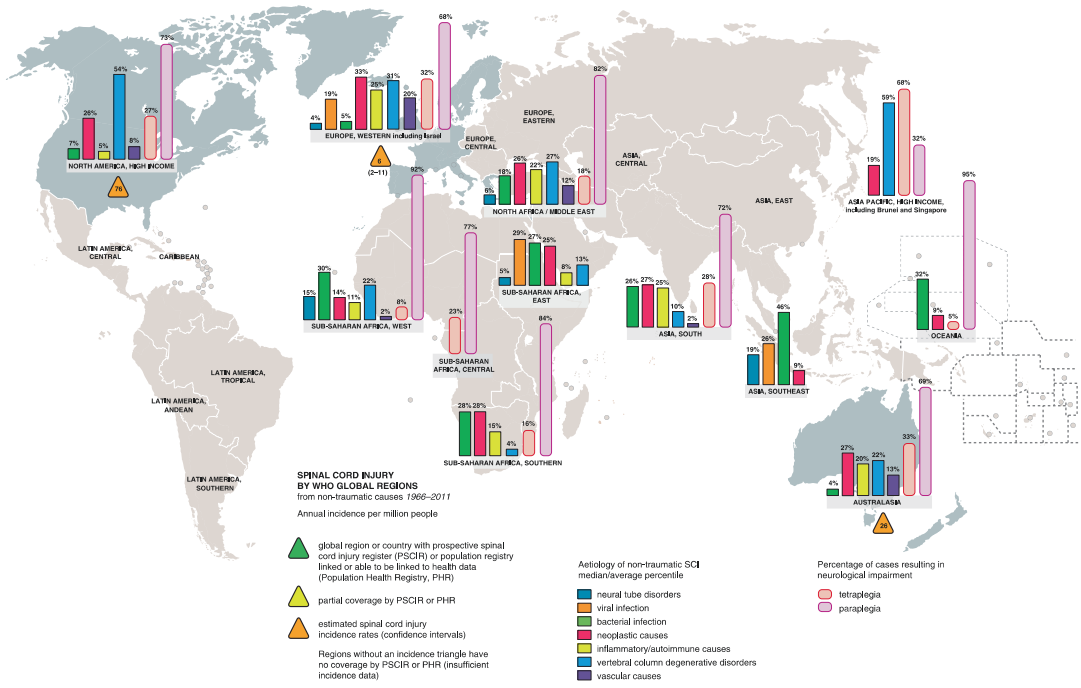

Fig. 12.3 Global maps of nontraumatic spinal cord injury epidemiological outcomes (1959–2011) by WHO global regions. From New et al. (2014), with permission

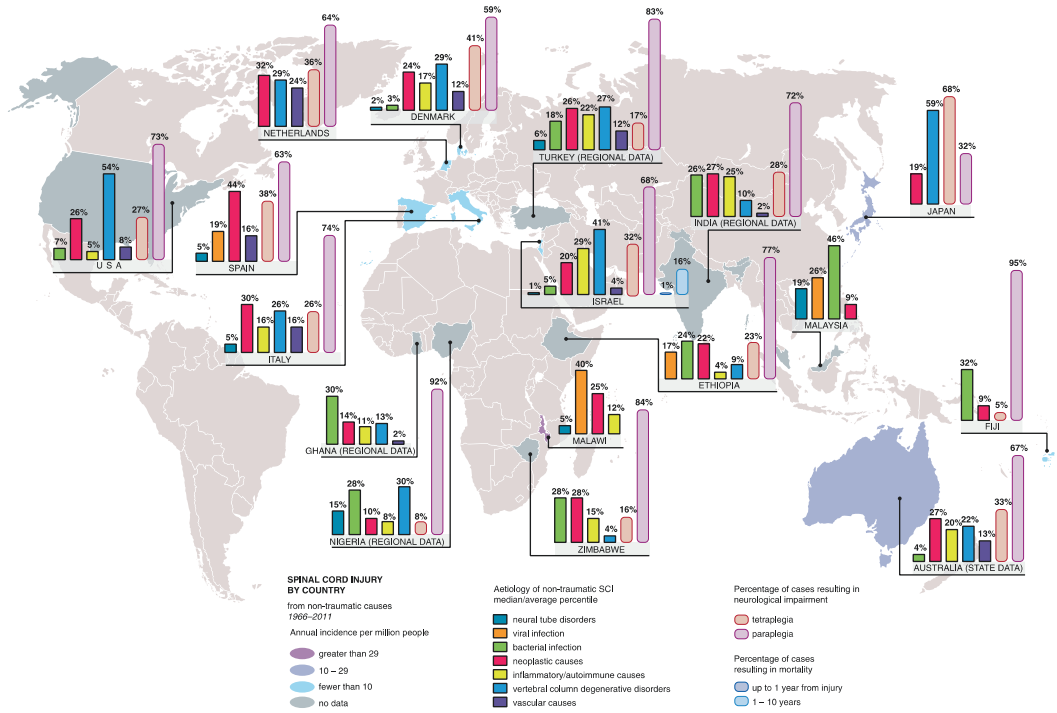

Fig. 12.4 Global maps of nontraumatic spinal cord injury epidemiological outcomes (1959–2011) by country. From New et al. (2014), with permission

The majority of people with traumatic spinal cord injury are male (male/women = 3:1), whereas in nontraumatic spinal cord injuries, it is almost equally distributed. Worldwide nontraumatic spinal cord injury increases significantly with the number of high-level tetraplegic patients requiring artificial ventilation. In general, the proportion of patients with tetraplegia has increased, and nowadays, it is equal to that of paraplegic patients. Most traumatic spinal cord injuries occur at younger ages below the age 30, whereas nontraumatic spinal cord disease occurs in elderly people over 55 years of age (DeVivo and Vogel 2004; Vogel et al. 2012).

12.3 Age at Injury

Spinal cord injuries affect young adults with the highest incidence rates in the late teens and the early 20s. The average age at injury for traumatic spinal cord injury increased from 28.3 to 37.1 years in the United States between 1970 and 2005 (DeVivo 2012; DeVivo and Chen 2011). It has been reported to be 42.6 years since 2010. The percentage of new injuries that are at least 60 years of age will continue to increase by 2% over the next decade and lesser amounts thereafter (Chen et al. 2015; Chen et al. 2013; DeVivo 2012). The mean age at traumatic spinal cord injuries in the United States between 2015 and 2020 was 43.2 years (NSCISC 2021a) (Fig. 12.5). A Canadian study reports a greater increase in age at injury from 34.5 to 45.5 years between 1995 and 2004. A bimodal peak in traumatic spinal cord injury between the ages of 15 and 35 years and a second, smaller peak at age 65 to 74 years are observed. It is expected the average age at injury will continue to increase by 2 years in the next decade and lesser amounts each decade through at least 2050 (Lenehan et al. 2012). Factors that can contribute to this trend might include changes in age-specific incidence rates, general population age, and survival rates of the elderly at injury.

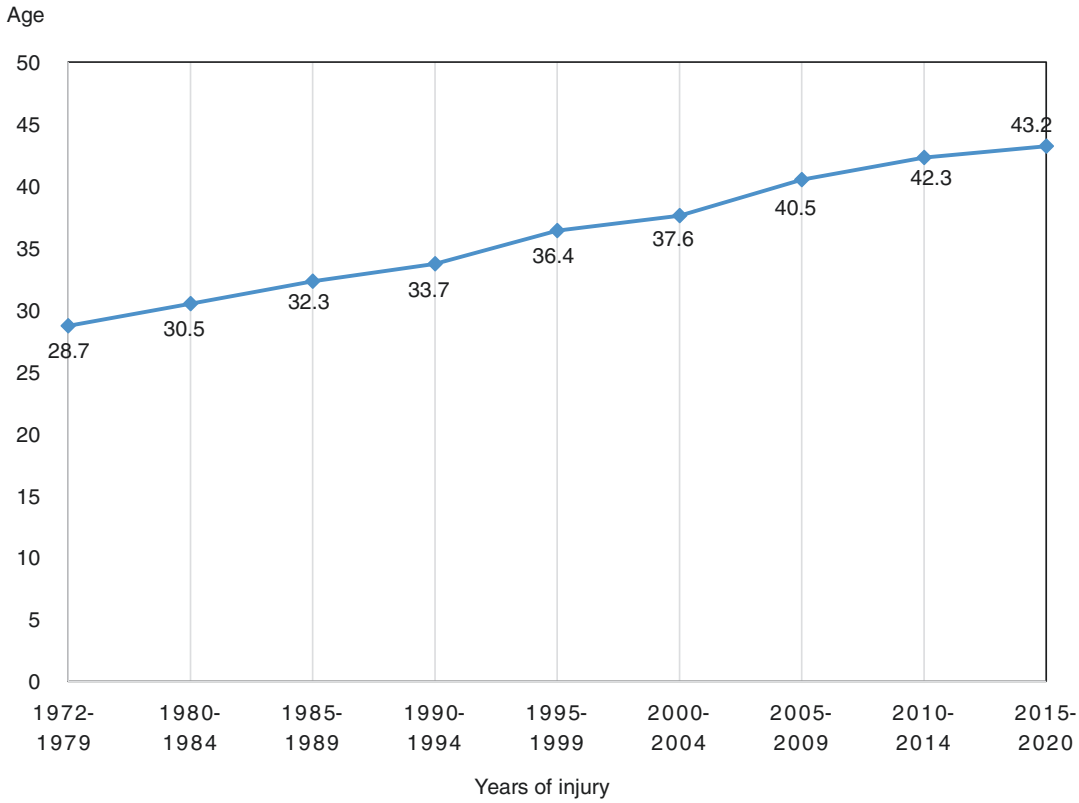

Fig. 12.5 Trends in age by year of injury. From NSCISC (2021a)

12.4 Cause of Injury

The most common causes for traumatic spinal cord injury are traffic accidents, falls, and results of violence. Motor vehicle accidents are the leading cause of spinal cord injury in the United States, accounting for about 36.6% in the database since 2010 (DeVivo and Chen 2011) and 32.0% according to the 2020 annual NSCISC report. Falls (23.1%) are the second common cause and have been increasing over time in the United States, followed by violence, mainly due to gunshot wounds and sports. Falls are a major cause of spinal cord injury in the elderly, 53.9% in 61–75 years and 66.7% over 76 years (Fig. 12.6). Violence as a cause of spinal cord injury, peaked in the 1990s, but has declined. Sports injuries have decreased slightly (Fig. 12.7). The percentage of injuries resulting from vehicular accidents, violence, and sports differed by sex. Women are more likely to be injured by a vehicular accident (females, 51.4%; males, 39.6%), but violence and sports are more likely the cause of male injuries (males, 18.4% and 11.1%, respectively; females, 11.2% and 5.6%, respectively) (NSCISC 2021a) (Fig. 12.8).

The main causes of nontraumatic spinal cord injuries are degenerative diseases and tumors in developed countries and infections, particularly tuberculosis and HIV, in developing countries. A study of 134 adults with nontraumatic spinal cord injury in a spinal cord injury unit in Australia showed the following etiologies: tumor (20.1%), multiple sclerosis (19.4%), degeneration (17.9%), vascular (11.9%), transverse myelitis (8.2%), and others (New et al. 2002).

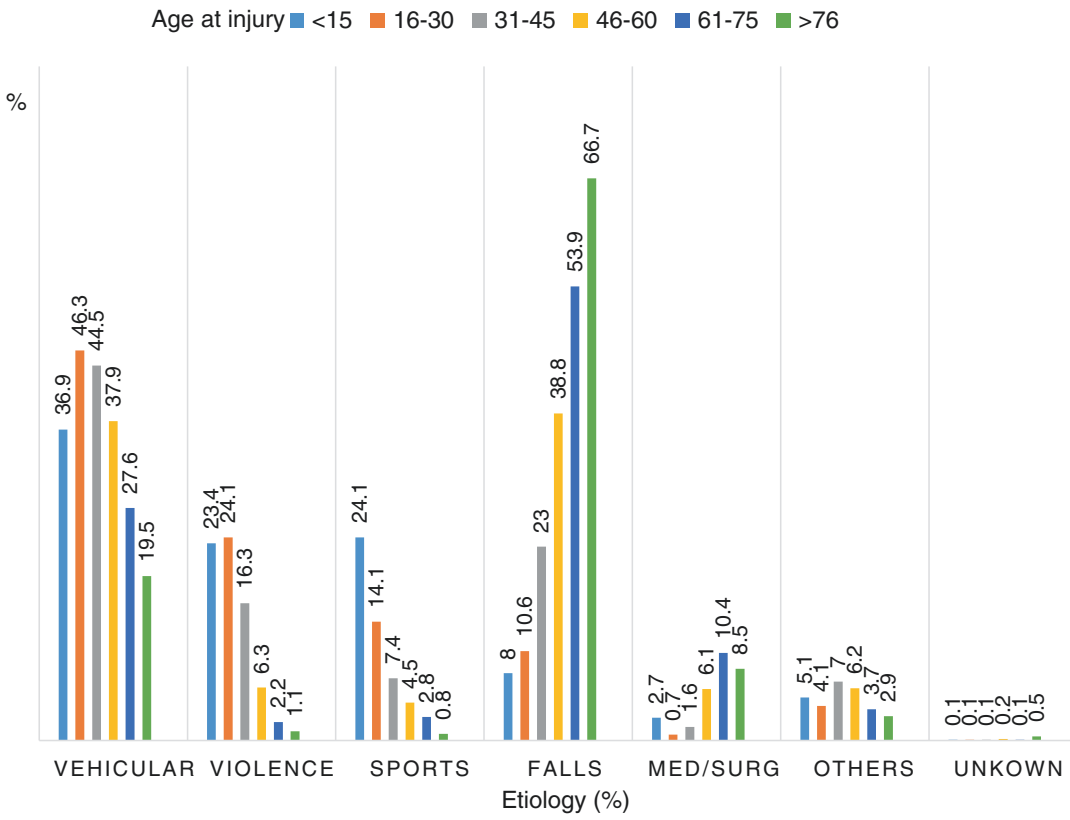

Fig. 12.6 Grouped etiology by age at injury. From NSCISC (2021a)

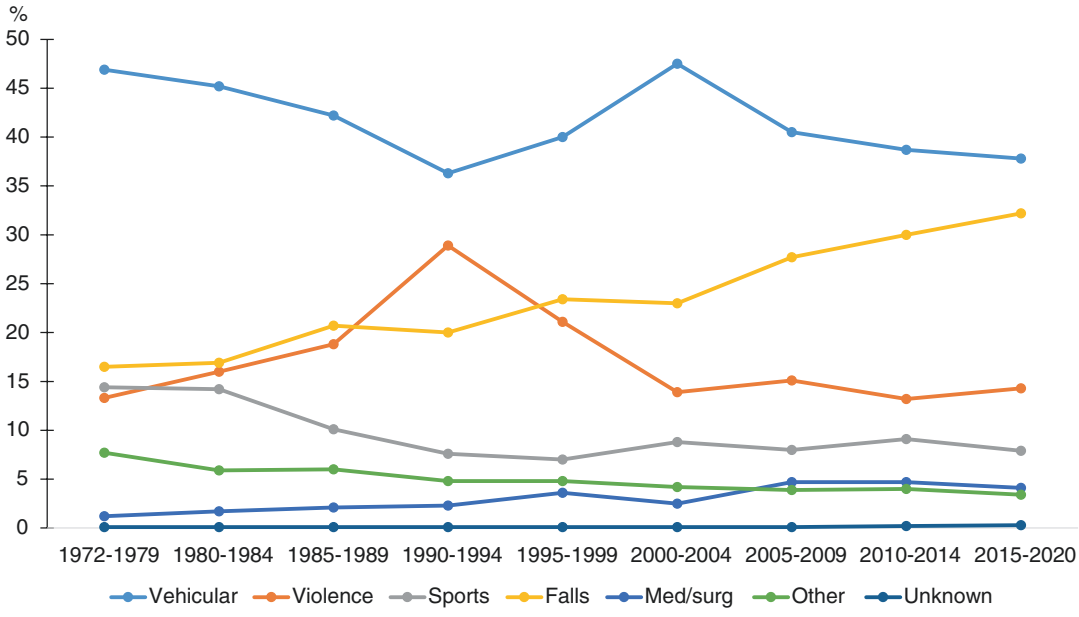

Fig. 12.7 Trend in grouped etiology by year of injury. From NSCISC (2021a)

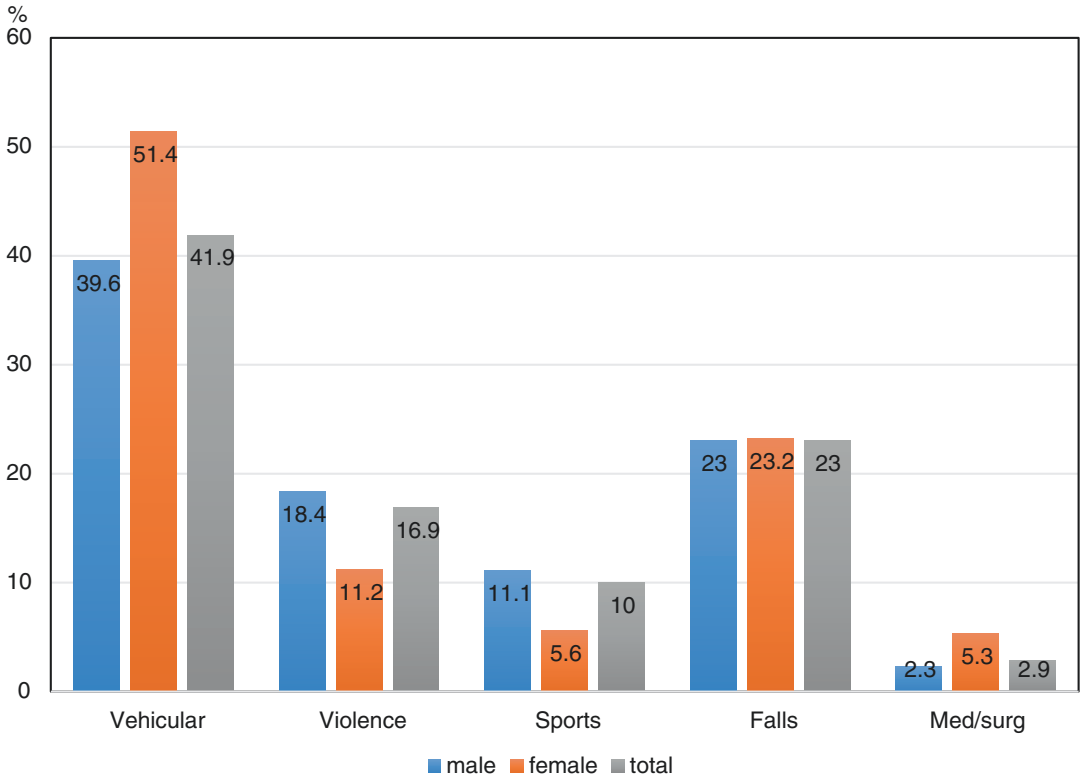

Fig. 12.8 Grouped etiology of spinal cord injury by sex. From NSCISC (2021a)

12.5 Type of Injuries

Cervical spine injuries are 54.3% of all traumatic spinal cord injuries, followed by thoracic (34.9%) and lumbosacral (10.4%) injuries (DeVivo 2012; Lenehan et al. 2012; NSCISC 2021a). Over the years, there has been a slight increase in the proportion of cervical injuries. The most common level of injury at discharge is C5 (15.1%), followed by C4, C6, T12, C7, and L1. Cervical injuries are most often either AIS A or D (NSCISC 2021a). Thoracic injuries are most likely AIS A. There is an increasing trend in the number of patients on the ventilator at discharge due to increased C1–C4 injuries and decreased C5–C8 neurological level of injury (DeVivo 2012; DeVivo and Chen 2011). The percentage of persons with high cervical injuries (C1–C4) increased from 12.3% in the 1970s to 27.2% since 2005. Ventilator dependency increased from 1.5% to 4.6% (DeVivo and Chen 2011).

Complete spinal cord injuries have decreased over time. According to US data, a decrease in complete injuries from 56% in the 1970s to 47% in the late 2000s has been reported (DeVivo 2012; DeVivo and Chen 2011). Incomplete tetraplegia is the most common injury, followed by complete paraplegia, complete tetraplegia and incomplete paraplegia (Jackson et al. 2004). The proportion of incomplete injuries has been increasing. There is a strong relationship between injury severity and age. Older individuals are most likely to have incomplete tetraplegia due to low-energy falls and underlying spinal degeneration (Lenehan et al. 2012).

12.6 Causes of Death

Although the survival of persons with spinal cord injury has improved dramatically in recent decades, there remains an increased risk of premature death due to, for example, pneumo-

nia or suicide. The main causes of long-term death for people with spinal cord injuries have changed from urological complications to cardiovascular and pulmonary diseases (van den Berg et al. 2010).

Mortality from spinal cord injury peaks during the initial hospitalization and period of treatment. Pneumonia, heart disease, accidents, poisoning, and septicemia are the leading causes of death in these patients. In the past, renal failure was once the leading cause of death, but diseases of genitourinary system as a cause of death have dramatically decreased over the last 40 years in relation to improvements in urological care. Genitourinary complications continue to be among the leading causes of morbidity, in addition to pulmonary complication, pressure injuries, deep vein thrombosis, and musculoskeletal complications such as heterotopic ossification and contractures. Complete spinal cord injury is more likely to occur in earlier death than an incomplete spinal cord injury. Several studies have shown that the causes of death in paraplegic patients are similar to the general population. Ischemic heart or brain events, tumors, and chronic obstructive lung disease are now common causes of death. However, about 15% of patients with spinal cord injury still die from pressure injuries and their medical consequences. A high number of pulmonary complications in tetraplegia have been consistently identified as a major cause of death.

According to causes of death following spinal cord injuries by a Dutch cohort study, the main causes of death were cardiovascular disease (37.0%), pulmonary disease (29.6%), and neoplasm (14.8%). In the US study, diseases of the respiratory system (21.4%) are the leading cause of death in people with spinal cord injuries. Of these, 65.2% are pneumonia. The second most frequent cause of death is infective and parasitic diseases (12.0%). This is usually caused by septicemia (90.6%) and is usually associated with pressure injuries, urinary tract infections, or respiratory infections. AIDS (5.0%) is also included in this category (Table 12.1). Cancer is the third most common cause, most prevalently lung cancer, followed by hypertensive and ischemic heart disease. Specific locations of cancer included the lungs (25.4%), followed by the bladder (9.1%), the colon/rectum (8.7%), the prostate (5.5%), and the liver (4.2%). Unintentional injuries are the sixth leading cause of death, followed by diseases of the digestive system, cerebrovascular disease, suicide, and diseases of pulmonary circulation. Pulmonary emboli account for 91.7% of the diseases of pulmonary circulation (NSCISC 2021a). In the first year after injury, the top five causes of death are respiratory diseases (31.1%), other heart diseases (13.8%), infective and parasitic diseases (9.4%), disease of pulmonary circulation (8.9%), and hypertensive and ischemic heart diseases (6.7%). Among those who survived the first year after injury, respiratory diseases are the leading cause of death (19.9%), followed by infective and parasitic diseases (12.4%), cancer (11.8%), hypertensive and ischemic heart diseases (10.9%), and other heart diseases (7.4%) (NSCISC 2021a).

In the last 40 years since the national spinal cord injury database in 1973, pneumonia and septicemia were the most common causes of death, which had the greatest impact on the

Table 12.1 Primary cause of death

Primary cause of death	Overall (%)	≤1 year	>1 year
Diseases of the respiratory system	21.4	31.1	19.9
Infective and parasitic diseases	12.0	9.4	12.4
Neoplasms	10.8	4.2	11.8
Hypertensive and ischemic heart disease	10.4	6.7	10.9
Other heart disease	8.3	13.8	7.4
Unintentional injuries	6.7	2.7	7.3
Diseases of the digestive system	4.9	3.4	5.1
Cerebrovascular disease	3.5	3.2	3.6
Suicide	3.0	1.4	3.2
Disease of pulmonary circulation	2.9	8.9	2.0
Diseases of the genitourinary system	2.9	2.6	2.9
Endocrine, nutritional, metabolic and immunity disorders	2.8	1.6	3.0

From NSCISC (2021a)

diminished life expectancy of this population. Mortality rates for cancer (Nahm et al. 2015), heart disease, stroke, arterial disease, pulmonary embolus, urinary tract disease, digestive diseases, and suicide are on the decline. However, these gains are offset by an increase in endocrine, metabolic, and nutritional disease mortality rates, accidents, nervous system disorders, musculoskeletal disorders, and mental disorders. The mortality rate for septicemia has not changed over the past 45 years, and mortality from respiratory disease has decreased only slightly. Regardless of the severity and the level of injury, there is evidence that incidence of suicide is a higher cause of death in people with spinal cord injuries than in the general population (Cao et al. 2013; McCullumsmith et al. 2015). Suicide accounts for about 3.0% of deaths (NSCISC 2021a). The suicide rate is about five times higher than the general population and the highest risk for the first 5 years. A higher suicide rate is reported in complete paraplegia (Cao et al. 2013; McCullumsmith et al. 2015).

12.7 Life Expectancy

Spinal cord injury due to pneumonia, pressure ulcers, or lower and upper urinary tract infections was fatal within days to months, depending on the neurological level of injury and severity. The advancement in the second half of the twentieth century in the development of surgical stabilization options and intensive care medicine and the strong desire not to accept the inevitable fate of victims of spinal cord injury have led to the introduction of rehabilitative and neurological therapies. These factors have fundamentally changed the situation of individuals suffering from the sequels of spinal cord injury. As a result, the life expectancy of people with traumatic spinal cord injury has steadily increased over the last 70 years (Middleton et al. 2012). However, the mortality rate in the spinal cord injury population is higher compared to the general population. Although advances in medical management have increased survival following spinal cord injury, overall life expectancy is still lower compared to the general population, particularly for persons with tetraplegia and ventilator dependency (DeVivo 2012; Shavelle et al. 2015a). Life expectancy following spinal cord injury is much lower in developing countries, particularly for individuals with tetraplegia (Lee et al. 2014).

The life expectancies for people with spinal cord injuries remain substantially below normal, particularly with tetraplegia and ventilator dependency. Although mortality rate has been steadily decreasing in the first post-injury since the 1970s, the annual mortality rate after the first post-injury year has not changed since the first year after the injury since the early 1980s. Therefore, although the life expectancy of the general population is generally increasing, life expectancy for persons with spinal cord injuries surviving the first year after injury has remained relatively constant, and the difference in life expectancy between persons with spinal cord injuries and the general population of comparable age, sex, and race is increasing (Shavelle et al. 2015a, b).

Crude standardized mortality ratios show that the overall mortality rate of patients with spinal cord injuries is up to three times higher than in the general population. Survival rates were statistically significantly lower in nontraumatic spinal cord injury than in traumatic spinal cord injury. Age at injury, neurological level of the lesion, extent of lesion, and year of injury were described as predictors of survival (van den Berg et al. 2010). In patients with spinal cord injuries who do not use a mechanical ventilator, life expectancy decreases by 4–5 years compared to the age of the general population. Overall, the life expectancy of patients with spinal cord injuries has been gradually increased but is shorter than the general population, accounting for approximately 80% of the general population. It is reported that the life expectancy of patients with paraplegia is about 4 years longer than that of patients with tetraplegia. In patients with spinal cord injuries AIS A–C, patients who were injured at the age of 20 will survive approximately 32.5 years with C1–C4, 39.2 years with C5–C8, and 44.8 years with paraplegia. This can be considered to be about 15–25 years shorter, considering that the life

Table 12.2 Life expectancy for persons with SCI surviving at least 24 h post-injury

		AIS D	AIS ABC			Vent dependent
Age at injury	No SCI	Any level	T1–S3	C5–C8	C1–C4	Any level
10 years	69.2	61.6	53.9	48.3	41.1	16.2
15 years	64.2	56.7	49.1	43.5	36.5	12.2
20 years	59.4	52.1	44.8	39.2	32.5	10.0
25 years	54.7	47.7	40.8	35.4	29.3	9.5
30 years	50.0	43.5	37.1	31.8	26.3	10.6
35 years	45.3	39.2	33.3	28.3	23.5	10.0
40 years	40.7	35.0	29.6	24.8	20.7	8.7
45 years	36.1	30.8	26.0	21.5	18.3	7.9
50 years	31.6	26.7	22.4	18.2	15.4	6.2
55 years	27.4	22.9	19.0	15.4	12.9	4.6
60 years	23.3	19.4	16.1	13.1	11.2	3.7
65 years	19.4	15.9	13.0	10.5	9.0	2.8
70 years	15.7	12.6	10.1	8.0	6.7	1.9
75 years	12.3	9.5	7.4	5.7	4.7	1.1
80 years	9.2	6.9	5.2	3.8	3.1	0.5

Values for persons with no SCI are from the 2017 life tables for the US general population
From NSCISC (2021a)

expectancy of the general population after age 20 is about 59.4 years (NSCISC 2021a) (Table 12.2).

12.8 Prognosis and Recovery After Spinal Cord Injury

The standards for clinical evaluation by segmental motor and sensory testing, the International Standards for Neurological Classification of Spinal Cord injury (ISNCSCI), lead to a five-grade impairment scale (A–E), ASIA Impairment Scale (AIS), which was jointly produced by the American Spinal Injury Association (ASIA) and the International Spinal Cord Society (ISCoS). It replaced earlier systems, the first of which was established in Stoke Mandeville by Dr. Frankel in 1969 (Frankel et al. 1969). This standardized assessment can predict clinical recovery and emphasizes the incompleteness of the lesion classified as the presence of sacral sparing (Kirshblum et al. 2011; Waters et al. 1991). Prognosis and recovery of acute traumatic spinal cord injuries depend mainly on the severity and on the level of injury. Persons who are motor complete with extended zones of sensory preservation but have no sacral sparing are less prone to becoming motor incomplete that they have sacral sparing of sensation (Curt et al. 2008; Kirshblum and O'Connor 2000; Marino et al. 1999).

Traumatic spinal cord injuries usually produce diffuse and irregularly damaged zones of the spinal cord over 2–3 segments or more, which are reflected by a zone of partial preservation. Traumatic spinal cord injuries represent a complex and combined injury of the spinal cord segments and peripheral neural structures (Dietz and Curt 2006). The distribution and extent of segmental damage are very important for recovery if spinal cord injury is incomplete. In addition to the severity and completeness of the lesion, clinical spinal cord syndromes are relevant as they may show pronounced recovery patterns due to the specific epidemiology and anatomical distribution of lesion in the spinal cord (McKinley et al. 2007).

Individuals with paraplegia are less likely to convert from complete to incomplete. Conversion to incomplete occurs more frequently as the level of injury is lower. In persons with high paraplegia (T2–T5), 9% are converted to incomplete compared to 16% of persons with midlevel paraplegia (T6–T9) and 29% of those with low paraplegia (T10–T12) (Zariffa et al. 2011). Among the components of the neurological examination for the lowest sacral segment, i.e., pin prick, light touch, deep anal pressure, and voluntary anal contraction (VAC), it has been reported that the more the other components are spared, including VAC, the better the prognosis for recovery. The initial sparing of all sacral sensory components correlated

with the greatest conversion to motor incomplete status at discharge and at 1 year. In patients with initial AIS C, it was most often observed that the presence of VAC in combination with other sacral sparing components improved to AIS D status at discharge. However, the presence of VAC alone as an initial sacral sparing component had the worst prognosis for recovery to AIS D. The presence of VAC alone does not appear to be a positive predictor of subsequent recovery in people with initial AIS C (Kirshblum et al. 2016).

12.8.1 Sensory Recovery

Sensory improvement in traumatic spinal cord injury is poor. Differences between tetraplegic and paraplegic subjects revealed only minor significant improvement, but not between complete and incomplete spinal cord injury. The light touch sensation was significantly increased in tetraplegia AIS A and C, whereas light touch sensation on average of all tested segments remained unchanged in most paraplegic patients. Pin prick was more stable and increased only moderately in tetraplegia AIS C patients (Curt et al. 2008).

12.8.2 Motor Recovery

Knowledge of motor recovery outcomes is particularly important for the prediction of functional outcomes since neurological/motor function is a major determinant of overall function in patients with spinal cord injuries. Neurological impairment is determined by the ISNCSCI (Chap. 7). The ISNCSCI examination performed after 72 h can be used to estimate prognosis for neurological recovery. For example, the reliability of earlier examination in the first 24 h is reduced because of several factors such as sedation, pain, intoxication, hemodynamic instability, and anxiety that may influence the examination results.

After a spinal cord injury, depending on severity and level of injury, motor, sensory, and functional recovery begins (Curt et al. 2008; Geisler et al. 2001; Marino et al. 1999). Factors that influence motor recovery of injury in tetraplegia include initial motor level, severity of injury, and length of the motor zone of partial preservation (Waters et al. 1998). Regardless of the level of injury and severity, most improvements are observed within 1 year of injury, with a steeper curve of recovery of strength and motor scores during the 3 months (Curt et al. 2008). However, late improvements are seen between 1 and 5 years after spinal cord injury, while the functional significance of these changes remains unclear (Kirshblum et al. 2004). The relative improvement of motor function is greater in the incomplete spinal cord injury and greater in tetraplegia than in paraplegic subjects (Curt et al. 2008). Spontaneous neurological recovery of 1–2 spinal cord segments was observed within 1–2 years after spinal cord injury (Marino et al. 1999; Waters et al. 1993). A motor-level deterioration is much less frequent (4.6%) but is more prevalent in lower cervical lesion (C6 or C7) and usually occurs within the first 4–8 weeks (van Hedel and Curt 2006). A gain of 1 or 2 motor segments was a highly significant improvement for a patient suffering from a complete spinal cord injury (Kramer et al. 2012; Steeves et al. 2011).

Individuals with complete tetraplegia and motor levels from C4 to C7 gain an average of 10 motor points 1 year post-injury. All persons with complete tetraplegia improved a motor level, with 70% at least one motor level and 20–30% two or more levels (Marino et al. 2011; Steeves et al. 2011). The distribution of gained motor score may be more functionally important than a given sum of improved motor score. Functional recovery does not just depend on the recovery of the motor score. There is no age-related difference in the recovery of motor score, but there is a significant age effect on the level of functioning (Jacob et al. 2009; Wilson et al. 2014; Wirth et al. 2008).

12.8.3 Recovery in Zone of Injury

Recovery of motor function in the zone of injury in complete tetraplegia has been studied. Since there is no key muscle in the thoracic segments

and lesions of lumbar level are usually associated with cauda equina injuries, so it is not possible to clinically assess the motor recovery of zone of injury in paraplegia. Although less than 10% of individuals with complete tetraplegia gain motor recovery in the legs, most patients with complete tetraplegia gain motor function in the upper extremity within two to three motor segments below the initial neurological level, and one level of motor is obtained as definition of neurological level of injury in ISNCSCI after injury (Marino et al. 1999, 2011).

Muscles with some motor power below an antigravity muscle, i.e., grade 1 or 2 strength, have a better prognosis than those without motor power. Studies have shown that 90% reach antigravity strength for up to 1 year when the next rostral key upper extremity muscle has some initial strength of grade 1 or 2. If the next rostral muscle has initial strength of 0, 45% will gain antigravity strength by 1 year and 64% for antigravity strength over 2 years (Marino et al. 2011).

12.9 Prognosis of Ambulation Function

Factors associated with ambulation after spinal cord injury include initial AIS grade, age, initial lower extremity strength, and type of sensory sparing. The chance of ambulating after spinal cord injury depends on AIS grade. For persons with AIS A injuries, only 3% will walk, and it increases to 50% for AIS B, 75% for AIS C and 95% for AIS D (van Middendorp et al. 2011). If some preservation of pin prick sensation in the lower extremities or sacral region is maintained, recovery of ambulation for persons with AIS B will be improved. 66–89% of persons with AIS B and pin prick preservation recover the ability to walk, compared with 11–33% for those with only light touch preserved (Scivoletto and Di Donna 2009). This can be partially explained by that the lateral corticospinal tract is very close to the spinothalamic tract. Age is one of most important factors influencing ambulation potential. People of young age with AIS C have a positive relationship with ambulation. 70–90% of people under the age of 50 with AIS C will walk, while persons over the age of 50 will recover their ability to walk only 25–40% (Scivoletto and Di Donna 2009).

Only 3% of the patients with AIS A spinal cord injury in the initial examination have enough strength to ambulate within 1 year after injury. Overall, about 50% of those initially classified as AIS B will become ambulatory. Those AIS B individuals with preserved sacral pin prick sensation will have a better prognosis for lower extremity recovery approaching that of motor incomplete individuals, while prognosis for recovery of ambulation in patients without pin prick sensation is between 10% and 33%. In patients with AIS C, approximately 75% will become community ambulators. A community ambulator is defined as an ability to walk 150 feet (46 m) or more and ability to transfer from sitting to standing and ability to don and doff the orthoses independently. Age and the amount of preserved spinal cord function below the lesion affect the recovery of ambulation (Hussey and Stauffer 1973). The greater the amount of function preserved, the better the prognosis for recovery of ambulation. The prognosis of patients above 50–60 years is not good. Those who were initially classified as AIS D have an excellent prognosis for walking, about 95% (van Middendorp et al. 2011). The prediction rule for independent ambulation outcomes after traumatic spinal cord injuries consists of five prognostic parameters: age (<65 vs. ≥65 years of age); motor scores of the quadriceps femoris (L3) and gastroc-soleus (S1); and light touch sensation of dermatomes L3 and S1 (van Middendorp et al. 2011).

While few patients with complete tetraplegia or complete paraplegia achieve significant improvement in motor score of the lower extremity over time, patients with incomplete tetraplegia or incomplete paraplegia gain an average of 12 points motor score in the lower extremity between 1 month and 1 year after injury. The motor score in the lower extremity 30 days after the injury was used to predict likelihood of community ambulation at 1 year. Patients with incomplete tetraplegia require more lower extremity strength to ambulate than patients with paraplegia because of decreased upper extremity weight-bearing ability.

12.10 Days Hospitalized at Acute and Rehabilitation Units

The median length of stay of the acute care decreased from 24 days in the period 1972–1979 to 11 days in the period 2015–2020. People with complete tetraplegia typically had the longest acute stays (an average of 25 days for all years), while those with minimal deficits had the shortest stay. The median rehabilitation length of stay also decreased from 91 days in 1972–1979 to 42 days in 2015–2020. The median days in the rehabilitation unit were greatest in those with complete tetraplegia (an average of 93 days for all years), ranging from 122 days in 1972–1979 to 64 days in 2005–2009, with a slight increase to 68 days for 2010–2014. For people with incomplete paraplegia, the rehabilitation length of stay ranged from 68 days in 1972–1979 to 33 days in 2015–2020 (NSCISC 2021a) (Fig. 12.9).

12.11 Place of Residence at Discharge

Most of people (87.4%) with spinal cord injuries were discharged to private residences. The proportion of people discharged to private residences ranged from 74.0% to 94.1%. The year following the injury, private residence was most common, ranging from 91.5% in the first year after injury to 97.3% in the 35th and 40th years after injury. The percentage of those reporting being in a nursing home residence has decreased over time, from 3.9% in the first year after injury to 1.2% in 35 and 40 years after injury (NSCISC 2021a).

12.12 Return to Work

The percentage of working over the post-injury years increases from 12.7% in the first year after injury to 33.7% in 25 years after injuries and then decreases to 27.6% in the later years for 40 years after injuries (NSCISC 2021a). However, relatively few persons are likely to return to their previous job, and many will return to less physically demanding jobs (Lidal et al. 2007). A study for the employment situation of people with spinal cord injury in 22 countries showed 38%, ranging from 10.3% to 61.4%, in which the observed employment was defined as performing paid work at least 1 h a week (Post et al. 2020).

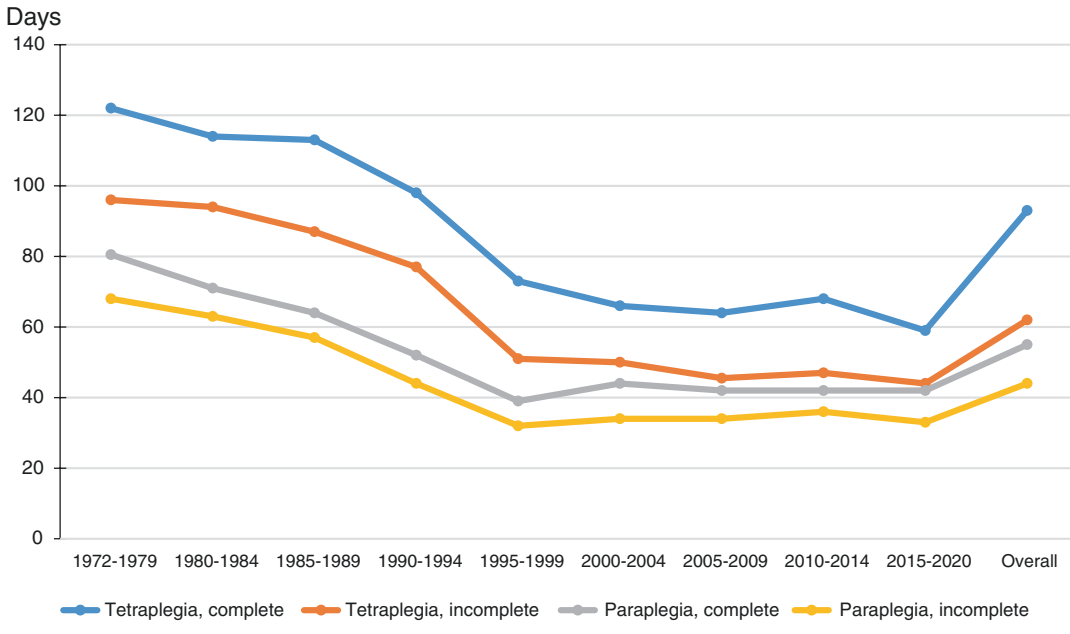

Fig. 12.9 Median days in the rehab unit by year of injury and neurologic category. From NSCISC (2021a)

The unemployed persons had medical complications more often. Pressure injuries, respiratory problems, serious urinary tract infections, spasticity, and hospitalization were related to the employment rate. The bowel continence has become an important predictors of employment. The most frequently reported employment barriers included transportation problems, health and physical limitation, lack of work experience, education or training, physical or architectural barriers, discrimination by employers, and loss of benefits (Lidal et al. 2007).

Many persons with disabilities benefit from home working employment. Telework can provide an opportunity for homework, and it can be a strategy for patients with spinal cord injury to return to work. The clear advantages of home-based teleworking are low dependency on transportation, community accessibility, less focus on physical limitations and medical complications, and decreased self-efficacy, as well as possible employer biases (Lidal et al. 2007).

References

Cao Y, Massaro JF, Krause JS, et al. Suicide mortality after spinal cord injury in the United States: injury cohorts analysis. Arch Phys Med Rehabil. 2013;95:230–5.

Chen Y, Tang Y, Vogel LC, et al. Causes of spinal cord injury. Top Spinal Cord Inj Rehabil. 2013;19:1–8.

Chen Y, Tang Y, Allen V, et al. Aging and spinal cord injury: external causes of injury and implications for prevention. Top Spinal Cord Inj Rehabil. 2015;21:218–26.

Cripps RA, Lee BB, Wing P, et al. A global map for traumatic spinal cord injury epidemiology: towards a living data repository for injury prevention. Spinal Cord. 2011;49:493–501.

Curt A, Van Hedel HJ, Klaus D, et al. Recovery from a spinal cord injury: significance of compensation, neural plasticity, and repair. J Neurotrauma. 2008;25:677–85.

DeVivo MJ. Epidemiology of traumatic spinal cord injury: trends and future implications. Spinal Cord. 2012;50:365–72.

DeVivo MJ, Chen Y. Trends in new injuries, prevalent cases and aging with spinal cord injury. Arch Phys Med Rehabil. 2011;92:332–8.

DeVivo MJ, Vogel LC. Epidemiology of spinal cord injury in children and adolescents. J Spinal Cord Med. 2004;27(Suppl 1):S4–S10.

Dietz V, Curt A. Neurological aspects of spinal-cord repair: promises and challenges. Lancet Neurol. 2006;5:688–94.

Fitzharris M, Cripps RA, Lee BB. Estimating the global incidence of traumatic spinal cord injury. Spinal Cord. 2014;52:117–22.

Frankel HL, Hancock DO, Hyslop G, et al. The value of postural reduction in the initial management of closed injuries on the spine with paraplegia and tetraplegia. Paraplegia. 1969;7:179–92.

Geisler FH, Coleman WP, Grieco G, et al. Measurements and recovery patterns in a multi center study of acute spinal cord injury. Spine (Phila Pa 1976). 2001;26(24 Suppl):S68–86.

Halvorsen A, Pettersen AL, Nilsen SM, et al. Non-traumatic spinal cord injury in Norway 2012-2016: analysis from a national registry and comparison with traumatic spinal cord injury. Spinal Cord. 2019;57:324–30.

Hao D, Du J, Yan L, et al. Trends of epidemiological characteristics of traumatic spinal cord injury in China, 2009-2018. Eur Spine J. 2021;30:3115–27.

Hussey RW, Stauffer ES. Spinal cord injury: requirements for ambulation. Arch Phys Med Rehabil. 1973;54(December):544–7.

Jackson AB, Dijkers M, DeVivo MJ, et al. A demographic profile of new traumatic spinal cord injuries: change and stability over 30 years. Arch Phys Med Rehabil. 2004;85:1740–8.

Jacob W, Wirz M, van Hedel HJ, et al. Difficulty of elderly SCI subjects to translate motor recovery-"body function" into daily living activities. J Neurotrauma. 2009;26:2037–44.

Jain NB, Ayers GD, Peterson EN, et al. Traumatic spinal cord injury in the United States, 1993–2012. JAMA. 2015;313:2236–43.

Kirshblum SC, Botticello AL, DeSipio GB, et al. Breaking the news: A pilot study on patient perspectives of discussing prognosis after traumatic spinal cord injury. J Spinal Cord Med. 2016;39:155–61.

Kirshblum SC, O'Connor KC. Levels of spinal cord injury and predictors for neurologic recovery. Phys Med Rehabil Clin N Am. 2000;11(1–27):vii.

Kirshblum S, Millis S, McKinley W, et al. Late neurologic recovery after traumatic spinal cord injury. Arch Phys Med Rehabil. 2004;85:1811–7.

Kirshblum S, Botticello A, Lammertse DP, et al. The impact of sacral sensory sparing in motor complete spinal cord injury. Arch Phys Med Rehabil. 2011;92:376–83.

Kramer JL, Lammertse DP, Schubert M, et al. Relationship between motor recovery and independence after sensorimotor-complete cervical spinal cord injury. Neurorehabil Neural Repair. 2012;26:1064–71.

Lasfargues JE, Custis D, Morrone F, et al. A model for estimating spinal cord injury prevalence in the United States. Paraplegia. 1995;33:62–8.

Lee BB, Cripps RA, Fitzharris M, et al. The global map for traumatic spinal cord injury epidemiology: update 2011, global incidence rate. Spinal Cord. 2014;52:110–6.

Lenehan B, Street J, Kwon BK, et al. The epidemiology of traumatic spinal cord injury in British Columbia, Canada. Spine (Phila Pa) 1976. 2012:321–9.

Lidal IB, Huynh TK, Biering-Sørensen F. Return to work following spinal cord injury: a review. Disabil Rehabil. 2007;29:1341–75.

Marino RJ, Ditunno JF Jr, Donovan WH, et al. Neurological recovery after traumatic spinal cord injury: data from the model spinal cord injury systems. Arch Phys Med Rehabil. 1999;80:1391–6.

Marino RJ, Burns S, Graves DE, et al. Upper- and lower-extremity motor recovery after traumatic cervical spinal cord injury: an update from the national spinal cord injury database. Arch Phys Med Rehabil. 2011;92:369–75.

McCullumsmith CB, Kalpakjian CZ, Richards JS, et al. Novel risk factors associated with current suicidal ideation and lifetime suicide attempts in individuals with spinal cord injury. Arch Phys Med Rehabil. 2015;96:799–808.

McKinley W, Santos K, Meade M, et al. Incidence and outcomes of spinal cord injury clinical syndromes. J Spinal Cord Med. 2007;30:215–24.

Middleton JW, Dayton A, Walsh J, et al. Life expectancy after spinal cord injury: a 50-year study. Spinal Cord. 2012;50:803–11.

Miyakoshi N, Suda K, Kudo D, et al. A nationwide survey on the incidence and characteristics of traumatic spinal cord injury in Japan in 2018. Spinal Cord. 2021;59:626–34.

Nahm LS, Chen Y, DeVivo MJ, et al. Bladder cancer mortality after spinal cord injury over 4 decades. J Urol. 2015;193:1923–8.

National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham: University of Alabama at Birmingham; 2021a. https://www.nscisc.uab.edu. Last access Nov 2021.

National Spinal Cord Injury Statistical Center (NSCISC). Spinal cord injury facts and figures at a glance. 2020 SCI data sheet. Birmingham: University of Alabama at Birmingham; 2021b. https://www.nscisc.uab.edu. Last access Nov 2021.

New PW, Sundararajan V. Incidence of non-traumatic spinal cord injury in Victoria, Australia: a population-based study and literature review. Spinal Cord. 2008;46:406–11.

New PW, Rawicki HB, Bailey MJ. Nontraumatic spinal cord injury: demographic characteristics and complications. Arch Phys Med Rehabil. 2002;83:996–1001.

New PW, Simmonds F, Stevermuer T. A population-based study comparing traumatic spinal cord injury and non-traumatic spinal cord injury using a national rehabilitation database. Spinal Cord. 2011;49:397–403.

New PW, Farry A, Baxter D, et al. Prevalence of non-traumatic spinal cord injury in Victoria, Australia. Spinal Cord. 2013;51:99–102.

New PW, Cripps RA, Lee BB. Global maps of non-traumatic spinal cord injury epidemiology: towards a living data repository. Spinal Cord. 2014;52:97–109.

New PW, Baxter D, Farry A, et al. Estimating the incidence and prevalence of traumatic spinal cord injury in Australia. Arch Phys Med Rehabil. 2015;96:76–83.

Nijendijk JH, Post MW, van Asbeck FW. Epidemiology of traumatic spinal cord injuries in the Netherlands in 2010. Spinal Cord. 2014;52:258–63.

Noonan VK, Fingas M, Farry A, et al. Incidence and prevalence of spinal cord injury in Canada: a national perspective. Neuroepidemiology. 2012;38:219–26.

O'Connor PJ. Prevalence of spinal cord injury in Australia. Spinal Cord. 2015;43:42–6.

Post MW, Reinhardt JD, Avellanet M, et al. Employment among people with spinal cord injury in 22 countries across the world: results from the international spinal cord injury community survey. Arch Phys Med Rehabil. 2020;101:2157–66.

Razdan S, Kaul RL, Motta A, et al. Prevalence and pattern of major neurological disorders in rural Kashmir (India) in 1986. Neuroepidemiology. 1994;13:113–9.

Scivoletto G, Di Donna V. Prediction of walking recovery after spinal cord injury. Brain Res Bull. 2009;78:43–51.

Shavelle RM, DeVivo MJ, Brooks JC, et al. Improvements in long-term survival after spinal cord injury? Arch J Phys Med Rehabil. 2015a;96:645–51.

Shavelle RM, Paculdo DR, Tran LM, et al. Mobility, continence, and life expectancy in persons with ASIA impairment scale grade D spinal cord injuries. Am J Phys Med Rehabil. 2015b;94:180–91.

Singh A, Tetreault L, Kalsi-Ryan S, et al. Global prevalence and incidence of traumatic spinal cord injury. Clin Epidemiol. 2014;6:309–31.

Steeves JD, Kramer JK, Fawcett JW, et al. Extent of spontaneous motor recovery after traumatic cervical sensorimotor complete spinal cord injury. Spinal Cord. 2011;49:257–65.

van den Berg ME, Castellote JM, de Pedro-Cuesta J, et al. Survival after spinal cord injury: a systematic review. J Neurotrauma. 2010;27:1517–28.

van Hedel HJ, Curt A. Fighting for each segment: estimating the clinical value of cervical and thoracic segments in SCI. J Neurotrauma. 2006;23:1621–31.

van Middendorp JJ, Hosman AJ, Donders AR, et al. A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: a longitudinal cohort study. Lancet. 2011;377:1004–10.

Vogel LC, Betz RR, Milcahey MJ. Spinal cord injuries in children and adolescents. Handb Clin Neurol. 2012;109:131–48.

Waters RL, Adkins RH, Yakura JS. Definition of complete spinal cord injury. Paraplegia. 1991;29:573–81.

Waters RL, Adkins RH, Yakura JS, et al. Motor and sensory recovery following complete tetraplegia. Arch Phys Med Rehabil. 1993;74:242–7.

Waters RL, Adkins R, Yakura J, et al. Donal Munro lecture: functional and neurologic recovery following acute SCI. J Spinal Cord Med. 1998;21:195–9.

Wilson JR, Davis AM, Kulkarni AV, et al. Defining age-related differences in outcome after traumatic spinal cord injury: analysis of a combined, multi center dataset. Spine J. 2014;14:1192–8.

Wirth B, van Hedel HJ, Kometer B, et al. Changes in activity after a complete spinal cord injury as measured by the spinal cord Independence Measure II (SCIM II). Neurorehabil Neural Repair. 2008;22:145–53.

World Health Organization (WHO). International perspectives on spinal cord injury. 2013. https://apps.who.int/iris/bitstream/handle/10665/94192/WHO_NMH_VIP_13.03_eng.pdf?sequence=1&isAllowed=y. Assessed 1 Nov 2021.

Wyndaele M, Wyndaele JJ. Incidence, prevalence and epidemiology of spinal cord injury: what learns a worldwide literature survey? Spinal Cord. 2006;44:523–9.

Zariffa J, Kramer JL, Fawcett JW, et al. Characterization of neurological recovery following traumatic sensorimotor complete thoracic spinal cord injury. Spinal Cord. 2011;49:463–71.

Recommended Additional Reading

Buchanan LE, Nawoczenski DA, editors. Spinal cord injury-concepts and management approaches. Baltimore: Williams & Wilkins; 1987.

Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. Wolters Kluwer: New Delhi; 2015.

Kirshblum S, Lin VM, editors. Spinal cord medicine. 3rd ed. New York: Demos Medical Publishing; 2019.

Vaccaro AR, Fehlings MG, Dvorak MF, editors. Spine and spinal cord trauma, evidence-based management. New York: Thieme Medical Publishers; 2011.

Vogel LC, Zebracki K, Betz RR, Mulcahey MJ, editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.

13 Standard Assessment and Neurological Classification of Spinal Cord Injuries

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) examination is universally recognized as the gold standard for the assessment and classification of neurological impairment after spinal cord injury. However, prior to evaluating a patient according to the ISNCSCI described in this chapter, a physical and neurological examination should be performed on patients with spinal cord injuries to identify spinal cord lesions from central nervous system disorders, and motor, sensory, proprioception, reflexes, muscle tone, and spasticity; The overall status of the activity, including the locomotor activity, should be assessed. A screening examination to determine the subject of further and more detailed examination, the localization of the lesion site, and the specifying spinal cord injury/lesion was mentioned in Chap. 11.

Performing standardized physical and neurological examinations on people with spinal cord injuries is mandatory for clinical and scientific purposes, as well as for accurate communication between clinicians and researchers. Such a standardized method is also important for documenting the course of recovery and the effect on the treatment of people with spinal cord injuries. Efforts have been made since the 1960s to develop a classification system for spinal cord injuries based on neurological examinations to provide a standard of assessment. The Frankel scale (Frankel et al. 1969) was adopted as the primary classification system for traumatic spinal cord injuries in the first booklet of the American Spinal Injury Association (ASIA) entitled "Standards for Neurological Classification of Spinal Cord Injury Patients" in 1982. The Frankel scale classifies patients as complete (grade A), sensory only (grade B), motor useless (grade C), motor useful (grade D), or no neurological deficit/recovered (grade E) (Table 13.1). The Frankel scale is a simple but nonspecific and subjective

Table 13.1 Frankel classification of degree of incompleteness

Grade	Frankel scale
A	*Complete*: All motor and sensory function is absent below the zone of partial preservation
B	*Incomplete, preserved sensory only*: Preservation of any demonstrable, reproducible sensation, excluding phantom sensations. Voluntary motor functions are absent
C	*Incomplete, preserved motor non-functional*: Preservation of voluntary motor function which is minimal and performs no useful purpose. Minimal is defined as preserved voluntary motor ability below the level of injury where the majority of the key muscle tests less than a grade of 3
D	*Incomplete, preserved motor functional*: Preservation of voluntary motor function which is useful functionally. This is defined as preserved voluntary motor ability below the level of injury, where the majority of the key muscles test at least a grade of 3
E	*Complete recovery*: Complete return of all motor and sensory function, but one may still have abnormal reflexes

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classification of acute spinal cord injury. It has major limitations. First, the neurological levels of injury were not incorporated into the classification system. Second, the subjective nature of determining motor function "useless" vs. "useful" potentially increases the variability of the classification system among observers. Finally, the Frankel scale showed limited responses to subtle changes in neurological function during the recovery phase after spinal cord injury (Furlan et al. 2008).

Over the past three decades, ASIA, in cooperation with the International Spinal Cord Society (ISCoS), has improved the classification system by organizing consensus meetings of experts in various medical fields related to the treatment of patients with acute spinal cord injuries. The results are the International Standards of Neurological Classification of Spinal Cord Injury. The latest revised edition was published in 2019. In the eighth edition of ISNCSCI in 2019, substantial revisions have been made in addition to the 2015 update of the seventh edition in 2011 (ASIA 2019; ASIA and ISCoS International Standards Committee 2019; Kirshblum et al. 2020). Clarifications and revisions in the seventh edition in 2011, the update of the seventh edition in 2015, and the eighth edition in 2019 are listed in Tables 13.2, 13.3, and 13.4, respectively. Figure 13.1 is the worksheet of the 2019 revision, eighth edition of ISNCSCI. The International Standards to Document Remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) were established in 2012 (ASIA 2012) and have been revised as the second edition in 2021 (Figs. 13.2 and 13.3). Figures 13.2 and 13.3 are the general autonomic function assessment form and the sacral autonomic function assessment form of the ISAFSCI (second edition), respectively (Wecht et al. 2021). The ISAFSCI will be described in detail in Chap. 21. The examination and classification of spinal cord injuries described in this chapter are essentially based on the eighth edition of ISNCSCI in 2019 (ASIA 2019).

The initial neurological examination is important to assess the severity and level of spinal cord injury. It helps to establish a rational treatment plan and to determine the prognosis and outcomes of neurological function (Calancie et al. 2004; Consortium for Spinal Cord Medicine 2008). It is generally accepted that the prediction of long-term outcomes after traumatic spinal cord injury can be more accurately predicted with neurological examinations performed days

Table 13.2 Clarifications, revisions, and changes of the 7th edition of ISNCSCI in 2011

Clarifications and revisions
More detailed description of the motor and sensory examination, including positions for motor tests to assess grade 4 or 5 muscle strength, e.g. elbow flexed at 90°, arm at the side of patient, and forearm supinated for grade 4 or 5 strength C5 test, wrist in full extension for C6
Definition of the motor level in a patient with no motor function to test (i.e., above C5, between T2-L1), with examples given, e.g., if the sensory level is C4, and there is no C5 motor strength (or strength graded <3), the motor level is C4, and if the sensory level is C4, with the C5 key muscle strength graded as ≥3, the motor level will be C5
When documenting the ZPP in a situation where there is no sparing of motor or sensory function below the motor and sensory levels, the motor and sensory levels are documented in the designated area on the worksheet. This term, ZPP, used only for complete injuries
Distinguishing a sensory vs. motor incomplete (AIS B from C) injury as well as between motor incomplete injuries (AIS C from D). Specifically, using the motor level on each side to differentiate AIS B from C, and the single neurological level of injury for AIS C from D
Utilization of non-key muscle functions in the AIS classification. Non-key muscles are used to determine sensory vs. motor incomplete status (AIS B vs. C)
Replacement of the term "deep anal sensation" by "deep anal pressure"
If the sensation is abnormal at C2, the level that should be designated is C1
If patients have light touch or pin prick sensation at S4–5, examination for DAP is not required
Revision of the definition of the ZPP levels: "The dermatomes and myotomes caudal to the sensory and motor levels on each side of the body remaining partially innervated in ASIA A" from "ZPP is determined from the NLI."

Table 13.3 Clarifications in the 2015 update of the 7th edition of ISNCSCI

Clarifications	Summary
ND (not determinable)	ND (not determinable) should be documented on the worksheet when any component of the scoring (e.g., upper and lower extremity motor scores, total motor and sensory scores) and classification (e.g., the sensory level, motor level, NLI, AIS grade, and ZPP) cannot be determined on the basis of the examination. For example, if NT (not testable) is used in the scoring for the examination, and the motor, sensory or NLI, or AIS grade, cannot be determined in a specific case based on this, then "ND" should be used for the designation of these scores, levels, and AIS grade on the worksheet. It is strongly recommended that the reason for the NT note be documented in the "comments box."
Non-key muscle function	The use of non-key muscle functions has been added to the booklet. This has been added to the worksheet available on the ASIA website as of 2013. If a patient is preliminarily classified as sensory incomplete (AIS B) where all key muscle functions on each side of the body are graded zero more than three levels below the motor level and there is no VAC, then non-key muscle functions more than three levels below the motor level on each side of the body should be examined to rule out or rule in a motor incomplete status. If there is no motor function in any non-key muscle function more than three segments below the motor level on each side, the patient is classified as AIS B, otherwise as AIS C.
Worksheet	The worksheet with format changes that was introduced in 2013 has been added to the booklet, with non-key muscle functions added in the "comments box."
Definition of motor incomplete	Definition of motor incomplete was clarified. Motor function is preserved at the most caudal sacral segments on VAC or the patient meets the criteria for sensory incomplete status with some sparing of motor functions at more than three levels below the ipsilateral motor level on either side of the body.
Additional terms	Additional terms have been added to the definitions, including "key muscle functions," "non-key muscle functions," "sacral sparing," complete injury," and "not determinable."

NLI, neurological level of injury; AIS, ASIA Impairment Scale; ZPP, zone of partial preservation; VAC, voluntary anal contraction

Table 13.4 Revisions of the 8th edition of ISNCSCI in 2019

Revisions	Summary
Documentation of non-SCI related impairments	A general "*"-concept is introduced, in which abnormal examination scores can be tagged with a "*" to indicate a non-SCI condition. This general "*"-concept is applied to both the motor and the sensory exam independent from the level of occurrence (above, at, or below the sensory/motor level). As such for motor strength, the "*" can be applied to motor scores from 0 to 4 and for NT, and this can be applied to sensory scores of 0, 1 or NT
Zone of partial preservation	In the 2011 ISNCSCI revision and the 2015 update, ZPPs were only defined for AIS A. The ZPP rules were changed and are no longer based on the AIS grade. Motor ZPPs are now defined and should be documented in all cases, including patients with incomplete injuries with absent VAC. The sensory ZPP on a given side is defined in the absence of sensory function in S4–5 (PP, LT) on this side as long as DAP is not present. This means that in cases with present DAP, sensory ZPPs are not defined on both sides and should be noted as "not applicable (NA)." In cases with absent DAP, a sensory ZPP can be defined on one side (assuming that there is also no PP and LT sensation in S4–5 on this side), while it may not necessarily be applicable (and should be noted as "NA") on the other side if PP or LT at S4–5 is present
Worksheet	The revised worksheet complies with the new ZPP definition and with documentation of non-SCI related conditions in the "comments box."
Patterns of incomplete injury	Although not a part of the ISNCSCI, the 2019 revision described incomplete injury syndromes in the booklet, which were retained as part of the introduction

NT, not testable; ZPP, zone of partial preservation; AIS, ASIA Impairment Scale; VAC, voluntary anal contraction; DAP, deep anal pressure; PP, pin prick; LT, light touch

a

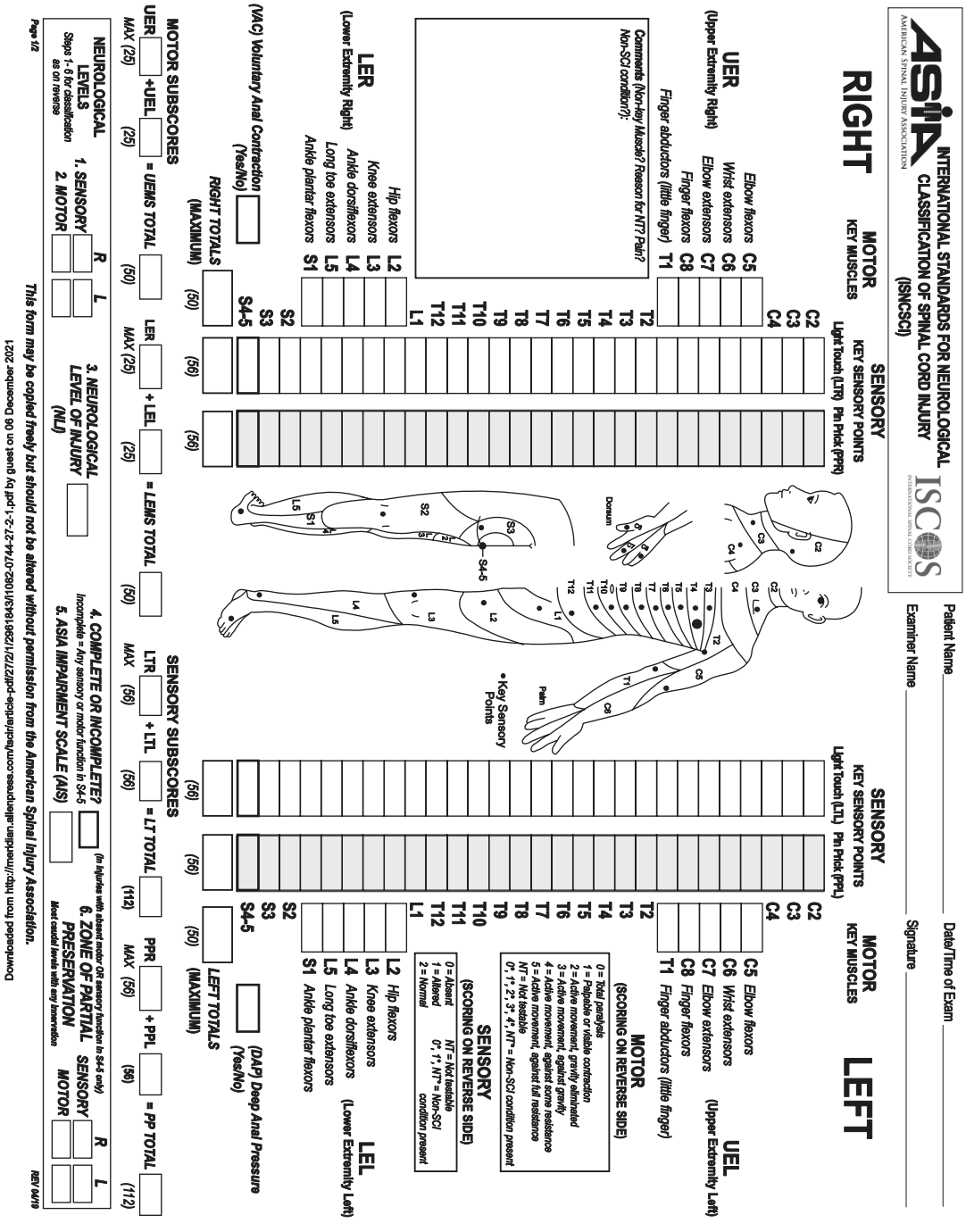
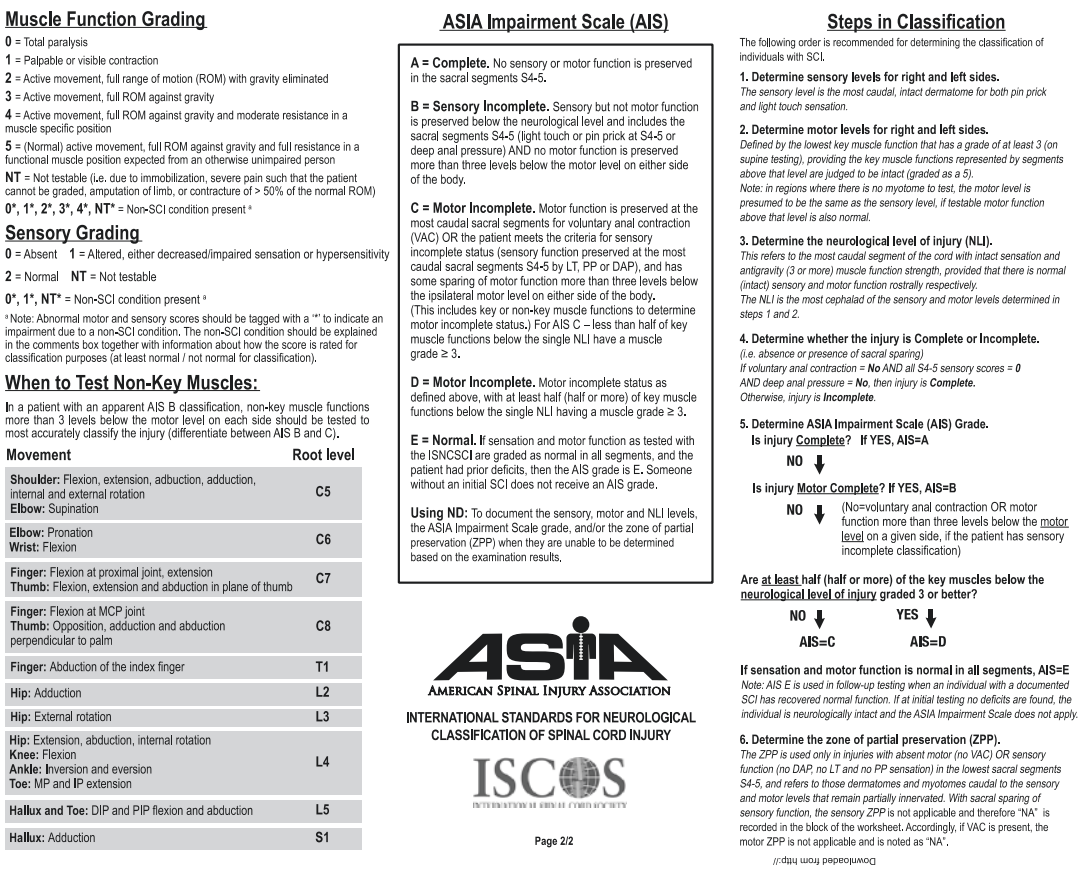


Fig. 13.1 (**a**) Worksheet of ISNCSCI, 8th edition in 2019 (front side). Download the full form at https://asia-spinalinjury.org/wp-content/uploads/2019/10/ASIA-ISCOS-worksheet_10.2019_PRINT-Page-1-2.pdf. (**b**) Worksheet of ISNCSCI, 8th edition in 2019 (backside)

b



Muscle Function Grading

0 = Total paralysis

1 = Palpable or visible contraction

2 = Active movement, full range of motion (ROM) with gravity eliminated

3 = Active movement, full ROM against gravity

4 = Active movement, full ROM against gravity and moderate resistance in a muscle specific position

5 = (Normal) active movement, full ROM against gravity and full resistance in a functional muscle position expected from an otherwise unimpaired person

NT = Not testable (i.e. due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of > 50% of the normal ROM)

0*, 1*, 2*, 3*, 4*, NT* = Non-SCI condition present [a]

Sensory Grading

0 = Absent **1** = Altered, either decreased/impaired sensation or hypersensitivity

2 = Normal **NT** = Not testable

0*, 1*, NT* = Non-SCI condition present [a]

[a] Note: Abnormal motor and sensory scores should be tagged with a '*' to indicate an impairment due to a non-SCI condition. The non-SCI condition should be explained in the comments box together with information about how the score is rated for classification purposes (at least normal / not normal for classification).

When to Test Non-Key Muscles:

In a patient with an apparent AIS B classification, non-key muscle functions more than 3 levels below the motor level on each side should be tested to most accurately classify the injury (differentiate between AIS B and C).

Movement	Root level
Shoulder: Flexion, extension, adbuction, adduction, internal and external rotation **Elbow:** Supination	C5
Elbow: Pronation **Wrist:** Flexion	C6
Finger: Flexion at proximal joint, extension **Thumb:** Flexion, extension and abduction in plane of thumb	C7
Finger: Flexion at MCP joint **Thumb:** Opposition, adduction and abduction perpendicular to palm	C8
Finger: Abduction of the index finger	T1
Hip: Adduction	L2
Hip: External rotation	L3
Hip: Extension, abduction, internal rotation **Knee:** Flexion **Ankle:** Inversion and eversion **Toe:** MP and IP extension	L4
Hallux and Toe: DIP and PIP flexion and abduction	L5
Hallux: Adduction	S1

ASIA Impairment Scale (AIS)

A = Complete. No sensory or motor function is preserved in the sacral segments S4-5.

B = Sensory Incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-5 (light touch or pin prick at S4-5 or deep anal pressure) AND no motor function is preserved more than three levels below the motor level on either side of the body.

C = Motor Incomplete. Motor function is preserved at the most caudal sacral segments for voluntary anal contraction (VAC) OR the patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segments S4-5 by LT, PP or DAP), and has some sparing of motor function more than three levels below the ipsilateral motor level on either side of the body. (This includes key or non-key muscle functions to determine motor incomplete status.) For AIS C – less than half of key muscle functions below the single NLI have a muscle grade ≥ 3.

D = Motor Incomplete. Motor incomplete status as defined above, with at least half (half or more) of key muscle functions below the single NLI having a muscle grade ≥ 3.

E = Normal. If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

Using ND: To document the sensory, motor and NLI levels, the ASIA Impairment Scale grade, and/or the zone of partial preservation (ZPP) when they are unable to be determined based on the examination results.

ASIA
AMERICAN SPINAL INJURY ASSOCIATION

INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

ISCOS

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Steps in Classification

The following order is recommended for determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
The sensory level is the most caudal, intact dermatome for both pin prick and light touch sensation.

2. Determine motor levels for right and left sides.
Defined by the lowest key muscle function that has a grade of at least 3 (on supine testing), providing the key muscle functions represented by segments above that level are judged to be intact (graded as a 5).
Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level, if testable motor function above that level is also normal.

3. Determine the neurological level of injury (NLI).
This refers to the most caudal segment of the cord with intact sensation and antigravity (3 or more) muscle function strength, provided that there is normal (intact) sensory and motor function rostrally respectively.
The NLI is the most cephalad of the sensory and motor levels determined in steps 1 and 2.

4. Determine whether the injury is Complete or Incomplete.
(i.e. absence or presence of sacral sparing)
*If voluntary anal contraction = **No** AND all S4-5 sensory scores = **0***
*AND deep anal pressure = **No**, then injury is **Complete**.*
*Otherwise, injury is **Incomplete**.*

5. Determine ASIA Impairment Scale (AIS) Grade.
Is injury Complete? If YES, AIS=A
NO
Is injury Motor Complete? If YES, AIS=B
NO (No=voluntary anal contraction OR motor function more than three levels below the motor level on a given side, if the patient has sensory incomplete classification)

Are at least half (half or more) of the key muscles below the neurological level of injury graded 3 or better?
NO → AIS=C **YES → AIS=D**

If sensation and motor function is normal in all segments, AIS=E
Note: AIS E is used in follow-up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact and the ASIA Impairment Scale does not apply.

6. Determine the zone of partial preservation (ZPP).
The ZPP is used only in injures with absent motor (no VAC) OR sensory function (no DAP, no LT and no PP sensation) in the lowest sacral segments S4-5, and refers to those dermatomes and myotomes caudal to the sensory and motor levels that remain partially innervated. With sacral sparing of sensory function, the sensory ZPP is not applicable and therefore "NA" is recorded in the block of the worksheet. Accordingly, if VAC is present, the motor ZPP is not applicable and is noted as "NA".

Fig. 13.1 (continued)

to weeks after injury (Evaniew et al. 2020). During the first 24 h after spinal cord injury, a variety of factors affect the neurological examination, such as unstable vital signs, including pain, sedation, and anxiety. Therefore, neurological assessment 72 h after injury is important in predicting future neurological recovery (Alexander et al. 2009; Herbison et al. 1992). In addition to the neurological examination performed during the acute phase of spinal cord injury, the classification of spinal cord injury should take into account the potential presence of spinal shock. Spinal shock is more pronounced when spinal cord injury is severe and neurological levels are high (Ko et al. 1999). The somatic components of spinal shock are flaccid motor paralysis and areflexia of deep tendon reflexes and cutaneous reflexes (Arnold et al. 2006). These alterations in the somatic component during spinal shock can mislead an accurate neurological examination.

13.1 History of the ISNCSCI

The first attempts for standardization of spinal cord injuries began with the questionnaire that Michaelis sent to clinicians and researchers in 1967 (Michaelis 1969). The results showed a consensus on the neurological terminology and neurological prognosis. The neurological terminologies defined are the definition of the level of a lesion, grading of active muscular power, and the definition of types of incomplete lesions. The

Cardiovascular	Scoring	Condition	Definitions	Score
Heart Rate	**Normal (2)**		61-99 bpm	
Supine_____mmHg	**Altered (1)**	Bradycardia	≤ 60 bpm	
		Tachycardia	≥ 100 bpm	
		Arrhythmias §		
Seated_____mmHg	**Not Tested (NT): indicate reason**			
Systolic BP	**Normal (2)**		91 -139 mmHg	
Supine_____mmHg	**Altered (1)**	Supine Hypotension	SBP ≤ 90 mmHg	
		Orthostatic Hypotension	Fall ≥ 20 mmHg within 10 minutes*	
		Neurogenic Shock	within 30 days of injury; heart rate ≤ 60 bpm; SBP ≤ 90 mmHg	
		Autonomic Dysreflexia**	increase in SBP > 20 mmHg above baseline	
Seated_____mmHg		Supine Hypertension	≥ 140 mmHg	
	Not Tested (NT): indicate reason			
Diastolic BP	**Normal (2)**		61-89 mmHg	
Supine_____mmHg	**Altered (1)**	Supine Hypotension	≤ 60 bpm	
		Orthostatic Hypotension	Fall ≥ 10 mmHg within 10 minutes*	
		Supine Hypotension	≥ 90 mmHg	
Seated_____mmHg	**Not Tested (NT): indicate reason**			

*§ define the arrhythmia; * within 3 minutes, but delayed orthostatic hypotension; within 10 minutes, may be more common in the SCI population. ** self-report "within the past 7-days". ***unanticipated i.e., not in response to known intervention (e.g., medication).*

Termoregulation Core Body Temp	Scoring	Conditions	Definitions	Score
	Normal (2)	Normal	36.4-37.6 °C (97.5-99.7 °F)	
	Altered (1)	Subnormal	35.1-36.3 °C (95.1-97.4 °F)	
		Elevated	37.7-37.9 °C (99.8-100.3 °F)	
		Hypothermia	≤35°C (≤95°F)	
		Hyperthermia	≥38.0°C (≥100.4°F)	
	Not Tested (NT): indicate reason			

*** Under ambient conditions: 20-25°C (68-77°F); 30-50% relative humidity; wearing single-layer, indoor gaments; after 10-minutes of rest; no acute illness or infection*

Fig. 13.2 General autonomic function assessment form of the ISAFSCI (2nd ed.). From Wecht et al. (2021)

Sudomotor*	Scoring	Conditions	Definitions	Score
	Normal (2)	Normal sweating	Sweating on all skin surfaces	
	Altered (1)	Hypohidrosis	Diminished sweating above NLI Diminished sweating below NLI	
		Hyperhidrosis	Excessive sweating above NLI Excessive sweating below NLI	
	Absent (0)	Anhidrosis	No sweating above or below NLI	
	Not Tested (NT): indicate reason			

** Record sweating response to high ambient heat or exercise only. Do not record sweating associated with AD, OH, or mental stress.*

Broncho-pulmonary System	Findings	Condition	Definitions	Score
	Normal (2)			
	Altered (1)	Invasive ventilation	24 hours/day	
		Partial invasive ventilatory support	< 24 hours/day	
		Impaired voluntary respiration not requiring ventilatory support	Continuous Positive Airway Pressure (CPAP) for sleep apnea	
	Not Tested (NT): indicate reason			

Forces Vital Capacity (FVC) *	**Supine_____seated_____** **abdominal binder: YES_____ NO_____** **mL ____; kg ____; mL/kg _____**

Fig. 13.2 (continued)

definitions of the level of a lesion and the assessment of active muscular power were adopted in the later development of the ISNCSCI. In another publication in the "Paraplegia" in the same year, a classification system that provided categories as A, B, C, D, and E was reported (Frankel et al. 1969). Subsequently, many classifications have been proposed according to neurological function, bony level of injury, injury mechanism, and functional outcome (Bracken et al. 1978; Alaca 2015).

The first published standard of the American Spinal Injury Association (ASIA) in 1982 was "Standards for Neurological Classification of Spinal Injury Patients" (ASIA 1982). The first edition of 1982 was heavily influenced by the work of Frankel et al., Michaelis, and Bracken et al. The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) is the most widely used classification standards in spinal cord injury research and clinical practice. It has been revised until the eighth edition in 2019, most recently, since its first publication in 1982, to define the standardized neurological examination and classification for spinal cord injuries. Such a standardized classification of spinal cord injuries is very important in order to document neurological impairment, neurological recovery, and the effect of treatments in the field of spinal cord medicine between researchers and clinicians. Prior to the ASIA standards for spinal cord injuries, Frankel and colleagues (Frankel et al. 1969) reported a 5-grade system for severity of traumatic spinal cord injuries that were classified as complete (A) and 4 incomplete (B-E) injuries. The first standards published in 1982 included the Frankel scale and introduced definitions for the following terms: (1) motor tests of key muscles; (2) sensory tests in 29 dermatomes; (3) neurological zone of injury; (4) zone of injury; (5) the terms of quadriplegia, paraplegia, tetraparesis, and paraparesis; (6) incomplete anatomical syndromes. S4 and S5 dermatomes were considered as separate dermatomes in the 29 dermatomes. Complete and incomplete spinal cord injuries were defined by sparing more than three

Bladder Emptying	Method Frequency Timing Voluntarily	Yes _____ No _____		
System/Organ	**Scoring**	**Anticipated Function (based on ISNCSCI)**	**Anticipated Functional Score**	**Patien Reported Score**
Awareness bladder fullness	Normal (2)	Any level injury with normal sensation in the T11-L2 and S3-S5 dermatomes		
	Altered (1)	Any level injury with partial preservation of sensation in the T11-L2 and/or S3-S5 dermatomes		
	Absent (0)	NLI at or above T9 no sensation below		
	Not Tested (NT): indicate reason			
Ability to prevent bladder leakage	Normal (2)	Individuals with normal sensation and motor function in the S3-S5 dermatomes		
	Altered (1)	Individuals with partial sensation and motor function in the S3-S5 dermatomes		
	Absent (0)	No motor function at the S3-5 dermatomes		
	Not Tested (NT): indicate reason			
Bowel Emptying	Method Frequency Timing Voluntarily	Yes _____ No _____		
System/Organ	**Scoring**	**Anticipated Function (based on ISNCSCI)**	**Anticipated Functional Score**	**Patien Reported Score**
Awareness of bowel fullness	Normal (2)	Normal sensation and motor function in the S3-S5 dermatomes		
	Altered (1)	Partial preservation of sensation or motor function in the S3-S5 dermatomes		
	Absent (0)	No sensation or motor function in the S3-5 dermatomes		
	Not Tested (NT): indicate reason			

Fig. 13.3 Sacral autonomic function assessment form of the ISAFSCI (2nd ed.). From Wecht et al. (2021)

Ability to prevent bowel leakage	Normal (2)	Individuals with normal sensation and motor function in the S3-S5 dermatomes		
	Altered (1)	Individuals with partial sensation and motor function in the S3-S5 dermatomes		
	Absent (0)	No motor function at the S3-5 dermatomes		
	Not Tested (NT): indicate reason			
System/Organ	**Scoring**	**Anticipated Function (based on ISNCSCI)**	**Anticipated Functional Score**	**Patien Reported Score**
Psychogenic arousal	Normal (2)	Normal sensation and reflex motor function at T11-L2		
	Altered (1)	Partial sensation and motor reflex function at T11-L2		
	Absent (0)	No sensation or reflex motor function at T11-L2		
	Not Tested (NT): indicate reason			
Reflex genital arousal	Normal (2)	Normal sensation and reflex function at S3-5		
	Altered (1)	Partial sensation and motor reflex function at S3-5		
	Absent (0)	No sensation or motor function in the S3-5		
	Not Tested (NT): indicate reason			
Orgasm	Normal (2)	Intact S3-5 sensation and or motor function with any degree of preserved sacral reflexes		
	Altered (1)	No S3-5 sensation or motor function and preserved sacral reflexes		
	Absent (0)	No S3-5 sensation or motor function and absent sacral reflexes		
	Not Tested (NT): indicate reason			
Ejaculation	Normal (2)	Normal T11-12 sensation and sacral reflexes		
	Altered (1)	Diminished sensation at T11-12 dermatomes and normal sacral reflexes		
	Absent (0)	No sensation at T11-12 dermoatomes and absent sacral reflexes		
	Not Tested (NT): indicate reason			

Fig. 13.3 (continued)

levels below the "neurological zone of injury." The extent of neurologically partially preserved segmental levels below the neurological zone of injury was defined as the "zone of injury" (ASIA 1982; Solinsky and Kirshblum 2018).

Revisions were repeated from the ASIA standards in 1982 to the eighth edition in 2019, with the following basic terms being defined and standardized: (1) specific sensory key areas with anatomic landmarks to define the sensory level with combining the S4 and S5 dermatomes into a single S4–5 dermatome (perianal area), reducing the total number of dermatomes to 28 (changed in 1989); (2) redefining the zone of injury as the zone of partial preservation (ZPP) of sensory and motor function (changed in 1989); (3) adopting sacral sparing concept (in 1992); (4) clarification of muscle strength grading in the determination of motor levels; (5) adoption of the ASIA Impairment Scale (in 1992); (6) discouraged the term of quadriparesis and paraparesis. In the fourth edition of the ASIA standards published in 1992, the Frankel classification was replaced by the ASIA Impairment Scale with adopting the definition of sacral sparing in determining the injury completeness. In the fourth edition, some important changes and revisions were made: inclusion of the Functional Independence Measure (FIM), separate testing pin prick and light touch in a 3-point scale (0-1-2), sensory index scoring, no longer consideration of muscle strength grade 4 as normal, revision of ZPP definition, the term tetraplegia as preferred to quadriplegia. These standards were endorsed by the International Medical Society of Paraplegia (currently International Spinal Cord Society, ISCoS) and subsequently known as the "International Standards for Neurological and Functional Classification of Spinal Cord Injury."

The fifth edition of the ASIA standards in 1996 included clarification for evaluating muscles strength that can be affected by inhibiting factors, further clarification of differentiation between AIS C and D, and instructions for determining the motor level when the sensory level falls in a region in which the key muscles cannot be clinically tested, for C1–C4, T2–L1, and S3–5. In the revision (sixth edition) in 2000, further clarifications were given on motor incomplete injuries and on documentation of the ZPP (Kirshblum and Waring III 2014). The FIM was removed from the sixth edition standards. The "International Standards for the Neurological Classification of Spinal Cord Injury" has been used as the title of the standards since their revision in 2000. Further minor revisions and reprints of the standards were made in 2002, 2003, 2006, and 2008. "Non-key muscles" were mentioned for the first time in 2003 (Kirshblum et al. 2011a, b, 2014). ASIA began developing an Internet-based learning course for the ISNCSCI called the International Standards Training eLearning Program (InSTeP) in 2006 (Kirshblum and Waring III 2014).

There were extensive changes in motor and sensory examinations in the seventh edition of 2011 (ASIA 2011; Kirshblum et al. 2011a, b). The statement that "if motor function is intact in the rostral at the levels of C1-4, T2-L1, and S2-5, which can be determined only as sensory, the sensory level is determined as motor level" was added. It was made clear that the motor ZPP in the regions with no key muscle function to be tested does not follow sensory function in determining motor ZPP. It was recommended to use the motor levels on either side to differentiate between AIS B and C, while the single neurological level is used to differentiate between AIS C and D. In addition, it was mentioned that non-key muscle functions can be used to determine AIS B vs. C. Clarifications and revisions in the seventh edition in 2011, the update of the seventh edition in 2015, and the eighth edition in 2019 are listed in Tables 13.2, 13.3, and 13.4, respectively.

13.2 Overview of the ISNCSCI

The ISNCSCI comprises elements of sensory and motor examinations that are ultimately used for impairment grades. However, the ISNCSCI is not a complete neurological examination as it does not include details that are not used in the classification standards, such as deep tendon reflexes and pathologic reflexes (Arnold et al. 2006; Calancie et al. 2004). For more details on the

physical and neurological examination of spinal cord injuries, see Chap. 3. The ISNCSCI examination is a standard for determining the neurological level of injury and the severity of spinal cord injury. It may not be the best screening assessment tool for the determination of all the neurological impairments caused by spinal cord injury. Nevertheless, the neurological examination described by the ISNCSCI is widely used for the standardized initial assessment of patients with spinal cord injuries, for follow-up examinations to determine neurological improvements or changes, and for research on the neurological recovery after spinal cord injuries (Marino et al. 2008).

The ISNCSCI consists of three components: a sensory examination of light touch and pin prick sensation in each dermatome, a manual muscle strength examination of ten key muscles on each side of the body, and a neurological rectal examination (voluntary anal contraction and deep anal pressure). Examination of specific dermatomes and myotomes is an important component of the ISNCSCI system. The sensory testing is usually performed first and examines light touch and pin prick sensation in 28 defined dermatomes. The sensory grade is obtained on a 3-point scale from 0 to 2, with absent sensation being noted 0, present but altered sensation noted 1, and normal sensation noted 2. The score 2 implies that the sensation of a key sensory point of a dermatome is the same as the face. The sensory examination also includes the perception of deep anal pressure. Any perception of deep anal pressure classifies patients as at least sensory incomplete injury. The deep anal pressure is not scored differently from scoring of light touch or pin prick sensation, but as present or absent. The motor examination comprises the examination of 10 myotomes (C5-T1 and L2-S1), which are defined by grading their strength on a 5-point Medical Research Council scale (Compston 2010; Medical Research Council 1943). And voluntary anal contraction is assessed. The presence of voluntary anal contraction classifies patients as at least a motor incomplete injury. A general "*"-concept applies in non-SCI conditions.

After a sensory and motor examination by ISNCSCI, the neurological level of injury as well as the sensory and motor level is determined. The sensory level is defined as the most caudal, intact dermatome (sensory grade of 2) for the sensation of pin prick and light touch. The most caudal segment with a motor function grade of at least three with normal grade in the just proximal segment defines the motor level. The neurological level of injury is defined as the most caudal segment with normal sensory and antigravity motor function on either side of the body, provided that there is normal sensory and motor function rostrally. The numbers obtained from the sum of the right and left sensory subscores, a total of 112 for pin prick and 112 for light touch, and the sum of the right and left motor subscores, a total of 100, are documented and will contribute to the subsequent neurological change.

Spinal cord injuries are classified as either complete or incomplete based on sensory or motor sparing in the lowest sacral segments. A complete spinal cord injury is characterized by the complete absence of sensory and motor function in the lowest sacral segments (S4–5). In comparison, there is partial preservation of sensory and/or motor function in S4–5 with incomplete injury. It is sacral sparing. This definition has been found to be the most reliable definition of completeness (Waters et al. 1991). It is intuitive in that, for sacral sparing to be present, some signals have traversed the entire length of the spinal cord as one would expect with incomplete conduction block. Although the center of the spinal cord is completely destroyed by severe compression or contusion, the outer area of the white matter tracts is not impaired in the majority of cases of clinically complete spinal cord injury (Kakulas 1999a). Descending motor pathways such as the corticospinal tract and ascending sensory tracts such as the spinothalamic tract and the proprioceptive pathways are presumed to be somatotopically organized (Hughes 1991). It is believed that the sacral axons are located in the most eccentric position, which are usually spared in severe but not complete spinal cord injury (Kakulas 1999a, b; Wolfe et al. 2007). Incomplete

injuries preserve the sacral sensation (pin prick or light touch) or deep anal pressure. Complete injuries are the absence of both the lowest sacral motor and sensory function. A zone of partial preservation is defined as myotomes and dermatomes caudal to the motor and sensory levels that have remained partially innervated. The zone of partial preservation is used in all motor complete or incomplete injuries with no VAC and all sensory complete or incomplete injuries with absent DAP and absent ipsilateral or bilateral light touch and pin prick sensations (ASIA 2019; Kirshblum et al. 2020).

Although it is not the ISNCSCI classification itself, a skeletal level of injury can be practically defined as the level of spinal column injury with the greatest bony spinal damage on radiographic examination. It is important to note that skeletal level and neurological level are not always correlated (Oner et al. 2017).

The ASIA Impairment Scale (AIS) can be used to classify the severity of spinal cord injury based on sensory and motor examinations, neurological level of injury, and classification of complete or incomplete injury. In addition, AIS has shown important prognostic value for determining the outcome after a spinal cord injury. The positive predictive value of the AIS for independent walking at 1 year after injury ranges from 8.3% for AIS A to 97.3% for AIS D (van Middendorp et al. 2011). The AIS was modified on the Frankel scale and uses a 5-point scale from A to E to rate the severity of spinal cord injury. There are some important differences between the AIS and Frankel scales. For example, while the Frankel scale is nonspecific for the definition of complete patients (Frankel A) or motor complete/sensory incomplete patients (Frankel B), AIS emphasizes the role of motor and sensory functions in the S4–S5 segments. The Frankel scale classifies C or D patients as subjective motor "useless" functions, but the AIS defines C or D injuries by the muscle grading system of the Medical Research Council.

Given the detailed and accurate nature of the ISNCSCI classification system, inter- and intra-observer variability were minimal (Furlan et al. 2011; Marino et al. 2008). Due to the high reliability of the ISNCSCI classification system, this system is widely accepted and is currently used worldwide to evaluate the severity and neurological level of spinal cord injury. This classification system ensures the accuracy of communication between clinicians and researchers treating patients with spinal cord injuries (Kirshblum et al. 2014).

13.3 Definitions of the Terms

The terms in the ISNCSCI are listed and summarized in Table 13.5.

13.3.1 Tetraplegia

The term tetraplegia is preferable to quadriplegia. For reference, "Quad" of "Quadriplegia" is a Latin derivation, and "-plegia" is a Greek derivation, so it is unified with "Tetra" (=4) and "-plegia" of Greek derivation and referred to as "Tetraplegia." The term change to tetraplegia is to maintain consistency with Greek derivation of the root and suffix of the language, like paraplegia. The term tetraplegia refers to the impairment or loss of motor and/or sensory function in the cervical segments of the spinal cord due to damage of the neural elements within the spinal canal. The body parts of impairment in tetraplegia include the upper extremities as well as the trunk, lower extremities, and pelvic organs, i.e., including the four extremities. Since the motor innervation in the upper extremity is from C5 to T1 and sensory innervation from C4 to T2, patients with a T1 motor neurological level of injury and a T2 sensory level of injury are not clinically included in tetraplegia.

13.3.2 Paraplegia

Paraplegia means impairment or loss of motor or sensory function in the thoracic, lumbar, or sacral

Table 13.5 Term definitions in ISNCSCI

Term	Definition
Tetraplegia	Impairment or loss of motor and/or sensory function in the cervical segments of the spinal cord due to damage of neural elements within the spinal canal. Tetraplegia results in impairment in the upper and lower extremities, including trunk and pelvic organs
Paraplegia	Impairment or loss of motor and/or sensory function in the thoracic, lumbar, or sacral segments of the spinal cord. The term is used to refer to lesions of the cauda equina and the conus medullaris
Tetraparesis/paraparesis	Use of these terms is discouraged, as they imprecisely describe incomplete lesions
Dermatome	The area of skin innervated by the sensory axons within each segmental nerve root
Myotome	The collection of muscle fibers innervated by the motor axons within each segmental nerve root
Key muscle functions	Ten key muscle functions that are tested in all patients and scores from the examination
Non-key muscle functions	Muscle functions that are not part of the "key muscle" functions. In a patient with an apparent AIS B, non-key muscle functions more than three levels below the motor level on each side should be tested to differentiate the injury between AIS B and C
Sensory level	The most caudal dermatome with normal function for both pin prick and light touch sensation
Motor level	The lowest key muscle function level that has a grade of at least 3, with normal muscle function in the just proximal segmental level
Neurological level of injury (NLI)	The most caudal segment of the spinal cord with normal sensory and antigravity motor function on both sides of the body, provided that there is normal sensory and motor function rostrally
Skeletal level	The spinal level with the greatest vertebral damage by radiographic examination
Sacral sparing	The presence of residual preserved neurological function at the most caudal spinal cord segment (S4–5) as determined by examination of sensory and motor functions. Sensory sacral sparing includes sensation preservation at the anal mucocutaneous junction (S4–5 dermatome) on one or both sides for light touch or pin prick, or the presence of deep anal pressure. Motor sacral sparing includes the presence of voluntary contraction of the external anal sphincter during the digital rectal examination
Complete injury	No motor and sensory sacral sparing
Incomplete injury	Presence of motor or sensory sacral sparing
Zone of partial preservation (ZPP)	Dermatomes and myotomes caudal to the sensory and motor levels with partially preserved functions
Not determinable (ND)	This term is used on the worksheet when any component of the scoring, including the motor or sensory scores, the NLI of sensory or motor, ZPP, AIS cannot be determined based on the examination results

spinal cord segments with no involvement of the cervical segments due to an injury to the neural elements within the spinal canal. In paraplegia, the function of the upper extremities is spared, but the trunk, legs, and pelvic organs may be involved, depending on the level of injury. The term paraplegia refers to injuries to the cauda equina and conus medullaris injuries. "Para" (=2) and "-plegia" are all Greek derivations.

13.3.3 Tetraplegia and Paraplegia Versus Tetraparesis and Paraparesis

The terms tetraplegia and paraplegia refer to the involvement of neural elements within the spinal canal. Impairments due to lesions outside the spinal canal, such as brachial plexus or lumbosacral plexus or peripheral nerve lesions, should not be

referred to in these terms. The use of the terms "tetraparesis" and "paraparesis" is discouraged, as they describe incomplete lesions imprecisely and incorrectly, that tetraplegia and paraplegia should only be used for neurologically complete injuries. Instead, the ASIA Impairment Scale describes the severity of the spinal cord injury more precisely.

13.3.4 Dermatome

The term dermatome refers to the area of skin innervated by the sensory axons within each segmental nerve (root). Since a dermatome is formed by at least two or more spinal cord segments, the result of the sensory test may differ depending on the test site within the distribution area of a dermatome. Therefore, the ISNCSCI standardized the test by designating the key point of each dermatome.

13.3.5 Myotome

The term myotome refers to the collection of muscle fibers innervated by the motor axons of each segmental nerve (root). Most muscles are innervated by more than one root, and most nerve roots innervate more than one muscle. It is conventionally believed that a muscle function that is at least a grade of 3 has complete innervation by the more rostral segment of the segment. When determining the motor level, the next most rostral key muscle function should be tested as 5 as it is believed that the muscles are not compromised both of its two innervating segments. Because multiple muscles are innervated by a spinal cord segmental nerve, communication between clinicians is limited when examining muscles of a particular segment are different, according to the examiners. Therefore, the ISNCSCI designated the key muscles of each spinal cord segment.

13.3.6 Key Muscle Functions

This term refers to the ten muscle functions that should be tested in all patients, and the scores from the examination are documented on the worksheet.

13.3.7 Non-key Muscle Functions

The term non-key muscle functions refer to muscle functions that are not part of the key muscle functions routinely examined and documented on the worksheet. It is not recommended that non-key muscle functions be assessed as a routine part of the ISNCSCI. In a patient with an apparent AIS B, non-key muscle functions more than three levels below the motor level on each side should be tested to most accurately classify the injury to differentiate between AIS B and C. The results are documented in the "Comments box" of the worksheet.

13.3.8 Sensory Level

The sensory level is the most caudal, normally innervated dermatome for both pin prick (sharp/dull discrimination) and light touch sensations. This can be different on the right and left sides of the body. The sensory level is determined by examining the key sensory points in each of the 28 dermatomes on each side of the body.

13.3.9 Motor Level

The motor level is defined by the lowest key muscle function with a grade of 3 or more on manual muscle testing in the supine position, and it is judged that the key muscle functions represented by the segment above that level are not impaired with a grade of 5 on manual muscle testing. This may be different for the right and left sides of the

body. The motor level is determined by examining a key muscle function within each ten myotomes on each side of the body.

13.3.10 Neurological Level of Injury (NLI)

The NLI refers to the most caudal segment of the spinal cord with normal sensory and antigravity motor function on both sides of the body, provided that there is normal sensory and motor function rostrally. Normally functioning segments of sensory and motor often differ on the side of the body and in terms of sensory and motor tests. There can be up to four different segments in determining the neurological level of injury, i.e., R-sensory, L-sensory, R-motor, L-motor. The most rostral segment of these levels is defined as the single NLI.

13.3.11 Skeletal Level

This term skeletal level has been used to indicate the level of the greatest vertebral damage by radiographic examination. The skeletal level is not part of the current ISNCSCI. Indeed, not all cases of spinal cord injury have bony injury, and bony injuries do not consistently correlate with the neurological injury to the spinal cord.

13.3.12 Sensory Scores

Sensory scores are a numerical summary score of sensory functions. There is a maximum total of 56 points each for light touch and pin prick modalities for a total of 112 points (key sensory points of 28 dermatomes, 0 to 2 grades each) on each side of the body.

13.3.13 Motor Scores

The term motor scores refer to a numerical summary score of motor functions. There is a maximum score of 25 for each extremity (five key muscles in each extremity graded from 0 to 5), totaling 50 for the upper limbs (upper extremity motor score, UEMS) and 50 for the lower limbs (lower extremity motor score, LEMS).

13.3.14 Sacral Sparing

Since 1992, "sacral sparing" has been used to define whether a spinal cord injury is neurologically complete or incomplete, and is based on examining the most caudal aspects of the spinal cord, including light touch and pin prick modalities at the S4–S5 dermatome, deep anal pressure (DAP), and voluntary anal contraction (Kirshblum et al. 2016). The term sacral sparing is defined as the presence of preserved neurological function in the most caudal segments of the spinal cord (S4–S5) by examining the sensory and motor functions. Sensory sacral sparing includes sensation preservation of light touch or pin prick at one or both anal mucocutaneous junctions (S4–S5 dermatome) or the presence of DAP. Motor sacral sparing is the presence of voluntary contraction of the external anal sphincter on digital rectal examination (Zariffa et al. 2012). In the ISNCSCI, sacral sparing is a key neurological presentation differentiating between complete and incomplete spinal cord injuries. Severe compression or contusion completely destroys the center of the spinal cord, but in most cases of clinically completed spinal cord injury, the outer region of the white matter tracts is not compromised (Kakulas, 1999a). This is thought to be reflected neuroanatomically; the sacral axon is located centrifugally toward the surface of the spinal cord in long ascending sensory and descending motor projections. It is usually believed that the sacral axon is located at the most eccentric position, which is usually spared in severe but not complete spinal cord injury (Kakulas 1999a, b).

Among the neurological examination components for the lowest sacral segment, that is, pin prick, light touch, deep anal pressure, and voluntary anal contraction, it has been reported that the more sparing of other components including vol-

untary anal contraction (VAC) is accompanied, the better the prognosis for recovery. The initial sparing of all sacral sensory components correlated with the greatest conversion to motor incomplete status at discharge and at 1 year. In patients with initial AIS C, it was most often observed that the presence of VAC in association with other sacral sparing improved to AIS D status at discharge. However, the presence of VAC alone as the initial sacral sparing component had the poorest prognosis for recovery to AIS D status (Kirshblum et al. 2016).

13.3.15 Complete Injury

A complete spinal cord injury is defined as the absence of sensory and motor function in the sacral segments S4–S5. It means the absence of light touch and pin prick sensation in the dermatomes S4–5 and deep anal pressure as well as the absence of voluntary anal sphincter contraction, i.e. no sacral sparing.

13.3.16 Incomplete Injury

This term is used when there is the preservation of any sensory and/or motor function below the neurological level, including the lowest sacral segments S4–S5, i.e. presence of "sacral sparing." Since 1992, voluntary anal contraction or motor sparing more than three levels below the motor level has been used as the criteria for a motor incomplete injury.

13.3.17 Zone of Partial Preservation (ZPP)

The term ZPP refers to those dermatomes and myotomes caudal to the sensory and motor levels that remain partially innervated and is used only in injuries with absent motor (no VAC) or sensory function (no DAP, no light touch, and no pin prick sensation). The most caudal segment with some sensory and/or motor function defines the extent of the sensory and motor ZPP, respectively, and is documented as four different levels (R-sensory, L-sensory, R-motor, and L-motor).

13.3.18 Not Determinable (ND)

This term is used on the worksheet when it is not possible to determine any component of the scoring, including the motor or sensory scores based on the examination results. If NT (not testable) is used in the scoring for the examination, and the motor, sensory scores and levels, the NLI, AIS grade or ZPP, cannot be determined in a specific case based on this, then ND is used for the designation of the sum scores, levels, and AIS grade on the worksheet. The reason for the NT is recommended to be documented in the "Comments box."

13.4 Two Major Changes with the Eighth Edition of ISNCSCI in 2019

13.4.1 General "*"-Concept

Previously, if there was a non-SCI-related condition such as peripheral nerve injuries, brachial plexus lesions, burns, pain, casts, amputations, joint contractures, or generalized weakness, it was predicted to be normal even though it was not normal in the muscle strength test, and described it as "5*." The new taxonomy is marked with "*" on the actual muscle strength presented in the current state. And the reasons for non-SCI-related conduction should be described in the Comments box. Also, for the sensory grade in the case of non-SCI condition, mark "*" on the currently presented sensory grade. If the motor or sensory test is not possible due to pain or immobilization, it is marked "NT*." Therefore, the muscle function grade of the non-SCI condition can be expressed as 0*, 1*, 2*, 3*, 4*, NT*, and the sensory grade can be expressed as 0*, 1*, NT*. If the non-SCI-related impairment influences the determination of AIS, AIS is deter-

mined based on current muscle function and sensory test and tagged with "*," such as AIS C* (Rupp et al. 2021).

Tagged with an asterisk ("*") for non-SCI conditions can be applied motor and sensory scoring including total scoring, sensory and motor levels or the neurological level of injury, AIS grade, complete vs. incomplete, and ZPP.

13.4.2 New Definition of Zone of Partial Preservation (ZPP)

Previously, the concept of ZPP was only applied to complete injuries, i.e., AIS A. In this revision, motor ZPP applies to all incomplete injuries without voluntary anal contraction (VAC). Therefore, motor ZPP is applicable to AIS C and D, as well as motor complete injuries (AIS A, B), which are determined by four more segments of partial preserved motor function or distribution of the segments motor function ≤3 below the neurological level of injury, but they do not have VAC. In AIS B with sacral sensory sparing, if there is a partially preserved motor function in more than four segments below the neurological level of injury, it can be classified as AIS C or D, accordingly, motor ZPP can be documented even if classified as AIS C or AIS D. Sensory ZPP is also documented if there is no pin prick or light touch on one or both sides and of course there is no deep anal pressure (DAP). According to the new definition of sensory ZPP, the previous assumption that the sensory function of the S4–5 must be present if VAC was present is no longer applicable. Previously, it was said the DAP test is not required if S4–5 has a pin prick and light touch. In this revision, DAP must be checked with or without a pin prick and light touch. It is assumed that DAP has no left–right bias. If there is a DAP, sensory ZPP documentation cannot be provided even if the pin prick and light touch on the S4–5 are not on both sides or on one side. The new definition of the ZPP is known to be advantageous in predicting the motor score of the lower extremity 1 year after injury (Schuld et al. 2012).

13.5 Neurological Examination

The International Standards examination is used to determine the sensory, motor, and neurological levels, to provide motor and sensory scores, and to determine the ZPP and the completeness of the injury. Tests for the International Standards do not indicate a comprehensive neurological examination of patients with spinal cord injuries because they do not include elements that are not used in determining classification, such as deep tendon reflexes, pathologic reflexes, spasticity, etc. They are performed with minimal equipment (safety pin and cotton wisp) in any clinical setting. Basically, the ISNCSCI test should examine the same area, posture, and method in all phases, from acute to chronic. It should be performed with the patient in the supine position, with the exception of the anorectal examination which can be performed side lying to allow a valid comparison of scores throughout the phases of care. The rectal examination can alternatively be performed in the supine position with hip and knee flexion if the examination in the lateral position is not possible. If the spine is unstable, the patient should be log-rolled so as not to twist the spinal column for the anorectal examination.

If a key sensory point or key muscle function is not testable for any reason, such as a cast, burn, and amputation, or if the patient is unable to appreciate sensation on the face, the examiner should record "NT" instead of a numeric score. In such cases, "ND" is documented because it cannot generate sensory and motor scores for the affected side of the body as well as total sensory and motor scores.

13.5.1 Sensory Examination

13.5.1.1 Required Elements

The required portion of the sensory examination is the examination of the key point in each of the 28 dermatomes (from C2 to S4–S5) on the right and left sides of the body that can be easily located in relation to bony anatomical landmarks, except S4–S5 (Table 13.6) (Fig. 13.4). At each of

Table 13.6 Sensory key points and key muscles

Segments	Sensory key points	Key muscles
C2	At least 1 cm lateral to the occipital protuberance (alternatively 3 cm behind the ear)	None
C3	Supraclavicular fossa (posterior to the clavicle) and at the midclavicular line	None
C4	Over the acromioclavicular joint	None
C5	Lateral (radial) side of the antecubital fossa (just proximal to elbow crease)	Elbow flexors: Biceps, brachialis
C6	Thumb, dorsal surface, proximal phalanx	Wrist extensors: ECRL and ECRB
C7	Middle finger, dorsal surface, proximal phalanx	Elbow extensors: Triceps
C8	Little finger, dorsal surface, proximal phalanx	Finger flexors (FDP) to the middle finger
T1	Medial (ulnar) side of the antecubital fossa, just proximal to the medial epicondyle of the humerus	Small finger abductors: ADQ
T2	Apex of the axilla	None
T3	Midclavicular line and the 3rd intercostal space. Alternatively by palpating the manubriosternal joint	None
T4	4th intercostal line (nipple line) at the midclavicular space	None
T5	Midclavicular line and 5th intercostal space (midway between T4 and T6)	None
T6	Midclavicular line and 6th intercostal space (level of xiphisternum)	None
T7	Midclavicular line and 7th intercostal space (midway between T6 and T8)	None
T8	Midclavicular line and 8th intercostal space (midway between T6 and T10)	None
T9	Midclavicular line and 9th intercostal space (midway between T8 and T10)	None
T10	Midclavicular line and 10th intercostal space (umbilicus)	None
T11	Midclavicular line and 11th intercostal space (midway between T10 and T12)	None
T12	Midclavicular line and midpoint of the inguinal ligament	None
L1	Midway between the key sensory point for T12 and L2	None
L2	Anterior-medial thigh at midpoint between midpoint of the inguinal ligament and medial femoral condyle	Hip flexors: Iliopsoas
L3	Medial femoral condyle above the knee	Knee extensors: Quadriceps
L4	Medial malleolus	Ankle dorsiflexors: Tibialis anticus
L5	Foot dorsum at the 3rd metatarsal phalangeal joint	Long toe extensors: EHL
S1	Lateral heel (calcaneus)	Ankle plantar flexors: Gastrocnemius, soleus
S2	Midpoint of the popliteal fossa	None
S3	Ischial tuberosity or infragluteal fold	None
S4–5	Perianal area less than 1 cm lateral to the mucocutaneous junction	None

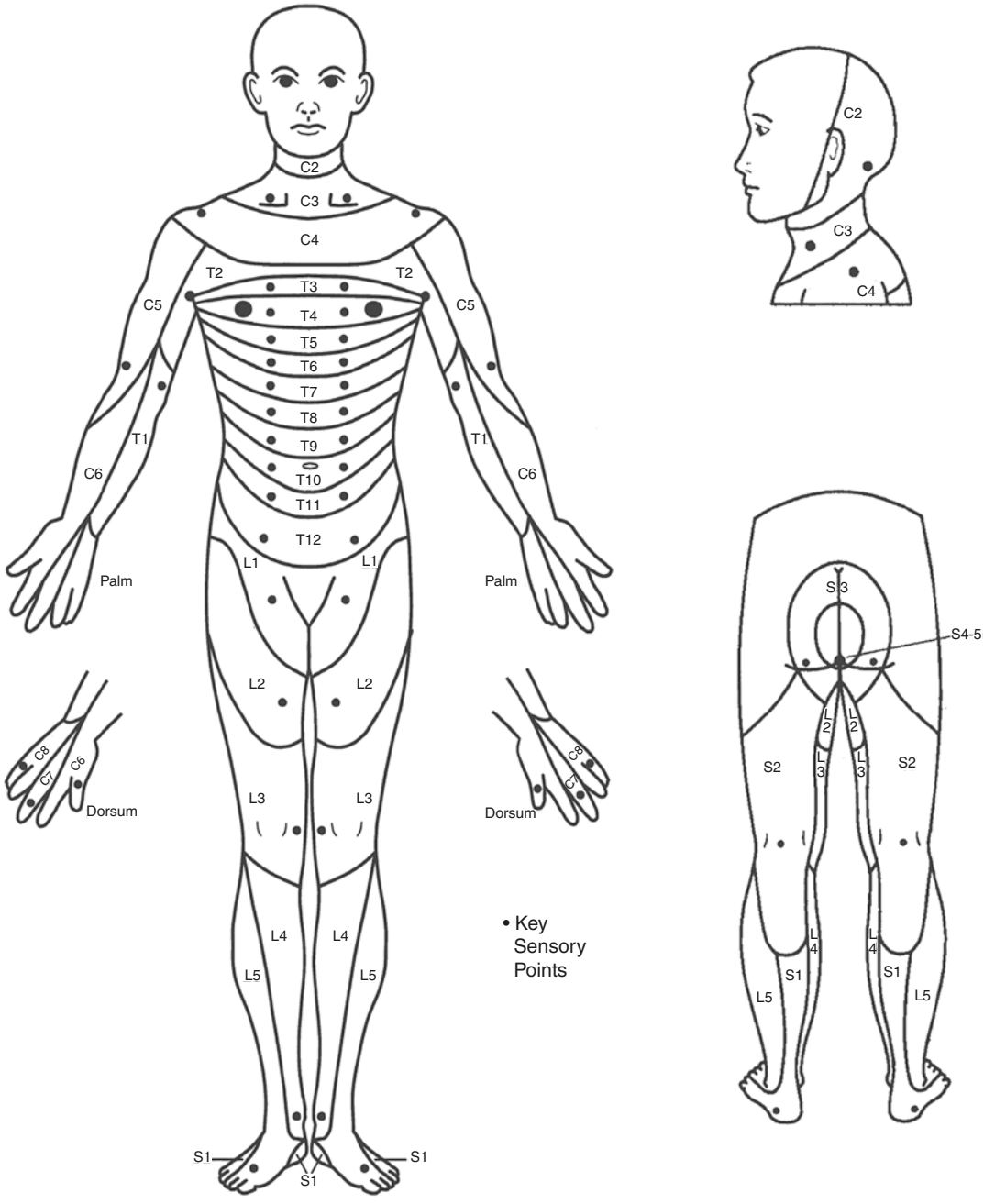

Fig. 13.4 Key sensory points

these key points, two aspects of sensation are examined: light touch and pin prick. Light touch and pin prick sensation at each key point are separately scored on a three-point scale and compared with the sensation on the patient's cheek as a normal reference frame.

- 0 = Absent
- 1 = Altered (impaired or partial appreciation, including hyperesthesia)
- 2 = Normal or intact (same as on the cheek)
- NT = Not testable
- 0*, 1*, NT* = non-SCI condition present.

Light touch sensation (feeling of touching or not) is tested with a tapered cotton wisp or the cotton being pulled away from the end of the cotton stick stroked once over an area of the key point so as not to exceed 1 cm of skin with the eyes closed or vision blocked. Pin prick sensation (sharp/dull discrimination) is performed with a disposable safety pin that is stretched to allow testing on both ends: using the pointed end for sharp and the rounded end of the pin for dull. Eight correct answers of ten tests at each dermatome are suggested as the criteria for accuracy. If sharp/dull sensation is altered, a grade of 1 for pin prick is given. In this case, the patient clearly distinguishes between the sharp and dull ends of the pin, but the intensity of sharpness is different in the key sensory point than the feeling of sharpness on the face. The intensity may be greater or lesser than the feeling on the face. The examination advances the key sensory point from the rostral to the caudal. In areas of hypersensitivity, the cotton wisp or pin prick may feel more intense than normal or may be uncomfortable. These dermatomes are scored as impaired, score 1.

Abnormal scores including NT, i.e., 0, 1, NT, should be tagged with a "*" to indicate that this score is affected by a non-SCI condition, such as brachial plexus or lumbosacral plexus injuries, limb amputation, and other lesions affecting sensory perception including burn wound, pain, and swelling. The reasons for the non-SCI condition should be documented in the "Comments box." If the non-SCI condition is clearly above the sensory level, the tagged scores should be noted as normal or intact for classification. If the non-SCI condition is at or below the sensory level, classification should be performed on the basis of the examined score and all other possible scores on an examiner's assumption.

13.5.1.2 Deep Anal Pressure (DAP)

DAP awareness is performed by inserting the index finger and applying gentle pressure to the anorectal wall. Pressure can be applied by using the thumb to squeeze the anus against the inserted index finger gently. Consistently perceived pressure is graded according to presence or absence. Any reproducible pressure sensation felt in the anal area during this examination indicates that the patient has a sensory incomplete lesion. The 2019 revision booklet also wrote "If patient has light touch or pin prick sensation at S4–S5, DAP examination is not required as the patient already has been designated as a sensory incomplete injury." However, in the new version of ISNCSCI in 2019, the definition of ZPP can be adapted to all incomplete injury, so if there is no pin prick and light touch sensation on one side, sensory ZPP can be determined in the case with no DAP, so the DAP test should not be omitted. Also, since DAP does not distinguish between right and left, it should not be assumed that DAP will be present if there is a light touch and a pin prick. It is necessary to clarify further the DAP and ZPP and related clinical implications, including the sentence from the above quotation.

13.5.1.3 Optional Elements

Optional elements of sensory functions are joint movement appreciation and position sense and awareness of deep pressure/deep pain.

1. For joint movement appreciation and position sense, the interphalangeal (IP) joint of the thumb, the proximal IP joint of the little finger, the wrist, the IP joint of the great toe, the ankle, and the knee can be tested. They are graded using the same sensory scale provided (absent, impaired, normal). A grade of 1 (impaired) means that the patient is able to consistently report joint movement with 8 of 10 correctly only on large movements of the joint, but small movements (about 10° of motion) of the joint cannot be reported consistently.
2. Deep pressure appreciation of the limb is tested by applying firm pressure to the skin for 3–5 s at different locations of the wrist, fingers, ankles, and toes. For the patient without light touch and pin prick sensation (grade 0), deep pressure appreciation test can be performed. Since deep pressure appreciation tests are performed electively in the absence of light touch and pin prick sensations, it is

graded as either a 0 for absent or 1 for present. The reference of this test is firm pressure on the patient's chin with the examiner's index finger or thumb.

13.5.2 Motor Examination

Motor examination in the ISNCSCI consists of ten key muscles, voluntary anal contraction, and non-key muscle functions, and presents standardized positions for examinations of grades 4 and 5 muscle strength of the ten key muscles. It is also important to examine other muscles in addition to the ten key muscles, such as pronators for C6, trapezius for C3 and C4, diaphragm, and abdominal muscles for Beevor's sign (McCarter et al. 2018; Pearce 2005). In a patient with a potentially unstable spine during the acute phase of spinal cord injury, care should be taken to ensure that the manual muscle testing does not cause spinal instability or further injury. For example, in patients who are suspected of acute traumatic injury below T8, the hip joints should not be actively or passively flexed beyond 90° to prevent increased kyphotic stress on the lumbar spine.

13.5.2.1 Required Elements

The required portion of the motor examination is completed by testing the key muscle groups corresponding to ten paired myotomes (C5–T1 and L2–S1) (Table 13.6). Each key muscle function should be examined in the supine position in a rostral-caudal sequence, and the individual muscles examined should be stabilized not to be substituted by other muscles. The strength of each muscle is graded on a 6-point scale from 0 to 5. Plus and minus scores are not used. In general, the manual muscle test requires that a muscle is tested for grade 3 first and then for the stronger or weaker grades based on the result. Before examining the muscles, passively move the joints to determine the available range. Existing contractures or increased tone may limit the range of motion but do not indicate weakness. If the ROM is limited to <50% of the normal ROM, "NT" should be recorded. Abnormal scores including NT, i.e., 0–4 and NT, should be tagged with a "*" to indicate that the score is affected by a non-SCI condition. The non-SCI condition should be explained in the "Comments box" with information on how the score is rated for classification purposes. As with the sensory examination, the tagged score should be rated as normal or intact for classification if the non-SCI condition is clearly above the motor level. If the non-SCI condition is at or below the motor level, the classification should be performed on the basis of the examined score and all other possible scores greater than the examined score, except normal. If the classification with the different possible scores, for an examined score of 2*, the classification should be performed with 2, 3, and 4, do not lead to consistent results, then "ND" should be used. Any classification parameter that was determined based on an examiner's assumption should be tagged with the "*."

The strength of each muscle function is graded on a six-point scale from 0 to 5.

- 0 = Total paralysis
- 1 = Palpable or visible contraction
- 2 = Active movement, full range of motion (ROM) with gravity eliminated
- 3 = Active movement, full ROM against gravity
- 4 = Active movement, full ROM against moderate resistance in a muscle specific position
- 5 = (Normal) active movement, full ROM against gravity and full resistance in a muscle specific position expected from an otherwise unimpaired person
- NT = Not testable (i.e., due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of >50% of the range of motion)
- 0*, 1*, 2*, 3*, 4*, NT* = non-SCI condition present.

When testing for grade 4 or 5 strength, the specific positions listed in Table 13.7 should be used.

Table 13.7 Positions of key muscle testing for grade 4 or 5 strength

Segment	Position
C5	Elbow flexed at 90°, arm at the patient's side, and forearm supinated
C6	Wrist in full extension
C7	Shoulder is neutral rotation, adducted and in 90° of flexion with elbow in 45° of flexion
C8	Full flexed position of the distal phalanx with the proximal finger joints stabilized in an extended position
T1	Full abducted position of fingers
L2	Hip flexed to 90°
L3	Knee flexed to 15°
L4	Full dorsiflexed position of ankle
L5	First toe fully extended
S1	Hip in neutral rotation, neutral flexion/extension, and neutral abduction/adduction, the knee is fully extended, and the ankle in full plantar flexion

13.5.2.2 Voluntary Anal Contraction (VAC)

The neurological rectal examination is important to determine whether the patient has a complete injury. This rectal examination consists of three elements: deep anal pressure, voluntary anal contraction, and reflex activity. The external anal sphincter is tested for reproducible voluntary contractions around the examiner's finger inserted into the rectum and graded as present or absent, i.e. Yes or No on the worksheet. The instruction to the patient is "squeeze my finger as if to hold back a bowel movement." In the presence of VAC, the patient has a motor incomplete injury. VAC should be distinguished from reflex anal contraction or reflex spasm. It is very important not to move the finger inserted into the anus or touch the buttocks around the anus while examining the anal sphincter contractions. If anal contraction is present only with Valsalva maneuver, it may be a reflex contraction and should be documented as absent.

13.5.2.3 Non-key Muscle Functions

Non-key muscle functions refer to muscle functions that are not part of the 10 key muscle function that are tested routinely. These muscle functions are not used in determining motor levels or scores. It is not recommended to examine non-key muscle functions as part of the ISNCSCI routine examination. There are still no standardized techniques that describe how to examine non-key muscle functions and how to detect muscle substitutions resulting in false positives. The motor levels for non-key muscle functions were selected by reviewing multiple key reference sources for myotomal distributions of each of the non-key muscles in the upper and lower extremities. Of these, the most rostral innervation of the muscles that usually performs the activity was chosen (ASIA 2019; Kirshblum and Waring III 2014). Non-key muscle functions are used to determine motor incomplete status, AIS B vs. C. In a patient with an AIS B, if there are non-key muscle functions more than three levels below the motor level on each side, it should be classified as AIS C (Table 13.8).

Table 13.8 Non-key muscle functions

Segments	Joints	Movements
C5	Shoulder	Flexion, extension, abduction, adduction, internal rotation, external rotation
	Elbow	Supination
C6	Elbow	Pronation
	Wrist	Flexion
C7	Finger	Flexion at proximal joint, extension
	Thumb	Flexion, extension, and abduction in the plane of thumb
C8	Finger	Flexion at MCP joint
	Thumb	Opposition, adduction, and abduction perpendicular to the palm
T1	Finger	Abduction of the index finger
L2	Hip	Adduction
L3	Hip	External rotation
L4	Hip	Extension, abduction, internal rotation
	Knee	Flexion
	Ankle	Inversion and eversion
	Toe	MP and IP extension
L5	Hallux and toe	DIP and PIP flexion and abduction
S1	Hallux	Adduction

13.5.3 Sensory and Motor Scores/ Levels

13.5.3.1 Sensory Level

The sensory level is the most caudal intact dermatome for pin prick and light touch sensations. The intact dermatome level that is located immediately above the first dermatome level with impaired or absent light touch or pin prick sensation is defined as the sensory level. The sensory level should be determined for each side. Up to four sensory levels per dermatome are generated: R-pin prick, R-light touch, L-pin prick, L-light touch. For a single sensory level, the most rostral of all is taken.

If the sensation at C2 is abnormal and intact on the face, the sensory level should be designated as C1. When sensation is intact on one side or both sides for light touch and pin prick at all dermatomes C2 through S4–S5, the sensory level on that side should be recorded as "INT" that indicates "intact," rather than as S5. If the sensory level is determined based on the examiner's assumptions, the level should be tagged with a "*."

13.5.3.2 Sensory Scores

A score of 2 for each of the 28 key sensory points tested on each side of the body would result in a maximum score of 56 for pin prick, 56 for light touch, and a total of 112. The sensory score cannot be calculated if any required key sensory point is not tested.

13.5.3.3 Motor Level

Most muscles are innervated by more than one segment. If a muscle is innervated by two segments, the muscle with the presence of innervation by one segment and absence of innervation by the other segment will result in a weakened muscle. The motor level is defined by the lowest key muscle function with a grade of at least 3, and it is judged that the key muscle function represented by the segment above that level is not compromised (graded as a 5). In determining the motor level, it is assumed that the muscles are not compromised by both innervation segments of the two, so the next most rostral key muscle function should be tested as 5. A single motor level is the more rostral of both sides. For those myotomes that are not clinically testable by a manual muscle testing, i.e., C1 to C4, T2 to L1, and S2 to S5, it is assumed that the motor level is the same as the sensory level. If the motor level is determined based on the assumption of an examiner, the level should be marked with a "*."

13.5.3.4 Motor Scores

A score of 5 for each of the five key muscle functions of the upper extremity results in a maximum score of 25 for each extremity, a total of 50 for the upper extremities. The same applies to the five key muscle functions of the lower extremity, and the maximum total score of the lower extremity is 50. The motor score cannot be calculated if any required muscle function is not tested. The scores for the upper limb and lower limb are not added together. It should be separated into two scales: 10 upper limb muscle functions and 10 lower limb muscle functions, with a maximum score of 50 each (Marino and Graves 2004).

13.5.4 Neurological Level of Injury (NLI)

The term NLI refers to the most caudal segment of the spinal cord with intact sensation and antigravity muscle function strength, i.e., the last normal spinal cord segment or the level above the first abnormal segment, provided that there is normal sensory and motor function rostrally. The single NLI is the most rostral level of sensory and motor level on both sides. The motor level where there is no key muscle, such as T2–L1, is the same as the sensory level. It is recommended to record each sensory and motor level of each side separately, as a single NLI can be misleading from a functional standpoint if the sensory level is rostral to the motor level.

If a sensory or motor level is determined based on the examiner's assumptions, the neurological level should also be tagged with a "*."

13.6 ASIA Impairment Scale (AIS)

Severity of spinal cord injury is rated using the ASIA Impairment Scale (AIS). The AIS remains the most widely used classification scheme for determining the severity of spinal cord injury and for predicting the probability of subsequent spontaneous recovery (Kirshblum et al. 2011a, b, 2016; Zariffa et al. 2012). Complete or incomplete injuries are based on the sacral sparing. "Sacral sparing" is defined as the presence of sensory or motor function in the most caudal sacral segments, S4–S5, by examination of sensory or motor functions (light touch, pin prick, deep anal pressure, or voluntary anal contraction). AIS, A to E, is used in grading the degree of impairment of spinal cord injury. When evaluating the extent of motor sparing level to distinguish between AIS B and C, the motor level on each side is used, whereas to differentiate between AIS C and D, depending on proportion of key muscle functions with strength grade 3 or greater, the single neurological level is used.

If the AIS is determined based on the examiner's assumption, the AIS should be marked with a "*." If there is NT (not testable) for a particular motor or sensory score, the neurological level of injury and the ASIA Impairment Scale should be documented as "ND" (not determinable).

Grades of the ASIA Impairment Scale are as follows (Table 13.9):

- A = *Complete*. No sensory or motor function is preserved in the sacral segments S4–S5.
- B = *Sensory Incomplete*. Sensory but not motor function is preserved at the most caudal sacral segments S4–S5, and no motor function is preserved more than three levels below the motor level on either side of the body.
- C = *Motor Incomplete*. Motor function is preserved at the most caudal sacral segments on voluntary anal contraction (VAC) or the patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segments, S4–S5, by light touch, pin prick, or deep anal pressure), with sparing of motor function more than three levels below the ipsilateral motor level on either side of the body. This includes key or non-key muscle functions more than three levels below the motor level to determine motor incomplete status. For AIS C, less than half of key muscle functions below the single NLI have a muscle grade ≥ 3.

Table 13.9 ASIA impairment scale (AIS)

Scale	Descriptions
A (complete)	• No sensory or motor function is preserved in the sacral segments S4–5.
B (sensory incomplete)	• Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4–5 (light touch or pin prick at S4–5 or deep anal pressure) AND • No motor function is preserved more than three levels below the motor level on either side of the body
C (motor incomplete)	• Motor function is preserved at the most caudal sacral segments for voluntary anal contraction OR • The patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segment (S4–5) by light tough, pin prick, or deep anal pressure), and has some sparing of motor function more than three level below the ipsilateral motor level on either side of the body • This includes key or non-key muscle functions to determine motor incomplete status. For AIS C, less than half of the key muscle functions below the single NLI have a muscle grade ≥3
D (motor incomplete)	• Motor incomplete status as defined above, with at least half (half or more) of key muscle functions below the single NLI having a muscle grade ≥3 • Non-key muscles are not used in determining in AIS D
E (normal)	• If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E • Someone without an initial SCI does not receive an AIS grade
Using ND	• To document the sensory, motor, and NLI levels, the AIS, and/or the ZPP when they are unable to be determined based on the examination results

- D = *Motor Incomplete*. Motor incomplete status as defined above (AIS C), with at least half (half or more) of key muscle functions below the single NLI having a muscle grade ≥ 3.
- E = *Normal*. If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without a spinal cord injury does not receive an AIS grade.

13.7 Zone of Partial Preservation (ZPP)

The term ZPP is used in injuries with absent motor (no VAC) or sensory function (no DAP, no light touch, and no pin prick sensation) in the lowest sacral segments S4–5, and is defined as the dermatomes and myotomes caudal to the sensory and motor levels that remain partially innervated. The most caudal segment with some sensory or motor function defines the extent of the sensory or motor ZPP, respectively. A single segment is designated on the worksheet. If there are no segments with partially preserved functions below a motor or a sensory level, the motor or sensory level should be recorded for the ZPP on the worksheet. The motor function does not follow sensory function in recording ZPP, but rather the caudal extent of the motor ZPP must be based on the presence of voluntary muscle contraction below the motor level. For example, if NLI is T4 with some sensation at the left T6 dermatome, T6 is recorded for the left sensory ZPP, but motor ZPP should remain T4. That is, while the motor level defers to the sensory level in the regions with no muscles to be tested by manual muscle testing, motor ZPP does not follow the sensory ZPP (Solinsky and Kirshblum 2018).

In general, non-key muscles are not used to determine ZPP. However, if a non-key muscle function was used to determine AIS C, the most caudal non-key muscle function level is recorded as motor ZPP. If DAP or VAC is present, sensory ZPP and motor ZPP on both sides are not applicable, "NA" is recorded in the ZPP box.

13.8 Clinical Syndromes

For spinal cord injuries due to trauma and vascular or other space-occupying lesions, the ISNCSCI included the clinical syndromes of spinal cord injuries prior to the seventh revision of 2011. The ISNCSCI defines five clinical syndromes of incomplete spinal cord injury that are not a part of the ISNCSCI examination or classification: central cord syndrome, Brown-Séquard syndrome, anterior cord syndrome, conus medullaris, and cauda equina syndrome (ASIA 2015, 2019) (Table 13.10). For each of the incomplete

Table 13.10 Patterns of common incomplete injuries

Syndrome	Cause	Examination findings
Central cord	Hyperflexion or extension, usually elderly with existing spinal stenosis; most common syndrome	Motor weakness of arms > legs with sacral sensory sparing
Brown-Séquard	Spinal cord hemisection, often gunshot or stab wound	Ipsilateral loss of motor and proprioception; contralateral loss of pain and temperature sensation; variations as Brown-Séquard plus syndrome
Anterior cord	Damage to anterior 2/3 of cord, usually direct injury or ischemia from anterior spinal artery injury	Loss of motor function and pain/temperature with preserved proprioception and light touch sensation
Cauda equina	Injury to lumbar/sacral nerve roots, lumbar (L2 or lower), or sacral fractures, also pelvic fractures, herniated disc, tumor	Weakness or flaccid leg paralysis, high lesions spare bowel/bladder, absent bulbocavernosus reflex
Conus medullaris	Injury to the sacral cord and lumbar nerve roots, upper lumbar (L1) fractures, disc herniation, tumor	Bowel, bladder, and sexual dysfunction with areflexia, normal leg motor function, present bulbocavernosus reflex with high lesion

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clinical syndromes, see Chap. 17. Previous versions of the International Standards included the posterior cord syndrome and a mixed syndrome. The posterior cord syndrome was removed from the ISNCSCI versions because of the rare occurrence of less than 1%, while the mixed syndrome was omitted because it does not present a definable syndrome (Hayes et al. 2000).

13.9 Expedited ISNCSCI

Although the full ISNCSCI examination remains the gold standard for evaluation and documentation of spinal cord injuries, there are circumstances where a more rapid but more limited examination may be required. The ISNCSCI examination requires a sensory test of 28 dermatomes for light touch and pin prick bilaterally, a manual muscle test for ten key limb muscles on both sides, and an anorectal test for sensation and motor function. This detailed examination of testable segments includes 134 items. Completion and recording of the exam can take over 45 min, even for an experienced examiner (Burns and Tansey 2020). Because of this time requirement, the E-ISNCSCI examination was developed to provide a more rapid option for determining the neurological level of injury (NLI) and ASIA Impairment Scale (AIS) with the minimum items of examination. This is achieved in part by omitting examination items that do not affect NLI and AIS determination and options that allow some examination findings to be assumed based on other findings. There are options to substitute S1 sensory and motor findings for the anorectal exam and S4–5 dermatomes if these cannot be performed. This is based on a study by Zariffa et al. (2012) that a preserved sensation at the S1 provided a good prediction (90.5%) for caudal sacral sensory sparing (S4–5) and a voluntary anal contraction was accurately predicted by a preserved motor function of the S1 in 85.4%.

Use of the E-ISNCSCI exam may be appropriate in some clinical or research situations, but it is not intended to replace the full ISNCSCI. The protocol uses the same motor and sensory examination techniques as the full ISNCSCI examination but allows omission of a large percentage of the individual examination components. Use of the E-ISNCSCI examination requires knowledge of and training in the full ISNCSCI examination (ASIA 2020).

References

Alaca R. ASIA assessment of spinal cord injury-history. Turk J Phys Med Rehabil. 2015;61(Supp. 1):S1–3.

Alexander MS, Anderson KD, Biering-Sorensen F, et al. Outcome measures in spinal cord injury: recent assessments and recommendations for future directions. Spinal Cord. 2009;47:582–91.

Arnold PM, Filardi TZ, Strang RD, et al. Early neurologic assessment of the patient with spinal cord injury. Top Spinal Cord Inj Rehabil. 2006;12:38–48.

ASIA. Standards for neurological classification of spinal injury patients. Chicago: ASIA; 1982.

ASIA. International standards for neurological classification of spinal cord injury. 7th ed. Revised 2011. Atlanta: ASIA; 2011.

ASIA. International standards to document remaining autonomic function after spinal cord injury. 1st ed. Atlanta: ASIA; 2012.

ASIA. International standards for neurological classification of spinal cord injury. 7th ed. updated 2015. Atlanta: ASIA; 2015.

ASIA. International standards for neurological classification of spinal cord injury. 8th ed. revised 2019. Richmond: ASIA; 2019.

ASIA. Expedited ASIA ISNCSCI Exam (E-ISNCSCI) Version 1 (February 2020). 2020. https://asia-spinalinjury.org/expedited-isncsci-exam/. Accessed 20 Nov 2021.

ASIA and ISCoS International Standards Committee. The 2019 revision of the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)-What's new? Spinal Cord. 2019;57:815–7.

Bracken MB, Webb SB Jr, Wagner FC. Classification of the severity of acute spinal cord injury: implications for management. Paraplegia. 1978;15:319–26.

Burns SP, Tansey KE. The expedited international standards for neurological classification of spinal cord injury (E-ISNCSCI). Spinal Cord. 2020;58:633–4.

Calancie B, Molano MR, Broton JG. Tendon reflexes for predicting movement recovery after acute spinal cord injury in humans. Clin Neurophysiol. 2004;115:2350–63.

Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: nerve injuries research committee. His Majesty's stationery office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 figures. Brain. 2010;133:2838–44.

Consortium for Spinal Cord Medicine. Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care providers. Washington, DC: Paralyzed Veterans of America; 2008.

Eckert MJ, Martin MJ. Trauma: spinal cord injury. Surg Clin North Am. 2017;97:1031–45.

Evaniew N, Sharifi B, Waheed Z, et al. The influence of neurological examination timing within hours after acute traumatic spinal cord injuries: an observational study. Spinal Cord. 2020;58:247–54.

Frankel HL, Hancock DO, Hyslop G, et al. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. Paraplegia. 1969;7:179–92.

Furlan JC, Fehlings MG, Tator CH, et al. Motor and sensory assessment of patients in clinical trials for pharmacological therapy of acute spinal cord injury: psychometric properties of the ASIA standards. J Neurotrauma. 2008;25:1273–301.

Furlan JC, Noonan V, Singh A, Fehlings MG, et al. Assessment of impairment in patients with acute traumatic spinal cord injury: a systematic review of the literature. J Neurotrauma. 2011;28:1445–77.

Hayes KC, Hsieh JT, Wolfe DL, et al. Classifying incomplete spinal cord injury syndromes: algorithms based on the international standards for neurological and functional classification of spinal cord injury patients. Arch Phys Med Rehabil. 2000;81:644–52.

Herbison GJ, Zerby SA, Cohen ME, et al. Motor power differences within the first two weeks post-SCI in cervical spinal cord-injured quadriplegic subjects. J Neurotrauma. 1992;9:373–80.

Hughes JT. Neuropathology of the spinal cord. Neurol Clin. 1991;9:551–71.

Kakulas BA. A review of the neuropathology of human spinal cord injury with emphasis on special features. J Spinal Cord Med. 1999a;22:119–24.

Kakulas BA. The applied neuropathology of human spinal cord injury. Spinal Cord. 1999b;37:79–88.

Kirshblum S, Waring W III. Updates for the international standards for neurological classification of spinal cord injury. Phys Med Rehabil Clin N Am. 2014;25:505–17.

Kirshblum S, Botticello A, Lammertse DP, et al. The impact of sacral sensory sparing in motor complete spinal cord injury. Arch Phys Med Rehabil. 2011a;92:376–83.

Kirshblum SC, Waring W, Biering-Sorensen F, et al. Reference for the 2011 revision of the international standards for neurological classification of spinal cord injury. J Spinal Cord Med. 2011b;34:547–54.

Kirshblum SC, Biering-Sorensen F, Betz R, et al. International standards for neurological classification of spinal cord injury: cases with classification challenges. Top Spinal Cord Inj Rehabil. 2014;20:81–9.

Kirshblum SC, Botticello AL, Dyson-Hudson TA, et al. Patterns of sacral sparing components on neurologic recovery in newly injured persons with traumatic spinal cord injury. Arch Phys Med Rehabil. 2016;97:1647–55.

Kirshblum S, Snider B, Rupp R, et al. Updates of the international standards for neurologic classification of spinal cord injury: 2015 and 2019. Phys Med Rehabil Clin N Am. 2020;31:319–30.

Ko HY, Ditunno JF Jr, Graziani V, et al. The pattern of reflex recovery during spinal shock. Spinal Cord. 1999;37:402–9.

Marino RJ, Graves DE. Metric properties of the ASIA motor score: subscales improve correlation with functional activities. Arch Phys Med Rehabil. 2004;85:1804–10.

Marino RJ, Jones L, Kirshblum S, et al. Reliability and repeatability of the motor and sensory examination of the international standards for neurological classification of spinal cord injury. J Spinal Cord Med. 2008;31:166–70.

McCarter SJ, Burkholder DB, Klaas JP, et al. Beevor's lasting contributions to neurology: more than just a sign. Neurology. 2018;90:513–7.

Medical Research Council (Nerve injuries committee). Aids to the examination of the peripheral nervous system. Memorandum No. 45 (superseding War Memorandum No. 7). London: Her Majesty's Stationery Office; 1943.

Michaelis LS. International inquiry on neurological terminology and prognosis in paraplegia and tetraplegia. Paraplegia. 1969;7:1–5.

Oner C, Rajasekaran S, Chapman JR, et al. Spine trauma-what are the current controversies? J Orthop Trauma. 2017;31(Suppl 4):S1–6.

Pearce JM. Beevor's sign. Eur Neurol. 2005;53:208–9.

Rupp R, Schuld C, Biering-Sørensen F, et al. A taxonomy for consistent handling of conditions not related to the spinal cord injury (SCI) in the International Standards for Neurological Classification of SCI (ISNCSCI). Spinal Cord. 2021. https://doi.org/10.1038/s41393-021-00646-0.

Schuld C, Wiese J, Hug A, et al. Computer implementation of the international standards for neurological classification of spinal cord injury for consistent and efficient derivation of its subscores including handling of data from not testable segments. J Neurotrauma. 2012;29:453–61.

Solinsky R, Kirshblum SC. Challenging questions regarding the international standards. J Spinal Cord Med. 2018;41:684–90.

van Middendorp JJ, Goss B, Urquhart S, et al. Diagnosis and prognosis of traumatic spinal cord injury. Global Spine J. 2011;1:1–8.

Waters RL, Adkins RH, Yakura JS. Definition of complete spinal cord injury. Paraplegia. 1991;29:573–81.

Wecht JM, Krassioukov AV, Alexander M, et al. International standards to document autonomic function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.

Wolfe D, Hsieh J, Curt A, et al. Neurological and functional outcomes associated with SCI rehabilitation. Top Spinal Cord Inj Rehabil. 2007;13:11–31.

Zariffa J, Kramer JL, Jones LA, et al. Sacral sparing in SCI: beyond the S4-S5 and anorectal examination. Spine J. 2012;12:389–400.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/ McGraw-Hill; 2005.

Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Durrant DH, True JM. Myelopathy, radiculopathy, and peripheral entrapment syndromes. Boca Raton: CRC Press; 2002.

Eagler GL, Cole J. Merton, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.

Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.

Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.

14 Spinal Shock: Definition and Reflex Evolution Pattern

Severe spinal cord injury results in a complete loss of motor and sensory function caudal to the injury site. It also leads to an immediate and prolonged depression of stretch reflex excitability in spinal cord segments caudal to the injury (Calancie et al. 2004). The term "spinal shock" refers to this condition, defined as a "… state of total abolition of all tendon reflexes and profound depression of other reflex activity below the level of cord transection which immediately follows such a lesion..." (Guttmann 1976; Kuhn 1950). Kuhn observed the most typical sequence of reflex activity after severing the spinal cord: (1) spinal shock (total flaccidity); (2) minimal reflex activity; (3) flexor spasms; (4) alternating flexor and extensor spasms; and (5) predominant extensor spasms (Kuhn 1950). After an acute onset of spinal cord injury, there is a sudden loss of reflexes and muscle tone below the level of injury known as spinal shock. The term "spinal shock" was first introduced in 1840 by Marshall Hall, which suddenly showed a decrease in muscular irritability and no reflexes in spinal paralysis (Hall 1840). Before Hall's description, Whyte reported the same motor phenomenon in 1750, but there was a fairly clear definition of the loss of sensation accompanying motor paralysis with the gradual recovery of the reflexes. The term shock was not used, however, and there was no anatomical basis for the reflexes understood at the time (Ditunno et al. 2004; Sherrington 1906).

Initially, it was defined by Bastian as a complete severance of the spinal cord, which leads to a complete loss of motor and sensory function below the level of the lesion, as well as permanent extinction of tendon reflexes and muscle tone although the reflex arc remains intact (Bastian 1890). Flaccid motor paralysis is observed immediately after the acute onset of complete spinal cord injury below the level of injury with no motor responses to external stimuli. Sherrington replaced Bastian's use of the term "permanent" with a "temporary" extinction of the reflex below the level of the lesion (Guttmann 1976; Sherrington 1906). Sherrington's definition has been used to date as a transient extinction of reflexes below the level of spinal cord injury (Sherrington 1906).

Spinal shock is pronounced only in primates, especially in humans, due to such a dominance of an inhibitory mechanism in the spinal cord (van Harreveld 1940). In general, the more severe the physiologic or anatomic transection of the spinal cord, the more profound the spinal shock. Spinal shock does not occur with slowly developing spinal cord diseases or injuries (Atkinson and Atkinson 1996).

The pattern of natural course following a spinal cord injury distinguishes between sudden onset and slow changes in the spinal cord. In the next days and weeks, motor reactions to external stimuli gradually reappear systematically

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(Christensen et al. 1990; Ditunno et al. 2004; Ko et al. 1999). The definition of spinal shock and the pattern of reflex recovery or evolution and muscle tone recovery remain issues of debate and controversy (Atkinson and Atkinson 1996; Ko et al. 1999). The lack of consensus on the clinical symptomatology defining the duration of spinal shock persists. Some clinicians interpret spinal shock to mean that it ends with the appearance of the bulbocavernosus reflex (Stauffer 1975; Holdsworth 1968). Others (Hiersemenzel et al. 2000; Wolpaw and Tennissen 2001) state that spinal shock ends with the recovery of deep tendon reflexes and may not reappear for several weeks if the human spinal cord is completely injured. Still, other clinicians define the resolution of spinal shock as the recovery of detrusor reflex after injury (Ditunno et al. 2004). If the duration of spinal shock is defined by the initial recovery of any reflex, it probably lasts no more than 20 min to 1 h. However, if the spinal shock is defined as the absence of deep tendon reflexes, its duration is several weeks (Hiersemenzel et al. 2000).

The terms "spinal shock" and "neurogenic shock" are often both used inappropriately or incorrectly or confused with each other in the clinical setting (Eckert and Martin 2017). Although neurogenic shock refers to a hemodynamic pattern, spinal shock refers to the neurologic examination results that may be seen after an acute spinal cord injury. Neurogenic shock results in severe hypotension and bradycardia, associated with an acute spinal cord injury. Neurogenic shock is the hemodynamic consequence of spinal cord injury, which is classically characterized by hypotension due to vasodilation and increased perfusion of the lower extremities, known as "warm shock" (Eckert and Martin 2017). Because of an intact parasympathetic influence via the vagal nerve and a loss of sympathetic tone due to disruption in supraspinal control, neurogenic shock occurs as a result of an imbalance in autonomic control.

This chapter describes the definition, pathophysiology, and clinical significance of spinal shock, which is not well established and has a lot of controversies.

14.1 Definition of Spinal Shock

The spinal shock was initially considered to be arterial hypotension after spinal cord injury (Hall 1841). The definition has evolved into a permanent extinction of tendon reflexes. Further definition changes have been revised to include all findings relating to the physiological and anatomical transection of the spinal cord that results in depression of spinal reflexes for a limited period. A complete or relatively complete spinal cord lesion is immediately followed by a complete loss of motor and sensory functions below the level of the lesion upon sudden onset, as well as a complete loss of tone with no deep and superficial reflexes. The phenomenon in which tone and reflex activity disappear completely below the level of injury is known as spinal shock. Spinal shock is defined as a condition of transient physiologic, rather than anatomic, reflex depression of spinal cord function below the level of injury. Spinal shock is usually temporary. Spinal shock should not be confused with neurogenic shock in the acute phase of spinal cord injury. Spinal shock is characterized by the loss of reflexes, detrusor activity, and muscle tone below the level of injury. Neurogenic shock is a hemodynamic change, one of the autonomic components during the acute phase of spinal cord injury, caused by a loss of sympathetic tone and unopposed parasympathetic function, leading to hypotension and bradycardia (Levi et al. 1993; White and Likavec 1999). It is commonly seen when the level of injury is above T6.

It has been observed that the most peripheral somatic reflexes of the sacral cord segments (the anal reflex and bulbocavernosus reflex) may never disappear or may return within minutes or hours of the injury, although classic teaching refers to generalized areflexia below the level of the lesion for days to months (Guttmann 1976). One study interpreted an existing bulbocavernosus reflex in persons with complete spinal cord injury as the end of the spinal shock and found that the bulbocavernosus reflex returned within 24 h in 99% of the patients (Stauffer 1975). According to other observations, there is no sig-

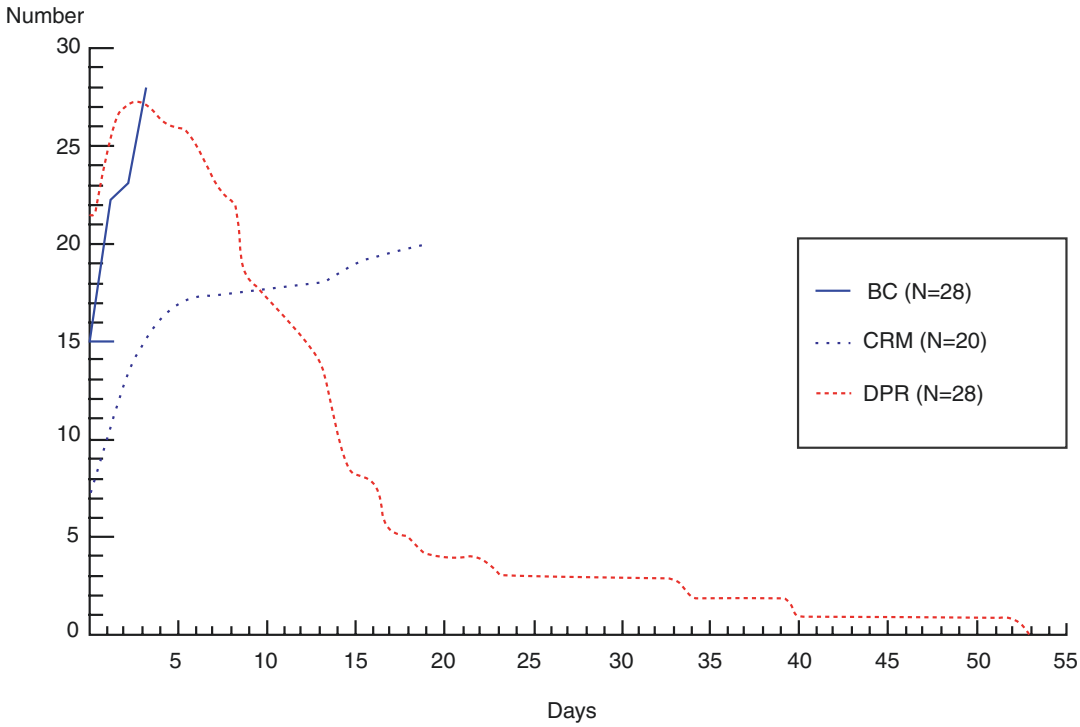

Fig. 14.1 Recovery of the cutaneous reflexes, which includes the bulbocavernosus (BC), the delayed plantar response (DPR), and the cremasteric reflex (CRM). DPRs appear first, followed by BC reflexes and CRMs, all appearing within days of injury. From Ko et al. (1999), with permission

nificant time difference between the evolution of the bulbocavernosus reflex and other cutaneous reflexes, so that is difficult to define the appearance of the bulbocavernosus reflex as the end of spinal shock (Ko et al. 1999) (Fig. 14.1). Preserved sacral reflex arcs such as bulbocavernosus and anal reflex during spinal shock due to high cervical cord injuries should not be confused with sacral sparing. If there is distal sacral reflex arc activity in the initial phase of high cervical spinal cord injury, they may be depressed, or they may become areflexic within hours to days after injury (Atkinson and Atkinson 1996). However, functions of proximal segments to the level of injury can also be depressed (Atkinson and Atkinson 1996).

It is known that spinal shock usually lasts days or weeks after a spinal cord injury, and the average duration is 4–12 weeks. Spinal shock is terminated earlier, and the pyramidal tract signs and defense reactions appear earlier in incomplete lesions than with complete transverse lesions. The identification of clinical signs that determine the duration of spinal shock is controversial. There is no uniform consensus on the definition of cessation of spinal shock. Most references define the end of spinal shock with a return of specific reflexes. However, not all reflexes are uniformly depressed in each patient. The reflex changes are individualized. Spinal shock resolves over a period of days to months, and spinal shock slowly transitions to spasticity. Various authors have defined the termination of spinal shock as the reappearance of the bulbocavernosus reflex, the recovery of deep tendon reflexes, or the return of reflexic detrusor activity. Still, there are many questions to be answered, such as: When should we define spinal shock as the end? What types of reflexes appear first among polysynaptic cutaneous reflexes, monosynaptic deep tendon reflexes, and pathological reflexes? Should it include changes in autonomic reflexes such as a detrusor reflex?

14.2 Pathophysiology

The underlying mechanisms of spinal shock are not clearly defined. There has not been a convincing explanation for reflex recovery. According to modern concepts, spinal shock can be mediated by synaptic changes in spinal cord segments below the level of injury, such as by enhancement of presynaptic inhibition (Calancie et al. 1993), a high concentration of glycine (Simpson et al. 1996), as a major inhibitory neurotransmitter, and by hyperpolarization of spinal motor neurons (Leis et al. 1996; Nacimiento and Noth 1999).

Many hypothetical mechanisms of spinal shock have been introduced. Sherrington's hypothesis was one of the most explainable mechanisms of spinal shock, in which a sudden withdrawal of facilitatory influences of the descending pathways leads to a disruption of synaptic transmission and interneuronal conduction (Sherrington 1906). The neurophysiological hypotheses are based essentially on the withdrawal of supraspinal facilitation and increased segmental inhibition. If the neurophysiological hypothesis is one aspect that explains the mechanism of spinal shock, another aspect depends on the neurotransmitter. The most explainable neurochemical mechanism is a threefold to fourfold increase of glycine, an amino acid neurotransmitter, in the absence or depression of reflexes during spinal shock (Simpson et al. 1993, 1996). A high concentration of the inhibitory amino acid neurotransmitter, glycine, is associated with flaccidity following spinal cord injury or spinal shock (Simpson et al. 1993).

The relative importance of different pathways causing spinal shock is not well understood, but in lower animals, the important descending influences appear to be reticulospinal and vestibulospinal tract, while in higher animals, including man, corticospinal connections are probably more important (Bach-y-Rita and Illis 1993). Spinal shock may occur due to the loss of normal facilitation and/or inhibition of interneurons and motor neurons of the spinal cord through several pathways, including corticospinal, rubrospinal, vestibulospinal, and reticulospinal tracts (Barnes and Schadt 1979; Mendell 1988). The supraspinal segmental inhibition has been confirmed by several electrophysiological studies during spinal shock, with results of presynaptic inhibition and blocking monosynaptic and polysynaptic reflex arcs (Calancie et al. 2004; Schadt and Barnes 1980).

Loss of tone and depression of reflexes can be the result of a disturbance of the fusiform, γ-efferent system that regulates the sensitivity of the muscle stretch receptors (Weaver et al. 1963). Gamma-motor neurons, which regulate muscle spindle tension, may potentially be fired to maintain background excitability in muscle spindles. Gamma-motor neurons may lose tonic descending facilitation distal to the level of spinal cord injury, resulting in decreased muscle spindle excitability and decreased segmental input to motor neurons by stretch reflex afferents. The disturbance of fusiform function is caused by the loss of normal spinal cord activity, which is dependent on continuous tonic discharges from higher centers through the vestibulospinal and reticulospinal tracts (Weaver et al. 1963).

After a few hours to a few weeks, the spinal neurons gradually regain their excitability. This phenomenon appears to be a natural feature of neurons in the nervous system. That is, after the source of facilitatory impulses has been lost, it at least partially increases the level of natural excitability to compensate for the loss. In most nonprimates, the excitability of the cord centers returns to nearly normal within a few hours to a day. In humans, however, they are often delayed for weeks and sometimes never completely. Conversely, recovery is sometimes excessive and, as a result, some or all spinal cord functions. Evolutionarily the higher species have greater degrees of spinal shock, suggesting that new descending tracts may be phylogenetically responsible (Sherrington 1906). Although the distal spinal cord below the level of injury has received the most attention, researchers have known for almost a century that the proximal spinal cord also changes, and these cephalic effects are known as the Schiff-Sherrington phenomenon (Atkinson and Atkinson 1996; Guttmann 1976; Ruch 1935; Sherrington 1906). In early clinical series, such loss was supposed to be an

extension of concussion in the area of injury, but later laboratory experiments suggest the phenomenon (Atkinson and Atkinson 1996).

There was a different hypothesis explaining the recovery of reflexes. Nonsynaptic diffusion neurotransmission (volume transmission) and unmasking were postulated to explain the recovery of reflexes. Reflex recovery may be associated with the upregulation of receptors in synapses and on the surface of partially denervated spinal cord cells, resulting in increased sensitivity to neurotransmitters and other neuroactive substances released at the surviving synapses or elsewhere and transported in the extracellular fluid (Bach-y-Rita and Illis 1993). Recovery from spinal shock and development of spasticity can be caused by synaptic reorganization such as augmentation of latent synapses on spinal motor neurons, which are normally present but ineffective (Tai and Goshgarian 1996), as well as collateral sprouting of axons from undamaged systems, which in turn can reinnervate partially denervated spinal neurons (McCouch et al. 1958; Nacimiento and Noth 1999).

14.3 Clinical Observations of Reflex Evolution During Spinal Shock

There is a clinical phenomenon of spinal shock with sequential rostrocaudal depression of reflex activities after spinal cord transection and recovery of reflexes in the caudorostral pattern (Guttmann 1970; Landau and Clare 1959; Riddoch 1917). If the duration of spinal shock is defined by the initial recovery of a reflex, it cannot last longer than 1 h. If spinal shock is defined as the absence of deep tendon reflexes or autonomic reflexes, its duration lasts several weeks or months (Ditunno et al. 2004; Ko et al. 1999). There are several characteristics of spinal shock. Spinal cord injuries first change the reflexes that occur in the nearest segment of the injury and then change the reflexes farther from the injured segment. Therefore, in high-level cervical injuries, the sacral reflexes such as bulbocavernosus and anal reflex can be preserved longer. The observation that reflex depression or extinguishment occurs in a proximal to distal pattern suggests a physiological explanation for this change. Spinal shock occurs immediately after spinal cord injury, but the reflexes do not decrease or disappear in some segments for some periods of time. The segment of the spinal cord most distal to the transection is more likely to retain some reflex activity. In clinical series, patients with high cervical cord injuries are likely to retain distal sacral reflex, such as bulbocavernosus and anal reflex, although all other reflexes are lost. Guttmann found that the ankle jerk, plantar response, and anal sphincter and bulbocavernosus reflexes are still present immediately after spinal cord transection and may disappear after a certain latent period. During this time, there may be some reflex activity in the sacral segments, but reflex activity in the detrusor muscle of the bladder may be absent (Guttmann 1970).

Spinal shock involves suppression of autonomic activity and somatic activity, and the bladder is acontractile and areflexic. However, there is one study in which a urodynamic examination revealed an acontractile detrusor in only 37%, but unfavorable urodynamic parameters, such as detrusor overactivity, detrusor-sphincter dyssynergia, high maximum detrusor pressure, and low detrusor compliance, in 63% in people with acute spinal cord injuries. In contrast to the well-known acontractile detrusor in acute spinal cord injuries, almost two-thirds of the patients showed unfavorable urodynamic parameters within the first 40 days after spinal cord injuries (Bywater et al. 2018). In addition, during experimental spinal shock, the urethral muscle responded to drugs earlier than the detrusor muscle. Stimulation with parasympathomimetic drugs caused some rise in intravesical pressure, but an unexpected and much greater rise in intraurethral pressure (Tulloch and Rossier 1975). Thus, the assumption that parasympathetic or sympathetic reflexes develop more slowly than somatic reflexes should be reconsidered and require further clarification. Radiologically, the bladder shows smooth contour with no trabeculation during spinal shock. The bladder neck is usually closed and competent unless previously undergone surgery or the

patient does not have a thoracolumbar spinal cord and sympathetic injury (Sullivan and Yalla 1996). Some electromyographic activity can be recorded in the striated sphincter, and the maximum urethral closure pressure is lower than normal but still maintained at the level of the external sphincter. However, there is no normal guarding reflex for the striated sphincter to contract during filling and no voluntary control (Fam and Yalla 1988). Since there is a sphincter tone, there is usually no incontinence unless there is no overdistention. The bladder storage pressure remains low. Catheterization is required to solve urinary retention. Almost all agree that clean intermittent catheterization is a preferred management method during this period (Lloyd 1986).

The autonomic component of spinal shock after spinal cord injury may last from days to weeks, but when a somatic component is present, it usually lasts for hours after injury. In fact, one-third of patients with spinal cord injuries cannot have significant loss of reflexes without somatic spinal shock after injury. An earlier observation showed that the sacral or caudal segment of the spinal cord after complete transection has less reflex depression than the rostral segments (Riddoch 1917). The reflex depression is usually more severe and lasts longer in segments of the isolated cord that are closer to the transection than in the distal segment (Guttmann 1970). Other observations showed greater depression of reflexes in the rostral segments due to the loss of a greater number of descending propriospinal and encephalospinal pathways (Landau and Clare 1959). A very important postulation has been suggested that cutaneous reflexes are the least depressed and recover earlier, as less obvious long descending fibers contribute to the central excitatory state (Dimitrijević and Nathan 1968).

Reflexes return sequentially rather than simultaneously. During the early return of reflexes, the stimulus should be strong or summated and the response can be easily fatigued (Bach-y-Rita and Illis 1993). According to Guttmann's classic study of spinal cord injuries, the resolution of the somatic component of spinal shock was traditionally signaled by the return of the bulbocavernosus reflex and the anal cutaneous reflex, a polysynaptic spinal reflex mediated by the S2–S4 via the conus medullaris (Guttmann 1952, 1970). Observations made before Guttmann show other phenomena of reflex activity during spinal shock. It is not consistent with the caudorostral recovery of reflexes, for example, a cremasteric reflex occurs as early as the bulbocavernosus reflex and delayed plantar response (Guillain and Barre 1917; Riddoch 1917; van Harreveld 1940). The cremasteric reflex comes from L1 and L2 (Schwarz and Hirtler 2017), the bulbocavernosus reflex from S3 and S4, and the delayed plantar reflex from S1. In the last few decades, at least since Guttmann, no detailed observation of the reflex behavior during spinal shock has been performed (Atkinson and Atkinson 1996). It is understood that clinical observation of change in reflexes since a spinal cord injury in humans cannot be an easy task. However, as much clinical observations as possible should be required to define the spinal shock more clearly. The questions remain: How do you define spinal shock? How can you define when the spinal shock stops? What is the first reflex after a spinal cord injury and during spinal shock? Are there differences in the reflex recovery pattern depending on the reflex types?

A study that examined the temporal return of reflexes after spinal cord injury challenged above traditional view (Calancie et al. 2004; Ko et al. 1999). The study is a sequential assessment of the reflexes on arrival at the emergency room after spinal cord injury. The reflexes assessed include delayed plantar response (reflex), bulbocavernosus reflex, cremasteric reflex, Babinski sign, ankle jerk, and knee jerk. The study found that the bulbocavernosus reflex may not be the first reflex to recover after spinal cord injury. However, the pathological reflex that is known as the delayed plantar response precedes or occurs simultaneously with the return of the bulbocavernosus reflex in most acute complete injuries (AIS A). The delayed plantar response requires an unusually strong stimulus, unlike the Babinski sign or normal plantar response (Weinstein et al. 1997). The delayed plantar response lasts from hours to a

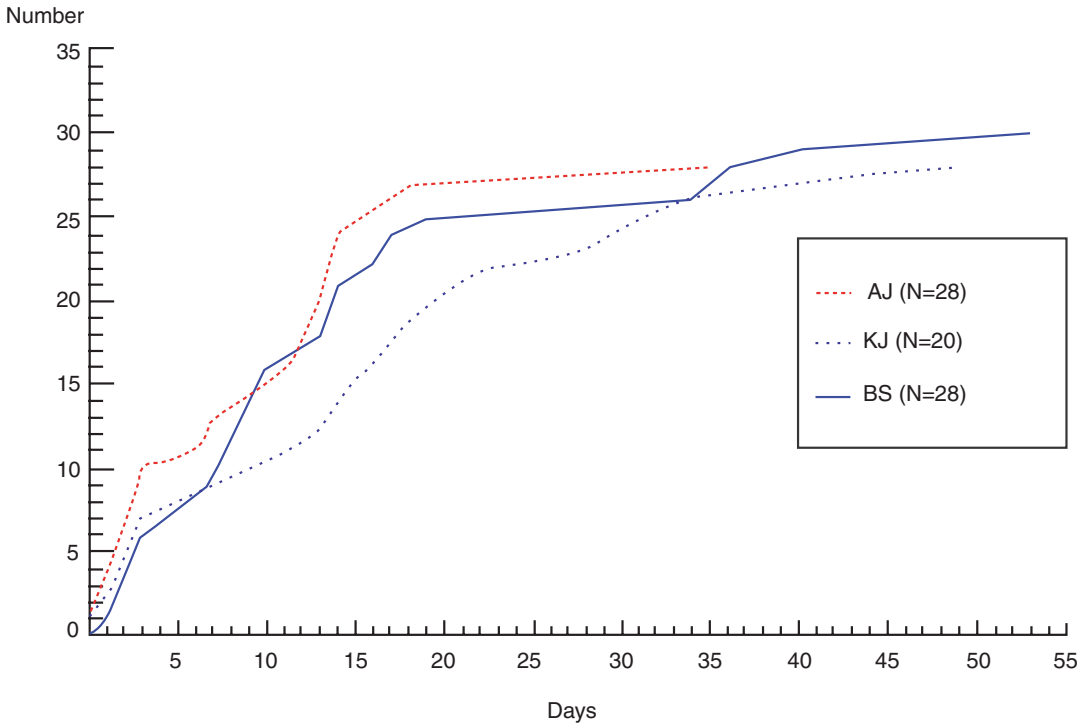

Fig. 14.2 Recovery of the deep tendon reflexes (AJ, KJ) and the Babinski sign in individuals with AIS A. The difference in the order of appearance depending on the duration between each of the reflexes is not clear. From Ko et al. (1999), with permission

few days until the extensor plantar reflex or Babinski sign develops, usually within 14 days in patients with complete injuries (Calancie et al. 2004; Ko et al. 1999) (Fig. 14.1). It shows a reciprocal relationship with the Babinski sign and the delayed plantar response is gradually replaced by the Babinski sign as observed by Riddoch (Guillain and Barre 1917; Ko et al. 1999; Riddoch 1917; van Harreveld 1940). If deep tendon reflexes are chosen as termination criteria for spinal shock, the duration of spinal shock is longer and lasts for several weeks or months. Clinical observation suggests that other reflexes occur after delayed plantar reflex in the following order: bulbocavernosus reflex, cremasteric reflex, ankle jerk, Babinski sign, and knee jerk. The pattern of reflex recovery appears to be cutaneous polysynaptic reflexes before monosynaptic reflexes (Ditunno et al. 2004; Ko et al. 1999; van Gijn 1978, 1996). There was no significant time difference in the recovery of deep tendon reflexes of ankle jerk and knee jerk and the development of Babinski sign in complete injuries (Fig. 14.2). Although Guttmann (Guttmann 1952, 1970) showed that the bulbocavernosus reflex recovered first, followed by deep tendon reflexes in a caudal to rostral direction, the study was unable to confirm this recovery pattern. The cremasteric reflex (L2) often precedes the ankle jerk (S1), and the delayed plantar response (S1) often precedes the bulbocavernosus reflex (S3–S5), which is not compatible with the caudorostral recovery pattern of the reflexes (Ko et al. 1999). Initially observable reflexes are the polysynaptic cutaneous reflexes such as delayed plantar response, bulbocavernosus reflex, and cremasteric reflex, rather than the monosynaptic deep tendon reflexes, and these distinctions are more obvious than caudorostral distinction (Ditunno et al. 2004). It appears that the polysynaptic cutaneous reflexes receive

less supraspinal facilitation and/or those synaptic areas are less disturbed because descending pathways provide less contributive (Illis 1967). The differences of reflex recovery in complete injuries according to age were significant. The younger, the more severe the spinal shock with delayed development to Babinski sign, the longer the presence of a delayed plantar response, and the more delayed the recovery of deep tendon reflexes (Ko et al. 1999; van Munster et al. 2012) (Table 14.1). The earlier recovery of deep tendon reflexes in the elderly suggests that spinal stenosis with preexisting subclinical myelopathy can contribute to the rapid recovery of reflexes (Bunge et al. 1993; Riddoch 1917). Conclusions of the study were as follows: (1) A delayed plantar response might be the first reflex. (2) Reflex recovery did not follow a caudorostral pattern. (3) Polysynaptic cutaneous reflexes may be less depressed compared to monosynaptic deep tendon reflexes. (4) The clinical presentation of reflex activities during or after spinal shock should be reconsidered and the definition of spinal shock, including autonomic reflex activities, should be reestablished (Ko et al. 1999). If spinal shock is defined as the absence of all reflexes, the definition of spinal shock may be reestablished since all reflexes are rarely absent, even with complete injuries. The view of spinal shock, that reflex return occurs in a caudal to rostral sequence, may also be reconsidered. A more accurate description of spinal shock should be characterized by a period of an altered appearance of cutaneous and deep tendon reflexes and the emergence of pathologic reflexes over days and weeks.

14.4 Clinical Implications of Spinal Shock

It is logical to determine whether an injury results in the acute phase leads to a profound depression of spinal reflexes, comparable to that which occurs in a neurologically complete spinal cord injury. If not, the absence of reflex depression following acute spinal cord injury should be associated with a better prognosis for recovery of neurologic function (Calancie et al. 2004). Spinal cord injury with concomitant spinal shock usually has a worse prognosis than the same degree of spinal cord injury without spinal shock, since the injury occurred over a shorter period of time (Christensen et al. 1990; Guttmann 1976). In addition, prognosis in patients with the same degree of spinal cord injury and spinal shock may be somewhat better if the reflexes are resumed earlier (Atkinson and Atkinson 1996; Guttmann 1976). The clinical implications of spinal shock can be summarized as follows: (1) the higher the species, the more profound the spinal shock; (2) the more severe the anatomical transection, the more profound the spinal shock; (3) the more distal segment from the level of injury, the later depression of the reflexes; (4) the more abrupt the injury, the more prominent the spinal shock; (5) the more profound spinal shock, the worse the prognosis. The presence of spinal shock appears to be prognostic only for the temporal profile of the injury mechanism.

Spinal shock mainly occurs when a spinal cord lesion suddenly occurs, such as traumatic, infectious, or vascular varieties of transverse

Table 14.1 Onset of the ankle jerk, Babinski sign, and the duration of the delayed plantar response in AIS A compared based on the age of two groups

	Age	Onset AJ	Onset BS	Duration DPR
Group I	48 years median	1 days median	7 days median	6 days median
$n = 9$	49 years mean	1.5 days mean	10 days mean	11 days mean
Group II	28 years median	14 days median	13 days median	15 days median
$n = 19$	33 years mean	14 days mean	14 days mean	15 days mean
	$p<0.05$	$p<0.001$	$p<0.01$	$p<0.05$

The younger, the more severe spinal shock with delayed development to Babinski sign, the longer duration of the presence of a delayed plantar response, and the delayed recovery of deep tendon reflexes. From Ko et al. (1999), with permission

myelopathy, and it is only rarely seen in slowly progressing lesions such as spinal cord tumors, degenerative myelopathy, or multiple sclerosis (Riddoch 1917). After a while, the cutaneous reflexes and the muscle stretch reflexes reappear, and the muscle stretch reflexes appear in exaggerated form and pathological reflexes and responses occur when the spinal shock subsides. If the reflex automatism of the isolated spinal cord is established, the result always leads to spasticity or hyperactive reflexes with abnormal spread to the adjacent isolated spinal cord segments (Atkinson and Atkinson 1996; Guttmann 1976). This usually occurs after an interval of 3 weeks to a month. Clinically, an infection such as a severe urinary tract infection or infected pressure injuries will prolong the duration of spinal shock (Guttmann 1976). If spinal shock is not physiologically identical, then the subsequent development of an infectious process, particularly severe sepsis, may be the cause.

Spinal shock is a commonly used term that represents a lack of descending facilitation after upper motor neuron lesions. It is sometimes difficult to clinically distinguish between upper and lower motor neuron lesions following spinal cord injury due to spinal shock. The somatic components of spinal shock are flaccid motor paralysis, loss of sensory function, and loss of deep tendon and cutaneous reflexes. Autonomic reflexes are variably influenced depending on the level of injury. The autonomic component is the loss of sympathetic tone and unopposed parasympathetic function, resulting in hypotension, bradycardia, and skin hyperemia (Atkinson and Atkinson 1996). When the distal segments of the spinal cord are not damaged but simply isolated from higher centers, a return of reflex detrusor contractility usually occurs. The return of reflex bladder activity typically occurs as an involuntary voiding between catheterizations and occurs with the recovery of deep tendon reflexes in the lower extremities. Clinically, it is believed that automatic reflex recovery including the parasympathetic detrusor reflex after a spinal cord injury, is slower than somatic reflexes such as bulbocavernosus reflexes or muscle stretching reflexes, but the changes in the autonomic reflex during the spinal shock period are not well established.

It is important to differentiate decreasing blood pressure between circulatory shock and neurogenic shock during spinal shock. Neurogenic shock is a type of distributive shock consisting of the hemodynamic triad of hypotension, bradycardia, and peripheral vasodilatation resulting from loss of sympathetic stimulation to the blood vessels and unopposed vagal activity (Levi et al. 1993). When spinal shock begins, arterial blood pressure drops almost immediately, sometimes down to about 40 mmHg, which indicates that activity of the sympathetic nervous system is almost blocked. The pressure normalizes within a few days, even in humans. Circulatory shock requires volume replacement, but neurogenic shock requires vasopressors (Levi et al. 1993). Although hypovolemic circulatory shock is associated with tachycardia, loss of thoracic sympathetic innervation (T1–T5) can inhibit tachycardia and vasoconstriction as signs of hypovolemia in patients with both conditions coexisting (Levi et al. 1993; White and Likavec 1999).

14.5 Changing Phases of Reflexes After Spinal Cord Injury

Reflex changes during spinal shock are individualized. The spinal shock resolves over a period of days to months, and spinal shock slowly develops into spasticity. It has been suggested that this transition consists of four phases: areflexia or hyporeflexia (0–24 h), initial reflex return (1–3 days), early hyperreflexia (4 days to 1 month), and spasticity/hyperreflexia (1–12 months) (Ditunno et al. 2004; Silver 2005) (Fig. 14.3). Four phases of spinal shock have been postulated, presumably paralleled by different pathophysiological processes, but the postulation may not be as well associated with human pathophysiology. In this observational postulation, delayed plantar response and evolution to Babinski sign, recovery of deep tendon reflexes and autonomic reflexes were used for

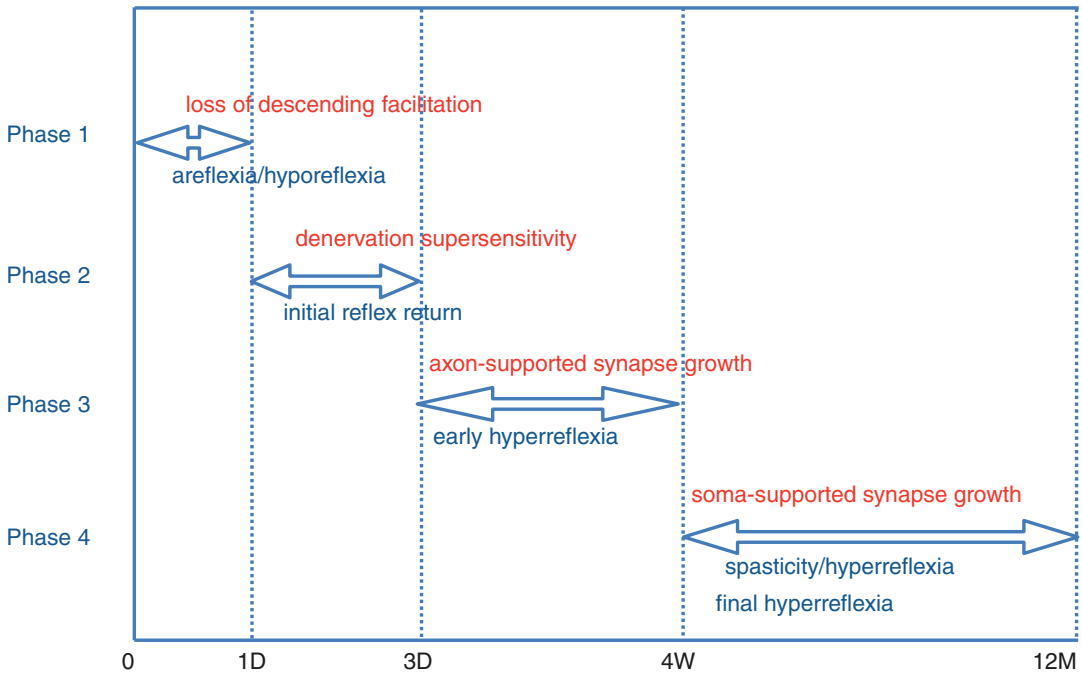

Fig. 14.3 Four phases of spinal shock resolution. Modified from Ditunno et al. (2004), with permission

the milestone of transmission to each phase. The first phase occurs between 0 and 24 h after injury and is characterized by areflexia or hyporeflexia. There is no deep tendon reflex. The first pathological reflex during this period is the delayed plantar reflex followed by a series of cutaneous reflexes such as the bulbocavernosus, abdominal wall, and cremasteric reflex. Sympathetic dysfunction may cause bradyarrhythmias, atrioventricular conduction block, and hypotension. Phase 2 occurs between day 1 and day 3 after injury. During this phase, polysynaptic cutaneous reflexes are more prominent, while deep tendon reflexes are still absent. It is not unusual for elderly individuals and children to experience recovery of deep tendon reflexes during this time. The Babinski sign can also be evident in the elderly. Denervation supersensitivity and receptor upregulation explain these changes in the second phase. The next phase (phase 3) occurs between 4 days and 1 month after injury. Deep tendon reflexes may be returned in the majority of patients and the Babinski sign may appear. It differs from the fourth phase (1–12 months) in which hyperactivity occurs in cutaneous and deep tendon reflexes in response to minimal stimuli. Deep tendon reflexes usually recover by 3 days after injury. The recovery of the Babinski sign is almost similar to the return of the ankle jerk. There is also a decrease in the delayed plantar reflex. Autonomic changes such as bradyarrhythmias and hypotension begin to subside. This period is reflected by axon-supported synapse growth. The fourth phase is dominated by hyperactive reflexes and occurs from 1 to 12 months after injury. Vasovagal hypotension and bradycardia generally improve within 3–6 weeks, but orthostatic hypotension may take 10–12 weeks to disappear. During this period, episodes of malignant hypertension or autonomic dysreflexia begin to appear (Silver 2005). Soma-supported synapse growth accounts for these findings (Table 14.2).

The physiology of the latter two phases is driven by synapse growth and short (phase 3) and long axon growth (phase 4) from intraspinal and segmental afferent sources that replace empty synaptic endings in axotomized supraspinal neurons. This hypothesis suggests that postinjury synaptic formation is axon-length dependent,

Table 14.2 Proposed possible neuronal mechanisms for the four phases of spinal shock

Phases	Possible neuronal mechanisms
1. 0–1 day, hyporeflexia Motoneurons hyperpolarized	1. Lost normal background supraspinal excitation 2. Increased spinal inhibition 3. Lost plateau potentials in spinal neurons due to 5HT loss 4. Reduced neuronal metabolism 5. Retraction of dendrites and synapses
2. 1–3 days, reflex return Denervation supersensitivity, receptor upregulation	1. Denervation supersensitivity 2. NMDA receptor upregulation (NR1 and NR2A subunits) 3. Inactivity-dependent receptor upregulation 4. NT and GF synthesis increase
3. 1–4 weeks, early hyperreflexia Synapse growth, short axons and axon supplied	1. New synapse growth to occupy vacated synaptic sites 2. NT retrograde signal to elicit synapse growth 3. Competitive and activity-dependent synapse growth 4. Most synapse growth by short-axoned interneurons • Rapid retrograde signaling and axon transport in short-axoned interneurons 5. Limited synapse growth by long-axoned neurons–for example, 1A afferents • Synapse place-holding function • "Disturbed sprouting program," axon cannibalization 6. Plateau potentials, possibly via Ca^{2+} channel synthesis in spinal neurons
4. 1–12 months, late hyperreflexia Synapse growth, long axons and soma supplied	1. New synapse growth by long-axoned neurons–for example, 1A afferents and interlimb afferents 2. Soma-supplied synapse growth via axon transport 3. Competitive and activity-dependent synapse growth

From Ditunno et al. (2004), with permission

activity dependent, and competitive, which leads to a gradual termination of spinal shock (Ditunno et al. 2004; Petersen et al. 2010). In the clinical presentation, the transition from spinal shock to spasticity is a continuum that gradually increases motor excitability with characteristic changes in muscle tone, spasm, and short- and long-latency reflex excitability (Hiersemenzel et al. 2000).

References

Atkinson PP, Atkinson JLD. Spinal shock. Mayo Clin Proc. 1996;71:384–9.

Bach-y-Rita P, Illis LS. Spinal shock: possible role of receptor plasticity and non synaptic transmission. Paraplegia. 1993;31:82–7.

Barnes CD, Schadt JC. Release of function in the spinal cord. Prog Neurobiol. 1979;12:1–13.

Bastian HC. On the symptomatology of total transverse lesions of the spinal cord; with special reference to the condition of the various reflexes. Med Chir Trans. 1890;73:151–217.

Bunge RP, Puckett WR, Becerra JL, et al. Observations on the pathology of human spinal cord injury. A review and classification of 22 new cases with details from a case of chronic cord compression with extensive focal demyelination. In: Seil FJ, editor. Advances in neurology. New York: Raven Press Ltd; 1993.

Bywater M, Tornic J, Mehnert U, et al. Detrusor acontractility after acute spinal cord injury-myth or reality? J Urol. 2018;199:1565–70.

Calancie B, Broton JG, Klose KJ, et al. Evidence that alterations in presynaptic inhibition contribute to segmental hypo-and hyperexcitability after spinal cord injury in man. Electroencephalogr Clin Neurophysiol. 1993;89:177–86.

Calancie B, Molano MR, Broton JG. Tendon reflexes for predicting movement recovery after acute spinal cord injury in humans. Clin Neurophysiol. 2004;115:2350–63.

Christensen PB, Wermuth L, Hinge HH, et al. Clinical course and long-term prognosis of acute transverse myelopathy. Acta Neurol Scand. 1990;81:431–5.

Dimitrijević MR, Nathan PW. Studies of spasticity in man: 3. Analysis of reflex activity evoked by noxious cutaneous stimulation. Brain. 1968;91:349–68.

Ditunno JF, Little JW, Tessler A, et al. Spinal shock revisited: a four-phase model. Spinal Cord. 2004;42:383–95.

Eckert MJ, Martin MJ. Trauma: spinal cord injury. Surg Clin North Am. 2017;97:1031–45.

Fam B, Yalla SV. Vesicourethral dysfunction in spinal cord injury and its management. Semin Neurol. 1988;8:150–5.

Guillain G, Barre JA. Etude anatomo-clinique de quinze cas de section totalle de la moelle. Ann Méd. 1917;2:178–222.

Guttmann L. Studies on reflex activity of the isolated cord in spinal man. J Nerv Ment Dis. 1952;116:957–72.

Guttmann L. Spinal shock and reflex behaviour in man. Paraplegia. 1970;8:100–16.

Guttmann L. Spinal cord injuries: comprehensive management and research. 2nd ed. Oxford: Blackwell Scientific Publications; 1976.

Hall M. Second memoir on some principles of the pathology of the nervous system. Med Chir Trans. 1840;23:121–67.

Hall M. On the diseases and derangements of the nervous system: in their primary forms and in their modifications by age, sex, constitution, hereditary predisposition, excesses, general disorder, and organic disease. London: H. Baillière; 1841.

Hiersemenzel LP, Curt A, Dietz V. From spinal shock to spasticity: neuronal adaptations to a spinal cord injury. Neurology. 2000;54:1574–82.

Holdsworth FW. Neurological diagnosis and the indications for treatment of paraplegia and tetraplegia, associated with fractures of the spine. Manit Med Rev. 1968;48:16–8.

Illis LS. The motor neuron surface and spinal shock. Mod Trends Neurol. 1967;4:53–68.

Ko HY, Ditunno JF, Graziani V, et al. The pattern of reflex recovery during spinal shock. Spinal Cord. 1999;37:402–9.

Kuhn RA. Functional capacity of the isolated human spinal cord. Brain. 1950;73:1–51.

Landau WM, Clare MH. The plantar reflex in man, with special reference to some conditions where the extensor response is unexpectedly absent. Brain. 1959;82:321–55.

Leis AA, Kronenberg MF, Stětkárová I, et al. Spinal motoneuron excitability after acute spinal cord injury in humans. Neurology. 1996;47:231–7.

Levi L, Wolf A, Belzberg H. Hemodynamic parameters in patients with acute cervical cord trauma: description, intervention, and prediction of outcome. Neurosurgery. 1993;33:1007–16.

Lloyd LK. New trends in urologic management of spinal cord injured patients. Cent Nerv Syst Trauma. 1986;3:3–12.

McCouch GP, Austin GM, Liu CN, et al. Sprouting as a cause of spasticity. J Neurophysiol. 1958;21:205–16.

Mendell LM. Physiological aspects of synaptic plasticity: the Ia/motoneuron connection as a model. Adv Neurol. 1988;47:337–60.

Nacimiento W, Noth J. What, if anything, is spinal shock? Arch Neurol. 1999;56:1033–5.

Petersen JA, Schubert M, Dietz V. The occurrence of the Babinski sign in complete spinal cord injury. J Neurol. 2010;257:38–43.

Riddoch G. The reflex functions of the completely divided spinal cord in man, compared with those associated with less severe lesions. Brain. 1917;40:264–402.

Ruch TC. Evidence of the non-segmental character of spinal reflexes from an analysis of the cephalad effects of spinal transection (Schiff-Sherrington phenomenon). Am J Physiol-Legacy Content. 1935;114:457–67.

Schadt JC, Barnes CD. Motoneuron membrane changes associated with spinal shock and the Schiff-Sherrington phenomenon. Brain Res. 1980;201:373–283.

Schwarz GM, Hirtler L. The cremasteric reflex and its muscle – a paragon of ongoing scientific discussion: a systematic review. Clin Anat. 2017;30:498–507.

Sherrington C. The integrative action of the nervous system. London: Constable & Company LTD.; 1906.

Silver JR. Spinal shock revisited: a four-phase model. Comment on spinal shock revisited: a four-phase model. Spinal Cord. 2005;43:450.

Simpson RK Jr, Robertson CS, Goodman JC. Glycine: an important potential component of spinal shock. Neurochem Res. 1993;18:887–92.

Simpson RK Jr, Robertson CS, Goodman JC. The role of glycine in spinal shock. J Spinal Cord Med. 1996;19:215–24.

Stauffer ES. Diagnosis and prognosis of acute cervical spinal cord injury. Clin Orthop Relat Res. 1975;112:9–15.

Sullivan MP, Yalla SV. Detrusor contractility and compliance characteristics in adult male patients with obstructive and nonobstructive voiding dysfunction. J Urol. 1996;155:1995–2000.

Tai Q, Goshgarian HG. Ultrastructural quantitative analysis of glutamatergic and GABAergic synaptic terminals in the phrenic nucleus after spinal cord injury. J Comp Neurol. 1996;372:343–55.

Tulloch AG, Rossier AB. The autonomic nervous system and the bladder during spinal shock—an experimental study. Paraplegia. 1975;13:42–8.

Van Gijn J. The Babinski sign and the pyramidal syndrome. J Neurol Neurosurg Psychiatry. 1978;41:865–73.

van Gijn J. The Babinski sign: the first hundred years. J Neurol. 1996;243:675–83.

van Harreveld A. On spinal shock. Proc Natl Acad Sci U S A. 1940;26:65–7.

van Munster CE, Weinstein HC, Uitdehaag BM, et al. The plantar reflex: additional value of stroking the lateral border of the foot to provoke an upgoing toe sign and the influence of experience. J Neurol. 2012;259:2424–8.

Weaver RA, Landay WM, Higgins JF. Fusimotor function: part II. Evidence of fusimotor depression in human spinal shock. Arch Neurol. 1963;9:127–32.

Weinstein DE, Ko HY, Graziani V, et al. Prognostic significance of the delayed plantar reflex following spinal cord injury. J Spinal Cord Med. 1997;20:207–11.

White RJ, Likavec MJ. Spinal shock-spinal man. J Trauma. 1999;56:979–80.

Wolpaw JR, Tennissen AM. Activity-dependent spinal cord plasticity in health and disease. Annu Rev Neurosci. 2001;24:807–43.

Recommended Additional Reading

Campbell WW, editor. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Fehlings MG, Vccaro AR, Roakye M, et al., editors. Essentials of spinal cord injury: basic research to clinical practice. New York: Thieme; 2013.

Fulton JF, Keller AD. The sign of Babinski: a study of the evolution of cortical dominance in primates. Springfield: Charles C Thomas; 1932.

Guttmann L. Spinal cord injuries. Comprehensive management and research. Oxford: Blackwell Scientific Publications; 1976.

Harrison P. Managing spinal injury: critical care. The international management of people with actual or suspected spinal cord injury in high dependency and intensive care unit. London: The Spinal Injury Association; 2000.

Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.

Jallo J, Vaccaro AR, editors. Neurotrauma and critical care of the spine. 2nd ed. New York: Thieme; 2018.

Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.

Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, vol. 109. 3rd series ed. London: Elsevier; 2012.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury. In: progress in brain research, vol. 152. New York: Elsevier; 2006.

Management in the Acute Phase of Traumatic Spinal Cord Injuries

15

Based on the pathophysiological changes in the spinal cord injury, the early acute phase is defined as 2–48 h after the injury, the subacute phase between 2 days to 2 weeks, the intermediate phase between 2 weeks to 6 months, and the chronic phase after 6 months (Rowland et al. 2008). However, the clinically acute phase is usually defined as the first 4–5 weeks after the injury. The physiopathological changes occurring in each phase of spinal cord injury are summarized in Table 15.1. Spinal cord injuries remain a clinical challenge. Goals of the acute phase management of spinal cord injuries are to minimize primary neurological damage and prevent secondary cord injury due to hypoperfusion, ischemia, and apoptotic, biochemical, and inflammatory changes (Baptiste and Fehlings 2006). Primary injury refers to the initial traumatic impact on the spinal cord resulting in neuronal damage. Secondary injury involves the delayed progression of injury occurring weeks to months after initial trauma and is defined by complex and interrelated molecular progresses that progressively damage central nervous system tissues (Karsy and Hawryluk 2017). The injury mechanisms of primary and secondary injury in spinal cord injuries are summarized in Table 15.2.

Traumatic spinal cord injuries are common in patients with concurrent traumatic injuries in other body systems, including the brain. These multiple trauma patients pose unique challenges for clinicians (Yue et al. 2017). Therefore, an appropriate systematic assessment of the spine/spinal cord and/or accompanying injuries is required at an early phase. Patients who survive the initial spinal cord injury are at significant risk of medical complications for the rest of their lives. A spinal cord injury is associated with a significant reduction in life expectancy across the injury spectrum and the age at the time of the injury (Eckert and Martin 2017). More than half of all patients with spinal cord injuries develop complications during the initial hospital stay, with higher rates corresponding to increased injury severity, the presence of an associated head injury, and cerebrovascular lesions associated with cervical spine injuries (Eckert and Martin 2017; Kushner and Alvarez 2014).

Spinal cord injuries can lead to numerous multisystem complications, especially during the acute phase of care (Stricsek et al. 2017) (Table 15.3). In the initial presentation and evaluation of patients with spinal cord injuries, almost all other injuries should be given priority in both evaluation and management, unless the spinal cord injury is not impair airway or hemodynamics, such as neurogenic shock (Eckert and Martin 2017). The evaluation, classification, and initial medical management of patients with spinal cord injuries have become increasingly standardized. Despite advances in the acute management of patients with spinal cord injuries, neurological outcomes have not improved significantly over

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Table 15.1 Physiopathological changes in each phase of spinal cord injuries

	≤2 h	≤48 h	≤14 days	≤6 months	>6 months
Phase	Primary immediate	Acute early	Secondary subacute	Intermediate	Chronic/late
Physiopathological process	Primary mechanical injury Gray matter hemorrhage Axonal disconnection Hemorrhagic necrosis Microglial activation with liberation of cytokines (IL-1β, TNFα, IL-6, among others)	Cytotoxic and vasogenic edema Production of ROS: lipid peroxidation Excitotoxicity mediated by glutamate Continuous hemorrhages and necrosis Neutrophil infiltration Loss of permeability of blood–brain barrier Early demyelination (oligodendrocyte apoptosis) Neuronal death Ischemic events (systemic shock, spinal shock, hypotension, hypoxia)	Macrophages infiltration Astroglial cicatrization (reactive astrocytosis) Blood–brain barrier repair and resolution of edema	Astroglial scar consolidation Cyst formation Stabilization of injury	Prolonged Wallerian degeneration Persistence of noninjured and nondemyelinated axons Beginning of structural plasticity and functional processes in noninjured medular tissue

IL-6, interleukin-6; IL-1β, interleukin-1 beta; ROS, reactive oxygen species; TNFα, tumor necrosis factor-alpha
From Azeez et al. (2020), with permission

Table 15.2 Injury mechanisms of primary and secondary injury in spinal cord injuries

Stages of spinal cord injuries	Time	Mechanism
Primary injury	Seconds	Compression, laceration, distraction, shearing, contusion, transection, stretching
Secondary injury	Seconds–minutes	Hemorrhage, decreased adenosine triphosphate, increased lactate
	Hours	Vasogenic and cytotoxic edema, microvessel vasospasm, thrombosis, ionic excitotoxicity, loss of Na/K gradient, release of neurotoxic opioids, inflammatory cascade, lipid peroxidation, glutamatergic excitotoxicity, oxidative stress
	Days–Weeks	Microglial stimulation, gliosis, macrophage activation, apoptosis

Adapted from Karsy and Hawryluk (2017), with permission

Table 15.3 Medical complications of organ systems during the acute phase of spinal cord injury

Organ system	Complications
Cardiovascular	Arrhythmia, bradycardia, cardiac arrest, myocardial infarction, shock, congestive heart failure, cardiogenic pulmonary edema, orthostatic hypotension
Pulmonary	Hypoventilation/respiratory failure, poor secretion control, acute respiratory distress syndrome, aspiration, pneumonia
Hematologic	Deep venous thrombosis, pulmonary embolus, thrombocytopenia, coagulopathy
Psychiatric	Depression, anxiety, cognitive changes, substance abuse
Neurologic	Neurogenic shock, spinal shock
Genitourinary	Hematuria, acute renal failure, urinary incontinence, urinary tract infection, priapism
Gastrointestinal	GI hemorrhage, ileus, obesity, pancreatitis, dysphagia, constipation
Skin	Pressure injuries

Modified from Stricsek et al. (2017), with permission

the past few decades. Long-term management strategies, including rehabilitation, will remain critical in optimizing outcomes (Ropper et al. 2015).

Injuries to the spine usually occur in areas of maximal mobility. Most typically, injuries occur when significant forces to the spinal column cause fracture, ligamentous disruption, or combined injuries that result in direct compression and injury to the spinal cord. Injuries to the spinal column are commonly classified according to the location of injury (craniocervical, subaxial cervical, or thoracolumbar) and the mechanism of injury (flexion, extension, or axial load). The three-column concept in thoracolumbar spines is used to define instability when at least two of the three columns of the spine are disrupted. Spinal cord injury should always be suspected and ruled out in any patient with a significant trauma mechanism. Precautions for the spine, such as transport using a long board, flat positioning, and log-roll turning and immobilization with cervical collars, should be taken in all major trauma patients until the spine is properly assessed. Figure 15.1 is the updated algorithm for Emergency Neurological Life Support (ENLS) traumatic spinal cord injury (version 4.0). This algorithm described the steps involved in treating airway, breathing, circulation, and spinal motion restriction (Chen et al. 2019).

This chapter provides an overview of acute spinal cord injuries with an emphasis on practical issues of initial evaluation and management.

15.1 Initial Management of Spinal Cord Injuries

The initial management of patients with spinal cord injuries is the same as for any patient with a traumatic injury. The principle of the primary survey is a rapid and systematic evaluation, which should be completed within the first few minutes of the patient's arrival and which follows

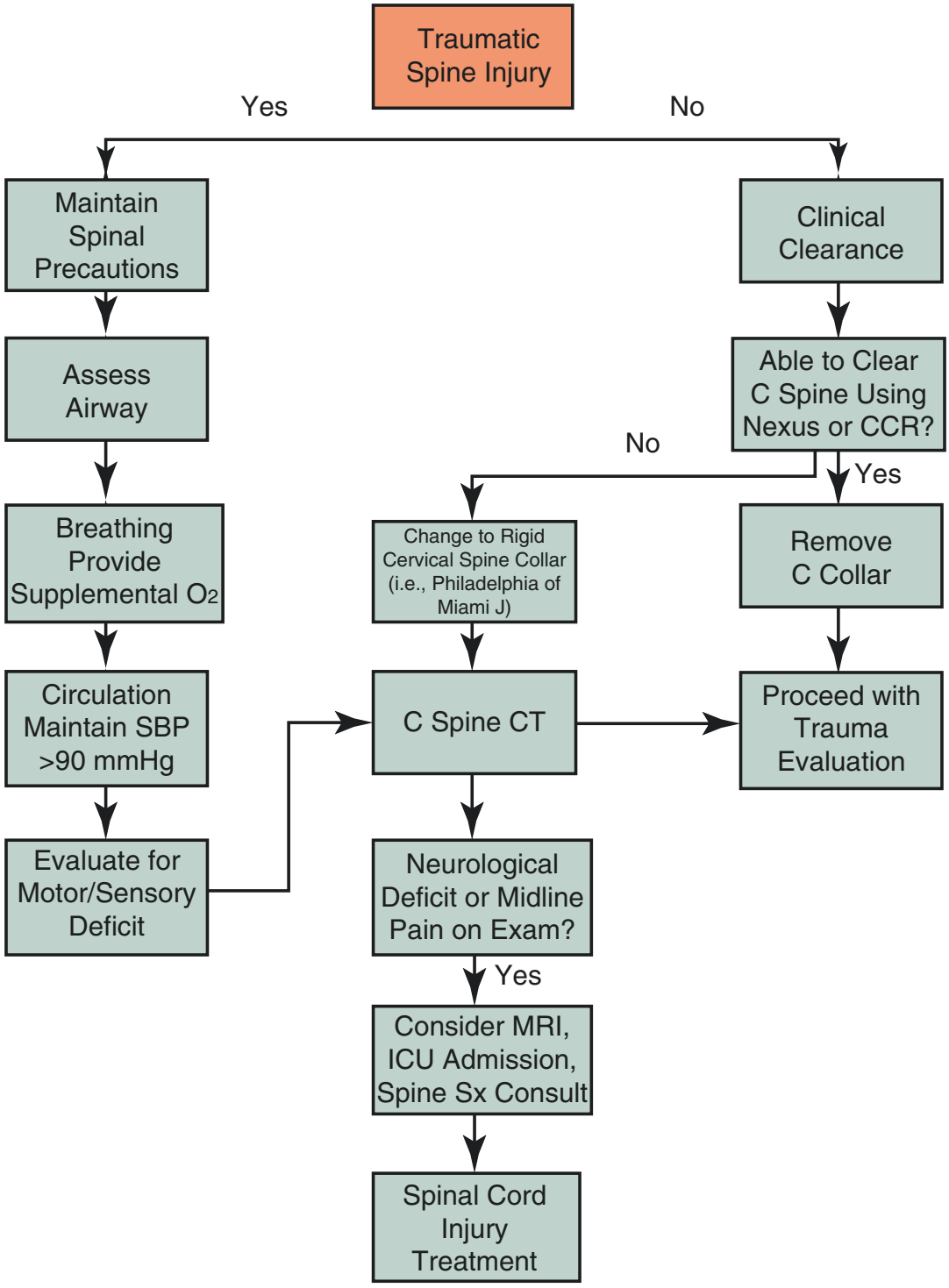

Fig. 15.1 ENLS traumatic spinal cord injury algorithm. From Chen et al. (2019). https://enls.neurocriticalcare.org/protocols

the ABCDEs (airway, breathing, circulation, disability, and exposure) of resuscitation. The physiologic consequence of the spinal cord injury, such as the risk of airway loss, inadequate oxygenation and ventilation, and hypotension, require immediate attention during the primary survey (Stein and Sheth 2015).

Any patient with a significant trauma mechanism should always be suspected of spinal cord injury, and spinal cord injury should be ruled out. Spine precautions should be taken until the spine is properly evaluated. Treatment for spinal cord injuries begins with spine precautions and protection against further injury (Eckert and Martin 2017). Appropriate treatment at the accident site for patients with spinal injuries includes immobilization, extrication, initial resuscitation, evaluation, and rapid transport of the patient to a medical center capable of diagnosis and treatment of spinal cord injuries. Prehospital care for patients with potential spinal cord injuries requires the minimization of secondary spinal cord injuries and possible morbidity due to improper immobilization of the spine (Ahn et al. 2011). A combination of a rigid cervical collar and support blocks on a backboard with straps, without flexing or extending the patient's neck, effectively limits cervical spine motion. A soft foam collar provides the least immobilization of all cervical orthoses available as it allows flexion, extension, and rotation of the neck. It is not recommended to immobilize the spine with sandbags and tape. Bivalved form cervical orthoses, like the Philadelphia or Miami cervical orthoses, provide maximum support and can easily be used in emergency situations for most patients. If the patient is found lying on the ground, the patient should be immobilized on a long spinal board after the application of the cervical collar. The use of rigid boards can lead to discomfort at the occiput and sacrum and increased pressures that can lead to tissue necrosis during prolonged transport and/or short periods of rigid immobilization. Cushioning the board can lead to more comfort and reduce the pressure at the occiput and sacrum without affecting the biomechanical immobilization (Sheerin and de Frein 2007). Two or four people are needed to safely log-roll a person with a spinal cord injury. All individuals suspected of having spinal injuries should be immobilized in the position before extrication (Kato et al. 2008). Immobilization of the spine in case of penetrating trauma, such as knife stab or gunshot wounds, is not recommended because of the low risk of spinal instability. Children under the age of 8 have relatively large heads in relation to their bodies. To avoid excessive neck flexion, use a child's spine board with an occiput cutout or recess, or with padding under the shoulders and chest, raise the upper body 2–3 cm and place the head at the board level (Ahn et al. 2011).

Important concepts of acute care include early recognition and detection of injuries, immediate on-site stabilization, proper resuscitation, and prevention of further deterioration due to medical complications or improper handling (Ahn et al. 2011). One of the primary concerns in the initial management of potential spinal injuries is that neurological function may be impaired by an unstable spine and pathologic movement of the injured vertebrae (Hadley et al. 2013). Precautions in spinal immobilization do not mean that the patient will lie flat and motionless after the initial trauma evaluation. A reverse Trendelenburg position up to 30° will benefit greatly, and a participatory pulmonary toilet should begin if they are not intubated.

The goal of initial management of the spinal cord injuries is an accurate diagnosis of bony, ligamentous, and neurological injuries as well as the immediate immobilization of the spine, the establishment of oxygenation and circulation (mean arterial pressure > 85 mmHg). Emergency intubation may be necessary in case of hypoventilation and when patients with high cervical injuries may have apnea. Manual in-line stabilization (MILS) of the cervical spine should be performed in the airway management of patients suspected of having spinal cord injury requiring intubation in the prehospital setting. Hyperextension of the neck when placing an endotracheal tube should be avoided. Adequate ventilation to prevent hypoxia and secondary ischemia of the spinal cord is important.

The initial treatment of the patients with spinal cord injuries is the evaluation and treatment of

impairment of ventilation and circulatory function. Patients with acute spinal cord injuries, especially those with complete or severe cervical spinal cord injuries, should be managed in an intensive care unit or the similar environment under cardiac, hemodynamic, and respiratory monitoring to detect cardiovascular dysfunction and respiratory insufficiencies (Lo et al. 2013). These patients often have hypotension, hypoxemia, pulmonary dysfunction, thermoregulatory dysfunction, and cardiovascular instability even after initial stable cardiac and pulmonary function. Hypotension may be the result of neurogenic shock when presented at first, but its classic presentation related to bradycardia is relatively rare. Therefore, the presentation of the shock must be evaluated for significant bleeding. Restoring normovolemia, correcting hypotension, and maintaining adequate oxygenation can reduce the risk of further ischemic cord damage. Avoidance of hypotension (systolic blood pressure < 90 mmHg) and hypoxia is crucial to avoid further secondary spinal cord injuries (Stevens et al. 2003). Neurogenic shock may manifest as hypotension that is poorly responsive to fluid resuscitation but is quick to respond to vasopressor agents. There is no associated tachycardia in pure neurogenic shock.

Almost half of the patients with spinal injuries have serious associated injuries, many of which are life threatening (Saboe et al. 1991). The most common associated injuries are injuries to the head, chest, and long bones. Emergent spine imaging is not required prior to a laparotomy or other life-saving surgical intervention (Eckert and Martin 2017). Ten percent have three or more such injuries. Injury of the cervical spine can cause occlusion of the vertebral arteries with related symptoms. Factors such as changes in mental status, pulmonary insufficiency requiring mechanical ventilation, major organ damage, and combined factors for the long bone fracture may limit critical neurological assessments. A complete and accurate neurological examination should be performed to indicate the presence of spinal shock, complete spinal cord lesion, or other types of spinal cord injury (Cole and Weller 1998).

The acute care physician or surgeon will address issues such as appropriate resuscitation and stabilization, type of spinal injury, neurological deficit secondary to spinal cord injury, lesion stability, and surgical or nonsurgical treatment. Early or acute hospital treatment includes diagnostic assessment and decision-making for surgery of spinal injuries and associated injuries, as well as management of complications, resulted from spinal cord injuries such as cardiac, respiratory, genitourinary, gastrointestinal, nutritional problems, venous thrombosis, and pressure injuries (Ball 2001; Lo et al. 2013). Gastric hyperacidity, paralytic ileus, and pancreatic sphincter dysfunction can cause stress ulcers, vomiting, aspiration, fecal impaction and pancreatitis. Bladder dysfunction leads to urinary stasis, which can lead to cystitis, pyelonephritis, hydronephrosis, stone formation, and renal failure. Table 15.4 lists the symptoms and signs and their causes that are commonly seen in people with spinal cord injuries. Early rehabilitation interventions and psychosocial intervention should begin with acute medical and surgical management.

There are important guidelines for early management following spinal cord injury: the Consortium for Spinal Cord Medicine Clinical Practice Guidelines on Early Acute Management

Table 15.4 Causes and common symptoms and signs in individuals with spinal cord injuries

Symptoms/signs	Causes
Daytime drowsiness	Medication side effect, sleep apnea, OH, depression
Diarrhea	Bowel management schedule, CD infection, bowel impaction, medication side effect
Headache	AD, BP change
Increased spasticity	UTI, pressure ulcer, bowel impaction, acute abdomen
Shoulder pain	Rotator cuff, adhesion, cervical radiculopathy, syringomyelia, visceral referred pain
Fever	UTI and other infection, pneumonia, pressure ulcer, cellulitis, DVT, HO, limb fracture, drug fever
Fatigue	Infection, cardiac/respiratory failure, depression, medication effect
Unilateral leg swelling	DVT, fracture, HO, cellulitis, hematoma, pelvic cancer
New weakness	Syringomyelia, entrapment neuropathy

in Adults with Spinal Cord Injury (Consortium for Spinal Cord Medicine 2008a, b), and the American Association of Neurological Surgeons/Central Nervous System (AANS/CNS) Guidelines for Management of Acute Cervical Spine and Spinal Cord Injuries, which were updated in 2013 (Hadley and Walters 2013).

15.2 Neurological Assessment of Spinal Cord Injury

Patients with suspected spinal injury or spinal cord injury should be performed an initial neurological examination to document the presence of spinal cord injury. If neurologic deficits are compatible with a spinal cord injury, the neurological level of injury and neurological completeness are determined by the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) (ASIA 2019). The neurological examination described by the ISNCSCI is commonly used for the standardized initial assessment of patients with spinal cord injuries, for follow-up examinations to determine neurological improvements or changes, and to research the neurological recovery after spinal cord injuries (Marino et al. 2008). However, the ISNCSCI is not a complete neurological examination as it does not contain details that are not used in the classification standards, such as deep tendon reflexes and pathologic reflexes (Arnold et al. 2006; Calancie et al. 2004). Serial examinations should be performed to detect neurological deterioration or neurological improvement. After the first 48–72 h, the clinical neurological assessment described by ISNCSCI can also be used to determine the prognosis of neurological recovery (Alexander et al. 2009; Herbison et al. 1992). For more information on the ISNCSCI, refer to Chap. 13.

15.3 Neuroprotective Medication

An increasing number of therapies for spinal cord injury are emerging from the laboratory and looking to translate into human clinical trials. Many of these are given as soon as possible after injury in the hope of attenuating secondary damage and maximizing the amount of neurological tissue spared. Since the clinical trials of methylprednisolone, the spinal cord injury community has sought additional interventions that follow the similar strategy of administration as early as possible after the injury to minimize secondary damage (Kwon et al. 2011). Methylprednisolone, based on the results of the National Acute Spinal Cord Injury (NASCIS) trial, has been administered intravenously for over 20 years after positive studies published in the 1990s (Hurlbert et al. 2013). The NASCIS I-III trials could not show any difference in the neurologic outcomes after high-dose methylprednisolone (Bracken et al. 1985, 1990, 1997). Post hoc subgroup analyses in the later NASCIS trials did not correlate with a measure of functional improvement or effect on disability (Eckert and Martin 2017). Although this study remains an option in individual cases, it has been extensively discussed due to the lack of consistent or convincing clinical evidence and significant adverse effects such as increased incidence of pneumonia, sepsis, gastrointestinal hemorrhage, venothrombotic events, and wound complications (Liu et al. 2009).

In addition to the NASCIS trial, a large number of agents were evaluated for early clinical trials with the aim of neuroprotection and neurogeneration in spinal cord injuries: vasopressors, minocycline, glyburide/glibenclamide, magnesium, riluzole, gacyclidine/GK-11, thyrotropin-releasing hormone (TRH), naloxone, and granulocyte colony-stimulating factor (G-CSF) for neuroprotective treatments; IN-1 (ATI355), cethrin (BA-210), gangliosides (GM-1)/Syngen, and fibroblast growth factor for neuroregenerative treatment (Karsy and Hawryluk 2017). The Consortium for Spinal Cord Medicine Clinical Practice Guidelines on Early Acute Management in Adults with Spinal Cord Injury (Consortium for Spinal Cord Medicine 2008b) and the 2013 AANS/CNS Guidelines for Management of Acute Cervical Spine and Spinal Cord Injuries (Walters et al. 2013) indicate that there is no clinical evidence to definitively recommend neuroprotective pharmacologic agent, including steroids, in the treatment of acute spi-

Table 15.5 Similarities and differences between neurogenic and hypovolemic shock

Neurogenic shock	Hypovolemic shock
Hypotension	Hypotension
Bradycardia	Tachycardia
Areflexia	Normal reflexes
Responsive to vasopressors	Responsive to volume replacement
Urine volume often maintained	Decreased urine volume
Warm and dry extremities	Cold and clammy extremities

nal cord injuries that improves functional recovery (Table 15.5).

15.4 Polytrauma in Spinal Cord Injury

More than 70% of patients with spinal cord injuries suffer multiple injuries associated with spinal cord injury, which contributes to the high complication rates in the acute and long-term phases of care (Hebert and Burnham 2000). Signs of spinal cord injury in multitraumatized patients are the response to pain above, but not below the level of injury, flaccid areflexic extremities, loss of anal sphincter tone, paradoxical breathing, unexplained bradycardia, inappropriate vasodilation with warm flushed extremities during hypotension, and priapism. Injuries such as limbs or pelvic bone fractures, traumatic brain injury, vascular injuries, and chest and abdomen injuries can complicate the evaluation and management of spinal cord injury. When investigating an injury in a traumatized person, the examiner may warn of the possibility of a spinal injury. For example, facial trauma may suggest the possibility of a cervical spine injury. Lap belt bruises should increase the suspicion of flexion-distraction lesions of the thoracolumbar spine. Calcaneal fractures from falls or motor vehicle accidents can be associated with fractures of the thoracolumbar and lumbar spines due to excessive axial loading.

The most common sites of extraspinal fractures associated with spinal cord injuries are the chest, lower extremity, upper extremity, head, and pelvis (Saboe et al. 1991). Early stabilization of extraspinal fractures is indicated. Patients with spinal cord injuries, especially those with high cervical injuries, have a high incidence of traumatic brain injury (NSCISC 2018). In addition to the Glasgow Coma Scale evaluated in the acute settings, the evaluation of posttraumatic amnesia appears to be a reliable test, such as the Galveston Orientation and Amnesia Test (GOAT). In addition to traumatic brain injury, medications, or hypoxia can affect test results. Patients with cervical spinal cord injury may have a concomitant injury to the carotid or vertebral artery, and screening using CT or magnetic resonance (MR) angiography should be considered as part of the assessment of cervical spinal cord injury. Chest and abdominal injuries are common in patients with thoracolumbar spinal injuries. Clinical examination is unreliable in the setting of impaired sensory function and requires additional diagnostic measures such as ultrasound and/or abdominal CT.

15.5 Decision of Surgery

The main role of surgery in acute spinal cord injury is to prevent further neurological deterioration through decompression, while stabilization reduces complications related to immobility and facilitates earlier rehabilitation which remains critical in optimizing outcomes (Sandean 2020). Surgery may improve neurological recovery if the spinal cord injury is incomplete, especially if neurological function deteriorates, but it remains controversial. The choice of surgical intervention often depends on the severity of the injury, the level of injury, the mechanism of injury, and the extent of compression. The timing of surgical decompression of the spine in compressive phenomena, such as epidural hematoma, cord edema or hemorrhage, or impinging bony fragments and foreign bodies, has been extensively studied. Although there is increasing evidence that early surgical decompression may be associated with safe and better neurological outcomes, the time of surgery in the management of spinal cord injuries is controversial (Agostinello

et al. 2017; Burke et al. 2019; Fehlings et al. 2012).

Early surgery may lead to a significantly shorter length of stay in rehabilitation, but the frequency of medical complications similar to those undergoing surgery more than 24 h after the injury (Agostinello et al. 2017; Burke et al. 2019). On the other hand, it has been reported that early surgical decompression is also associated with decreased pulmonary morbidity and duration of mechanical ventilation, as well as the reduced duration of intensive care unit and hospital stay (Liu et al. 2016). However, surgical decompression in patients with ASIA A injury did not show significant improvement in neurological outcomes (Bourassa-Moreau et al. 2016). Surgical treatment of penetrating spinal injuries is often not warranted, as neither bullet removal nor spinal debridement has been associated with a low risk of infection, reduced pain, or improved neurological recovery (Eckert and Martin 2017).

15.6 Acute Medical Management

15.6.1 Acute Cardiovascular Management

Hypotension in the prehospital setting is treated with fluid resuscitation after appropriate intravenous access. The goal is to maintain optimal tissue perfusion and resolve the shock. After the initial traumatic spinal cord injury, a transient hypertensive state is often produced by the release of peripheral catecholamines. However, this period is short and followed by a neurogenic shock. Patients with acute cervical or high-thoracic spinal cord injuries often experience hypovolemic and neurogenic shock (Table 15.5). The terms "spinal shock" and "neurogenic shock" are often both used inappropriately or incorrectly in the clinical setting. Neurogenic shock is the hemodynamic consequence of the spinal cord injury, which is classically characterized by hypotension due to vasodilation and increased perfusion of the lower extremities. In pure neurogenic shock, there is no associated tachycardia; the extremities may be warm and dry rather than cold and clammy. In cases of upper cervical cord injury, hypotension may often be accompanied by paradoxical bradycardia. This pattern is a relatively unique and specific hemodynamic pattern for spinal cord injury and should be given immediate assessment and interventions. Cervical spine and high-thoracic spine injuries can result in loss of sympathetic cardiac stimulation (bradycardia) and vasomotor tone in the lower body (hypotension), which will benefit from early initiation of a vasopressor medication with standard trauma resuscitation to restore intravascular volume (Eckert and Martin 2017).

Care should be taken to distinguish these symptoms from neurogenic shock characterized by hypotension, bradycardia, and hypothermia. The combination of hypotension and bradycardia may cause secondary neurological injury, as well as pulmonary, renal, and cerebral insults (Ball 2001). These cardiovascular events are more common in patients with a neurological level at or above T6. This mechanism is a reduction in sympathetic outflow levels with cervical or high-thoracic lesions, which leaves parasympathetic effects relatively unopposed. As mentioned above, if the neurological level of injury is above T1, uncontrolled vagal activity can induce heart rates of less than 60/min because of sympathetic innervation of the heart from T1 to T5 (T6) (Consortium for Spinal Cord Medicine 2008b; Furlan and Fehlings 2008).

Aggressive management of hypotension and/or neurogenic shock is recommended with aggressive fluid resuscitation and may be associated with improvements in neurological outcomes. Avoidance of hypotension (systolic blood pressure < 90 mmHg) and hypoxia is critical to preventing further secondary spinal cord injury (Stevens et al. 2003). A systolic blood pressure of 90–100 mmHg, a heart rate of 60–100 beats/min, urine output >30 ml/h, and normothermia are suggested as therapeutic goals (Walters et al. 2013). The recommended goal is to maintain mean arterial pressure (MAP) above 85 mmHg (Tee et al. 2017; Wilkerson and Dailey 2021). The 2013 AANS/CNS Guidelines for Management of Acute Cervical Spine and Spinal Cord Injuries included level III recommendations

to maintain MAP 85 to 95 mmHg for the first 7 days after injury and correct hypotension (systolic blood pressure < 90 mmHg) as quickly as possible (Hawryluk et al. 2015; Ryken et al. 2013; Walters et al. 2013). Maintaining MAP at 85–90 mmHg after acute spinal cord injury for the first 7 days is associated with improved neurological outcomes for cervical and upper thoracic injuries. Longer duration of treatment with vasopressor may interfere with renal function due to the adrenergic effect on the renal arteries (Ploumis et al. 2010). There are no recommendations for the optimal vasopressor agent (Jia et al. 2013; Ryken et al. 2013; Squair et al. 2017; Vale et al. 1997; Walters et al. 2013). MAP is dependent on the peripheral resistance and the cardiac output. MAP increases when cardiac output is greater than peripheral resistance. MAP can be determined by the formula: MAP = diastolic + (pulse pressure/3) or (systolic + diastolic × 2)/3. Because of the risk of intramedullary hemorrhage and edema, hypertension should be avoided.

Bradycardia is common in patients with complete cervical cord injuries, and although the bradycardia is often self-limited, treatment with atropine or vasopressors may be necessary in severe cases (Table 15.6). If persistent bradycardia associated with hypotension is unresponsive to anticholinergic therapy such as atropine, transcutaneous/transthoracic pacing may be required as a temporary step prior to permanent pacemaker implantation. Bradycardia seen in spinal cord injuries can be significant, but serious episodes usually resolve after approximately 6 weeks and permanent cardiac pacemakers are rarely required (Royster et al. 2004). Bradycardia is a hallmark of neurogenic shock, but the clinician must maintain a high level of suspicion that other hemodynamic patterns of shock may coexist, especially in the polytrauma patient, since bradycardia can occur with concomitant blood loss and neurogenic shock. Treatment of hypotension and neurogenic shock following spinal cord injury initially involves volume resuscitation, taking care to avoid volume overload, followed by vasopressors as needed. The indwelling urinary catheter should be placed at least until the patient is hemodynamically stable. Care should be taken to determine the cause of persistent hypotension after hydration (Ryken et al. 2013). Patients with neurogenic shock who are continuously infused intravenously with impaired ability to mediate vasoconstriction may increase the risk of capillary leak and pulmonary edema (Stevens et al. 2003; Yue et al. 2017). Neurogenic shock can manifest as hypotension, which is poorly responsible for fluid resuscitation but which responds briskly to vasopressor agents (Eckert and Martin 2017). Therefore, it is better to use the vasopressors early than to continue intravenous fluid infusion (Ball 2001; Consortium for Spinal Cord Medicine 2008a).

Although no consensus has been reached on the best vasoactive agent of choice, it is recommended to use an agent with both α-adrenergic and β-adrenergic activity to treat both hypotension and bradycardia associated with sympathetic denervation and unopposed vagal tone in high cervical/thoracic injuries (Consortium for Spinal Cord Medicine 2008a). Initial vasopressors for hypotension and bradycardia in patients with spi-

Table 15.6 Management of bradycardia in cervical spinal cord injuries

Drugs/Modality	Administration route	Action mechanism
Atropine	IV	Reduces vagal tone by muscarinic receptor blockade
Dopamine	IV infusion	β1-receptors on the heart
Epinephrine	IV infusion	β1-receptors on the heart
Aminophylline	IV	Inhibition of PDE enzyme thus increasing cAMP with subsequent rise in catecholamines
Theophylline	Enteral or parenteral	Inhibition of PDE enzyme thus increasing cAMP with subsequent rise in catecholamines
Pacemaker	Invasive	

PDE phosphodiesterase

nal cord injuries include dopamine (2.5–5 μg/kg/min) with both α- and β-agonist properties and norepinephrine bitartrate (0.01–0.2 μg/kg/min, usually 0.05 μg/kg/min) as a secondary agent, if necessary. Dopamine and phenylephrine have historically been the primary vasopressors used in spinal cord injuries with both inotropic and chronotropic as well as vasoconstrictive properties (Ploumis et al. 2010). Peripheral vasoconstrictors are required for lesions in the lower thoracic region. Phenylephrine specifically regulates peripheral vasodilation by acting only on α1 receptors and can be used for lower thoracic and lumbar cord injuries, but not for upper thoracic or cervical injuries. Epinephrine and dobutamine were generally avoided because of their cardiac side effects (Inoue et al. 2014). The dosing of dopamine starts in the renal dose range (3–5 μg/kg/min) and is titrated up to the cardiac dose (>10 μg/kg/min) as necessary. Because phenylephrine is a pure α-agonist and can aggravate existing bradycardia, it is not an appropriate initial choice in patients with spinal cord injury (Consortium for Spinal Cord Medicine 2008a; Hughes 1990; McMahon et al. 2009; Stein et al. 2012) (Table 15.7).

Although the use of vasopressors can help achieve MAP goals and improve spinal cord perfusion, there are risks (Table 15.8). It has been reported that incidence of vasopressor-associated complications was higher with dopamine than with phenylephrine in both complete and incomplete spinal cord injuries. More vasopressor and dopamine-specific complications were observed in elderly spinal cord injuries (Yue et al. 2019). Dopamine has been found to cause major complications at a rate of 10% compared to phenylephrine, which has a rate of 3% to cause serious complications (Saadeh et al. 2017). These major complications included ST-segment elevation on electrocardiography, troponin elevations, atrial fibrillation, and ventricular tachycardia. Atrial fibrillation, ventricular tachycardia, or elevated troponins occurred in 30% of patients receiving dopamine. Only 4.5% of patients receiving phenylephrine experienced these complications (Readdy et al. 2015).

After the acute phase, baseline systolic and diastolic blood pressure in tetraplegics are reduced to about 15 mmHg lower than in non-spinal cord injury individuals due to the interruption of supraspinal sympathetic input. This may be because the influence of sympathetic vasoconstrictors does not affect below the level of injury. Autonomic dysreflexia rarely occurs during the first few weeks of injury. It is important to monitor and adjust the temperature and avoid prolonged exposure to extreme temperatures, as patients with cervical or high-thoracic injury may be at risk for poikilothermia (Furlan and Fehlings 2008).

15.6.2 Acute Pulmonary Management

Pulmonary complications are the most common short- and long-term cause of morbidity and mortality after spinal cord injuries and also affect the hospital stay length and costs. Respiratory disorders are the third most common cause of hospitalization in the first year after spinal cord injury

Table 15.7 Vasoactive agents to treat neurogenic shock

Agent	α-activity	β-activity	Considerations
Norepinephrine	+++	++	Probably the preferred agent
Dopamine Low dose (3–10 μg/kg/min) High dose (10–20 μg/kg/min)	+ ++	++ +++	May lead to inadvertent diuresis at low dose
Phenylephrine	++	None	May worsen bradycardia
Epinephrine	+++	++	Rarely needed
Dobutamine	None	+++	May cause hypotension if not euvolemic

+ = small effect, ++ = moderate effect, +++ = large effect
From Stein et al. (2012), with permission

Table 15.8 Physiologic response and complications of commonly used vasopressors/inotropes

Medication	Mean arterial pressure	Heart rate	Cardiac output	Systemic vascular resistance	Activity	Complications
Norepinephrine	Increase	Increase	Increase	Increase	$\alpha > \beta$	Arrhythmia, peripheral ischemia
Dopamine	Increase	Increase	Increase	Increase	$\alpha = \beta$	Hypotension with low dose, tachyarrhythmia, tissue ischemia
Phenylephrine	Increase	Decrease	Decrease	Increase	α	Reflex bradycardia, peripheral ischemia
Dobutamine	Similar	Increase	Increase	Decrease	$\alpha < \beta$	Tachyarrhythmia, cardiac ischemia
Epinephrine	Increase	Increase	Increase	Increase	$\alpha > \beta$	Tachyarrhythmia, stress cardiomyopathy, cardiac ischemia
Milrinone	Similar	Increase	Increase	Decrease	cAMP > inotropic	Vasodilation, can decrease blood pressure

cAMP, cyclic adenosine monophosphate
From Eli et al. (2021), with permission

(Burns 2007). Pneumonia occurs in 50% of patients with acute tetraplegia during acute hospitalization and rehabilitation (Fishburn et al. 1990). People with complete tetraplegia die from pneumonia at a rate that is 150 times higher than a matched population without spinal cord injuries (DeVivo et al. 1999). The highest incidence of atelectasis and pneumonia occurs within the first 5–7 days and is often primarily in the left lower lobe (Carter 1987). Ventilator-dependent patients have less than half the life expectancy of similarly injured but not ventilator-dependent patients (NSCISC 2021).

Respiratory management of patients with spinal cord injury should ideally include a combination of chest physiotherapy, secretion clearance devices, bronchodilators, mucolytics, respiratory muscle training, assisted breathing, and assisted coughing devices and techniques (Stein and Sheth 2015). Patients should be carefully monitored for respiratory failure within days of spinal cord injury. Reference parameters of respiratory function, including vital capacity, forced expiratory volume in 1 s (FEV1), and arterial blood gases, should be obtained until the patient is stabilized at regular intervals when initially evaluated (Cook 2003). Serial forced vital capacity (FVC) for evaluation of respiratory function is measured. A serial FVC less than 1 L is a predictor of ventilatory failure requiring airway protection and mechanical ventilation. The main consequence of expiratory muscle weakness is a decrease in peak cough flow, which is ineffective for clearance of bronchial secretions. With a peak cough flow of less than 2.7 L/s (160 L/min), air flow is insufficient to mobilize secretions out of the bronchi and trachea (Bach and Saporito 1996). Measures to promote the mobilization of secretions are listed in Table 15.9. In patients with acute tetraplegia, production of bronchial mucus may exceed 1 L per day, and the secretions are often tenacious. Aspiration is relatively common in patients with acute tetraplegia, especially in patients with predisposing factors such as mechanical ventilation, tracheostomy, anterior cervical spine surgery, or concomitant brain injury (Kirshblum et al. 1999).

Table 15.9 Methods of secretion mobilization

Method	Remarks
Manually assisted coughing	• Insufflation using AmbuBag (air stacking) • Contraindications: IVC filter, recent abdominal surgery, rib fractures
Mechanical insufflation-exsufflation	• Effective cough at inspiration/expiration pressure of +40/−40 cmH_2O • For patient using device first time, begin with pressures of 15 cm H_2O to familiarize patient with procedure • 3 s inhalation phase, 2 s exhalation phase, then pause for 5 s • Perform cycle of 4 or 5 assisted coughs, then rest for 30 s • Monitor symptoms and oxygen saturation • Contraindications: Bullous emphysema, pneumothorax, pneumomediastinum, recent barotrauma
Percussion	Manual or mechanical
Postural drainage	
High-frequency chest wall oscillation	
Intrapulmonary percussive ventilation	
Suctioning	
Bronchoscopy	
Inhaled mucolytics or hydrating agents for thick, tenacious secretions	

Modified from Burns (2007), with permission

Mechanical ventilation should be considered for patients with high tetraplegia and poor respiratory parameters. A tracheostomy should be performed early in the hospital for patients if the treatment center is likely to rely on the ventilator in the absence of specific expertise in the use of noninvasive ventilation. Noninvasive ventilation often eliminates the need for intubation and tra-

cheostomy (Bach 2012). Patients who are intubated should receive a nasogastric tube as soon as possible to avoid vomiting and aspiration. Succinylcholine is a drug for intubation in patients with spinal cord injury within 48 h of injury. Succinylcholine is safe to use in the first 48 h after injury. Succinylcholine is not recommended after this period because of a potential risk of a fatal hyperkalemic reaction of succinylcholine. General parameters for urgent intubation are obvious respiratory distress, dyspnea, complaints of inability to "catch my breath," inability to hold breath for 12 s, vital capacity <10 ml/kg or decreasing vital capacity, occurrence of "belly breathing" or "quad breathing," and pCO_2 >20 mmHg above baseline (Stein and Knight IV 2017). Tracheal or laryngeal manipulation can also stimulate a bradycardic response, as can any degree of hypoxia. Atropine should always be immediately available when the airway is manipulated in a patient with an acute cervical spinal cord injury. All patients with cervical cord injuries should be given supplemental oxygen to maintain an arterial saturation > 92%, as hypoxemia is extremely detrimental to patients with neurological injury. Hypoxemia can lead to severe bradycardia in patients with high cervical cord injuries due to unopposed vagal stimulation.

Patients who require mechanical ventilation are susceptible to ventilator-associated pneumonia (VAP). Measures to prevent VAP in patients with acute spinal cord injury requiring mechanical ventilation due to respiratory failure are very important. Patients with spinal cord injuries with the level of injury above T12 are initially difficult to remove pulmonary secretions and are at risk for pulmonary complications. In addition to suctioning, secretions that are retained due to expiratory muscle weakness should be treated with manually assisted coughing, pulmonary hygiene, mechanical insufflation-exsufflation, or similar expiratory aids. Tracheal suctioning alone is often not sufficient for secretion mobilization because bronchial anatomy suction catheters do not enter the left main bronchus properly (Fishburn et al. 1990).

15.6.3 Venous Thromboembolism

Venous thrombosis is a major cause of morbidity and mortality in patients with acute spinal cord injuries. Patients with traumatic spinal cord injury are more likely to have thromboembolic disorders, including deep vein thrombosis and pulmonary embolism. The risk of venous thrombosis in people with spinal cord injuries is approximately 2.5 times higher for deep venous thrombosis and 1.6 times higher for pulmonary embolism compared to controls. The risks are greatest within the first 3 months after the injury and with increasing age (Chung et al. 2014). They often have all of the risk factors described by Virchow (Virchow's triad): stasis due to muscle paralysis and vessel wall damage related to immobility, hypercoagulability due to transient coagulation factor and platelet aggregation abnormalities, and endothelial damage. Motor complete spinal cord injury, older age, smoking, obesity, associated injuries such as lower limb fracture, a history of thromboembolism coexisting coagulopathies, and comorbidities such as congestive heart failure or cancer further increase the risk of venous thromboembolism (Hull et al. 2013).

15.6.3.1 Prophylaxis of Deep Vein Thrombosis

The occurrence of deep vein thrombosis in acute spinal cord injuries depends on the prophylaxis of deep vein thrombosis. The incidence of venous thromboembolism with prophylaxis is between 6 and 14%, with no prophylaxis between 50 and 100% (Christie et al. 2011; Jones et al. 2005). The overall incidence of pulmonary embolism is between 8 and 14%. The incidence is highest within 2 weeks after injury and was observed as early as 72 h after the injury. Thromboembolic disorders are rare in children, but the incidence in adolescents is similar to that of adults (Fehlings et al. 2017).

Deep vein thrombosis can lead to pulmonary embolism and death, so prophylaxis is essential. Therapeutic options include intermittent pneumatic compression devices, thigh-high graded

compression stockings, coumadin, low-dose subcutaneous unfractionated heparin, adjusted dose subcutaneous unfractionated heparin, or low molecular weight heparin. However, all of these compounds had some limitations, including parenteral administration of heparins and the need for routine coagulation monitoring and dose adjustments for warfarin (Ageno et al. 2012). To overcome some of these limitations, direct oral anticoagulants (DOACs) have been developed (Barnes et al. 2015). DOACs have a favorable pharmacologic profile (e.g., rapid onset and short half-life) and a predictable anticoagulant response, which makes their use particularly attractive for both the acute phase treatment and for the long-term secondary prevention of venous thromboembolism. However, studies on the use of DOAC to prevent and treat deep venous thrombosis in patients with spinal cord injuries have not been well conducted (Hamidi et al. 2019). Anticoagulation may be appropriate immediately if the bleeding is stabilized (Consortium for Spinal Cord Medicine 1999). Unless there is a contraindication to low molecular weight heparin, such as active bleeding, profound thrombocytopenia, enoxaparin can be an intervention to prevent deep vein thrombosis. Some surgeons and critical care physicians are concerned about the risk of bleeding in the spinal cord and are reluctant to start anticoagulant therapy in the acute phase of spinal cord injury. If there is a high reserve for low molecular heparin in the acute phase of injury, the use of intermittent compression devices and compression stockings in addition to serial doppler monitoring may be appropriate. Duplex and Doppler ultrasonography are the most common and most convenient screening methods used today (Zierler 2004). There is no clear consensus on the timing or schedule for screening after acute spinal cord injuries, but it is suggested that weekly screening for asymptomatic deep vein thrombosis may be appropriate in the early high-risk period after spinal cord injury (Furlan and Fehlings 2008). Serial Doppler studies are costly and cannot detect a significant number of calf thrombosis. In some cases, a Greenfield filter may be indicated. Greenfield filers can be considered in high-risk groups such as complete high tetraplegia with femur fracture that cannot prescribe enoxaparin. Later, in the rehabilitation phase, low molecular weight heparin can be instituted (Jones et al. 2005).

Unless it is contraindicated, the mechanical compression devices should be placed immediately, and chemoprophylaxis should be initiated within 72 h. Low-dose heparin therapy alone or oral anticoagulation alone is not recommended as a prophylactic treatment strategy. Low molecular weight heparin should be started in all patients as soon as possible, when primary hemostasis becomes apparent. Intracranial bleeding, spinal hematoma, or hemothorax are contraindications to the initial administration of anticoagulants, but if bleeding is stable, anticoagulants may be appropriate. If trauma to the lower extremities interferes with the use of stockings or devices, the use of a foot pump may be considered. If initiation of venous thromboembolism prophylaxis is delayed by more than 3 days, a duplex scan of the leg may be performed to rule out deep vein thrombosis before placing the compression devices (Consortium for Spinal Cord Medicine 1999).

Chemoprophylaxis is usually performed with unfractionated heparin (5000 IU tid) or low molecular weight heparin. Patients with uncomplicated motor complete spinal cord injury o patients with no other major risk factors for venous thromboembolism should continue chemoprophylaxis for 8 weeks or 8 to 12 weeks (Christie et al. 2011). Patients with motor complete spinal cord injury and other risk factors such as fractures of the lower extremities, previous thrombosis, cancer, congestive heart failure, obesity, age over 70 years of age, or presence of an inferior vena cava filter with high risk of thromboembolism should receive chemoprophylaxis for 12 weeks. Prophylaxis may be discontinued earlier in patients with useful motor function in the lower extremities because they appear to have a low risk of venous thromboembolism. Patients with AIS C injuries should receive chemoprophylaxis for up to 8 weeks, and patients with AIS D should receive chemoprophylaxis during hospitalization, including reha-

bilitation (Consortium for Spinal Cord Medicine 1999). Pharmacological prophylaxis should be stopped several hours before elective surgery, depending on the half-life of the drug. When emergency surgery is needed, administration of protamine neutralizes unfractionated heparin and partially neutralizes low molecular weight heparin. If bleeding is controlled, low molecular weight heparin prophylaxis can be resumed 24 h after surgery (Christie et al. 2011; Consortium for Spinal Cord Medicine 1999).

Vena cava filters are not recommended as a routine preventive measure but are recommended for patients who cannot perform anticoagulation or who do not use anticoagulation and/or mechanical devices (Li et al. 2020). An inferior vena cava filter should only be considered for active bleeding if the expected duration is more than 72 h, and anticoagulants should be started as soon as possible after bleeding is stabilized. Although the efficacy of inferior vena cava filters has been demonstrated in the preventing pulmonary embolism in trauma patients, the placement of inferior vena cava filters has a potential risk of complications. Early complications include post-procedural bleeding, vessel penetration, malposition of the filter, and failure of filter opening. Complications can occur several weeks to months after placement of the filter and may include intraperitoneal erosion, inferior vena cava thrombosis, venous stasis, and distal migration of the inferior vena cava filter (Grewal et al. 2020; Li et al. 2020). It has been suggested that loss of abdominal muscle tone and use of the "quad cough" maneuver as an assisted coughing may increase the risk of inferior vena cava filter migration in patients with spinal cord injuries. Temporary filters may be more appropriate because permanent filters are associated with 26–36% of deep vein thrombosis occurrences in long-term follow-up observations (Hull et al. 2013).

Early mobilization and passive exercise should begin as soon as the patient stabilizes, either medically or surgically, with other prophylactic measures. If deep vein thrombosis is diagnosed, the affected lower extremity should not be mobilized for 48 h until the appropriate medication is administered. Patients with spinal cord injuries should resume prophylaxis if they are immobilized for a long time, readmitted for medical problems or surgery.

15.6.3.2 Diagnosis of Venous Thromboembolism

Clinical features include unilateral leg edema, increased calf diameter, localized tenderness, and/or low-grade fever, but deep venous thrombosis may occur even in the absence of these findings. Pulmonary embolism should be considered immediately if a patient with an acute spinal cord injury develops sudden onset of shortness of breath, hypotension, tachycardia, pleuritic chest pain, or unexplained hypoxia. Diagnostic tests or screening for deep vein thrombosis usually involve duplex ultrasound. Diagnostic tests for pulmonary embolism include ventilation-perfusion scan, electrocardiogram with a right ventricular strain pattern, and spiral CT of the lungs. Test for D-dimer levels has low specificity, although the negative predictive value of venous thromboembolism is good.

15.6.3.3 Treatment of Venous Thromboembolism

For patients with known venous thromboembolism, anticoagulant treatment should be started immediately with low molecular weight heparin, which is usually recommended because of its safety and efficacy compared to unfractionated heparin. Warfarin is started with an initial dosage of 5–10 mg/day at the same time, with heparin overlap, and warfarin treatment overlap for 4–5 days before heparin discontinuation. Warfarin doses are adjusted through frequent tests of the International Normalized Ratio (INR) to maintain the INR within the recommended therapeutic range of 2–3. The optimal duration of treatment is unclear, but anticoagulation is continued for 3–6 months for known deep vein thrombosis and 6 months for established pulmonary embolism. For more information on anticoagulants, see Chap. 10.

15.6.4 Bladder Management

Micturition requires an intact central and peripheral nervous system. The cortical and subcortical areas of the brain regulate the function of the sacral and pontine micturition centers. The bladder is innervated by sympathetic (T10–L2, hypogastric nerve), parasympathetic (S2–S4, pelvic nerve), and somatic (S2–S4, pudendal nerve) fibers. If the lesion is above the sacral micturition center, the result will be an upper motor neuron bladder. A lower motor neuron bladder dysfunction can lead to the absence or decrease of the sphincter and/or bladder tone.

The clinical abnormalities of upper and lower motor neuron bladder dysfunction in the acute phase are similar. The classic finding of an upper motor neuron bladder can be obvious when the spinal shock is resolved. Urinary retention is common immediately after spinal cord injury. Patients use a Foley catheter during the most acute phase of injury. In cases of contraindication due to urethral injury, urgent urological consultation is needed, and emergent suprapubic drainage may be initiated. Priapism in acute spinal cord injury is usually self-limited and does not require treatment. The urethral catheter can be placed in the presence of priapism after acute spinal cord injury. If the patient is stable not to require supplemental fluids and total urine volume is less than 3000 mL, an intermittent catheterization program should be initiated. Initially, the intermittent catheterization should be performed every 4–5 h, and the target volume is between 400 mL and 500 mL. The bladder management program can be individualized during the rehabilitation phase of the treatment (Wirtz et al. 1996). Some patients with spinal cord injuries can manage bladder dysfunction by other methods, such as the Valsalva maneuver, Credé maneuver, suprapubic tapping, or condom catheters.

15.6.5 Bowel Management

During the first month of spinal cord injury, there is a risk of gastrointestinal complications such as ileus, gastroduodenal ulceration and bleeding, and pancreatitis. Most patients with upper motor neuron pathology, lesions above the conus medullaris, are likely to be constipated. Fecal incontinence is possible with lower motor neuron lesion during acute hospitalization, but most patients develop constipation after the acute phase. However, the clinical abnormalities of upper and lower motor neuron bowel dysfunction are similar during spinal shock in the acute phase. Decreased intestinal motility and ileus after acute spinal cord injury are common. Bowel distention and inadequate evacuation can cause nausea and vomiting, high gastric residuals, anorexia, and decreased respiratory excursion. To ensure regularly scheduled evacuations, an early bowel program should be initiated during hospitalization. The initial bowel management should include bowel care as manual disimpaction at least once daily.

When medically appropriate, a more formal comprehensive bowel program should be initiated. Narcotics and tricyclic agents can aggravate constipation. Stool softeners like Colace and Senokot can be used in the acute phase. The patient should be placed on the commode after breakfast to utilize the gastrocolic reflex as possible. If constipation is suspected, a KUB film should be obtained, and a gentle enema should be considered. The first measure to avoid constipation is prevention by digital stimulation and laxatives such as bisacodyl at a dose of 10 mg once daily. In cases where there is no defecation 72 h after the initial dosage, the dose can be increased up to 10 mg bid (Azeez et al. 2020). Abdominal distention, pancreatitis, and gastric ulcers can occur in the acute phase of injury. Patients are recommended to eat when paralytic ileus is relieved. Stress ulcer prophylaxis should start and continue for 4 weeks or until other risk factors for gastrointestinal bleeding are resolved. Patient should not be treated prophylactically for more than 4 weeks unless there are other risk factors. A bowel program should be started as soon as possible. Typically, a bowel program includes a stool softener, laxative, and daily suppository.

15.6.5.1 Stress Ulcer Prophylaxis

Enteral feeding must begin early, preferably before 72 h after the traumatic spinal cord injury. Patients with acute spinal cord injury are at high risk for peptic ulceration or stress ulcer bleeding within the first 4 weeks, with the risk of ulceration diminishing thereafter. Proton pump inhibitors or histamine H_2-receptor antagonists are used as a preventive measure, starting at admission and continuing for 4 weeks. These drugs are safe and effective, but without any other risk factors, the risk is significantly reduced and should be discontinued after 4 weeks. Use of acid-reducing agents beyond 4 weeks is not indicated unless other risk factors for peptic ulceration are present, such as a bleeding disorder, mechanical ventilation, history of ulcer disease, liver failure, or ongoing use of corticosteroids (Consortium for Spinal Cord Medicine 2008a). Prolonged use of proton pump inhibitors or acid-reducing agents may be associated with an increase of the risk of *C. difficile* infection.

The delay in the gastric emptying manifests as nausea, vomiting, and abdominal distension. In the patients with a tube for enteral feeding, the gastric residue should be monitored strictly every 4 h, and should never exceed 250 mL. In the case of delayed gastric emptying, it is recommended to start treatment with metoclopramide, and in case of persistence, progress the nasogastric tube to post-pyloric tube (Azeez et al. 2020).

15.6.5.2 Swallowing Dysfunction

Patients with cervical spinal cord injury, halo fixation, cervical spine surgery, especially anterior cervical spine surgery (discectomy and fusion), long-term intubation, tracheostomy, presence of halo orthosis, or accompanying traumatic brain injury have previously been shown an increased risk of dysphagia after acute spinal cord injury, and swallowing function should be evaluated prior to oral feeding in these patients. If a feeding tube must be placed for long-term enteral feeding, it is preferable to use a jejunostomy tube rather than a gastrostomy tube to reduce the risk of aspiration.

15.6.6 Hyponatremia

Hyponatremia, an electrolyte abnormality found in critically ill patients, can be associated with significant morbidity and mortality. Because hyponatremia can arise in hypervolemic, euvolemic, and hypovolemic states, clinicians may not recognize its presence and cause. Incorrect management can lead to significant morbidity and mortality. Physicians need to recognize risk factors and symptoms and use appropriate treatment guidelines for hyponatremia (Patel and Balk 2007). Hyponatremia can develop due to (a) the dilution of total body sodium with excessive free water; (b) the reduction of total body sodium reserves as a result of abnormal sodium loss; or (c) a combination of these mechanisms because of the integrity of complex metabolic and autonomic interactions (Peruzzi et al. 1994).

Hyponatremia is a common electrolyte disorder during the early stage after traumatic spinal cord injury. The prevalence of hyponatremia in acute spinal cord injury is much higher than that of the general medical or surgical patient population. This abnormality usually occurs within the first week after injury. The most significant predictor of hyponatremia is the type rather than the level of spinal cord injury (Peruzzi et al. 1994). Hyponatremia occurs in 85.7% in patients with acute cervical spinal cord injuries, which is at least threefold higher than in individuals with acute cervical spine trauma without neurological impairment during the first 2 weeks of hospitalization after injury (Furlan and Fehlings 2009). Patients with spinal cord injuries with hyponatremia also show greater evidence of neurogenic hypotension than normonatremic individuals with spinal cord injury (Furlan and Fehlings 2009). Hyponatremia persisted from 24 h to 12 days after spinal cord injury (mean of 3.3 days), while hyponatremia lasted from 2 to 3 days after acute spine trauma without spinal cord injury (mean of 2.7 days) (Furlan and Fehlings 2009).

Although asymptomatic hyponatremia is usually seen in patients with serum sodium concentration between 130 and 135 mmol/L, vari-

Table 15.10 Symptoms and signs of hyponatremia

Classification	Plasma sodium concentration (nmol/L)	Symptoms and signs
Asymptomatic hyponatremia	130–135	Usually asymptomatic
Mild hyponatremia	125–130	Anorexia, nausea, vomiting, abdominal cramps, disorientation, headaches
Moderate hyponatremia	115–125	Agitation, confuction, hallucinations, impaired mental function, incontinence
Severe hyponatremia	<115	Seizures, coma

From Furlan and Fehlings (2009) and Moore et al. (2003), with permission

ous signs and symptoms may occur in patients with serum sodium concentration lower than 130 mmol/L (Moore et al. 2003; Patel and Balk 2007) (Table 15.10). The mortality rate for hyponatremic patients with a serum sodium concentration less than 130 mmol/L is 60-fold higher than in patients without documented hyponatremia (Anderson et al. 1985). In addition to the extent and duration of hyponatremia, the balance between increased cerebral edema and loss of electrolytes in the brain are key determinants of neurologic sequelae associated with hyponatremia (Furlan and Fehlings 2009; Patel and Balk 2007). Management of hyponatremia is initially aimed at restoring serum sodium concentration at least until symptoms and signs disappear. Treatment methods for hyponatremia include isotonic saline infusion (0.9% NaCl), hypertonic saline infusion (3% NaCl), fluid restriction, loop or thiazide diuretics, and arginine vasopressin receptor antagonists (Patel and Balk 2007).

15.6.7 Autonomic Vascular Dysfunction

In acute spinal cord injuries, blood pressure is lower than normal, and during rehabilitation with a level above T5 (T6), pronounced postural hypotension may occur when lifted from the horizontal, causing syncope. This is partly due to the lack of coordinated sympathetic vasoconstriction. Posture-dependent problems decrease over time, although this is not completely clear, but can decrease orthostatic hypotension with changes in hormonal body fluid regulation and alterations in vasomotor reflexes (wirtz et al. 1996).

Autonomic dysreflexia is a syndrome characterized by headache, flushing, piloerection, and hypertension. During the first few weeks of spinal cord injury, it is not a frequent occurrence, but rather when a patient emerges from spinal shock. Patients with T6 or higher lesions are most at risk. This condition is an emergency and requires immediate intervention. Without treatment, autonomic dysreflexia can lead to stroke, seizures, and even death. Any noxious stimulus below the level of injury can cause autonomic dysreflexia. Common causes of autonomic dysreflexia include bladder distention or fecal impaction. Less common causes include pressure injuries, ingrown toe nails, renal stone, tight clothing, and heterotopic ossification. Acute abdominal pathologies such as cholecystitis or perforated viscus can also cause autonomic dysreflexia. The causes must be identified and eliminated or treated. If the cause is not immediately recognized, the hypertension must be treated.

15.6.8 Noninfectious Fever and Abnormal Temperature Regulation

Acute spinal cord trauma can lead to a severe clinical fever reaction during intensive care follow-up, which can be attributed to both infectious and noninfectious etiologies as well as thermoregulatory dysfunction secondary to trauma (Ülger et al. 2019). Pyrexia, hyperthermia, and even hypothermia are common in the acute phase of spinal cord injury and may be accompanied by infections. However, an unknown cause of fever may also be the cause of increased body temperature (McKinley et al.

2006; Ülger et al. 2019). Because of the clinical importance of fever as a potential secondary injury mechanism, mechanisms underlying the detrimental effects of mild hyperthermia after injury should be evaluated (Dietrich and Bramlett 2007). In patients with tetraplegia, disorders of temperature regulation often occur. "Quad fever" occurs when patients with spinal cord injuries have high temperatures, i.e., 104 °F (40 °C) or higher, but have no other evidence of infection. Although these patients have very high body temperatures, they look well. Patients may also experience poikilothermia, in which body temperature is influenced by the ambient temperature. Perhaps the most important cause of noninfectious fever in patients with spinal cord injuries is the loss of supraspinal control of the sympathetic nervous system and defective thermoregulation due to loss of sensation (Ülger et al. 2019).

15.6.9 Pressure Injuries

Pressure injuries are a complication that can be avoided in patients with spinal cord injuries. The length of time of suspected pressure on vulnerable areas should be minimized. The most common area of pressure injuries in the acute period is the scrum, followed by the heel. Excessive shear and moisture should be avoided. Maceration of the skin due to urine, feces, and excessive sweating can cause pressure injuries. Careful skin care is important to relieve pressure and change posture at least every 2 h while keeping skin precautions clean and dry and inspecting the skin under medical equipments, pressure garments, or splints. Care should be taken with assisted bed mobility and transfers. The use of heel protector such as Prevalon Heel Protector Boot that off-loads the foot and keeps the foot in a neutral position. In assessing the risk of pressure injury, the Braden scale is a widely used tool that assesses the risk of pressure injury based on six factors: sensory perception, moisture, activity, mobility, nutrition, and friction and shear.

15.6.10 Contractures

Immobility leads to contractures. Muscles that cross two joints, such as the gastrocnemius, hamstrings, iliopsoas, and biceps brachii, are particularly at risk. Contracture can be prevented by passive range of motion of the joints and correct positioning. An ankle-foot orthosis can prevent the progression of gastrocnemius and soleus contractures. However, an orthosis is not a substitute for a passive range of motion exercise program. In patients with C5 and C6 tetraplegia, contractures should be encouraged, as if the MCP, PIP, and DIP joints, as the target joints, may need to be contracted in about 20 degrees of flexion for effective tenodesis. These flexion contractures may contribute to a functional grasp by passive or active tenodesis effects. A volar wrist hand orthosis can support this favorable contracture.

15.6.11 Pain

Patients with acute lesions can experience significant pain. Many patients complain of neuropathic pain, which may be manifested by poorly localized dysesthesias. Pharmacological management of the pain should be performed to balance the risk of side effects such as oversedation or respiratory depression. Anti-epileptic drugs may relieve neuropathic pain, including gabapentin, pregabalin, carbamazepine, and phenytoin. Low-dose tricyclic antidepressants, such as amitriptyline, nortriptyline, or imipramine, may also be helpful. These agents have anticholinergic side effects such as dry mouth, lightheadedness, blurred vision, and orthostatic hypotension. Non-pharmacological interventions for pain control include transcutaneous electrical nerve stimulation and psychological intervention.

15.7 Nutritional Support

Proper nutritional support is important for the acute phase after spinal cord injury. Patients with severe injuries are exposed to nitrogen losses and

malnutrition within 2–3 weeks after injury, resulting in increased susceptibility to infections, difficulty in wound healing, and difficulty in weaning from mechanical ventilation (Dhall et al. 2013a, b). Protein catabolism occurs after acute, severe spinal cord injury and significant loss in lean body mass due to muscle atrophy results in large nitrogen losses, long-term negative nitrogen balance, and rapid weight loss.

Nutritional support and early enteral nutrition to meet caloric and nitrogen needs is safe and can reduce the adverse effects of the catabolic nitrogen wasting process following an acute spinal cord injury. Enteral nutrition rather than parenteral nutrition is recommended. A standard polymeric enteral formula may be initiated at a semirecumbent position to prevent aspiration, if possible. Enteral nutrition should begin to be as tolerated within 24–48 h. Enteral feeding has been shown to reduce gastric stress ulceration in patients with acute spinal cord injuries. Other potential benefits of enteral feeding compared with parenteral administration include maintenance of intestinal integrity and function, lower costs, lower incidence of hypoglycemia, lower risk of infection, and avoidance of IV catheter-related complications. If enteral feeding is not allowed, nasoduodenal or nasojejunal tubal feeding should be done. Nasoduodenal or nasojejunal feeding usually provides full-caloric, high-nitrogen, large-volume feeding within days of injury (Dhall et al. 2013a, b). Parenteral nutrition is recommended for patients with bowel injury, mechanical bowel obstruction or prolonged ileus until the bowel recovery is complete. The need for long-term nutritional support and gastric decompression are indications for gastrostomy for acute spinal cord injuries. Percutaneous endoscopic gastrostomy (PEG) is one of the easiest methods to apply in the ICU setting.

High fat and low carbohydrate enteral diet have beneficial physiological effects on CO_2 production and respiratory quotient, which may make this type of diet useful in patients with impaired ventilatory reserves, but there are no definitive recommendations due to lack of conclusive evidence about the outcomes on the duration of ventilation and weaning success. Hyperglycemia should be managed to maintain normal blood glucose levels in critically ill and/or mechanically ventilated patients as medical outcomes will deteriorate. Complex changes in the metabolic effects of hypoglycemia have been found in tetraplegics, often without the usual clinical signs of the disease (Matthias et al. 1979).

15.8 Psychological Adaptation

Patients with spinal cord injuries can experience a variety of emotional status, including denial, anger, guilt, disbelief, and frustration. There is no normal coping pattern. Families may need emotional and psychological support. Rehabilitation psychologists, social workers, and pastoral services can provide comfort and support. The risk of mental health problems and psychosocial problems should be addressed after admission and throughout the acute care program.

References

Ageno W, Gallus AS, Wittkowsky A, et al. American College of Chest Physicians. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e44S–88S.

Agostinello J, Battistuzzo CR, Skeers P, et al. Early spinal surgery following thoracolumbar spinal cord injury. Spine. 2017;42:E617–23.

Ahn H, Singh J, Nathens A, et al. Pre-hospital care management of a potential spinal cord injured patient: a systematic review of the literature and evidence-based guidelines. J Neurotrauma. 2011;28:1341–61.

Alexander MS, Anderson KD, Biering-Sorensen F, et al. Outcome measures in spinal cord injury: recent assessments and recommendations for future directions. Spinal Cord. 2009;47:582–91.

Anderson RJ, Chung HM, Kluge R, et al. Hyponatremia: a prospective analysis of its epidemiology and the pathogenetic role of vasopressin. Ann Intern Med. 1985;102:164–8.

Arnold PM, Filardi TZ, Strang RD, et al. Early neurologic assessment of the patient with spinal cord injury. Top Spinal Cord Inj Rehabil. 2006;12:38–48.

ASIA. International standards for neurological classification of spinal cord injury. 8th ed. revised 2019. Richmond: ASIA; 2019.

Azeez MMA, Moscote-Salazar LR, Alcala-Cerra G, et al. Emergency management of traumatic spinal cord injuries. Indian J Neurotrauma. 2020;17:57–61.

Bach JR. Non-invasive respiratory management of high level spinal cord injury. J Spinal Cord Med. 2012;35:72–80.

Bach JR, Saporito LR. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure. A different approach to weaning. Chest. 1996;110:1566–71.

Ball PA. Critical care of spinal cord injury. Spine (Phila Pa 1976). 2001;(15):S27–30.

Baptiste DC, Fehlings MG. Pathophysiology of cervical myelopathy. Spine J. 2006;6(6 Suppl):190S–7S.

Barnes GD, Ageno W, Ansell J, et al. Subcommittee on the control of anticoagulation of the international society on thrombosis and haemostasis. Recommendation on the nomenclature for oral anticoagulants: communication from the SSC of the ISTH. J Thromb Haemost. 2015;13:1154–6.

Bourassa-Moreau E, Mac-Thiong JM, Li A, et al. Do patients with complete spinal cord injury benefit from early surgical decompression? Analysis of neurological improvement in a prospective cohort study. J Neurotrauma. 2016;33:301–6.

Bracken MB, Shepard MJ, Hellenbrand KG, et al. Methylprednisolone and neurological function 1 year after spinal cord injury. Results of the National Acute Spinal Cord Injury Study. J Neurosurg. 1985;63:704–13.

Bracken MB, Shepard MJ, Collins WF, et al. A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the second national acute spinal cord injury study. N Engl J Med. 1990;322:1405–11.

Bracken MB, Shepard MJ, Holford TR, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA. 1997;277:1597–604.

Burke JF, Yue JK, Ngwenya LB, et al. Ultra-early (<12 hours) surgery correlates with higher rate of American spinal injury association impairment scale conversion after cervical spinal cord injury. Neurosurgery. 2019;85:199–203.

Burns SP. Acute respiratory infections in persons with spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:203–16.

Calancie B, Molano MR, Broton JG. Tendon reflexes for predicting movement recovery after acute spinal cord injury in humans. Clin Neurophysiol. 2004;115:2350–63.

Carter RE. Respiratory aspects of spinal cord injury management. Paraplegia. 1987;25:262–6.

Chen JW, Meurer WJ, Dangayach NS, et al. Emergency Neurological Life Support (ENLS) traumatic spinal cord injury protocol, version 4.0. Last updated October 2019. https://higherlogicdownload.s3.amazonaws.com/NEUROCRITICALCARE/fdc4bb32-6722-417b-8839-f68ac1ef3794/UploadedImages/ENLS_Documents/ENLS_V4.0_protocol%20files/ENLS_V_4_0_Protocol_TSI_FINAL.pdf. Accessed Nov 2021.

Christie S, Thibault-Halman G, Casha S. Acute pharmacological DVT prophylaxis after spinal cord injury. J Neurotrauma. 2011;28:1509–14.

Chung WS, Lin CL, Chang SN, et al. Increased risk of deep vein thrombosis and pulmonary thromboembolism in patients with spinal cord injury: a nationwide cohort prospective study. Thromb Res. 2014;133:579–84.

Cole J, Weller R. Introduction to the clinical presentations of spinal cord disease from a pathophysiological perspective. In: Engler GL, Cole J, Merton WL, editors. Spinal cord diseases. Diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.

Consortium for spinal cord medicine. Prevention of thromboembolism in spinal cord injury. 2nd ed. Washington, DC: Paralyzed Veterans of America; 1999.

Consortium for spinal cord medicine. Early acute management in adults with spinal cord injury: a clinical practice guidelines for health-care professionals. J Spinal Cord Med. 2008a;31:403–78.

Consortium for Spinal Cord Medicine. Early acute management in adults with spinal cord injury. Clinical practice guidelines for health-care professionals. Washington, DC: Paralyzed Veterans of America; 2008b.

Cook N. Respiratory care in spinal cord injury with associated traumatic brain injury: bridging the gap in critical care nursing interventions. Intensive Crit Care Nurs. 2003;19:143–53.

DeVivo M, Krause J, Lammertse D. Recent trends in mortality and causes of death among persons with spinal cord injury. Arch Phys Med Rehabil. 1999;80:1411–9.

Dhall SS, Hadley MN, Aarabi B, et al. Deep venous thrombosis and thromboembolism in patients with cervical spinal cord injuries. Neurosurgery. 2013a;72(Suppl 2):244–54.

Dhall SS, Hadley MN, Aarabi B, et al. Nutritional support after spinal cord injury. Neurosurgery. 2013b;72(Suppl 2):255–9.

Dietrich WD, Bramlett HM. Hyperthermia and central nervous system injury. Prog Brain Res. 2007;162201–17.

Eckert MJ, Martin MJ. Trauma: spinal cord injury. Surg Clin North Am. 2017;97:1031–45.

Eli I, Lerner DP, Ghogawala Z. Acute Traumatic Spinal Cord Injury. Neurol Clin. 2021;39:471–88.

Fehlings MG, Vaccaro A, Wilson JR, et al. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the surgical timing in acute spinal cord injury study (STASCIS). PLoS One. 2012;7:e3203.

Fehlings MG, Tetreault LA, Aarabi B, et al. A clinical practice guideline for the management of patients with acute spinal cord injury: recommendations on the type and timing of anticoagulant thromboprophylaxis. Grobal Spine J. 2017;7(3 Suppl):212S–20S.

Fishburn M, Marino R, Ditunno JJ. Atelectasis and pneumonia in acute spinal cord injury. Arch Phys Med Rehabil. 1990;71:197–200.

Furlan JC, Fehlings MG. Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis and management. Neurosurg Focus. 2008;25:E13.

Furlan JC, Fehlings MG. Hyponatremia in the acute stage after traumatic cervical spinal cord injury: clinical and neuroanatomic evidence for autonomic dysfunction. Spine (Phila Pa 1976). 2009;(34):501–11.

Grewal S, Lewandowski RJ, Ryu RKW, et al. Inferior vena cava filter retrieval: patient selection, procedural planning, and postprocedural complications. AJR Am J Roentgenol. 2020;215:790–4.

Hadley MN, Walters BC. Introduction to the guidelines for the management of acute cervical spine and spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):5–16.

Hadley MN, Walters BC, Aarabi B, et al. Clinical assessment following acute cervical spinal cord injury. Neurosurgery. 2013;72(Suppl 2):40–53.

Hamidi M, Zeeshan M, Kulvatunyou N, et al. Operative spinal trauma: thromboprophylaxis with low molecular weight heparin or a direct oral anticoagulant. J Thromb Haemost. 2019;17:925–33.

Hawryluk G, Whetstone W, Saigal R, et al. Mean arterial blood pressure correlates with neurological recovery after human spinal cord injury: analysis of high frequency physiologic data. J Neurotrauma. 2015;32:1958–67.

Hebert JS, Burnham RS. The effect of polytrauma in persons with traumatic spine injury. A prospective database of spine fractures. Spine (Phila Pa 1976). 2000;(25):55–60.

Herbison GJ, Zerby SA, Cohen ME, et al. Motor power differences within the first two weeks post-SCI in cervical spinal cord-injured quadriplegic subjects. J Neurotrauma. 1992;9:373–80.

Hughes MC. Critical care nursing for the patient with a spinal cord injury. Crit Care Nurs Clin N Am. 1990;2:33–40.

Hull RD, Merali T, Mills A, et al. Venous thromboembolism in elderly high-risk medical patients: time course of events and influence of risk factors. Clin Appl Thromb Hemost. 2013;19:357–62.

Hurlbert RJ, Hadley MN, Walters BC, et al. Pharmacological therapy for acute spinal cord injury. Neurosurgery. 2013;72(Suppl 2):93–105.

Inoue T, Manley GT, Patel N, et al. Medical and surgical management after spinal cord injury: vasopressor usage, early surgerys, and complications. J Neurotrauma. 2014;31:284–91.

Jia X, Kowalski RG, Sciubba DM, et al. Critical care of traumatic spinal cord injury. J Intensive Care Med. 2013;28:12–23.

Jones T, Ugalde V, Franks P, et al. Venous thromboembolism after spinal cord injury: incidence, time course, and associated risk factors in 16,240 adults and children. Arch Phys Med Rehabil. 2005;86:2240–7.

Karsy M, Hawryluk G. Pharmacologic management of acute spinal cord injury. Neurosurg Clin N Am. 2017;28:49–62.

Kato H, Kimura A, Sasaki R, et al. Cervical spinal cord injury without bony injury: a multicenter retrospective study of emergency and critical care centers in Japan. J Trauma. 2008;65:373–9.

Kirshblum S, Johnston M, Brown J, et al. Predictors of dysphagia after spinal cord injury. Arch Phys Med Rehabil. 1999;80:1101–5.

Kushner DS, Alvarez G. Dual diagnosis: traumatic brain injury with spinal cord injury. Phys Med Rehabil Clin N Am. 2014;25:681–96, ix–x.

Kwon BK, Okon E, Hillyer J, et al. A systematic review of non-invasive pharmacologic neuroprotective treatments for acute spinal cord injury. J Neurotrauma. 2011;28:1545–88.

Li X, Haddadin I, McLennan G, et al. Inferior vena cava filter – comprehensive overview of current indications, techniques, complications and retrieval rates. Vasa. 2020;49:449–62.

Liu JC, Patel A, Vaccaro AR, Lammertse DP, et al. Methylprednisolone after traumatic spinal cord injury: yes or no? PM R. 2009;1:669–73.

Liu JM, Long XH, Zhou Y, et al. Is urgent decompression superior to delayed surgery for traumatic spinal cord injury? A meta-analysis. World Neurosurg. 2016;87:124–31.

Lo V, Esquenazi Y, Han MK, et al. Critical care management of patients with acute spinal cord injury. J Neurosurg Sci. 2013;57:281–92.

Marino RJ, Jones L, Kirshblum S, et al. Reliability and repeatability of the motor and sensory examination of the international standards for neurological classification of spinal cord injury. J Spinal Cord Med. 2008;31:166–70.

Matthias CJ, Frankel HL, Turner RC, et al. Physiological responses to insulin hypoglycaemia in spinal man. Paraplegia. 1979;17:319–26.

McKinley W, McNamee S, Meade M, et al. Incidence, etiology, and risk factors for fever following acute spinal cord injury. J Spinal Cord Med. 2006;29:501–6.

McMahon D, Tutt M, Cook AM. Pharmacological management of hemodynamic complications following spinal cord injury. Orthopedics. 2009;32:331.

Moore K, Thompson C, Trainer P. Disorders of water balance. Clin Med (Lond). 2003;3:28–33.

National Spinal Cord Injury Statistical Center (NSCISC). The 2017 annual statistical report for the spinal cord injury model systems, Birmingham: National Spinal Cord Injury Statistical Center; 2018.

National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham: University of Alabama at Birmingham; 2021. https://www.nscisc.uab.edu. Last accessed Nov 2021.

Patel GP, Balk RA. Recognition and treatment of hyponatremia in acutely ill hospitalized patients. Clin Ther. 2007;29:211–29.

Peruzzi WT, Shapiro BA, Meyer PR Jr, et al. Hyponatremia in acute spinal cord injury. Crit Care Med. 1994;22:252–8.

Ploumis A, Yadlapalli N, Fehlings MG, et al. A systematic review of the evidence supporting a role for vasopressor support in acute SCI. Spinal Cord. 2010;48:356–62.

Readdy WJ, Whetstone WD, Ferguson AR, et al. Complications and outcomes of vasopressor usage in acute traumatic central cord syndrome. J Neurosurg Spine. 2015;23:574–80.

Ropper AE, Neal MT, Theodore N. Acute management of traumatic cervical spinal cord injury. Pract Neurol. 2015;15:266–72.

Rowland JW, Hawryluk GW, Kwon B, et al. Current status of acute spinal cord injury pathophysiology and emerging therapies: promise on the horizon. Neurosurg Focus. 2008;25:E2.

Royster RA, Barboi C, Peruzzi WT. Critical care in the acute cervical spinal cord injury. Top Spinal Cord Injury Rehabil. 2004;9:11–32.

Ryken TC, Hurlbert RJ, Hadley MN, et al. The acute cardiopulmonary management of patients with cervical spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):84–92.

Saadeh YS, Smith BW, Joseph JR, et al. The impact of blood pressure management after spinal cord injury: a systematic review of the literature. Neurosurg Focus. 2017;43:E20.

Saboe LA, Reid DL, Davis LA, et al. Spinal trauma and associated injuries. J Trauma. 1991;31:43–8.

Sandean D. Management of acute spinal cord injury: a summary of the evidence pertaining to the acute management, operative and non-operative management. World J Orthop. 2020;11:573–83.

Sheerin F, de Frein R. The occipital and sacral pressures experienced by healthy volunteers under spinal immobilization: a trial of three surfaces. J Emerg Nurs. 2007;33:447–50.

Squair JW, Bélanger LM, Tsang A, et al. Spinal cord perfusion pressure predicts neurologic recovery in acute spinal cord injury. Neurology. 2017;89:1660–7.

Stein DM, Knight WA IV. Emergency neurological life support: traumatic spinal injury. Neurocrit Care. 2017;27:S170–80.

Stein DM, Sheth KN. Management of acute spinal cord injury. Continuum (Minneap Minn). 2015;21:159–87.

Stein DM, Roddy V, Marx J, et al. Emergency neurological life support: traumatic spine injury. Neurocrit Care. 2012;17(Suppl 1):S102–11.

Stevens RD, Bhardwaj A, Kirsch JR, et al. Critical care and perioperative management in traumatic spinal cord injury. J Neurosurg Anesthesiol. 2003;15:215–29.

Stricsek G, Ghobrial G, Wilson J, et al. Complications in the management of patients with spine trauma. Neurosurg Clin N Am. 2017;28:147–55.

Tee JW, Altaf F, Belanger L, et al. Mean arterial blood pressure management of acute traumatic spinal cord injured patients during the pre-hospital and early admission period. J Neurotrauma. 2017;34:1271–7.

Ülger F, Pehlivanlar Küçük M, Öztürk ÇE, et al. Non-infectious fever after acute spinal cord injury in the intensive care unit. J Spinal Cord Med. 2019;42:310–7.

Vale FL, Burns J, Jackson AB, et al. Combined medical and surgical treatment after acute spinal cord injury: results of a prospective pilot study to assess the merits of aggressive medical resuscitation and blood pressure management. J Neurosurg. 1997;87:239–46.

Walters BC, Hadley MN, Hurlbert RJ, et al. Guidelines for the management of acute cervical spine and spinal cord injuries: 2013 update. Neurosurgery. 2013;60:82–91.

Wilkerson C, Dailey AT. Spinal cord injury management on the front line: ABCs of spinal cord injury treatment based on American Association of Neurological Surgeons/Congress of Neurological Surgeons Guidelines and Common Sense. Neurosurg Clin N Am. 2021;32:341–51.

Wirtz KM, La Favor KM, Ang R. Managing chronic spinal cord injury: issues in critical care. Crit Care Nurse. 1996;16:24–35.

Yue JK, Winkler EA, Rick JW, et al. Update on critical care for acute spinal cord injury in the setting of polytrauma. Neurosurg Focus. 2017;43:E19.

Yue JK, Tsolinas RE, Burke JF, et al. Vasopressor support in managing acute spinal cord injury: current knowledge. J Neurosurg Sci. 2019;63:308–17.

Zierler BK. Ultrasonography and diagnosis of venous thromboembolism. Circulation. 2004;109(12 Suppl 1):I9–4.

Recommended Additional Reading

Buchanan LE, Nawoczenski DA, editors. Spinal cord injury-concepts and management approaches. Baltimore: Williams & Wilkins; 1987.

Cairo JM, editor. Pilbeam's mechanical ventilation. Physiological and clinical applications. 5th ed. St. Lois: Elsevier; 2012.

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. Wolters Kluwer: New Delhi; 2015.

Harrison P. Managing spinal injury: critical care. The international management of people with actual or suspected spinal cord injury in high dependency and intensive care unit. London: The Spinal Injury Association; 2000.

Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.

Preston RA. Acid-base, fluids and electrolytes: made ridiculously simple. 2nd ed. Miami: MedMaster, Inc.; 2011.

Russel C, Matta B. Tracheostomy a multiprofessional handbook. Cambridge: Cambridge University Press; 2004.

Sykes K, Yong JD. Respiratory support in intensive care. London: BMJ Books; 1999.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury. In: progress in brain research, vol. 152. New York: Elsevier; 2006.

16 Nontraumatic Spinal Cord Injuries/ Lesions

Spinal cord dysfunction can have an obvious traumatic or compressive cause. In addition, the lack of pathological specificity of the clinical and imaging features means that patients are often treated empirically based on the prevalence and the treatability of the differential diagnoses; multiple sclerosis and isolated inflammatory myelitis are the most likely diagnoses in the western world (Mariano et al. 2018). There are few reports of epidemiologic studies on nontraumatic spinal cord injury vs. traumatic spinal cord injury. In the western developed countries, the proportion of nontraumatic spinal cord injuries has increased steadily over the past decade, as demographic changes have a profound impact on the cause of spinal cord injuries due to the rapid increase in the elderly population (NSCISC 2020). Nontraumatic spinal cord injury is closely related to age and is more common than traumatic spinal cord injury (New and Sundararajan 2008). The incidence of nontraumatic spinal cord injury varies from 12 to 76 per million population (New et al. 2014; Nijendijk et al. 2014; Noonan et al. 2012; O'Connor 2015). The average age-adjusted incidence rate of nontraumatic spinal cord injury in Victoria, Australia between 2000 and 2006, was 26.3 cases per million per year for adults and 0.7 cases per million per year for those under 15 years. The median age of onset of nontraumatic spinal cord injury in Australia is 67 years, range 52–77 (New et al. 2013). The prevalence of nontraumatic spinal cord injury in Victoria, Australia, in June 2010 was 367.2 per million (New et al. 2013).

A variety of nontraumatic conditions can affect the spinal cord (McKinley 2008). Causes of nontraumatic spinal cord lesion/disease include vertebral spondylosis, cancerous, and infectious-related compression, vascular ischemia, and multiple sclerosis. Other vascular injuries, inflammatory disease, motor neuron disease, radiation myelopathy, syringomyelia, paraneoplastic syndrome, developmental and genetic diseases, and malnutrition, including vitamin B12 deficiency, are the causes of nontraumatic spinal cord injury (McKinley 2008; Thurnher et al. 2007). Vascular causes of myelopathy (infarction or, less often, hemorrhage) should be suspected if symptoms onset abruptly (hyperacute onset). Several spinal cord syndromes have an onset of days to weeks (acute/subacute onset). Inflammatory transverse myelitis is the most common in adults. Short spinal cord lesions (<3 vertebral segments) that are partial and asymmetrical in axial views of MRI, are classic of multiple sclerosis. Acute to subacute infective myelitis is most commonly viral. It is noteworthy that longitudinally extensive transverse myelitis of ≥3 vertebral segments can be the first sign of neuromyelitis optica spectrum disorder. Sarcoidosis, B12 deficiency, and chronic infections (e.g., human T cell lymphotropic virus myelitis, tuberculosis, schistosomiasis, HIV vacuolar myelopathy, and tertiary syphilis) may

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present with a more slowly progressive picture. Progressive multiple sclerosis is the leading cause of a non-compressive myelopathy in the western world, although multiple sclerosis typically results in a very slowly progressive condition that worsens over decades. It is important to note, however, that compressive myelopathy is sometimes misdiagnosed as inflammatory. Table 16.1 shows a summary of the nontraumatic spinal cord lesions according to speed of symptom onset and lesion length on MRI (Mariano et al. 2018).

The number of nontraumatic spinal cord injuries increases as the elderly population increases. After degenerative cervical myelopathy, spinal tumors are the leading cause of nontraumatic spinal cord injury in the USA and other developed countries. On the other hand, infections, including tuberculosis and HIV, are the predominant cause of nontraumatic myelopathy in many developing countries. Neurological manifestations are similar to traumatic spinal cord injury but tend to be older and more frequent in women. Elderly individuals with nontraumatic spinal

Table 16.1 Differential diagnosis of nontraumatic spinal cord lesions by speed of symptom onset and lesion length on MRI

Onset	MRI sagittal	Differential
Hyperacute	Long	Spinal Cord infarction Neuromyelitis optica spectrum disorder (rare; documented only in AQP4-antibody positive cases) Hemorrhage
	Short	Hemorrhage
Acute/ subacute	Long	Neuromyelitis optica spectrum disorder Autoimmune Infective (most commonly viral) Acute disseminated encephalomyelitis Paraneoplastic Sarcoidosis Vascular (spinal cord infarction, malformation) Neoplastic (ependymoma)
	Short	Multiple sclerosis Infective (viral, tuberculosis, parasitic) Autoimmune Sarcoidosis Atypical neuromyelitis optica spectrum disorder (14%)
Chronic/ progressive	Long	Paraneoplastic Sarcoidosis Atypical multiple sclerosis (long-standing or primary progressive) Chronic infection (syphilis, HTLV-1, HIV) Vascular Metabolic Neoplastic (ependymoma, astrocytoma)
	Short	Sarcoidosis Multiple sclerosis (primary or secondary progressive) Neoplastic (astrocytoma, ependymoma, metastatic)
Relapsing/ fluctuating	Long	Neuromyelitis optica spectrum disorder Vascular (malformation) Sarcoidosis
	Short	Multiple sclerosis

AQP4, aquaporin-4; HTLV-1, human T cell lymphotropic virus type 1
From Mariano et al. (2018), with permission

cord injury/disease may present with associated medical complications, such as cardiopulmonary disease or diabetes, which could adversely affect medical and functional outcomes. In addition, the degree of damage in nontraumatic spinal cord lesions is usually incomplete, and it is likely to be accompanied by underlying disease (Aebli et al. 2013a). The incidence of complications such as skin, bowel, and bladder dysfunction is similar to that of traumatic spinal cord injury, but the incidence of deep vein thrombosis, autonomic dysreflexia, orthostatic hypotension, and pneumonia is significantly less common in nontraumatic spinal cord injury patients compared to traumatic spinal cord injury (McKinley et al. 1998, 1999) (Table 16.2).

A nontraumatic spinal cord injury is assessed according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI). However, diseases such as multiple sclerosis and amyotrophic lateral sclerosis are not examined according to ISNCSCI.

Table 16.2 Characteristics of traumatic and nontraumatic myelopathies

	Traumatic	Nontraumatic
Onset age	Younger, increasing incidence in older adults	Depending on the underlying causes
Gender distribution	80% male, 20% females	Higher prevalence of females
Neurological level	Tetra or paraplegia	More often paraplegia
Completeness	Complete or incomplete	More often incomplete
Neurological examination	Based on ISNCSCI	Basically using ISNCSCI. Diseases such as MS and ALS are not examined according to ISNCSCI
Comorbidities	Few comorbidities with younger age	Higher prevalence of age-related comorbidities
Complications	Multiple complications, can affect all body systems	Same complications as in traumatic but less prevalence of AD, OH, and pneumonia

ISNCSCI, International Standards of Neurological Classification of Spinal Cord Injury; MS, multiple sclerosis; ALS, amyotrophic lateral sclerosis; AD, autonomic dysreflexia; OH, orthostatic hypotension

16.1 Degenerative Cervical Myelopathy

Age-related changes in the spinal column lead to a degenerative cascade known as spondylosis. These spondylotic changes may result in direct compression or ischemic dysfunction of the spinal cord known as cervical spondylotic myelopathy (Fehlings et al. 2017; Lebl et al. 2011). Degenerative cervical myelopathy, formerly known as cervical spondylotic myelopathy, is an umbrella term for a collection of pathologic entities that include cervical spondylotic myelopathy, ossification of the posterior longitudinal ligaments, and degenerative disc disease that cause partly or a combination of myelopathy in the cervical spine, that is, a neurological disorder caused by the degeneration of the spinal axis and the resulting compression of the spinal cord (Gibson et al. 2018; Moghaddamjou et al. 2020). Degenerative cervical myelopathy is a progressive disease caused by age-related degeneration of the facet joints, intervertebral discs, or vertebral bodies, hypertrophy of the ligamentum flavum, and, in some cases, OPLL or progressive cervical kyphosis (Baptiste and Fehlings 2006; Kalsi-Ryan et al. 2013). The degenerative pathologies under the umbrella term degenerative cervical myelopathy are listed in Table 16.3. In

Table 16.3 Degenerative pathologies of degenerative cervical myelopathy

Degenerative arthritic change
Facet hypertrophy
Facet joint instability
Degenerative spondylolisthesis
Subluxation
Disc herniation
Spondylosis/osteophytosis
Ligamentous degeneration
Hypertrophy of the ligamentum flavum
Ossification of the posterior longitudinal ligament
Ossification of the ligamentum flavum
Calcification of spinal ligaments

2015, the term degenerative cervical myelopathy was proposed to encompass osteoarthritic changes in the spine, including spondylosis, disc herniation, and facet arthropathy, as well as ligamentous hypertrophy, calcification, or ossification (Nouri et al. 2015; Tetreault et al. 2015). Cervical spondylosis is a degenerative condition that occurs with aging and gets worse with repetitive use. Spondylotic myelopathy of the cervical spinal cord is a very common cause of spinal cord dysfunction in the elderly. Degenerative cervical myelopathy is the leading cause of spinal cord impairment in adults worldwide, with the increasing rate in an aging population (Kalsi-Ryan et al. 2013; Nouri et al. 2015).

Degenerative spondylosis begins with biomechanics changes in the anterior element, the intervertebral discs, and follows degeneration of the posterior elements, facet joints, resulting in destabilization of the motion segment of the vertebrae. Reactive bone proliferation leads to the formation of osteophytes, which occur in combination with hypertrophy and ossification of the posterior longitudinal ligament and ligamentum flavum (Toledano and Bartleson 2013). They can compress the nerve root and narrow the spinal canal. Radiographically, cervical spondylosis and degenerative cervical myelopathy are very common. Degenerative cervical myelopathy is a condition in which the spinal cord is damaged either directly by traumatic compression and abnormal movement, or indirectly by ischemia due to arterial compression, venous stasis, or other consequences of the degenerative changes that characterize cervical spondylosis. The mean anteroposterior diameter of the spinal canal is approximately 17 mm from C3 to C7. The space requirement for the spinal cord is an average 10 mm. Absolute spinal canal stenosis has a sagittal diameter of less than 10 mm. The relative stenosis refers to a diameter of 10–13 mm (Bakhsheshian et al. 2017; Ghogawala and Whitmore 2013). As the degenerative cervical disc becomes narrower, the vertebral bodies are accompanied by the opposition of the vertebral bodies, resulting in deformity of the uncovertebral joints and narrowing of the intervertebral foramina and formation of the osteophytes along the anterior spinal canal, causing myelopathy (Kettler et al. 2007). In addition to anterior compression by osteophytes and disc material, the spinal cord can be compressed posteriorly by the ligamentum flavum if the neck is hyperextended (Shedid and Benzel 2007).

16.1.1 Epidemiology

Degenerative cervical myelopathy is the leading cause of spinal cord dysfunction in people over 55 years of age in North America. Men are more affected than women. The incidence and prevalence of myelopathy caused by degenerative pathology of the spine in North America is estimated to be 41 and 605 per million, respectively (Nouri et al. 2015). A global epidemiological study of nontraumatic spinal cord injuries estimates that 59% of nontraumatic spinal cord injuries in Japan, 54% in the USA, 31% in Europe, 22% in Australia, and between 4% and 30% in Africa (New et al. 2014). The most commonly affected levels are the more mobile segments of C5–C6, C6–C7, and C4–C5. Patients over the age of 60 often have a multisegmental disease (Klineberg 2010). A congenitally narrow canal lowers the threshold for minor trauma or early degenerative changes that can lead to myelopathy. Early onset of cervical spondylosis (early spondylotic myelopathy) in some patients, such as those with athetoid cerebral palsy, can be an overuse phenomenon. Repetitive overuse can contribute to the early onset or progression of cervical spondylotic myelopathy in some patients. Patients with a constitutionally narrow spinal canal are at higher risk of developing myelopathy with a spondylotic narrow canal, so the possibility of myelopathy due to spondylotic reduction in the spinal canal diameter is more likely. Less common causes are ossification of the posterior longitudinal ligament, which is particularly prevalent in the Asian/Japanese population (Klineberg 2010). In some cases, early symptoms of myelopathy due to amyotrophic lateral sclerosis are mistakenly diagnosed as spondylotic myelopathy, and unnecessary surgery may be performed. MRI, electromyography,

SEP, and MEP should be performed to rule out spinal cord lesions associated with disease-related pathologic processes.

16.1.2 Pathophysiology

The pathophysiology of degenerative cervical myelopathy is thought to be multifactorial. The pathogenesis contributing to degenerative cervical myelopathy can be divided into three main components: static, dynamic, and histopathologic and biomolecular factors (Table 16.4). Static factors cause acquired or developmental stenosis of the cervical spinal canal and dynamic factors result in repetitive injury to the spinal cord (Baptiste and Fehlings 2006; Lebl et al. 2011). These mechanical factors, in turn, result in direct injury to neurons and glial cells and a secondary cascade of events including ischemia, excitotoxicity, and apoptosis (Baptiste and Fehlings 2006). It has been postulated that the absolute size of the spinal canal may be an important factor in the development of symptoms of degenerative cervical myelopathy. The neurological symptoms of this disorder are generally related to the degree of compression of the various spinal cord tracts of the spinal cord.

Table 16.4 Pathophysiological factors contributing to degenerative cervical myelopathy

Factors	Pathophysiology
Static factors	• Spondylosis • Disc degeneration • Ossification of the posterior longitudinal ligament • Ossification of the ligamentum flavum • Congenital stenosis • Other acquired compression pathology, e.g. tumors and calcification
Dynamic factors	• Changes in neck flexion/extension, which narrow the cervical spinal canal dynamically and place increased strain and shear forces on the spinal cord
Histopathologic or biomolecular factors	• Ischemic injury due to chronic compression of spinal cord vasculature • Glutamate-mediated excitotoxicity • Oligodendrocyte and neuronal apoptosis

Adapted from Baptiste and Fehlings (2006), with permission

Although the changes in spondylosis, especially in anterior–posterior diameter of the spinal canal, lead to a narrowing of the spinal canal, in most cases, no neurological complications develop, so additional factors must contribute to the development of myelopathy. The initial constitutional diameter of the spinal canal is an important factor. Abnormal spinal movements also play an important role in the pathogenesis and progression of degenerative cervical myelopathy. The center of rotation of the cervical spine is located anterior to the vertebral bodies, so the length of the spinal cord increases in flexion and decreases in extension. It is believed that stretching of the spinal cord in flexion and movement against anterior spondylotic structures results in repeated spinal cord trauma. An enlarged cord cross-sectional area of the spinal cord in extension with the concomitant reduction in cross-sectional area of the spinal canal results in intermittent pinching of the spinal cord between anterior spondylotic structures and intervertebral disc material and the ligamentum flavum (Baptiste and Fehlings 2006). There is considerable debate as to whether myelopathy is the result of direct compression of neural tissue or whether it is a secondary effect resulting from impairment of the vascular supply of the spinal cord (Karadimas et al. 2013). Pathological changes in the spinal cord are most noticeable at areas of maximal compression site opposite spondylotic structures at the level of the intervertebral disc. The gray matter can exhibit neuronal loss and ischemia, leading to necrosis and cavitation. The white matter often shows minimal change but can show signs of demyelination and necrosis.

16.1.2.1 Static Factors

The static factors are structural factors that cause canal narrowing. The degenerative cascade of degenerative cervical myelopathy typically begins with the deterioration of the intervertebral disc (Baptiste and Fehlings 2006; de Oliveira

et al. 2016). Static factors include narrowing of the spinal canal from the decreased height of the degenerative intervertebral disc leading to the increased sagittal diameter of the disc and bulging of the disc, reactive hypertrophy and osteophyte formation at the vertebral end plates, projection of osteophytes from the uncovertebral and facet joints, ossification of the posterior longitudinal ligament, and hypertrophy of the ligamentum flavum.

16.1.2.2 Dynamic Factors

The dynamic factors relate to abnormal repetitive movement of the cervical spine during flexion and extension that cause irritation and compression of the spinal cord. The spinal cord stretches with flexion of the cervical spine and shortens and thicken with extension. With the extension of the cervical spine, the posterior half of the spinal cord is shortened more than the anterior portion of the cord, and the axons in the posterior column assumed a spiral course and occupied a larger cross-sectioned area on a transverse section. Therefore, the dynamic shortening of the posterior cord and posterior columns in extension may explain the difficulties with balance in the early phase of patients with degenerative cervical myelopathy (Breig et al. 1966).

The dynamic factors can also affect the dimensions of the spinal canal–the cross-sectional area of the spinal canal increases in flexion and decreases in extension. During hyperextension, the ligamentum flavum buckles into the canal and the degenerated disc bulges posteriorly, reducing the space available for the spinal cord and pinching the spinal cord between the vertebral body anteriorly and the hypertrophied buckled ligamentum flavum posteriorly. In patients with a kyphotic sagittal alignment, the spinal cord can become tethered over spondylotic anterior elements during flexion, although the canal diameter is increased (Breig and el-Nadi 1966; Breig et al. 1966; Holmes et al. 1996). If the spinal segments become stiff due to spondylotic change, adjacent segments may become relatively hypermobile or may result in subluxation contributing to the impact of the spinal cord (Breig et al. 1966; Lawrence et al. 2012).

16.1.2.3 Histopathologic and Biomolecular Factors

Mechanical compression of the spinal cord leads to vascular compromise that cause ischemia and inflammation (Baptiste and Fehlings 2006). Anterior compression impairs perfusion through the transverse arterioles arising from the anterior sulcal arteries, while compression of the posterior cord reduces perfusion to the intramedullary branches of the central gray matter (Hashizume et al. 1984). The oligodendrocytes are hypersensitive to ischemic injuries. Therefore, the death of oligodendrocyte after the onset of ischemia may explain the demyelination associated with chronic cervical myelopathy. Chronic cord compression can lead to neuronal cell loss, degeneration of the posterior columns and anterior horn cells, and endothelial damage, which results in an impaired blood–spinal cord barrier (Baptiste and Fehlings 2006; Kim et al. 2013; Lebl et al. 2011). Because degenerative cervical myelopathy is related to chronic compression by the degenerated structures of the spine, it can be progressive. It is estimated that 20–60% of people with myelopathy symptoms will further deteriorate over time (Badhiwala and Wilson 2018; Milligan et al. 2019).

16.1.3 Physical/Neurological Examination and Clinical Presentation

Nonspecific and subtle early features that overlap with other neurological conditions can delay the diagnosis. Incomplete neurological assessment by professionals with poor awareness of the disease further contributes to delay. Symptoms and signs of degenerative cervical myelopathy include variable degrees of both motor and sensory impairment, often mixed patterns of upper and lower motor neuron lesion signs, sensory loss of the spinothalamic tract and/or posterior column, and pain in the cervical region and the upper extremities (Table 16.5). With chronic degenerative cervical myelopathy, patient may notice subtle changes in balance or hand dexterity. Physician's history taking should identify dif-

Table 16.5 Symptoms and signs of degenerative cervical myelopathy

Symptoms associated with myelopathy
• Posterior neck pain
• Unilateral or bilateral pain of the upper extremities
• Clumsy hands
• Weakness, numbness, lack of dexterity of the upper extremities
• Lower extremity weakness and sensory loss
• Bladder and bowel problem
Signs associated with myelopathy
• Hyperreactive DTRs
• Inverted brachioradialis reflex
• Hoffman signs
• Babinski sign, Chaddock sign, Oppenheim sign, Gordon sign
• Romberg sign
• Lhermitte sign
• Limb spasticity
• Gait disturbance
• Bladder and bowel dysfunction

ficulties with motor tasks such as clumsiness or slowness in activities such as buttoning buttons, using keys, or changes in handwriting. Difficulties with common modern tasks such as using a computer keyboard, pressing buttons on a cellular phone, or text messaging may be noticed as early signs of cervical myelopathy. Often the earliest manifestations of balance problems are reported by the patient as the recent need to use a handrail when climbing stairs (Lebl et al. 2011). Degenerative cervical myelopathy is often a slow gradual deterioration with symptoms of gait abnormalities, weakness, sensory changes, and dexterity problems (Milligan et al. 2019). Symptoms are usually bilateral but may be asymmetrical. The pattern of sensory loss is also variable and depends on the compression area. A typical feature of degenerative cervical myelopathy is the "numb clumsy hand." In severe cases of degenerative cervical myelopathy, changes in bladder or bowel dysfunctions can occur.

Basically, assessments of manual muscle testing, deep tendon reflexes, pathological reflexes including Babinski, Hoffman's sign, and clonus, and balance tests such as heel-walking, toe-walking, and Romberg's sign should be included in physical examination.

Spastic paraplegia is a typical finding that reflects the initial involvement of the corticospinal tracts. Pathological reflexes such as Hoffman sign, Babinski sign, hyperreflexia in lower extremity muscle stretch reflexes, and clonus correspond to the spinal cord compression. Although the presence of a Hoffman sign and a Babinski sign indicates corticospinal tract injury, the absence of a Babinski sign or a Hoffman sign does not exclude corticospinal tract dysfunction (Cho and Bhattacharyya 2018). In a retrospective review of patients with degenerative cervical myelopathy, a Hoffmann sign was found in 68% and a Babinski sign in 33%. In patients with milder disability (mJOA Scores 14–16), a Hoffmann sign was present in 46%, while a Babinski sign occurred in 10%; in patients with severe myelopathy and mJOA scores of $\leq$10, a Hoffmann sign was present in 81% and the Babinski sign in 83% (Houten and Noce 2008). Normal jaw muscle stretch reflexes help distinguish degenerative cervical myelopathy from intracranial pathology. Upper motor neuron lesion signs may be accompanied by lower motor neuron lesion signs such as hyporeflexia and fasciculations in the upper extremities at the level of spinal cord injury or root compression, i.e. shoulder girdle muscle wasting and fasciculations at C5–C6 or intrinsic hand muscle atrophy at C8–T1 with intrinsic minus hand deformities. The presence of the associated lumbar stenosis may mask lower extremity hyperreflexia. Sensory changes vary depending on the location and extent of spinal cord dysfunction. Often there are changes in vibration and proprioceptive sense (Tsutsumimoto et al. 2012).

Posterior column dysfunction can lead to ataxia, a positive Romberg's sign, and a wide-based gait. In patients with degenerative cervical myelopathy who develop central cord syndrome after a hyperextension injury, the upper extremities usually show disproportionately much more than lower extremity weakness and a relative sacral sensory sparing (Yadla et al. 2010). Muscle strength of the lower extremity tends to be weaker in the muscles of the proximal muscles such as the iliopsoas and quadriceps. The limited range of motion of the neck reflects the underlying spondylosis. Patients can show Lhermitte's sign during flexion of the neck and are characterized

by a brief shock-like sensation of the spine and extremities (Harrop et al. 2007). Cervical spondylosis can cause dysphagia due to physical compression of the esophagus or inflammatory compression caused by swelling of the soft tissue in front of the vertebrae.

The assessment of grip strength with a dynamometer, the 10-s step test, and the 10-s open-and-close-hand test are valid measures for assessing impairment and useful tools for measuring the natural history and effectiveness of the treatment. Normal subjects can perform the latter two tests more than 15 and 20 times, respectively. Gait analysis, including changes in walking speed, has been shown to be a reliable method to monitor treatment response. The rating scales for degenerative cervical myelopathy include the modified Japanese Orthopedic Association (mJOA) scale (Table 16.6) for evaluating items related to motor and sensory function of the upper and lower extremities and bladder function. The mJOA remains the current "gold standard" in assessing degenerative cervical myelopathy (Moghaddamjou et al. 2020). The Myelopathy Disability Index is another tool that contains items related to activities of daily living (Casey et al. 1996) (Fig. 16.1). The Myelopathy Disability Index was originally developed to assess the level of difficulty in performing ten usual activities for patients with rheumatoid involvement of the cervical spine. It provides useful information for predicting outcome after surgical intervention (Casey et al. 1996). The myelopathy Assessment Scale Nurick is also often used as the clinical staging scale in the evaluation of cervical myelopathy (de Oliveira et al. 2016) (Table 16.7).

Table 16.6 Modified Japanese Orthopedic Association (mJOA) scales for Cervical Myelopathy

Score	Definition
Motor dysfunction score of the upper extremities	
0	Inability to move hands
1	Inability to eat with a spoon, but able to move hands
2	Inability to button shirt, but able to eat with a spoon
3	Able to button shirt with great difficulty
4	Able to button shirt with slight difficulty
5	No dysfunction
Motor dysfunction score of the lower extremities	
0	Complete loss of motor and sensory function
1	Sensory preservation without ability to move legs
2	Able to move legs, but unable to walk
3	Able to walk on flat floor with a walking aid (cane or crutch)
4	Able to walk up and/or down stairs with hand rail
5	Moderate-to-significant lack of stability, but able to walk up and/or down stairs without hand rail
6	Mild lack of stability but walks with smooth reciprocation unaided
7	No dysfunction
Sensory dysfunction score of the upper extremities	
0	Complete loss of hand sensation
1	Severe sensory loss or pain
2	Mild sensory loss
3	No sensory loss
Sphincter dysfunction score	
0	Inability to micturate voluntarily
1	Marked difficulty with micturition
2	Mild to moderate difficulty with micturition
3	Normal micturition

16.1.4 Imaging Study

Anteroposterior, lateral, and oblique radiographs should be performed in patients with suspected degenerative cervical myelopathy. Spinal degenerative changes such as narrowing of disc space, osteophyte formation, and listhesis are frequently seen. Decrease or loss of lordotic curvature and loss of motion segmental rhythm in the cervical spine are common. The absolute sagittal diameter of the spinal canal should be measured from the posterior aspect of the midvertebral body to the spinolaminar line. In C3–C7, the sagittal diameter of the spinal canal less than 13 mm is regarded as stenosis, but the absolute measurement is influenced by the magnification of the X-ray image. In standard lateral radiographs, the ratio of the sagittal canal diameter to the midvertebral body diameter (Torg–Pavlov ratio) of less than

Rising are you able to stand up from an armless straight chair?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Rising are you able to get in and out of bed?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Eating are you able to cut your meat?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Eating are you able to lift a full cup or glass to your mouth?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Walking are you able to walk outdoors on flat ground?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Walking are you able to climb up five steps?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Hygiene are you able to wash and dry your entire body?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Hygiene are you able to get on and off the toilet?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Grip are you able to:Open jars which have been previously opened?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Activities are you able to:Get in and out of a car?

- Without ANY difficulty ☐
- With SOME difficulty ☐
- With MUCH difficulty / assistance required ☐
- Unable to do ☐

Fig. 16.1 Myopathy disability index

Table 16.7 Nurick clinical scale for myelopathy assessment

Grading	Nurick clinical scale
Grade 0	Signs and symptoms of root involvement but without evidence of spinal cord disease
Grade 1	Signs of spinal cord diseases but no difficulty in walking
Grade 2	Slight difficulty in walking which does not prevent full-time employment
Grade 3	Difficulty in walking that prevents full-time employment and occupation or the ability to do all housework, but which is not so severe someone else's help to walk
Grade 4	Able to walk only with someone else's help or with the aid of a walker
Grade 5	Chairbound or bedridden

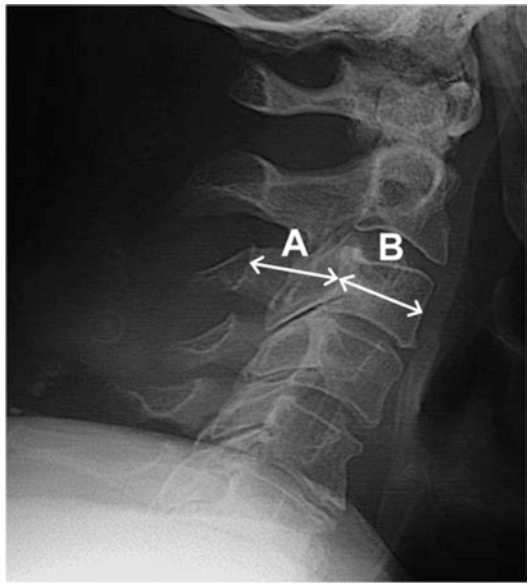

Fig. 16.2 Lateral view of the cervical spine with the measurements for calculating the Torg–Pavlov ratio. (A) developmental sagittal diameter of the spinal canal measured from the midpoint of the posterior surface of the vertebral body to the closest point of the opposite spinal lamina. (B) sagittal diameter of the vertebral body measured between the midpoints of the anterior and posterior surfaces. From Aebli et al. (2013b), with permission

0.8 is considered to be indicative of spinal stenosis (Aebli et al. 2013b) (Fig. 16.2). Calculation of the Torg–Pavlov ratio eliminates the influence of differences in magnification between X-ray images and provides a universally comparable numerical value. Although several correlations have been suggested, the role of the Torg–Pavlov ratio in predicting the clinical risk of traumatic spinal cord injury has not been conclusively proven.

Lateral flexion and extension radiographs allow the range of motion and instability to be assessed. MRI is useful for the assessment of soft tissues and neural elements. There is a relatively good correlation between the clinical severity of degenerative cervical myelopathy and the presence of high signal intensity in T2-weighted images (Table 16.8). CT myelography has a limited role, but it can provide additional information about the bony structures (Edwards et al. 2003).

Table 16.8 Poor prognostic surgical outcome signs of degenerative cervical myelopathy

Patient factors
• Older
• Longer duration of symptoms and signs
Imaging factors
• Intramedullary T1WI hypointensity
• Intramedullary T2WI hyperintensity
• Small cross-sectional area or atrophy of the spinal cord
• Intramedullary gadolinium enhancement

16.1.5 Differential Diagnosis

The great variability and lack of consistency in the pattern of onset of degenerative cervical myelopathy can make diagnosis clinically difficult. Although degenerative cervical myelopathy is the most common cause of cervical myelopathy, it is important to consider an extensive differential diagnosis. These include motor neuron disease; multiple sclerosis and other demyelinating conditions; other causes of spinal cord dysfunction such as syringomyelia; tumors; inflammatory, infectious, and nutritional myelopathies; peripheral and entrapment neuropathies; intracranial pathology; and systemic causes of hyperreflexia (Edwards et al. 2003). It is important to know that these conditions can coexist with degenerative cervical myelopathy.

16.1.6 Management

Nonsurgical treatment for degenerative cervical myelopathy may include simple observation and monitoring of the patient or treatment with a soft or hard collar, physical therapy, medications (steroids, NSAID, gabapentin/pregabalin), spinal injections, and cervical traction. Patients with no major neurological deficits but with radiological evidence of spinal cord compression can be treated conservatively and monitored conservatively. The role of surgical decompression is controversial in this context (Matz et al. 2009). A soft cervical collar can limit extreme movements and additional injuries, but the evidence is limited. It has been reported to be associated with neuro-

logical improvement. More rigid collars are often discarded when prescribed for long-term use. Nonsteroidal anti-inflammatory drugs are used for pain management. Surgical intervention is common in patients with moderate (mJOA score of 12–14) to severe (mJOA score of <11) neurological deficits and/or progressive disease. The goal of surgery is to decompress the spinal cord, stabilize the spinal column, and prevent any further neurologic damage. Prior to surgery, a clear diagnosis of cervical spondylotic myelopathy should be made on the basis of careful clinical history, examination, and imaging studies. Surgical procedures can be performed through an anterior or posterior approach (Nikolaidis et al. 2010). Surgical decompression should be considered despite the limited consensus on the long-term efficacy of surgical interventions and the specific surgical approach in relation to the progressive neurological deficit in degenerative cervical myelopathy. Patients need to know enough about the risk, benefits, and limitations of various surgical and nonsurgical treatment options to make informed decisions about their care. Successful surgery occurs in a third of individuals, 40% show no change and 25% show signs of worsening (Kalsi-Ryan et al. 2013; Moussellard et al. 2014). Despite treatment, many patients may present with residual spinal cord deficits such as neurogenic bladder or bowel, spasticity, and pain (Milligan et al. 2019).

The rehabilitation measures depend on the extent and type of neurological deficit. Patients with upper extremity weakness and impaired hand dexterity are candidates for assessment and training of activities of daily living and for appropriate prescriptions of adaptive equipment. Mobility assessment, gait training, and fall risk management are important components for those with significant neurological involvement of the lower extremity. Patients with spinal cord dysfunction due to degenerative cervical myelopathy have been proven to achieve significant functional gains with inpatient rehabilitation and achieve functional outcomes similar to traumatic spinal cord injuries. Management and secondary prevention of complications such as urinary incontinence, urinary tract infections, pressure injuries, venous thromboembolism, etc. are the same as for traumatic spinal cord injuries.

16.2 Adjacent Segment Disease

Adjacent segments disease includes various complications on the adjacent proximal or distal segments to the spinal fusion, including listhesis, herniated disc, facet joint degeneration, or vertebral compression fracture with spinal instability (Lawrence et al. 2012). Adjacent segment disease is caused by the biomechanics of excessive stress, which leads to further degenerative processes in adjacent segments after fusion. Treatment options for the adjacent segment disease include the extension of the number of fused vertebrae and/or decompression (Virk et al. 2014).

16.3 Cauda Equina Lesion

Cauda equina has a characteristic orientation of the lumbosacral roots in the spinal canal. The spinal roots of the proximal segment are anterior and lateral in the spinal canal, and the roots of the distal segment are posterior and medial. Therefore, it is likely that the pathology from the anterior element, such as disc herniation, affects the proximal segments, and if the pathology of the posterior element or traumatic injury invades the spinal canal, it is likely to result in neurological symptoms due to involvement of the lowest sacral segments. It can be assumed that neurological symptoms affecting the lowest sacral segment including the bladder and bowel due to a lesion of the anterior element of the spine are serious in pathology.

16.4 Spine and Spinal Cord Tumors

The spinal canal is a confined space, and tumors as a space-occupying lesion growing in this space can have a devastating effect on the function of the spinal cord and nerve roots. The destruction of the bones by a tumor may cause instability of

the spine with the collapse of vertebrae and compression of the nerve roots or the spinal cord itself. Metastatic tumors in the extradural space and primary or metastatic tumors arising in the spinal cord and its meningeal coverings cause compression or ischemia of nerve roots and the spinal cord (Mechtler and Nandigam 2012).

The classification given in Table 16.9 is based not only on the type of tumor but also on the anatomical location of the tumor. Tumors of the spine and spinal cord can be classified based on origin as primary or secondary tumors and based on location as extradural or intradural. Intradural tumors are further divided into extramedullary or intramedullary. Primary lesions are usually benign, arising from the bony spinal column, the meningeal coverings of the spinal cord, or from the spinal cord parenchyma itself. Secondary metastatic spinal tumors are common than primary lesions. Fifty-five percent to sixty percent of all spinal tumors are extradural, 35–40% are intradural-extramedullary, and 5% are intramedullary. The most common benign spinal neoplasms are intradural-extramedullary, followed by extradural and intramedullary. The most common intradural-extramedullary tumors (neurofibromas and schwannomas) and meningioma account for 80–90% of the cases, followed by congenital lesions (dermoids, epidermoids, teratomas, enteric cysts, and arachnoid cysts).

Table 16.9 Classification of spinal tumors

Vertebral column (bone tumors)	Primary	Chordoma Osteosarcoma Osteoclastoma (giant cell tumor of bone) Hemangioma Myeloma
	Secondary	Carcinoma (bronchus, prostate, breast) Lymphoreticular tumors
Extradural tumors		Metastatic carcinoma Malignant melanoma Lymphoma
Intradural tumors	Extramedullary-primary	Meningioma Schwannoma Neurofibroma Hemangioblastoma Malignant melanoma Lipoma Epidermoid and dermoid cysts
	Extramedullary-metastatic	Astrocytoma Primary neuroectodermal tumor (medulloblastoma) Ependymoma Metastatic carcinoma-seeding Spinal cord deposits Carcinomatous meningitis
Intramedullary tumors		Astrocytoma Anaplastic astrocytoma Glioblastoma multiforme Ependymoma, including myxopapillary ependymoma Primary neuroectodermal tumor Gangliocytoma Neurocytoma Lipoma Epidermoid cyst Hemangioma
Leukemias		Invasion of nerve roots and spinal cord

Modified from Engler et al. (1998)

Meningiomas are the second most common intradural-extramedullary tumors (Thakur et al. 2012).

Fifteen percent of all primary tumors of the central nervous system and its coverings occur in the spine. The primary tumors of the spine are 29% schwannomas, 25.5% meningiomas, 22% gliomas (63% of which are ependymomas), and 12% sarcoma. Primary bone tumors involving the spine are less common than metastatic tumors. Primary osteogenic sarcomas and osteoclastomas of the spine are rare but can cause bone destruction and compression of the spinal cord or cauda equina due to vertebral collapse or tumor extension into the spinal canal. Most hemangiomas occur in the thoracic or lumbar region. Treatment by excision of the lesion in the bone can be used to prevent or alleviate circulatory problems in the spinal cord. Metastatic tumors can involve any part of the spine. They destroy bone and cause vertebral collapse, or metastasis can spread into the spinal canal, causing compression of the spinal cord or cauda equina (Zairi et al. 2013). Chordomas, derived from tissue similar to the notochord, appear almost exclusively in the sacral regions of the spine and in the clivus of the skull. Nearly all carcinomas can be metastasized to the spine, most commonly carcinomas of the bronchus, breast, lung, and prostate. Lymphoreticular tumors, particularly plasmacytoma or myeloma, also involve the bone of the spine.

Primary tumors of the spinal cord are less common than those of the brain, but they form the majority of intramedullary tumors. Most tumors within the spinal cord, intramedullary tumors, originate from glial or neuronal tissue and are only very rarely metastatic origin (Raj and Lofton 2013). Intramedullary tumors are ependymomas, astrocytomas, or others including hemangioblastoma and, rarely, intramedullary metastases. Ependymoma is the most common primary intrinsic tumor of the spinal cord and is more common in adults. Astrocytomas represent the majority of intramedullary tumors in children. Ependymomas originate from cells lining the central canal. Almost all ependymomas are benign, and ependymomas are most often located in the cervical cord or in the cauda equina or filum terminale. The degree of invasiveness of astrocytomas may vary from low to high grade. Tumors within the confines of the dural sleeve or sac may either arise outside the spinal cord, extramedullary tumors, from leptomeninges (meningiomas from the arachnoid), from nerve roots (schwannomas and neurofibromas), or from the adipose tissue (lipoma) or remnants of epidermal tissue (epidermoid cysts). Meningiomas are often located posterior to the thoracic cord or near the foramen magnum and are more common in females and most commonly in the thoracic spine. Neurofibromas and schwannomas originate from Schwann cells of the nerve root. Multiple neurofibromas present the possibility of neurofibromatosis. Meningiomas and schwannomas are the most common intradural-extramedullary tumors in the spine. Extramedullary tumors are mostly benign.

Spinal metastases are common in cancer, but cause spinal cord compression only if that extend from the bone into the epidural space (Ropper and Ropper 2017). Metastatic carcinomas are the most common tumors involving extradural space in the spinal canal, and metastatic tumors account for more than 98% of extradural spinal tumors (Loblaw et al. 2012). Almost all types of cancers can metastasize to the spine, but the most common sources are lung, breast, and prostate cancers, and renal-cell cancer, non-Hodgkin's lymphoma, and myeloma are also common causes (Schiff et al. 1997; Stark et al. 1982). Sarcoma, neuroblastoma, and lymphoma have been reported as the most frequent causes of spinal cord compression in children (Lewis et al. 1986). The thoracic spine part of the vertebrae most frequently involved in metastasis, except in prostatic cancer, where the lumbar spine is more frequently involved (Fattal et al. 2011a, b). The compression occurs in 60%, 25%, and 15% of cases in the thoracic, lumbar, and cervical segments, respectively (Bach et al.). About 1 in 20 cancer patients cause spinal cord compression. If extradural compression of the spinal cord occurs elsewhere in the body without any evident primary tumor, high-grade non-Hodgkin's lymphoma is frequently found.

The distribution of metastatic lesions is a function of both the number of metastatic emboli produced and the survival rate of each embolus (Roos and Dingemans 1979). Metastatic emboli may spread through special lymphatic or venous channels. Lung carcinomas can spread to the bone through direct segmental arteries. Breast and prostate carcinomas can be metastasized through the Batson paravertebral venous plexus that connects the intra-abdominal venous supply with the epidural and paravertebral venous supplies. The azygos vein, which is the main venous drainage of the breast, communicates with the paravertebral venous plexus of the thoracic region. The prostate drains through the pelvic plexus, which communicates in the lumbar region. During Valsalva maneuver, there may be a flow back from these organs to the spine. The distribution of the tumor involves aspects of tissue susceptivity. The bone marrow provides a biochemically suitable environment for the proliferation of tumor cells. In the vertebrae, the vertebral body is the most common part of metastatic seeding, occurring 20 times more often than the posterior element (Asdorian et al. 1990). The cancellous bone is almost always invaded before the cortical bone.

16.4.1 Symptoms and Signs

The most common symptom of spinal tumors is pain. Aching thoracic or back pain and tenderness on percussion over the affected site are typical and can precede neurological symptoms by several weeks (Ropper and Ropper 2017). Pain is often persistent, and the supine position worsens and becomes more prominent at rest. As pain causes awakening from sleep at night and the cough or sneeze causes the consistent pain in the thoracic spine to worsen, the possibility of spine metastasis should be considered. Patients often have a known history of the primary tumors, but about 20% of cases of spinal metastases are an early symptom of cancer. Local tenderness is usually present.

Neurological deficits can be caused by spinal cord compression and/or local nerve root involvement. The distribution of neurological deficits is based on the location of the lesion. Segmental pain and sensory loss may occur at the level of the tumor due to dorsal root irritation or compression. Segmental lower motor neuron lesions may also occur at the level of the tumor, and the signs of upper motor neuron lesion may also occur below the level of the tumor lesion. The spinal cord syndrome develops over a period of hours or days and includes hyperreflexia and Babinski's signs, but is rarely characterized by sphincter dysfunction alone. With bony destruction and pathologic vertebral compression fracture, the spinal column becomes unstable, which leads to more severe back pain (Ropper and Ropper 2017). Sensory loss below the level of lesion and sphincter involvement may also occur. Intramedullary tumors often extend to multiple segments and may show clinical signs similar to that of syringomyelia or central cord syndrome. The clinical features of the extramedullary tumors and intramedullary tumors are summarized in Table 16.10.

16.4.2 Diagnosis

MRI is the imaging of choice and provides excellent visualization of the tumor and tumor-related structures. It can also distinguish tumors from other masses, such as an abscess or hematoma. Location and shape can characterize the type of spine or spinal cord tumor. Plain radiographs and bone scans have a limited role in tumor identification. If there is a suspicion of metastatic lesion on MRI, the whole spine should be visualized because there is an additional silent metastasis (Wald 2012).

16.4.3 Management

Treatment of malignant spinal cord compression with radiation therapy and surgical decompression is partly palliative, but relief of paraplegia and pain reduction may be possible for considerable periods (Ropper and Ropper 2017). Spinal cord compression due to metastatic tumor should

Table 16.10 Clinical differentiation between extramedullary and intramedullary tumors of the spinal cord

	Extramedullary tumors	Intramedullary tumors
Sensory changes	Contralateral loss of pain and temperature; ipsilateral loss of proprioception; Brown–Sequard type lesion	Dissociation of sensation; spotty changes
Changes in pain and temperature sensations in saddle area	More marked than at level of lesion. Sensory level may be located below the lesion	Less marked than at level of lesion. Sensory loss can be suspended
Spontaneous pain	Radicular or regional in type and distribution; an early and important symptom	Funicular; burning in type; poorly located
Upper motor neuron type paralysis and hyperreflexia	Prominent	Can be late and less prominent
Lower motor neuron involvement	Segmental	Can be marked and widespread with atrophy and fasciculations
Spinal subarachnoid block and changes in CSF	Early and marked	Late and less marked
Trophic changes	Usually not marked	Can be marked

Adapted from Campbell (1992)

be treated urgently with steroids and radiation. Once the tumor type is identified, specific therapy for the tumor is initiated. In the absence of a medical contraindication, steroids are recommended for patients with suspected or confirmed neurologic deficits with metastatic extradural compression of the spinal cord. There is no consensus on the dose of steroids. A bolus of 8–10 mg dexamethasone or equivalent may be administered, followed by 16 mg/day, usually two to four divided doses for tolerance. Patients with complete paraplegia should be considered for a higher bolus up to 100 mg and high maintenance doses. However, the risk of serious side effects should be considered. If motor deficit persists for more than 12 h and does not improve within 48 h, the prognosis for recovery is poor (Huang and Sliwa 2011). Steroids are generally administered at lower doses until the end of radiation therapy and gradually decrease over several days. Steroids are generally not necessary for patients who have radiographic compression but do not have neurologic deficits.

A vertebral infiltration with a tumor that does not compress the spinal cord can be managed with radiation therapy if the spine is stable. Radiation therapy for tumor compression is also commonly performed and should be performed as soon as possible. A typical prescription is 3000 cGY administered for 15 days. Surgical decompression with laminectomy is rarely performed or is necessary with the use of radiation in this situation. However, with advances in surgical techniques, surgical interventions to control neurological involvement, pain, and instability have been advocated as a treatment option, including minimally invasive surgery. Postoperative radiation has been suggested to give better results to patients in certain situations than radiation alone.

Surgical removal is the treatment of choice for most extramedullary tumors, which are usually benign. Intramedullary tumors are also surgically removed. Ependymomas are often well demarcated and separated and completely removable. Postoperative radiation is usually performed if removal of astrocytoma is incomplete or if there are histological evidences of malignancy. Circumferential resection of the tumor yields better results than the posterior decompression (laminectomy), since the laminectomy does not reduce the ventral tumor originating from the vertebral body and the surgery can lead to spinal instability (Ropper and Ropper 2017). Radiation therapy is not an effective treatment for spinal instability. Surgery is also an option for treating recurrent spinal tumor after radiation therapy. Separation surgery consists of resecting part of the tumor to create a margin surrounding the spinal cord for the application of radiosurgery, thus reducing radiation damage to the spinal cord (Bate et al. 2015).

Survival in patients with multiple spinal metastases and cord compression is generally less than 6 months, but a retained ability to walk before treatment is associated with longer survival (Rades et al. 2006; Sioutos et al. 1995). Patients with functional impairment due to neoplastic spinal cord compression can achieve significant functional benefits through inpatient rehabilitation. Rehabilitation treatment may focus on mobility, self-care, management of bladder and bowel dysfunction, and management of pain and psychological problems. Surviving patients should continue rehabilitation after discharge in order to maintain their function of self-care and mobility after discharge.

16.5 Multiple Sclerosis

Multiple sclerosis is the most common autoimmune demyelinating disease of the central nervous system. Multiple sclerosis is a major cause of neurological disability in young adults. In many parts of the world, it has steadily increased over the last 40–50 years. There are very different prevalence around the world, ranging from near zero at the equator to above 130/100,000 in the northern USA or Europe. This has led to causative hypotheses focusing on environmental factors. However, so far, the disease is better characterized with findings substantiating an autoimmune pathology (Nichtweiß et al. 2015). It affects approximately 400,000 in the USA and about 2.5 million people worldwide. This is rare in children. Its onset is steadily increasing from adolescence through age 35 and then gradually decreases. It shows a female predominance (Compston and Coles 2002). Women are affected two to three times more often than men. The white population is at a higher risk than blacks or Asians. Multiple sclerosis is more common in countries with mild climates and more common in the northern USA and Canada than in the south. The environmental relevance of high altitude exposure to sunlight supports the suggested role of lower levels of vitamin D in the pathogenesis.

Multiple sclerosis is a disease of the central nervous system that is particularly associated with periventricular white matter of the cerebral hemispheres, spinal cord, brain stem, optic nerve, and cerebellum. In general, the disorder progresses through the relapsing and remitting course leading to spasticity, visual loss, and ataxia. Multiple sclerosis is characterized by immune-mediated inflammation, demyelination, glial scarring, and neuronal loss, leading to multifocal white matter disorders. They are typically spatially distributed. In other words, lesions occur at different times and at different sites of the central nervous system. Spinal cord symptoms or signs are almost always present in the course of multiple sclerosis. In particular, cervical and thoracic cords are affected, and occasionally lumbosacral cords are affected. Episodes from myelitis due to multiple sclerosis usually result in partial spinal cord disturbance that is often limited to sensory disturbance. Spinal cord lesions of multiple sclerosis are typically shortened in one or two segments and localized laterally in the spinal cord. A longitudinal myelitis is not typical of multiple sclerosis, and alternative diagnoses such as neuromyelitis optica spectrum disorders should be considered (Wingerchuk et al. 2006).

The onset of multiple sclerosis can be abrupt or insidious. The severity and course of the illness vary widely among individuals (Samkoff and Goodman 2011). Multiple sclerosis was defined by the 2013 revisions by the US National Multiple Sclerosis Society Advisory Committee as the clinical subtypes as a relapsing-remitting disease or a primary or secondary progressive disease (Lublin et al. 2014). *Relapsing-remitting multiple sclerosis* (RRMS) is the most common form of over 85% of all cases. Patients have discrete attacks that develop over hours, days, to weeks with recovery in the ensuing weeks to months and remain neurologically stable between relapses. *Secondary progressive multiple sclerosis* (SPMS) begins with RRMS; as the disease progresses, patients begin to experience gradual deterioration that is not associated with acute relapses. The risk of developing SPMS is esti-

mated to be about 2% per year in patients with RRMS, so the majority of these patients eventually develop into SPMS. *Primary progressive multiple sclerosis* (PPMS) accounts for about 10–15% of all multiple sclerosis diagnoses. These patients are consistently neurologically and functionally deteriorated, but discrete attacks do not occur. PPMS is often older than other forms of multiple sclerosis and is more even sex distribution. *Progressive-relapsing multiple sclerosis* (PRMS) is characterized by persistent deterioration after onset with an incidence of about 5% but characterized by superimposed acute attacks as in SPMS.

In addition, a clinically isolated syndrome has been described, which refers to patients who have a demyelinating event with MRI and cerebrospinal fluid findings supporting multiple sclerosis, although a single episode of the inflammation process, whether unifocal or multifocal, is not classified as multiple sclerosis. Some patients do not have other symptoms of the disease, but many eventually develop into future relapses and a diagnosis of multiple sclerosis (Ben-Zacharia 2011). After 20 years, the probability of developing multiple sclerosis is about 60%, and the initial MRI increases to 80% when there is abnormality other than clinically significant lesions according to the expression.

Inflammatory and demyelinating plaques may be visualized in the spinal cord, and multiple lesions are highly suggestive of multiple sclerosis. Spinal MRI plays an important role in eliminating spinal cord compression and can be useful for finding arteriovenous malformation. A brain MRI is abnormal in 99% of patients with definite multiple sclerosis. The characteristic appearance is multiple lesions in the periventricular and subcortical white matter.

16.6 Neuromyelitis Optica Spectrum Disorder

Neuromyelitis optica spectrum disorder is an autoimmune disease of the central nervous system, characterized mainly by optic nerves and spinal cord inflammation. Neuromyelitis optica, known as Devic's disease, has long been considered a variant of multiple sclerosis (Sahraian et al. 2013). However, when 60–80% of patients are found to have specific serum autoantibodies against aquaporin 4 (AQP4) in their nervous system, neuromyelitis optica is a distinct disease entity from multiple sclerosis (Wingerchuk et al. 2006). Spinal cord affection is characterized by spanning over at least three vertebral segments with central lesions in the spinal cord.

16.7 Idiopathic Transverse Myelitis

Pathogenesis of about 40% of acute transverse myelitis remains unexplained (Scotti and Gerevini 2001). The diagnosis of acute transverse myelitis requires evidence of inflammation within the spinal cord. In addition to a clinical presentation of a spinal cord lesion, the diagnosis of idiopathic transverse myelitis includes signs of inflammation by MRI of hyperintensities in T2-weighted images and contrast enhancement, in the cerebrospinal fluid with pleocytosis or intrathecal immunoglobulin production (elevated IgG index) (Beh et al. 2013; Transverse Myelitis Consortium Working Group 2002). The Transverse Myelitis Consortium Working Group described the nosology in 2002 (Jacob and Weinshenker 2008; Scott 2007; Transverse Myelitis Consortium Working Group 2002) (Table 16.11). For the onset a progression of deficits to a nadir between 4 h and 3 weeks was regarded as typical and now seems to be generally accepted for broader use in describing of inflammatory spinal cord disease (Jacob and Weinshenker 2008; Scott 2007; Nichtweiß et al. 2015).

16.8 Amyotrophic Lateral Sclerosis

Motor neuron diseases are a heterogeneous group of diseases associated with irreversible loss of motor neurons. Amyotrophic lateral sclerosis (ALS) is the most common form of progressive

Table 16.11 Diagnostic criteria for transverse myelitis

	TMCWG	Complete acute transverse myelitis	Acute partial transverse myelitis
Deficits attributable to the spinal cord	• Sensory, motor, or autonomic dysfunction • Bilateral signs and/or symptoms (not necessarily symmetric), clearly defined sensory level	• Moderate or severe symmetrical weakness and autonomic (bladder) dysfunction • Symmetric sensory level	• Mild sensory and motor dysfunction, bilateral or unilateral; when severe, marked asymmetry is observed • Sensory signs or symptoms attributable to a sensory level or hemi-level or MR lesion typical of myelitis
Sign of inflammation	• Demonstrated by CSF findings or Gd-enhanced MRI • CSF or MRI evidence of inflammation within the spinal cord may or may not be present		
Development	Progression to nadir between 4 h and 21 days following the onset of symptoms		
Exclusion criteria	Radiation within 10 years, vascular disease, brain abnormalities suggestive of MS or other demyelinating disease, presence of NMO, ADEM, connective tissue diseases, sarcoidosis, and proven infection with known agents		

TMCWG, Transverse Myelitis Consortium Working Group; NMO neuromyelitis optica, ADEM acute disseminated encephalomyelitis. From Nichtweiß et al. (2015), with permission

motor neuron disease in adults. ALS affects both the lower motor neurons in the spinal cord and brainstem and the upper motor neurons of the motor cortex. The phenotypic variants of ALS include primary lateral sclerosis, progressive muscular atrophy, and progressive bulbar palsy (Ludolph et al. 2012; Rezania and Roos 2013; Williams 2013).

ALS is increasingly being suggested as a spectrum of disorders rather than a single entity. ALS has traditionally been divided into two very similar clinical categories: familial and sporadic, sporadic cases accounting for more than 90%. Familial ALS accounts for about 5–10% of cases, most of which are autosomal dominant in inheritance. It causes mutations in a heterogeneous group of genes. At least 16 gene mutations have been identified. The first mutation identified in the enzyme superoxide dismutase 1 (SOD1) accounts for about 20% of familial ALS cases.

16.8.1 Prognostic Factors

There are unfavorable and favorable prognostic factors for progression rate and life expectancy. The younger the age, the better the prognosis. Disease starting from the limbs has a better prognosis than bulbar or respiratory onset. Women are more likely to show bulbar symptoms than men and the overall prognosis is somewhat worse. Patients with lower extremity-onset disease appear to have a better prognosis than upper extremities. Significant weight loss, vital capacity less than 50% of normal, and executive and cognitive dysfunction at the time of presentation are also negative prognostic factors.

16.8.2 Clinical Presentations

ALS is presented in a gradually insidious and progressive manner. Symptoms at onset are usually asymmetric. As more muscles are involved over time, the condition becomes more symmetrical. A typical feature of ALS for examination is the presence of a wide range of pure motor signs of both upper and lower motor neuron dysfunctions. Lower motor neuron lesion signs may occur in the same limb as upper motor neuron lesion signs. Weak and debilitating muscles with persistent or hyperreactive reflexes should raise ALS suspicions. Lower motor neuron lesion signs include weakness, fasciculations, atrophy, and hyporeflexia. Fasciculations and atrophy may be found in the tongue as well as the limbs. Facial and bulbar muscle weakness can be observed on cranial nerve examinations. Eye

movement is usually preserved. Neck muscles are weak, and head may drop. Upper motor neuron lesion signs include hyperreflexia, clonus, spasticity, and pathological reflexes such as Babinski sign, Hoffmann sign, palmomental reflexes, and jaw jerk.

Early symptoms can be nonspecific and include muscle spasms or cramping, twitching, fatigue, and poorly defined weakness. Involvement of the lower extremities may cause gait impairment such as tripping or dragging one leg. Weakness of the upper extremities can cause problems with fine motor skills such as difficulty in performing buttons with distal involvement or difficulty in raising the arms for activities such as brushing hair due to proximal muscle weakness. Twenty-five percent of patients have a bulbar onset, which can lead to drooling (sialorrhea), dysarthria, difficulty chewing, or nasal regurgitation resulted from dysphagia. Up to 50% of patients with ALS can get pseudobulbar effects or emotional lability with uncontrollable laughter or crying. In some cases, there may be cognitive and/or behavioral disorders. Up to 15% of patients may have related characteristics of frontotemporal dementia characterized by personality changes, irritability, and persistent impairment of executive function such as impaired judgment and impulsivity (Turner et al. 2013).

Respiratory symptoms may develop as the disease progresses. Symptoms of respiratory insufficiency include dyspnea, orthopnea, sleep deprivation and sleep fragmentation, nightmares, early morning headaches, worsening of daytime somnolence, and attention and concentration problems. Sphincter disturbances do not usually appear, at least initially. Mild sensory symptoms may be present, but they should not be noticeable. Fasciculations are painless, but painful cramps in the extremities, abdominal, and paraspinal muscles can develop as the disease progresses.

16.8.3 Diagnostic Criteria

The diagnosis of ALS requires simultaneous association of upper and lower motor neuron lesions with progressive weakness and exclusion of alternative diagnoses (Costa et al. 2012; EFNS Task Force 2012). A committee of the World Federation of Neurology has established diagnostic guidelines for ALS (Andersen et al. 2012). El Escoril's original clinical criteria for ALS have been modified to include electrodiagnostic testing with enhanced diagnostic sensitivity without increasing false positives. According to the criteria, the diagnosis of ALS is classified as "definite," "probable," and "possible."

16.8.4 Management

Several studies have suggested multidisciplinary approaches to improve the quality of life in ALS patients. The multidisciplinary team includes a physician specializing in neuromuscular diseases, nurses, physical therapists, occupational therapists, speech and language therapists, nutritionists, social workers, and respiratory therapists. Professional consulting includes pulmonology, gastroenterology, psychology, and spiritual counseling. Good communication and coordination within the team and with the patient's primary care provider are essential (Phukan and Hardiman 2009).

Symptomatic management is the mainstay of ALS treatment to treat disturbing symptoms, alleviate the problems, and improve quality of life (Blackhall 2012; Phukan and Hardiman 2009) (Table 16.12). Sialorrhea caused by bulbar involvement may be common and may be socially disabling. It is treated with anticholinergic drugs and treated with botulinum toxin injection or salivary gland irradiation if it shows resistance. If there is bulbar weakness, swallowing and nutrition should be evaluated and managed. Percutaneous endoscopic gastrostomy is a standard procedure for enteral nutrition. Patients with respiratory dysfunction require mild sedation and must be performed before the vital capacity below 50%. It requires mild sedation, which is a risk for patients with advanced respiratory impairment, so it should be performed before vital capacity falls below 50%. Percutaneous radiologic gastrostomy is an alternative that does

Table 16.12 Management summary for multiple symptoms in amyotrophic lateral sclerosis

Symptom/sign	Management
Respiratory dysfunction	• Avoid unnecessary oxygen • Consider NIPPV if FVC <50% • Need informed decision about tracheostomy and mechanical ventilation • Anxiety control, avoid benzodiazepine or opiates • Mechanical I/E • Air stacking, manual assist cough • Hydration, acetylcysteine 200–400 mg tid, nebulizer
Swallowing/ nutrition	• Swallowing evaluation, FESS • Semisolid or modified food consistency • Carefully monitor bulbar dysfunction and nutrition • Protein supplements • Consider early PEG
Drooling	• Anticholinergic medication, amitriptyline 10 mg tid, atropine sublingual drop 3–4 times/day, transdermal scopolamine patch q 3 days • Botulinum toxin into parotid or submandibular glands • Irradiating of salivary glands in refractory cases
Insomnia	• Control contributing factors: depression and anxiety, excessive drooling, hypoventilation, and unable position change • Hypnotic medications, zolpidem
Depression and anxiety	• Behavioral intervention, psychological support, counseling • Antidepressant medication, SSRI, SNRI, NDRI, TCA • Benzodiazepine for anxiety
Fatigue	• Energy conservation techniques • Amantadine 100 mg bid, Methylphenidate 5–10 mg bid, Amphetamine and dextroamphetamine combination tablet 5–10 mg every 4–5 h, Pyridostigmine 60 mg tid
Dry mouth and thick secretions, phlegm	• Assisted cough, insufflator–exsufflator and chest wall oscillation, reduced intake of dairy • Humidifier • Guaifenesin tablets, capsules, oral solution 200–400 mg every 4 h as needed, Guaifenesin extended release capsules 600–1200 mg every 12 h with maximum of 2400 mg/day, Carbocisteine 750 mg tid and reduce to 750 mg bid when satisfactory response is obtained
Cramps and fasciculations	• Positioning, stretching, massage, pool therapy • Magnesium oxide 400–600 mg/day, Vitamin E 400 IU bid or tid, Carbamazepine 200 mg bid, Phenytoin 100 mg tid or qid
Jaw quivering or clenching	• Stretching • Clonazepam 0.5 mg tid as needed, Lorazepam 0.5 mg tid or qid as needed, Diazepam 2.5–5 mg tid as needed, Botulinum toxin injection
Care for end of life	• Opioids and benzodiazepine for dyspnea and/or pain • Hospice care, including home hospice • Discussion about end-of-life decisions

not require sedation. In cases with severe dysarthria, communication can be improved using a variety of low-tech and high-tech alternatives. As limb weakness progresses, a variety of mobility aids and assistive devices can be provided, depending on the degree of impairment (de Almeida et al. 2012; Hardiman et al. 2011). Spasticity and painful muscle cramps may require treatment. Sleep disorders, fatigue, depression, and anxiety can occur in various factors, and causative factors must be identified and properly managed. Cognitive and/or executive dysfunctions can occur at a significant rate, so it is important to identify and manage the problems.

A number of potentially promising drugs are currently in clinical trials, but the evidence-based neuroprotectant is currently not available. The only evidence-based neuroprotective agent is riluzole. The mechanism of action in ALS is unknown, but it reduces glutamate-induced excitotoxicity. Analysis of published literature revealed that riluzole increases the probability of survival for 1 year by 10–15% and contributes to the average survival rate of the patient for about

3 months. It is generally well tolerated. Fatigue, gastrointestinal side effects, and elevated liver enzymes occasionally occur. Realistic expectations about the effectiveness of the treatment and possible adverse effects should be discussed with patients and caregivers. Riluzole 50 mg twice a day should be started as soon as possible after diagnosis, once a treatment decision is made after considering the expected therapeutic benefits and potential adverse effects (Robberecht and Philips 2013).

16.8.4.1 Respiratory Care

Respiratory failure, with or without pneumonia, is the leading cause of death in ALS. Early symptoms of respiratory dysfunction should be actively detected at each clinic visit. Pulmonary functions should be checked every few months to measure respiratory muscle strength. The most common testing measurement is vital capacity. Additional evaluations may include maximum inspiratory pressure, maximum expiratory pressure, sniff nasal inspiratory pressure, and nocturnal pulse oximetry. The effect of cough can be assessed by measuring peak cough flow (Gruis and Lechtzin 2012).

16.8.4.2 Secretion Management and Cough Assistance

Breath stacking and manual assisted cough techniques can also be used to improve peak cough flow. Breath stacking induces multiple inspiratory volumes without expiration. Thus, when inspiratory volumes are combined or accumulated, large lung volumes are used for spontaneous or stack to result in a larger lung volume used for spontaneous or manual assisted cough. Breath stacking requires the patient to be able to voluntarily close the glottis between inspiratory efforts to prevent loss of inspired volume. This can be difficult for ALS patients. Therefore, the inspiratory volume with an alternative expiration can be occluded with a one-way valve that allows the only airflow of inspiration. The inspired volumes for breath stacking can be manually provided with a resuscitation bag.

In addition to the weakness of the inspiratory muscles, patients with ALS also have expiratory muscle weakness with impaired cough. Cough assist devices that provide mechanical insufflation–exsufflation (MI-E) may be useful in patients with reduced peak cough flow (2–3 L/s or less). Target MI-E pressures are +40 cmH_2O for insufflation and −40 cmH_2O for exsufflation. + 35/−35 cmH_2O are the minimum pressures required to clear airway secretions. Techniques to reduce the risk of aspiration should be introduced, including suction machines, changing food texture, and teaching swallowing. Tenacious secretions should be treated by proper hydration, the use of mucolytic agents such as acetylcysteine (200–400 mg three times a day), or the use of a saline nebulizer with β-receptor antagonists.

16.8.4.3 Noninvasive Positive Pressure Ventilation

Noninvasive positive pressure ventilation (NIPPV) has several advantages in ALS. If tolerated, NIPPV may prolong survival, especially in patients who can use it for more than 5 h a day and those without severe bulbar dysfunction, and may improve symptoms of hypoventilation such as fragmented sleep, morning headache, daytime somnolence, and cognitive function. It can improve quality of life without increasing caregiver burden or stress. Decisions to prescribe NIPPV should be based on a combination of respiratory muscle weakness and respiratory symptoms, but there is no consensus on explicit criteria. NIPPV should be considered in ALS patients with symptoms of respiratory insufficiency and forced vital capacity (FVC) less than 50%. Some evidence supports consideration of NIPPV at FVC less than 50% even in the absence of respiratory symptoms or higher FVC in symptomatic respiratory weakness.

NIPPV is usually supplied with bi-level positive airway pressure devices. Various nasal or oronasal mask interfaces can be used. Treatment is usually initiated at night to relieve symptoms of nocturnal hypoventilation. Patients dependent on NIPPV need to have an alternative power source. ALS patients and caregivers need troubleshooting training and emergency contact information for equipment malfunction. Oxygen therapy is not necessary and should be avoided in

most cases of respiratory insufficiency in patients with ALS. Carbon dioxide retention and dry mouth may be exacerbated.

16.8.4.4 Mechanical Ventilation

Less than 10% of patients choose tracheostomy and long-term invasive mechanical ventilation. Patients and families should be fully informed of the burdens and benefits before making a decision, and they should be interviewed before the occurrence of severe respiratory impairment, not in an emergency, and should be included in advance directives. The inadvertent initiation of tracheostomy and mechanical ventilation in an emergency situation in a patient without advance directives is ethically and clinically difficult since most patients cannot wean the ventilator once initiated. Although tracheostomy with mechanical ventilation can prevent death due to respiratory failure, median ALS patient survival after its initiation is about 1–3 years; respiratory infection is the leading cause of death. Caregivers of ALS as patients with tracheostomy and mechanical ventilation report poor quality of life and may require psychosocial support. The right of the patient with ALS to refuse or withdraw treatment, including mechanical ventilation should be respected. If mechanical ventilation is stopped, an appropriate dose of the opiate and benzodiazepine should be used to alleviate dyspnea and anxiety.

16.9 Vascular Disease and Ischemic Injury

Spinal cord ischemia differs significantly from patients with cerebral ischemia in terms of age, clinical presentation and course, risk factors, and underlying pathology. The clinical severity depends on the extent of the lesion and the level of lesion (Novy et al. 2006). Recovery of spinal cord ischemia is usually incomplete and approximately 50% of patients remain in a wheelchair. There is a clinical presentation of spinal cord ischemia as the sudden onset of spinal stroke characterized by transverse myelopathy in a limited vascular territory such as the anterior spinal artery. The range of extraspinal diseases that causes spinal ischemia is extensive. Atherosclerotic change in the aorta is the most common and manifests as a dissecting or a nondissecting aneurysm. Adult-type coarctation of the aorta may present as a progressive upper thoracic myelopathy (Salvador de la Barrera et al. 2001). Usually, abnormal circulation occurs through the enlarged vertebral, thyrocervical, and costocervical arteries to the anterior spinal artery, with retrograde flow through radicular artery and then intercostal vessels to the aorta below the coarctation. Knowing the principal anatomical features of spinal cord blood supply of individual patients receiving thoracic or abdominal interventions, regardless of whether they are open or endovascular, offers several potential benefits (Caragine et al. 2002; Melissano et al. 2010; Perera and Gibbs 2014).

The blood supply to the thoracic spinal cord arises from a single anterior spinal artery that was formed by the union of two branches of the vertebral arteries and two posterior spinal arteries that also derive from the vertebral arteries, which run the length of the spinal cord (McGarvey et al. 2007). The vascular anatomy is variable, and these arteries may not be continuous along their course. Both the anterior and posterior spinal arteries are supplemented by segmental radicular arteries, which are small branches of the cervical, thoracic, and lumbar vessels. The largest of the radicular arteries is the artery of Adamkiewicz, which is often seen at the T10 level, but it can vary in its position from T7 to L4 (Bicknell et al. 2009). This artery supplies the conus medullaris but has a poor connection with the upper part of the spinal cord. It arises from the left intercostal or lumbar artery in more than 75% of people and can be recognized by its characteristic hairpin bend. Another important radicular artery is the midthoracic radicular branch, which emerges from the T7 posterior intercostal artery and supplements the blood supply to the T4–T8 segments.

16.9.1 Vascular Disease of the Spinal Cord

Spinal cord infarction is a relatively rare cause of myelopathy. The distribution of age and gender depends on the underlying etiology. It is most often seen in middle to older ages. Paraplegia is much more common than tetraplegia; the mid-thoracic spinal cord is most commonly affected. Spinal cord ischemia can occur due to systemic hypoperfusion or interruption of blood supply. The most common causes of spinal cord infarction are aortic surgery, dissecting aortic aneurysm, and profound systemic hypotension (Kamin and Garstang 2008). Other causes include cardiac embolism, atherosclerosis, dissection of the vertebral artery due to cervical trauma or manipulation (Zaina et al. 2003), vertebral or aortic angiography, arteritis (e.g., collagen vascular diseases such as polyarteritis nodosa, systemic lupus erythematosus, or Sjögren syndrome, sarcoidosis, syphilis, tuberculosis, or cocaine use), venous thrombophlebitis, hematological diseases (procoagulant states, thrombocytosis, or sickle cell disease), fibrocartilaginous embolism (from nucleus pulposus material following intervertebral disc rupture or trauma), the complication of epidural injection, and air embolism (from nitrogen bubbles in decompression sickness). In aortic aneurysm surgery, spinal cord infarction occurs in up to 5–10% of thoracoabdominal aneurysm surgeries, but very rarely in operations below the infrarenal segment (Kamin and Garstang 2008).

Radicular pain or band-like circular pain in the trunk or back can sometimes indicate the onset. Depending on the area affected, the pain may be interscapular and refer to the shoulders or chest mimicking cardiac pain, abdomen, anterior thighs, or buttocks. Weakness and sensory loss are based on the level of the lesion and the distribution of ischemia. Typical clinical presentations may include anterior cord syndrome, Brown–Séquard syndrome, central cord syndrome, and rare posterior cord syndrome (Table 16.13). Bladder, bowel, and sexual dysfunction are common. As with the motor paralysis, the initial flaccid bladder with urinary retention and bowel paralysis with ileus may evolve to features consistent with upper motor neuron lesion. Depending on the level of lesion, additional symptoms and signs of autonomic dysfunction

Table 16.13 Clinical presentation of vascular spinal cord syndromes

Syndrome	Artery involved	Tracts involved	Symptoms/signs
Central cord	Sulcocommissural, within the watershed between the anterior and posterior spinal arteries in hypotension	Corticospinal, spinothalamic	Upper limb weakness more than lower limb weakness, bilateral loss of pain/temperature only at level of injury or bilateral loss below lesion
Anterior cord	Anterior spinal	Corticospinal, spinothalamic, sympathetic	Tetraplegia or paraplegia, bilateral loss of pain/temperature below lesion, autonomic symptoms
Brown–Séquard	Sulcocommissural	Corticospinal, spinothalamic, sympathetic, dorsal columns	Ipsilateral motor weakness; contralateral loss of pain/temperature beginning two dermatomes below lesion; ipsilateral loss of proprioception, and vibration below lesion
Complete	Segmental	Corticospinal, spinothalamic, sympathetic, dorsal columns	Tetraplegia or paraplegia; bilateral loss of pain/temperature below lesion; autonomic symptoms; bilateral loss of light touch, proprioception, and vibration below lesion
Posterior cord	Posterior spinal	Dorsal columns	Bilateral loss of light touch, proprioception, and vibration below lesion

Modified from Kramer (2018)

such as orthostatic hypotension, impaired thermoregulation, and autonomic dysreflexia may occur (Rubin and Rabinstein 2013).

MRI is the imaging of choice. However, it is sometimes normal for the first few hours. Subsequently, lesions with or without gadolinium enhancement can be observed on T2-weighted images, which may indicate edema that may extend to multiple segments. In the more chronic stage, the infarct region of the spinal cord is often atrophic, with low signal intensity in MRI. Additional diagnostic testing may be required to determine the cause of the infarction, including tests for immune-mediated diseases, sarcoidosis, or infections.

16.9.2 Arteriovenous Malformations

Spinal arteriovenous malformations (AVMs) are the second most common spinal vascular malformation after spinal dural arteriovenous fistulas and account up to 15% of all spinal vascular malformations. AVM may be congenital or acquired. Age and gender distribution varied depending on the type; overall, it is more common in middle-aged or older men. Type I AVM is the most common, and in most cases is considered acquired. These are usually located in the lower thoracic cord or in the conus medullaris (Bostroem et al. 2007). AVM can affect the spinal cord in several mechanisms: spinal cord compression, venous hypertension due to congestion, vascular steal, and hemorrhage. Venous hypertension is believed to play an essential role in the pathophysiology of myelopathy associated with type I arteriovenous fistulas. Hemorrhage within the spinal cord can be caused by type II AVM (Bostroem et al. 2007; Zozulya et al. 2006).

Patients often undergo a gradual progressive course, especially in those with type I lesions. A gradual course can only be observed in a few patients, but is considered classic. It is believed that this saltatory evolution is due to fluctuating venous congestion in the spinal cord. Acute onset of symptoms can occur if there is significant hemorrhage (Rodesch and Lasjaunias 2003).

Sensory disturbances and/or weakness are common initial symptoms. Leg weakness and atrophy, as well as concomitant numbness and paresthesia, can occur in the same distribution. Some patients may experience pain in the form of back pain or sciatica. Claudication symptoms have also been reported. Gait disturbance and urinary problems often occur. Sometimes the AVM has a bruit on the spine. In some cases, patients may have other cutaneous angiomas, or a nevus may be found on the skin of the back overlying the site of the AVM. The development varies and ranges from abrupt and worsening over several months. With progressive or gradual progression, symptoms may appear for years before a diagnosis is made. The severity and distribution of symptoms are also variable.

MRI or CT myelography can reveal the presence of enlarged serpiginous blood vessels, but in some cases may not be identifiable. MRI may show myelomalacia, edema, or bleeding. The appearance and signal intensity of bleeding on MRI can help determine the duration, but the correlation can be variable. Spinal angiography is used for the definitive diagnosis and determination of the vascular anatomy for surgical planning. AVM associated with progressive neurological impairment or recurrent bleeding should be evaluated for possible therapeutic interventions. Endovascular techniques, embolization, and microsurgical correction of AVM are becoming increasingly possible. In some cases, more extensive surgical resection or ligation may be required, and successful correction is not always possible. Focal radiation therapy has also been used, but its effect is unclear.

16.10 Ossification of the Posterior Longitudinal Ligament

Ossification of the posterior longitudinal ligament (OPLL) is a progressive degenerative disease of the spine and differs from spondylosis. It is widely known as a cause of degenerative cervical myelopathy. The posterior longitudinal ligament (PLL) is formed between the sixth and

ninth week from the mesodermally derived mesenchymal sclerotomes (Epstein 1992). The PLL extends from the axis adjacent to the tectorial membrane to the sacrum on the dorsal surface of the vertebral body. The PLL is cranially wider, tapers caudally, and is the thickest in the thoracic region. The PLL is wider over the intervertebral disc and the contiguous margin of the vertebral bodies. It is narrow and looser over the middle of the vertebral bodies and is separated by the basivertebral veins. It is designed as layers. The superficial layer forms a strap spanning several vertebral bodies, while the deeper layer spans only two vertebral bodies and makes up the lateral expansion at each intervertebral disc. In contrast to the anterior longitudinal ligament, the PLL is smaller in cross-sectional area, but the fibers of the PLL are more compact. Due to its anatomical orientation, the PLL can bear loads in flexion and shares resistance to flexion moments with the other posterior element ligaments such as the interspinous, supraspinous, and ligamentum flavum (Epstein 2002).

The prevalence of OPLL has been better classified in Japanese individuals compared to other Asian or non-Asian populations (Tetreault et al. 2015). The prevalence of cervical OPLL has been estimated at 4.3% in men, 2.4% in women, and 3.2% for the total Japanese population (Ohtsuka et al. 1987). The incidence of OPLL in whites from North America has been estimated to be 0.12% (Resnick 1994). OPLL is often most severe at the C4 and C5 levels and is usually in the cephalad direction. Although OPLL can occur at any level of the spine, 70–95% of cases are found in the cervical spine. The rest are found in the upper thoracic spines and the upper lumbar spines. Cervical OPLL originates at higher levels than most other degenerative spine diseases, usually at C5, and usually extends in the cephalad direction. This cephalad–caudad progression occurs at an average rate of 4 mm per year, while the ossification increases in the anteroposterior direction at an average of 0.67 mm per year (Epstein 1992; Hirabayashi et al. 1983).

Mizuno et al. (1992) proposed a staging system for spinal cord damage secondary to OPLL (Table 16.14). Based on the radiographic findings, OPLL is usually divided into four subtypes according to Hirabayashi: segmental (39%), which is limited by the vertebral bodies; continuous (27%), which crosses multiple levels and disc spaces; mixed (29%), which has features of both segmental and continuous; and other (or localized) (7.5%), where the ossification is found over the disc spaces (Hirabayashi et al. 1981) (Fig. 16.3). OPLL can further be classified based on axial images such as square, mushroom, or hill-type (Hirabayashi et al. 1989) (Fig. 16.4).

16.11 Arachnoiditis

The arachnoid itself is avascular, but the reactive inflammatory response may be due to irritation or injury in the surrounding vascular pia and dura. This leads to adhesions and chronic thickening of the arachnoid with obliteration of the subarachnoid space. Adjacent nerve roots and spinal cord can be damaged by compression and vascular occlusion from the fibrous connective tissue (Koyanagi et al. 2005). Arachnoiditis is an inflammation process of the spinal meninges that increases the fibrous tissue in the subarachnoid space (the inner aspect of the arachnid membrane). Arachnoiditis can be caused by spinal surgery, intrathecal administration of some agents such as certain contrast media used for

Table 16.14 Pathological stages form compression by OPLL

Stage	Description
0	Normal or mild compression of the anterior horn without neuronal loss
1	Mild compression of the anterior horn with partial neuronal loss
2	Marked deformity of the anterior horn with severe neuronal loss
3	Severe spinal cord damage with cystic cavitation

From Mizuno et al. (1992), with permission

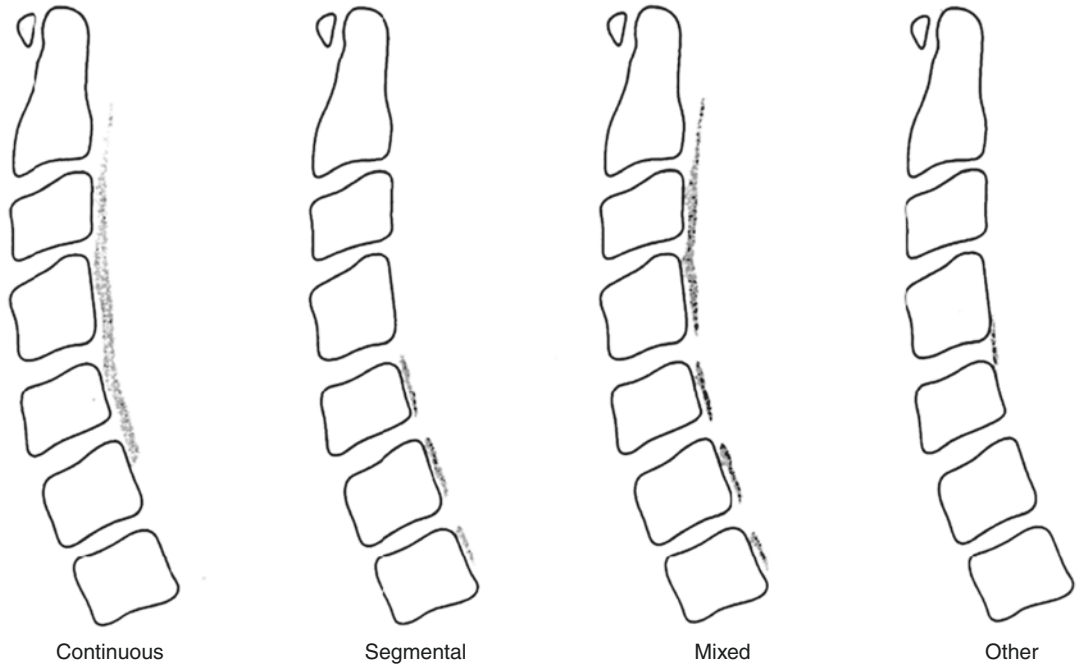

Fig. 16.3 Classification of OPLL into four subtypes. From Hirabayashi et al. (1981)

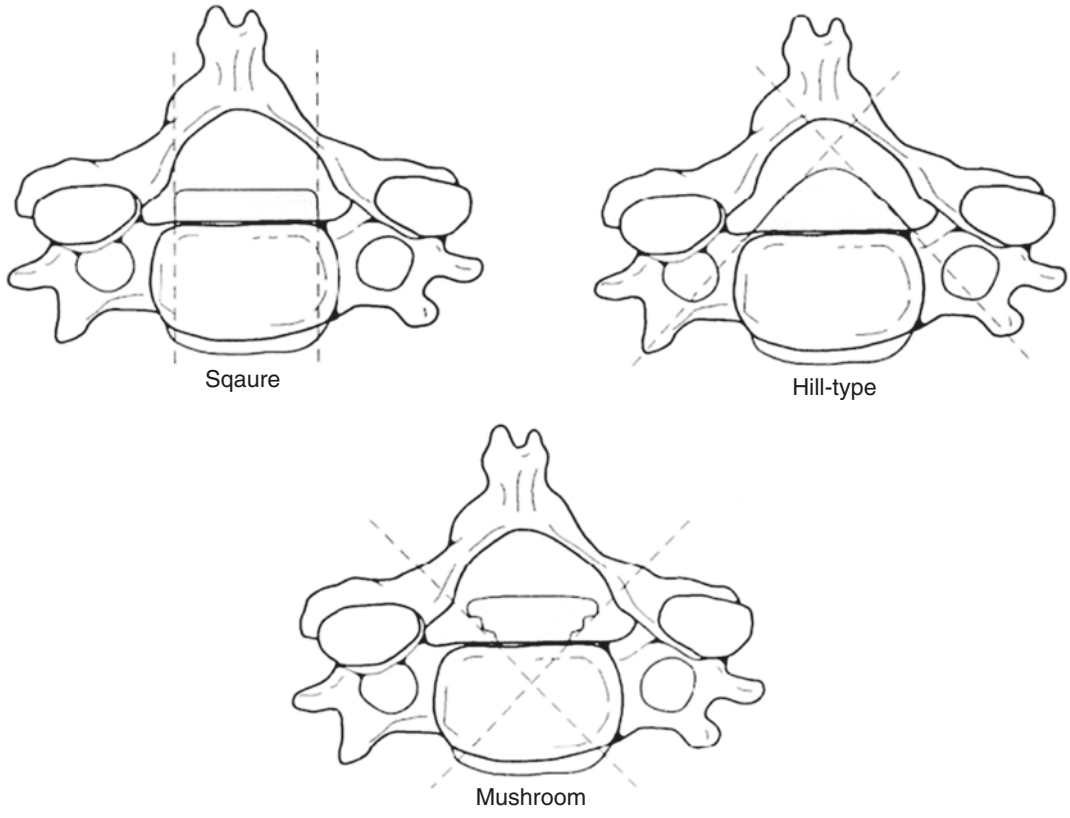

Fig. 16.4 Classification of OPLL into three subtypes based on axial images. From Hirabayashi et al. (1989)

myelography, infectious meningitis, or subarachnoid hemorrhage (Koyanagi et al. 2005; Vloeberghs et al. 1992).

Clinical presentations can be delayed weeks, months, or even a year after exposure to the triggering cause. In rare cases, arachnoiditis may be complicated by the development of a syrinx, which is believed to be associated with an altered cerebrospinal fluid flow. This condition is generally resistant to curative treatment. Steroids have proven to be ineffective. If the condition is confined to a relatively localized area, surgery may be helpful, but this is not common practice. Pain and other chronic symptoms require symptomatic treatment (Wright and Denney 2003).

16.12 Poliomyelitis

Poliomyelitis is caused by a highly infectious enterovirus whose main reservoir of infection is in the human gastrointestinal tract. There are three subtypes. The major epidemic poliovirus is type I, which accounted for 85% of cases of paralytic illness, while the other two types usually have sporadic cases and minor outbreaks. The route of infection is oral-oral and fecal-oral. Four clinical groups can be identified: asymptomatic, abortive, nonparalytic, and paralytic. The severity is determined by the host's immune response. The abortive cases show prodromal symptoms of a viral infection. Nonparalytic cases develop features of meningeal involvement but do not progress to paralysis. The paralytic cases reach the maximum weakness in 3–5 days, usually by 72 h. The poliovirus disseminates rapidly and widely throughout the central nervous system. Early changes involve neuronal chromatolysis, particularly affecting the cytoplasmic Nissl substance and a perivascular inflammatory cell infiltrate. The severity of the paralysis correlates with the proportion of the neurons destroyed. Pain in the spine and the limbs precedes the onset of weakness. The spinal and bulbar muscles are affected to varying degrees (Kidd et al. 1996). Weakness is usually asymmetrical and often shows patchy involvement. There is no sensory loss and no upper motor neuron lesion sign.

Many patients with previous paralytic poliomyelitis may develop late functional deterioration resulting in impairment of mobility, upper extremity function, respiratory capacity, and activities of daily living after a prolonged period of stability, usually 20–30 years after the initial infection and paralysis. This late deterioration has been referred to as postpolio syndrome or postpoliomyelitis neuromuscular atrophy (Pascuzzi 1992). Symptoms vary from mild to moderate deterioration of function, with fatigue, muscle pain, fasciculations, and weakness that can stabilize or progress to muscle atrophy.

16.13 Spine and Spinal Cord Infection

The microorganisms associated with myelopathy are numerous and include bacteria, viruses, fungi, and parasites. Spine infection include vertebral osteomyelitis due to a pyogenic, mycobacterial, or fungal infection as well as disc space infection (Go et al. 2012). Tuberculosis of the spine is common in developing countries. It is rare in the USA, but there is a high prevalence among immigrants and immunocompromised or homeless people (Garg and Somvanshi 2011). The clinical presentation may be similar to pyogenic infections, but onset is often subacute or chronic. Vertebral destruction and paravertebral abscess formation are observed in imaging studies, but unlike pyogenic infections, vertebral end plates and intervertebral discs are often preserved. Treatment requires several months of multidrug chemotherapy for tuberculosis after tissue biopsy and culture (Garg and Somvanshi 2011).

Bacterial infections of the spinal cord itself in the form of intramedullary abscesses are very rare. The spinal cord can be involved in neurosyphilis. Tabes dorsalis due to untreated syphilis affects the posterior columns of the spinal cord (Ho 2012). Some viruses can affect the spinal cord. Human immunodeficiency virus (HIV) is associated with vacuolar myelopathy, which mainly affects the posterior and lateral columns and occurs in the late stages of the disease (Gray et al. 1990). Other viral infections can occur in

people with HIV or other immunocompromised individuals such as cytomegalovirus, herpes simplex, or varicella zoster. In HIV positive individuals, parasitic infections of the spinal cord such as toxoplasmosis can occur. Other parasitic infections include cysticercosis and schistosomiasis, which are rare in the USA, but are prevalent worldwide (Richie and Pruitt 2013).

16.14 Nutritional Myelopathy

The most significant nutritional myelopathy is the subacute combined degeneration of vitamin B12 deficiency and copper deficiency (Kumar 2010, 2012). Vitamin B12 (cobalamin) is involved in enzymatic reactions for myelin and neurotransmitter synthesis, but the role in the pathogenesis of subacute combined degeneration is unclear (Scalabrino 2001). Lesions of the subacute combined degeneration arise in the center of the dorsal column and on the surface of the lateral columns, and occasionally in the anterior columns (Nichtweiß et al. 2015). The most common cause is pernicious anemia due to intrinsic factor antibodies that prevent absorption of vitamin B12 from the terminal ileum. Other causes include malabsorption, gastric resection, terminal ileum disease, and dietary deficiency. It has been reported that nitrous oxide anesthesia or inhalation causes subacute combined degeneration of the spinal cord by inactivating vitamin B12 metabolism. Degenerative changes can also be observed in the peripheral (peripheral neuropathy) and central nervous system (cognitive difficulties and dementia), presenting with myelin breakdown and vacuolation, with early involvement of the posterior columns and later spread to the corticospinal tracts (Kumar 2010). Routine CBC studies can show evidence of megaloblastic anemia with increased mean corpuscular volumes. Peripheral blood smears may reveal hypersegmented polymorphonuclear leukocytes. Erythrocyte macrocytosis may precede the neurological manifestations of the disorder. The suspicion should exist with mean corpuscular volume (MCV) exceeding 95 μm^3 on a CBC (normal 82–92 μm^3). Serum cobalamin levels can be normal despite the presence of neurological deficit. Neurologic symptoms may appear prior to the development of the hematologic abnormalities of vitamin B12 deficiency. Low serum cobalamin levels may be the only information needed to confirm the diagnosis. However, borderline or normal levels can occur (Schwendimann 2018).

Characteristic clinical manifestations of subacute combined degeneration are early symmetrical sensory symptoms in the legs with loss of vibration and position sense and spasticity, which sometimes appear within weeks. Combined features of upper motor neuron and lower motor neuron involvement in the legs, such as loss of ankle jerks with hyperreflexia at the knees, muscle atrophy with spasticity, and positive Babinski sign. Sensory ataxia and/or spastic paraplegia may be predominant. However, sphincter involvement is rare. The clinical symptoms and signs may be reversible by vitamin B12 replacement, oral supplementation 1000 μg daily, or intramuscular injection.

Folate deficiency occurs much often than vitamin B12 deficiency. It is well known that folate deficiency is a cause of neural tube defects. Folate deficiency can cause myelopathy, myeloneuropathy, peripheral neuropathy, and cognitive dysfunctions.

Copper is a component of numerous metalloenzymes and proteins that have a key role in maintaining the structure and function of the nervous system. Copper deficiency is a rare cause of myelopathy that has been recognized in the last decade and may resemble subacute combined degeneration of the spinal cord. Case reports have been associated with upper gastrointestinal bariatric surgery, malabsorption, and zinc overload, all of which affect copper absorption (Jaiser and Winston 2010; Schwendimann 2013, 2018). Zinc toxicity leading to copper deficiency can occur as a result of excessive zinc intake from various over-the-counter nutritional supplements, medications of the common cold, and dental adhesives. Zinc interferes with intestinal copper absorption by upregulating intestinal synthesis of metallothionein, which has a greater affinity for copper. Therefore, the copper bound by the enterocytes is eliminated by their sloughing off into the intestinal lumen (Nichtweiß et al. 2015).

Table 16.15 Common nutritional deficiency associated with metabolic myelopathy

Nutritional deficiency	Causes	Laboratory tests	Treatment
Vitamin B12 deficiency	Pernicious anemia, aging, gastric surgery, malabsorption, nitrous oxide toxicity, fish tapeworm	Vitamin B12, methylmalonic acid, and homocysteine levels; hematologic studies; parietal cell antibodies	Cobalamin 1000 μg/day IM for 5 days, monthly afterward
Copper deficiency	Gastrointestinal surgery, especially bariatric surgery; malabsorption; zinc toxicity	Serum and urinary copper, serum ceruloplasmin, zinc levels, hematologic tests	Copper 8 mg/day orally for 1 week, 6 mg/day for 1 week, 4 mg/day for 1 week, then 2 mg/day
Folate deficiency	Gastrointestinal disease, folate antagonists, alcoholism, association with other nutritional deficiencies	Serum folate, red blood cell folate, plasma total homocysteine	Folate 1 mg orally 2 times per day for several days followed by 1 mg/day; increase dietary intake of green leafy vegetables and citrus fruits
Vitamin E deficiency	Chronic cholestasis, pancreatic insufficiency, hypobetalipoproteinemia, abetalipoproteinemia, chylomicron retention disease	Serum vitamin E, ratio of vitamin E to serum cholesterol and triglycerides	Vitamin E 200 IU/day–1000 IU/day

Copper displaces zinc from metallothionein and remains in the enterocytes, which are later sloughed off and excreted in the feces. This leads to a reduction in the absorbed copper and often elevated levels of zinc (Schwendimann 2018).

Copper deficiency is recognized as a treatable cause of myelopathy and myeloneuropathy. It is necessary to limit oral intake of zinc, including the excessive use of dental adhesives. Treatment of copper deficiency and neurologic problems involves replacing elemental copper. Copper is administered orally at 8 mg/day for 1 week, 6 mg/day for 1 week, 4 mg/day for 1 week, followed by maintenance doses of 2 mg/day. IV copper can be used but is generally not needed (Kumar 2012; Schwendimann 2018). Table 16.15 summarizes the common nutritional deficiencies associated with metabolic myelopathy.

16.15 Myelopathy Due to Electrical or Lightning Injuries

The exact incidence is unknown, but it is a rare cause of spinal cord injury. Spinal cord injury may be caused by direct injury from the electrical current or indirectly by falling from a height following an electrical injury (Yarnell and Lammertse 1995). Current exposure of cord parenchyma causes tissue damage due to heating, altered cell membrane permeability, or denaturation of cellular protein. Injuries caused by electrical shock or lightning strike include skin burns, brain injury, muscle injury, compartment syndrome, vascular injury, autonomic dysfunction, peripheral nerve injury, etc. (Lammertse 2005). Clinical presentations are distinguished from acute and transient flaccid paralysis, which resolves after 24 h with a delayed onset of myelopathy after days or weeks that usually persist. The most common site of injury is the cervical spinal cord due to the frequency of hand contact in electrical injury. The current flows from one hand to the other and crosses the cervical region. This can cause severe cervical cord injuries.

16.16 Myelopathy Due to Decompression Sickness

Injury to the spinal cord can occur as a result of a rapid change in atmospheric pressure. Myelopathy can be a sign of decompression sickness in recreational scuba divers who return quickly to the surface after underwater diving. Rapid decompression leads to intravascular

coalescing of nitrogen bubbles with subsequent occlusion of spinal cord blood supply. This contributes to infarction following embolization and petechial hemorrhage. The signs and symptoms tend to occur abruptly, suggesting a vascular etiology. During rapid ascent and decompression, nitrogen gas that was previously forced into the bloodstream and tissues under pressure bubbles back out into bloodstream and tissues. Spinal cord injury are more prevalent in the thoracic region. Neurological symptoms usually appear immediately but may be delayed for several hours. Management requires first rapid recompression in a specialized chamber (Hawes and Massey 2008, 2009; Vollmann et al. 2011).

16.17 Radiation Myelopathy

Radiation has been identified as a potential source of CNS damage and myelopathy. Radiation myelopathy is a rare form of myelopathy caused by radiation to the spinal cord during radiation therapy for primary or metastatic spinal cord tumors or for malignancies in adjacent areas. A tumor involvement of the spinal cord must be ruled out before radiation myelopathy is diagnosed (Dropcho 2010). The spinal cord is exposed to potentially detrimental radiation effects if it lies in the center of the radiation field during radiation treatment of carcinoma. The necrosis of tissue within the CNS in the area of maximal radiation exposure occurs slowly and is cumulative over a few months to 5 years. In some cases, the symptoms of radiation myelopathy may be similar to those of a transverse myelopathy. The neurological decline and damage from progressive radiation myelopathy is usually irreversible.

Radiation myelopathy is classified into four general categories: transient myelopathy, chronic progressive radiation myelopathy, lower motor neuron dysfunction, and acute transverse myelopathy. Transient myelopathy is characterized by positive Lhermitte's sign and subjective sensory complaints. The presentation is usually dominated by spinothalamic symptoms. Chronic progressive radiation myelopathy is the most common form of severe radiation-induced myelopathy. Progressive neurological deterioration usually develops over a few months to a few years. Spontaneous recovery is not common. The third classification of radiation myelopathy, the lower motor neuron presentation, is rare but may occur with greater spinal cord damage. The stage is characterized by painless amyotrophy and weakness that predominantly affects the lower extremities. Radiation-induced acute transverse myelitis is extremely rare and is associated with the acute development of paraplegia or tetraplegia following after radiation. The acute transverse myelitis occurs secondary to radiation-induced damage of the intrinsic spinal cord blood supply, resulting in hemorrhage and associated parenchymal damage (Sadowsky et al. 1976).

16.18 COVID-19 and Spinal Cord Injuries/Lesions

With over 259 million cases worldwide as of November 25, 2021, COVID-19 disease has had an huge impact since it first emerged in December 2019. Known risk factors for negative outcomes after COVID-19, such as obesity, diabetes, and cardiovascular disease, disproportionally affect people with spinal cord injuries and raise concerns about the mortality risk among persons with spinal cord injuries (Hoogenes et al. 2021). The most common neurological symptoms in COVID-19 patients are anosmia, myalgia, headache, altered mental status or brain fog, transverse myelitis, Guillain–Barre syndrome, acute flaccid myelitis, etc. (Ali et al. 2021). There are several case reports and clinical experiences on Covid-19-associated acute transverse myelitis and acute transverse myelitis after COVID-19 vaccination (Ali et al. 2021; Hsiao et al. 2021; Román et al. 2021). Acute transverse myelitis is an unexpectedly common neurological complication of COVID-19 and accounts for 1.2% of all COVID-19 neurological complications (Román et al. 2021). Most cases (68%) had a latency of 10 days to 6 weeks, which may indicate post-infectious neurological complications mediated by the host's response to the virus (Román et al.

2021). The mechanism by which COVID-19 causes acute transverse myelitis is not fully understood, but it is assumed to be similar to that of Severe Acute Respiratory Syndrome Coronavirus 1 (SARS-CoV-1), which emerged in 2002 due to the structural resemblance between the two RNA viruses (Ali et al. 2021).

People with spinal cord injuries are potentially at risk for severe COVID-19 disease for a variety of reasons (Thomas and Murphy 2020). People with higher spinal cord lesions often have decreased lung capacity and may lack the ability to effectively clear their lungs. People with spinal cord injuries often have sedentary lifestyles and are at higher risk for chronic health conditions, such as obesity, diabetes, and cardiovascular disease, compared to people without physical disabilities (Myers et al. 2007). Additionally, there is preclinical evidence that people with spinal cord injuries may have a compromised immune system, making them vulnerable to infection and increasing their risk of severe COVID-19 disease. In addition, symptoms of COVID-19 in persons with spinal cord injuries may be different from those without spinal cord injuries, which can delay the SARS-CoV-2 testing and start treatment on time (López-Dolado and Gil-Agudo 2020). The clinical presentation of COVID-19 in people with spinal cord injuries was similar to the general population, and although adverse events and ICU admission were low, the mortality rate was high (19%) (Hoogenes et al. 2021).

References

Aebli N, Ruegg TB, Wicki AG, et al. Predicting the risk and severity of acute spinal cord injury after a minor trauma to the cervical spine. Spine J. 2013a;3:597–604.

Aebli N, Wicki AG, Rüegg TB, et al. The Torg-Pavlov ratio for the prediction of acute spinal cord injury after a minor trauma to the cervical spine. Spine J. 2013b;13:605–12.

Ali L, Mohammed I, Zada Y, et al. COVID-19-associated acute transverse myelitis: a case series of a rare neurologic condition. Cureus. 2021;13:e18551.

Andersen PM, Abrahams S, Borasio GD, et al. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)-revised report of an EFNS task force. Eur J Neurol. 2012;19:360–75.

Asdorian PL, Weidenbaum M, Hammerberg KW, et al. The pattern of vertebral involvement in metastatic vertebral breast cancer. Clin Orthop Relat Res. 1990;250:164–70.

Badhiwala JH, Wilson JR. The natural history of degenerative cervical myelopathy. Neurosurg Clin N Am. 2018;29:21–32.

Bakhsheshian J, Mehta VA, Liu JC. (2017) current diagnosis and management of cervical spondylotic myelopathy. Global Spine J. 2017;7:572–86.

Baptiste DC, Fehlings MG. Pathophysiology of cervical myelopathy. Spine J. 2006;6:190S–7S.

Bate BG, Khan NR, Kimball BY, et al. Stereotactic radiosurgery for spinal metastases with or without separation surgery. J Neurosurg Spine. 2015;22:409–15.

Beh SC, Greenberg BM, Frohman T, et al. Transverse myelitis. Neurol Clin. 2013;31:79–138.

Ben-Zacharia AB. Therapeutics for multiple sclerosis symptoms. Mt Sinai J Med. 2011;78:176–91.

Bicknell CD, Riga CV, Wolfe JH. Prevention of paraplegia during thoracoabdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg. 2009;37:654–60.

Blackhall LJ. Amyotrophic lateral sclerosis and palliative care: where we are, and the road ahead. Muscle Nerve. 2012;45:311–8.

Bostroem A, Thron A, Hans FJ, et al. Spinal vascular malformations – typical and atypical findings. Zentralbl Neurochir. 2007;68:205–13.

Breig A, el-Nadi AF. Biomechanics of the cervical spinal cord. Relief of contact pressure on and overstretching of the spinal cord. Acta Radiol Diagn (Stockh). 1966;4:602–24.

Breig A, Turnbull I, Hassler O. Effects of mechanical stresses on the spinal cord in cervical spondylosis. A study on fresh cadaver material. J Neurosurg. 1966;25:45–56.

Campbell WW, editor. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Caragine LP Jr, Halbach VV, Ng PP, et al. Vascular myelopathies-vascular malformations of the spinal cord: presentation and endovascular surgical management. Semin Neurol. 2002;22:123–32.

Casey AT, Bland JM, Crockard HA. Development of a functional scoring system for rheumatoid arthritis patients with cervical myelopathy. Ann Rheum Dis. 1996;55:901–6.

Cho TA, Bhattacharyya S. Approach to myelopathy. Continuum (Minneap Minn). 2018;24(2, Spinal Cord Disorders):386–406.

Compston A, Coles A. Multiple sclerosis. Lancet. 2002;359:1221–31.

Costa J, Swash M, de Carvalho M. Awaji criteria for the diagnosis of amyotrophic lateral sclerosis: a systematic review. Arch Neurol. 2012;69:1410–6.

de Almeida JP, Silvestre R, Pinto AC, et al. Exercise and amyotrophic lateral sclerosis. Neurol Sci. 2012;33:9–15.

de Oliveira VC, Orsini M, Leite MA, et al. Cervical spondylotic myelopathy: what the neurologist should know. Neurol Int. 2016;8:6330.

Dropcho EJ. Neurotoxicity of radiation therapy. Neurol Clin. 2010;28:217–34.

Edwards CC 2nd, Riew KD, Anderson PA, et al. Cervical myelopathy. Current diagnostic and treatment strategies. Spine J. 2003;3:68–81.

EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis, Andersen PM, Abrahams S, et al. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)-revised report of an EFNS task force. Eur J Neurol. 2012;19:360–75.

Engler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.

Epstein NE. Ossification of the posterior longitudinal ligament: diagnosis and surgical management. Neurosurg Quarterly. 1992;2:223–41.

Epstein N. Diagnosis and surgical management of cervical ossification of the posterior longitudinal ligament. Spine J. 2002;2:436–49.

Fattal C, Fabbro M, Gelis A, et al. Metastatic paraplegia and vital prognosis: perspectives and limitations for rehabilitation care. Part 1. Arch Phys Med Rehabil. 2011a;92:125–33.

Fattal C, Fabbro M, Rouays-Mabit H, et al. Metastatic paraplegia and functional outcomes: perspectives and limitations for rehabilitation care. Part 2. Arch Phys Med Rehabil. 2011b;92:134–45.

Fehlings MG, Tetreault LA, Riew KD, et al. A clinical practice guideline for the management of patients with degenerative cervical myelopathy: recommendations for patients with mild, moderate, and severe disease and nonmyelopathic patients with evidence of cord compression. Global Spine J. 2017;7(3 Suppl):70S–83S.

Garg RK, Somvanshi DS. Spinal tuberculosis: a review. J Spinal Cord Med. 2011;34:440–54.

Ghogawala Z, Whitmore RG. Asymptomatic cervical canal stenosis: is there a risk of spinal cord injury? Spine J. 2013;13:613–4.

Gibson J, Nouri A, Krueger B, et al. Degenerative cervical myelopathy: a clinical review. Yale J Biol Med. 2018;91:43–8.

Go JL, Rothman S, Prosper A, et al. Spine infections. Neuroimaging Clin N Am. 2012;22:755–72.

Gray F, Gherardi R, Trotot P, et al. Spinal cord lesions in the acquired immune deficiency syndrome (AIDS). Neurosurg Rev. 1990;13:189–94.

Gruis KL, Lechtzin N. Respiratory therapies for amyotrophic lateral sclerosis: a primer. Muscle Nerve. 2012;46:313–31.

Hardiman O, van den Berg LH, Kiernan MC. Clinical diagnosis and management of amyotrophic lateral sclerosis. Nat Rev Neurol. 2011;7:639–49.

Harrop JS, Hanna A, Silva MT, et al. Neurological manifestations of cervical spondylosis: an overview of signs, symptoms, and pathophysiology. Neurosurgery. 2007;60:S14–20.

Hashizume Y, Iijima S, Kishimoto H, et al. Pathology of spinal cord lesions caused by ossification of the posterior longitudinal ligament. Acta Neuropathol (Berl). 1984;63:123–30.

Hawes J, Massey EW. Neurologic injuries from scuba diving. Neurol Clin. 2008;26:297–308.

Hawes J, Massey EW. Neurologic injuries from scuba diving. Phys Med Rehabil Clin N Am. 2009;20:263–72.

Hirabayashi K, Miyakawa J, Satomi K. Operative results and postoperative progression of ossification among the patients with ossification of cervical posterior longitudinal ligament. Spine. 1981;6:354–63.

Hirabayashi K, Watanabe K, Suzuki N, et al. Expansive open door laminoplasty for cervical spinal stenotic myelopathy. Spine. 1983;8:693–9.

Hirabayashi K, Satomu K, Sasaki T. Ossification of the posterior longitudinal ligament in the cervical spine. In: the cervical spine. 2nd ed. Philadelphia: J. B. Lippincott; 1989.

Ho EL. Infectious etiologies of myelopathy. Semin Neurol. 2012;32:154–60.

Holmes A, Han ZH, Dang GT, et al. Changes in cervical canal spinal volume during in vitro flexion-extension. Spine (Phila Pa 1976). 1996;(21):1313–9.

Hoogenes B, Querée M, Townson A, et al. COVID-19 and spinal cord injury: clinical presentation, clinical course, and clinical outcomes: a rapid systematic review. J Neurotrauma. 2021;38:1242–50.

Houten JK, Noce LA. Clinical correlations of cervical myelopathy and the Hoffmann sign. J Neurosurg Spine. 2008;9:237–42.

Hsiao YT, Tsai MJ, Chen YH, et al. Acute transverse myelitis after COVID-19 vaccination. Medicina (Kaunas). 2021;57:1010.

Huang ME, Sliwa JA. Inpatient rehabilitation of patients with cancer: efficacy and treatment considerations. PM R. 2011;3:746–57.

Jacob A, Weinshenker BG. An approach to the diagnosis of acute transverse myelitis. Semin Neurol. 2008;28:105–20.

Jaiser SR, Winston GP. Copper deficiency myelopathy. J Neurol. 2010;257:869–81.

Kalsi-Ryan S, Karadimas SK, Fehling MG. Cervical spondylotic myelopathy: the clinical phenomenon and the current pathobiology of an increasingly prevent and devastating disorder. Neuroscientist Rev J Bringing Neurobiol Neurol Psychiatry. 2013;19:409–21.

Kamin S, Garstang S. Vascular disease of the spinal cord. Top Spinal Cord Inj Rehabil. 2008;14:42–52.

Karadimas SK, Erwin WM, Ely CG, et al. The pathophysiology and natural history of cervical spondylotic myelopathy. Spine (Phila Pa 1976). 2013;38(Suppl 1):S21–36.

Kettler A, Werner K, Wilke HJ. Morphological changes of cervical facet joints in elderly individuals. Eur Spine J. 2007;16:987–92.

Kidd D, Williams AJ, Howard RS. Poliomyelitis. Postgrad Med J. 1996;72:641–7.

Kim HJ, Tetreault LA, Massicotte EM, et al. Differential diagnosis for cervical spondylotic myelopathy: litera-

ture review. Spine (Phila Pa 1976). 2013;38(22 Suppl 1):S78–88.
Klineberg E. Cervical spondylotic myelopathy: a review of the evidence. Orthop Clin North Am. 2010;41:193–202.
Koyanagi I, Iwasaki Y, Hida K, et al. Clinical features and pathomechanisms of syringomyelia associated with spinal arachnoiditis. Surg Neurol. 2005;63:350–5.
Kramer CL. Vascular disorders of the spinal cord. Continuum (Minneap Minn). 2018;24(2, Spinal Cord Disorders):407–26.
Kumar N. Neurologic presentations of nutritional deficiencies. Neurol Clin. 2010;28:107–70.
Kumar N. Metabolic and toxic myelopathies. Semin Neurol. 2012;32:123–36.
Lammertse DP. Neurorehabilitation of spinal cord injuries following lightning and electrical trauma. NeuroRehabilitation. 2005;20:9–14.
Lawrence BD, Wang J, Arnold PM, et al. Predicting the risk of adjacent segment pathology after lumbar fusion: a systematic review. Spine. 2012;37(22 Suppl):S123–S32.
Lebl DR, Hughes A, Cammisa FP Jr, et al. Cervical spondylotic myelopathy: pathophysiology, clinical presentation, and treatment. HSS J. 2011;7:170–8.
Lewis DW, Packer RJ, Raney B, et al. Incidence, presentation, and outcome of spinal cord disease in children with systemic cancer. Pediatrics. 1986;78:438–43.
Loblaw DA, Mitera G, Ford M, et al. A 2011 updated systematic review and clinical practice guideline for the management of malignant extradural spinal cord compression. Int J Radiat Oncol Biol Phys. 2012;84:312–7.
López-Dolado E, Gil-Agudo A. Lessons learned from the coronavirus disease 2019 (Covid-19) outbreak in a monographic center for spinal cord injury. Spinal Cord. 2020;58:517–9.
Lublin FD, Reinggold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2014;83:278–86.
Ludolph AC, Brettschneider J, Weishaupt JH. Amyotrophic lateral sclerosis. Curr Opin Neurol. 2012;25:530–5.
Mariano R, Flanagan EP, Weinshenker BG, et al. A practical approach to the diagnosis of spinal cord lesions. Pract Neurol. 2018;18:187–200.
Matz PG, Anderson PA, Holly LT, et al. Joint section on disorders of the spine and peripheral nerves of the American Association of Neurological Surgeons and Congress of Neurological Surgeons. The natural history of cervical spondylotic myelopathy. J Neurosurg Spine. 2009;11:104–11.
McGarvey ML, Mullen MT, Woo EY, et al. The treatment of spinal cord ischemia following thoracic endovascular aortic repair. Neurocrit Care. 2007;6:35–9.
McKinley W. Nontraumatic spinal cord injury/disease: etiologies and outcomes. Top Spinal Cord Inj Rehabil. 2008;14:1–9.
McKinley WO, Tellis AA, Cifu DX, et al. Rehabilitation outcome of individuals with nontraumatic myelopathy resulting from spinal stenosis. J Spinal Cord Med. 1998;21:131–6.
McKinley WO, Seel RT, Hardman JT. Nontraumatic spinal cord injury: incidence, epidemiology, and functional outcome. Arch Phys Med Rehabil. 1999;80:619–23.
Mechtler LL, Nandigam K. Spinal cord tumors: new views and future directions. Neurol Clin. 2012;31:241–68.
Melissano G, Civilini E, Bertoglio L, et al. Angio-CT imaging of the spinal cord vascularisation: a pictorial essay. Eur J Vasc Endovasc Surg. 2010;39:436–40.
Milligan J, Ryan K, Fehlings M, et al. Degenerative cervical myelopathy: diagnosis and management in primary care. Can Fam Physician. 2019;65:619–24.
Mizuno J, Nakagawa H, Iwata K, et al. Pathology of spinal cord lesion caused by ossification of the posterior longitudinal ligament, with special reference to reversibility for the spinal cord. Neurol Res. 1992;14:312–4.
Moghaddamjou A, Badhiwala JH, Fehlings MG. Degenerative cervical myelopathy: changing frontiers. World Neurosurg. 2020;135:377–8.
Moussellard HP, Meyer A, Biot D, et al. Early neurological recovery course after surgical treatment of cervical spondylotic myelopathy: a prospective study with 2-year follow-up using three different functional assessment tests. Eur Spine J. 2014;23:1508–14.
Myers J, Lee M, Kiratli J. Cardiovascular disease in spinal cord injury: an overview of prevalence, risk, evaluation, and management. Am J Phys Med Rehabil. 2007;86:142–52.
National Spinal Cord Injury Statistical Center (NSCISC). The 2019 annual statistical report for the spinal cord model systems. Birmingham: NSCISC; 2020.
New PW, Sundararajan V. Incidence of non-traumatic spinal cord injury in Victoria, Australia: a population-based study and literature review. Spinal Cord. 2008;46:406–11.
New PW, Frry A, Baxter D, et al. Prevalence of non-traumatic spinal cord injury in Victoria. Australia Spinal Cord. 2013;51:99–102.
New PW, Cripps RA, Lee BB. Global maps of non-traumatic spinal cord injury epidemiology: towards a living data repository. Spinal Cord. 2014;52:97–109.
Nichtweiß M, Hattingen E, Weidauer S. Metabolic-toxic diseases and atrophic changes of the spinal cord. In: Hattingen E, Weidauer S, Setzer M, et al., editors. Diseases of the spinal cord. Novel imaging, diagnosis and treatment. Heidelberg: Springer; 2015.
Nijendijk JH, Post MW, van Asbeck FW. Epidemiology of traumatic spinal cord injuries in the Netherlands in 2010. Spinal Cord. 2014;52:258–63.
Nikolaidis I, Fouyas IP, Sandercock PA, et al. Surgery for cervical radiculopathy or myelopathy. Cochrane Database Syst Rev. 2010;CD001466.
Noonan VK, Fingas M, Farry A, et al. Incidence and prevalence of spinal cord injury in Canada: a national perspective. Neuroepidemiology. 2012;38:219–26.
Nouri A, Tetreault L, Singh A, et al. Degenerative cervical myelopathy: epidemiology, genetics, and pathogenesis. Spine. 2015;40:E675–E93.

Novy J, Carruzzo A, Maeder P, et al. Spinal cord ischemia: clinical and imaging patterns, pathogenesis, and outcomes in 27 patients. Arch Neurol. 2006;63:1113–20.
O'Connor PJ. Prevalence of spinal cord injury in Australia. Spinal Cord. 2015;43:42–6.
Ohtsuka K, Terayama K, Yanagihara M, et al. A radiological population study on the ossification of the posterior longitudinal ligament in the spine. Arch Orthop Trauma Surg. 1987;106:89–93.
Pascuzzi RM. Poliomyelitis and the postpolio syndrome. Semin Neurol. 1992;12:193–9.
Perera AH, Gibbs RGJ. Chapter 2. Paraplegia as a complication of thoracic and thoracoabdominal aortic interventions. In Dionyssiotis Y, editor. Topics in paraplegia. InTech. 2014, p. 25–51. https://www.intechopen.com/books/topics-in-paraplegia/paraplegia-as-a-complication-of-thoracic-and-thoracoabdominal-aortic-interventions. Accessed 10 Sept 2021.
Phukan J, Hardiman O. The management of amyotrophic lateral sclerosis. J Neurol. 2009;256:176–86.
Rades D, Fehlauer F, Schulte R, et al. Prognostic factors for local control and survival after radiotherapy of metastatic spinal cord compression. J Clin Oncol. 2006;24:3388–93.
Raj VS, Lofton L. Rehabilitation and treatment of spinal cord tumors. J Spinal Cord Med. 2013;36:4–11.
Resnick D. Diagnosis of bone and joint disorders. London: WB Saunders; 1994.
Rezania K, Roos RP. Spinal cord: motor neuron diseases. Neurol Clin. 2013;31:219–39.
Richie MB, Pruitt AA. Spinal cord infections. Neurol Clin. 2013;31:19–53.
Robberecht W, Philips T. The changing scene of amyotrophic lateral sclerosis. Nat Rev Neurosci. 2013;14:248–64.
Rodesch G, Lasjaunias P. Spinal cord arteriovenous shunts: from imaging to management. Eur J Radiol. 2003;46:221–32.
Román GC, Gracia F, Torres A, et al. Acute transverse myelitis (ATM): clinical review of 43 patients with COVID-19-associated ATM and 3 post-vaccination ATM serious adverse events with the ChAdOx1 nCoV-19 vaccine (AZD1222). Front Immunol. 2021;12:653786.
Roos E, Dingemans KD. Mechanisms of metastasis. Biochem Biophys Acta. 1979;560:135–66.
Ropper AE, Ropper AH. Acute spinal cord compression. N Engl J Med. 2017;376:1358–69.
Rubin MN, Rabinstein AA. Vascular diseases of the spinal cord. Neurol Clin. 2013;31:153–81.
Sadowsky CH, Sachs E Jr, Ochoa J. Postradiation motor neuron syndrome. Arch Neurol. 1976;33:786–7.
Sahraian MA, Radue EW, Minagar A. Neuromyelitis optica: clinical manifestations and neuroimaging features. Neurol Clin. 2013;31:139–52.
Salvador de la Barrera S, Barca-Buyo A, Montoto-Marqués A, et al. Spinal cord infarction: prognosis and recovery in a series of 36 patients. Spinal Cord. 2001;39:520–5.
Samkoff LM, Goodman AD. Symptomatic management in multiple sclerosis. Neurol Clin. 2011;29:449–63.
Scalabrino G. Subacute combined degeneration one century later. The neurotrophic action of cobalamin (vitamin B12) revisited. J Neuropathol Exp Neurol. 2001;60:109–20.
Schiff D, O'Neill BP, Suman VJ. Spinal epidural metastasis as the initial manifestation of malignancy: clinical features and diagnostic approach. Neurology. 1997;49:452–6.
Schwendimann RN. Metabolic, nutritional, and toxic myelopathies. Neurol Clin. 2013;31:207–18.
Schwendimann RN. Metabolic and toxic myelopathies. Continuum (Minneap Minn). 2018;24:427–40.
Scott TF. Nosology of idiopathic transverse myelitis syndromes. Acta Neurol Scand. 2007;115:371–6.
Scotti G, Gerevini D. Diagnosis and differential diagnosis of acute transverse myelopathy. The role of neuroradiological investigations and review of the literature. Neurol Sci. 2001;22(Suppl 2):S69–74.
Shedid D, Benzel EC. Cervical spondylosis anatomy: pathophysiology and biomechanics. Neurosurgery. 2007;60:S7–13.
Sioutos PJ, Arbit E, Meshulam CF, et al. Spinal metastases from solid tumors. Analysis of factors affecting survival. Cancer. 1995;76:1453–9.
Stark RJ, Henson RA, Evans SJ. Spinal metastases. A retrospective survey from a general hospital. Brain. 1982;105(Pt 1):189–213.
Tetreault L, Goldstein CL, Arnold P, et al. Degenerative cervical myelopathy: a spectrum of related disorders affecting the aging spine. Neurosurgery. 2015;77(Suppl 4):S51–67.
Thakur NA, Daniels AH, Schiller J, et al. Benign tumors of the spine. J Am Acad Orthop Surg. 2012;20:715–24.
Thomas FP, Murphy C. COVID-19 and spinal cord injury professionals: maintaining a scholarly perspective. J Spinal Cord Med. 2020;43:279.
Thurnher MM, Cartes-Zumelzu F, Mueller-Mang C. Demyelinating and infectious diseases of the spinal cord. Neuroimaging Clin N Am. 2007;17:37–55.
Toledano M, Bartleson JD. Cervical spondylotic myelopathy. Neurol Clin. 2013;31:287–305.
Transverse Myelitis Consortium Working Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology. 2002;59:499–505.
Tsutsumimoto T, Shimogata M, Yui M, et al. The natural history of asymptomatic lumbar canal stenosis in patients undergoing surgery for cervical myelopathy. J Bone Joint Surg Br. 2012;94:378–84.
Turner MR, Hardiman O, Benatar M, et al. Controversies and priorities in amyotrophic lateral sclerosis. Lancet Neurol. 2013;12:310–22.
Virk SS, Niedermeier S, Yu E, et al. Adjacent segment disease. Orthopedics. 2014;37:547–55.
Vloeberghs M, Herregodts P, Stadnik T, et al. Spinal arachnoiditis mimicking a spinal cord tumor: a case report and review of the literature. Surg Neurol. 1992;37:211–5.

Vollmann R, Lamperti M, Magyar M, et al. Magnetic resonance imaging of the spine in a patient with decompression sickness. Clin Neuroradiol. 2011;21:231–3.
Wald JT. Imaging of spine neoplasm. Radiol Clin N Am. 2012;50:749–76.
Williams TL. Motor neurone disease: diagnostic pitfalls. Clin Med. 2013;13:97–100.
Wingerchuk DM, Lennon VA, Pittock SJ, et al. Revised diagnostic criteria for neuromyelitis optica. Neurology. 2006;66:1485–9.
Wright MH, Denney LC. A comprehensive review of spinal arachnoiditis. Orthop Nurs. 2003;22:215–9.
Yadla S, Klimo P Jr, Harrop J. Traumatic central cord syndrome: etiology, management, and outcomes. Top Spinal Cord Inj Rehabil. 2010;15:73–84.
Yarnell PR, Lammertse DP. Neurorehabilitation of lightning and electrical injuries. Semin Neurol. 1995;15:391–6.
Zaina C, Grant R, Johnson C, et al. The effect of cervical rotation on blood flow in the contralateral vertebral artery. Man Ther. 2003;8:103–9.
Zairi F, Marinho P, Bouras A, et al. Recent concepts in the management of thoracolumbar spine metastasis. J Neurosurg Sci. 2013;57:45–54.
Zozulya YP, Slin'ko EI, Al-Qashqish II. Spinal arteriovenous malformations: new classification and surgical treatment. Neurosurg Focus. 2006;20:E7.

Recommended Additional Reading

Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation. Phys Med Rehabil Clinics of North America. Philadelphia: Elsevier; 2014.
Durrant DH, True JM. Myelopathy, radiculopathy, and peripheral entrapment syndromes. Boca Raton: CRC Press; 2002.
Engler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.
Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston: Butterworth-Heinemann; 1996.
Hattingen E, Weidauer S, Setzer M, et al., editors. Diseases of the spinal cord. Novel imaging, diagnosis and treatment. Heidelberg: Springer; 2015.
Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia: Elsevier; 2016.
Passias PG, editor. Cervical myelopathy. Philadelphia: Jaypee Brothers Medical Publishers (P) Ltd; 2016.
Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part I. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976.
Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part II. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976.
Vogel LC, Zebracki K, Betz RR, et al., editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.
Weidner N, Rupp R, Taney KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.

Patterns of Incomplete Spinal Cord Injury Syndromes

17

When examining a patient with tetraplegia or paraplegia, careful neurological examination is essential to plan for further diagnostic workup and management. Identifying various spinal cord syndromes and determining the likely location of the underlying pathological process will guide subsequent imaging and electrodiagnostic studies. The clinical picture of a spinal cord injury depends on whether the injury is complete or whether selected tracts of the white matter are spared. A number of clinically characterized incomplete spinal cord syndromes can develop due to the involvement of different parts of the gray and white matter of the spinal cord. Incomplete spinal cord syndromes are clinical syndromes that present with typical clinical signs in incomplete spinal cord injuries or lesions, when the injuries or lesions affect specific anatomical regions of the spinal cord, with some preservation of sensory or motor function below the lesion. The clinical presentation of the incomplete spinal cord syndromes is largely determined by the involvement of the three tracts: corticospinal tract, spinothalamic tract, and posterior column of the spinal cord. There are eight types of incomplete spinal cord syndromes based on clinical presentations: central cord syndrome, Brown–Séquard syndrome (unilateral cord syndrome), anterior cord syndrome, posterior syndrome, caudal equine syndrome, conus medullaris syndrome, subacute combined degeneration myelopathy, and cruciate paralysis. Table 17.1 summarizes the incomplete spinal cord syndromes, including the tracts involved, the lesions involved, the common causes, and the typical clinical manifestations. Knowledge of the spinal cord anatomy and the ability to identify the typical clinical signs of common spinal cord syndromes are essential in the examination and treatment of the patient (Kunam et al. 2018). This chapter describes the relevant anatomy of three important white matter tracts (corticospinal tract, spinothalamic tract, and posterior columns), the understanding of which is crucial in diagnosing the type of incomplete spinal cord syndrome and the clinical features of incomplete spinal cord syndromes.

In addition to the classification of patients according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), incomplete patients classified according to specific clinical syndromes provide information on the injury mechanism and recovery prognosis. In spinal cord injuries due to trauma, vascular, or other space-occupying lesions, the ISNCSCI prior to the seventh revision of 2011 provided a worksheet to specify the clinical syndromes of spinal cord injuries. The ISNCSCI defines five clinical syndromes with incomplete spinal cord injury (i.e., central cord syndrome, Brown–Séquard syndrome, anterior cord syndrome, conus medullaris, and cauda equina syndrome) that are not part of the ISNCSCI examination or classification of ASIA

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Table 17.1 Summary of characteristics of incomplete spinal cord syndromes

Incomplete syndrome	Involving tracts	Lesion localized	Common causes	Clinical presentations
Central cord				
Small lesion	Anterior commissure where STT fibers cross	Near the central canal	Syringomyelia, hyperextension injury in cervical spondylosis, intramedullary tumor	Suspended sensory deficit, classic cape distribution in lesion of cervical cord
Large lesion	Bilateral STT, CST, posterior columns (variable), autonomic center, and anterior horn cells	Large central lesion	Syringomyelia, hyperextension injury in cervical spondylosis, intramedullary tumor	Disproportionate motor (UMN type) and sensory deficits-greater in upper extremities than in the lower extremity, LMN deficit at level of lesion (anterior horn cells), variable loss of proprioception, autonomic dysfunction
Brown–Séquard	Ipsilateral CST and posterior column, and contralateral STT	Hemicord lesion	Knife or bullet injury, multiple sclerosis, transdural migration of spinal cord	Ipsilateral weakness (UMN type) and loss of proprioception, contralateral loss of pain and temperature senses, small band of LMN type weakness, and sensory deficits at the level of lesion
Anterior cord	Bilateral STT, CST, and autonomic center	Anterior two-thirds of spinal cord	Spinal cord infarction, trauma, multiple sclerosis, disk herniation	Loss of pain and temperature sensations, weakness, bladder dysfunction
Conus medullaris	Distal spinal cord containing lumbosacral segments	Spinal cord at level of T12 through L2 vertebrae	Disk herniation, trauma, tumors	Bladder or rectal dysfunction, saddle anesthesia, leg weakness (mixed UMN and LMN types)
Cauda equina	Lumbosacral nerve roots in spinal canal	Lesion compressing or involving nerve roots of cauda equina	Disk herniation, arachnoiditis, trauma, tumor, lumbar spine stenosis	Asymmetric multiradicular pain, leg weakness (purely LMN type) and sensory loss, bladder dysfunction, areflexia
Posterior cord	Predominately posterior columns; large lesions involve bilateral CST and bilateral autonomic fibers	Dorsal one-thirds of cord	Multiple sclerosis, tabes dorsalis, vit B12 deficiency, AIDS myelopathy, epidural metastases	Loss of proprioception and vibration sensations, sensory ataxia with positive Romberg test, variable weakness, bladder dysfunction
Subacute combined degeneration myelopathy	Bilateral CST and posterior columns	Posterior column and lateral column of white matter	Atrophic gastritis, gastric surgery, acid reduction therapy, parasitic infestation, strict vegetarianism	Impaired proprioception and vibration sensations, autonomic dysfunction, weakness, bladder and bowel and erectile dysfunctions
Cruciate paralysis	Lateral CST at pyramid of medulla	Injury to upper portion of pyramidal decussation	Odontoid process fracture, C1–C2 instability	Weakness of upper extremities with no weak legs

STT, spinothalamic tract; CST, corticospinal tract
Adapted from Kunam et al. (2018)

Impairment Scale (ASIA 2015). Incomplete injury syndromes are described as part of the introduction of the 2019 ISNCSCI booklet (ASIA 2019). Previous versions of the International Standards included the posterior cord syndrome and a mixed syndrome (Hayes

et al. 2000). The posterior cord syndrome was removed from recent ISNCSCI versions because of the rare occurrence of less than 1%, while the mixed syndrome was omitted because it does not present a definable syndrome. According to a study, 20.9% of cases admitted to acute spinal cord injury centers were diagnosed with clinical syndromes of spinal cord injury (McKinley et al. 2007). Central cord syndrome was the most common (44.0%), followed by cauda equina syndrome (25.1%) and Brown–Séquard syndrome (17.1%).

17.1 Anatomy of the Relevant White Matter Tracts to Incomplete Spinal Cord Syndromes

The white matter in the spinal cord consists of three columns or funiculi (anterior, lateral, and posterior), which are bundles of nerve axons that make up the neural pathways. The anterior columns (anterior funiculi) are located between the anterior median fissure and ventral nerve roots. The lateral columns are between the anterolateral and posterolateral sulci, where ventral and dorsal nerve roots enter and exit, respectively. The posterior columns are between the posterior median sulcus and posterolateral sulci on each side. In the cervical and upper thoracic regions, the posterior intermediate sulci are divided into fasciculus gracilis and cuneatus. When examining patients who have incomplete cord syndromes, it is important to know the location, function, and somatotopic organization of three important spinal cord pathways: the corticospinal tract, spinothalamic tract, and dorsal columns, as the symptom presentations of incomplete spinal cord syndrome are largely determined by involvement of these tracts.

17.1.1 Corticospinal Tract

The corticospinal tract is the largest and most important descending tract of the human spinal cord that controls voluntary movements. The corticospinal tracts are the spinal components of the pyramidal system and are occupied by the neurons in the parts of the ventral medulla oblongata called pyramids (Coppola 1973; Dumitru and Lang 1986). Approximately 40–50% of the corticospinal tract fibers are formed in the primary motor cortex of the frontal lobes (in the precentral gyrus). The remainder occurs in the other cortical regions of frontal and parietal lobes, including the premotor cortex, supplementary motor area, and sensory cortex. These fibers descend through the cerebral white matter, posterior limb of the internal capsule, cerebral peduncle, and ventral pons. In the medulla, 85–90% of the fibers in the corticospinal tract decussate in the pyramid and continue as the lateral corticospinal tract in the lateral column. The descending fibers that do not decussate in the medullar oblongata enter the spinal cord as the anterior corticospinal tracts (Armand 1982). The size of these tracts varies individually and on both sides. Damage to neurons in the motor cortex or corticospinal tract leads to upper motor neuron lesion. Table 17.2 summarizes the signs of differentiation between upper motor neuron lesion and lower motor neuron lesion. Topographically, the sacral fibers are located laterally, followed by lumbar, thoracic, and cervical medially.

Table 17.2 Differentiation between UMNL vs. LMNL

Clinical feature	UMNL	LMNL
Lesion	Above anterior horn cell: spinal cord, brainstem, motor cortex	Anterior horn cell or distal to anterior horn cell: nerve root, plexus, peripheral nerve
Muscle bulk	Not changed or mild atrophy	Severe atrophy
Muscle tone	Increased, spasticity	Decreased, flaccid
Stretch reflex	Increased	Decreased or absent
Babinski sign, ankle clonus	Positive	Negative

Adapted from Kunam et al. (2018)

17.1.2 Posterior Columns

The posterior column tract is responsible for transmitting sensations of position, vibration, two-point discrimination, proprioception, and quality of tactile sensation, and information from muscle, tendon, and joint receptors. The posterior column system consists of the fasciculus gracilis and the fasciculus cuneatus. The medial component (fasciculus gracilis) is located medially and transmits sensation for the lower half of the body, i.e., from the lower thoracic, lumbar, and sacral regions, to the brain. The lateral component (fasciculus cuneatus) is located more laterally and carries proprioceptive input on the levels rostral T5. Topographically, the sacral fibers are innermost, followed by lumbar, thoracic, and cervical. None of these fibers decussate or have synapses in the spinal cord. The posterior columns ascend and synapse at the nucleus gracilis and cuneatus of the lower medulla. The axons of these second-order neurons decussate as the internal arcuate fibers and travel rostrally as the medial lemniscus to the ventral posterolateral nucleus in the thalamus (VPL), terminating in the primary somatosensory cortex of the postcentral gyrus.

17.1.3 Spinothalamic Tract

The spinothalamic tract is located in the lateral column and carries pain, temperature, and touch sensation. The fibers can also transmit impulses such as tickling, itching, sexual sensations, and feeling of muscle fatigue. The anterior spinothalamic tract is associated with light touch and pressure. Touch and pressure are expressed bilaterally and are not lost after severing the nerve fibers of the spinothalamic system on one side. The spinothalamic tract consists of contralateral projections of second-order neurons that receive afferent input from the dorsal root ganglion cells. The second-order neurons are located in the gray matter of the spinal cord and project via the ventral commissure to the contralateral side after ascending about two or three segments. That is, the decussation fibers ascend at least two or three segments before reaching the opposite side. Therefore, a lesion involving the spinothalamic tract causes contralateral loss of pain and temperature sensations from some segments below the level of the lesion. The spinothalamic tract is the only one that decussates at the level of the spinal cord. Axons of the spinothalamic tract are also somatotopically arranged: within the spinothalamic tract such that sensory fibers from the upper extremities are more centrally located than the fibers from the lower extremities that are located peripherally. Pain and temperature sensations are transmitted more dorsally than the touch sensation. Because of these anatomical characteristics, small lesions involving the anterior spinal commissures, such as syringomyelia or central canal lesions, eliminate pain and temperature sensations on both sides, but do not affect tactile perception. The spinothalamic tract ascends to synapse with the ventral posterolateral (VPL) nucleus of the thalamus.

17.2 Incomplete Spinal Cord Syndrome

17.2.1 Central Cord Syndrome

Among the defined incomplete spinal cord injury syndromes, central cord syndrome is the most frequent type, accounting for 44% of the individuals with the incomplete syndrome of spinal cord injury, followed by cauda equina syndrome (25.1%), Brown–Séquard syndrome (17.1%), and conus medullaris syndrome (8%), while anterior cord syndrome (5%) and posterior cord syndrome (1%) were the least common (McKinley et al. 2007). Central cord syndrome was originally thought to be due to posttraumatic centro-medullary hemorrhage and edema (Schneider et al. 1954) or a Wallerian degeneration as a result of spinal cord compression in the narrow canal (Molliqaj et al. 2014). It occurs secondary to injury or lesions around the central canal, mainly in the cervical cord. The mechanism of injury in central cord syndrome has generally been low-speed/low-impact trauma (e.g.,

ground level fall) vs. high-impact trauma causing fracture dislocations. The most common level of neurologic injury in central cord syndrome is C4 and C5 (McKinley et al. 2007).

In acute traumatic central cord syndromes, there was a primary injury to the lateral corticospinal tract with evidence of Wallerian degeneration distal to the injury epicenter, with minimal Wallerian degeneration within the anterior corticospinal tracts (Jimenez et al. 2000). Most commonly central cord syndrome occurs in elderly individuals. Hyperextension injury is the classic mechanism of injury in elderly patients with underlying spinal stenosis secondary to the degenerative cervical spine, with or without fracture and dislocation (Pouw et al. 2010; Sweeney 1995). In younger patients, they can occur during water sports injuries or football. In older patients, this is often the result of a fall. It is believed that the resulting hyperextension of the narrowed spinal canal traps the spinal cord by a "pincer-like" effect between anterior degenerative bony or disk components and posteriorly through an inward bulging of folded hypertrophic ligamentum flavum.

Anatomically, the greatest impairment of the pyramidal tracts is caused by an expanding hematoma of the central cord (Morse 1982). Clinically, the central cord syndrome shows marked motor impairment of the upper extremities with lesser impairment of the lower extremities because the motor tracts of the lower extremity are located in the more lateral position of the spinal cord (van Middendorp et al. 2010). The somatotopic orientation of corticospinal axons in the cervical spinal cord is responsible for the predominant dysfunction of upper extremity motor performance in the central cord syndrome, which is somatotopically organized, with a laminated distribution of the location of the cervical, thoracic, lumbar, and sacral segments from medial to lateral. Alternatively, the corticospinal tract-mediated skilled upper extremity and hand movement are more severely affected than voluntary lower extremity movement, so that central cord lesions, which mainly affect the corticospinal tract, cause disproportionate functional deficits in the upper extremities (Levi et al. 1996). The main function of the corticospinal tract is to maintain fine motor movements to the distal musculature, especially the upper limbs (Levi et al. 1996). In addition, as second-order sensory fibers cross the anterior spinal commissure in front of the central canal before joining the opposite side spinothalamic tract, a process of central cord syndrome or syringomyelia that causes the central canal to expand along several segments may show selective loss of pain and temperature sensation, i.e., dissociated sensory loss (loss of pain and temperature sensation with preservation of position, vibration, and touch), due to involvement of the crossing spinothalamic tract fibers (Fig. 17.1). A term of sensory dissociation can rarely be used in the case of a small-sized syrinx or central cord syndrome when the senses of the lateral spinothalamic tract (pain and temperature) are impaired or absent and the senses of the anterior spinothalamic tract (light touch and light pressure) are preserved due to disproportional involvement.

The clinical manifestations of central cord syndrome correlate with the lesion size. Small lesions in the central cord region involve the spinothalamic tract, where they cross the anterior spinal commissure to the contralateral side and cause bilateral segmental loss of pain and temperature sensations. Since the decussating fibers ascend at least two to three spinal segments before reaching the opposite side, loss of pain and temperature sensations begins two to three segments below the level of the lesion. Sensations above and below this level are normal, with a band of sensory loss. Patients with cervical spinal cord lesions caused by either canal stenosis and underlying degenerative cervical spine or syringomyelia in the cervical spinal cord show a loss of pain and temperature sensations in the upper thorax, both shoulders, and upper arms, in a classic "cape" distribution. Large central cord lesions can involve the anterior horn cells, corticospinal tract, posterior columns, spinothalamic tract, and autonomic centers in the lateral horn (Fig. 17.2). Due to the somatotopic organization of fibers in the corticospinal tract and spinothalamic tract,

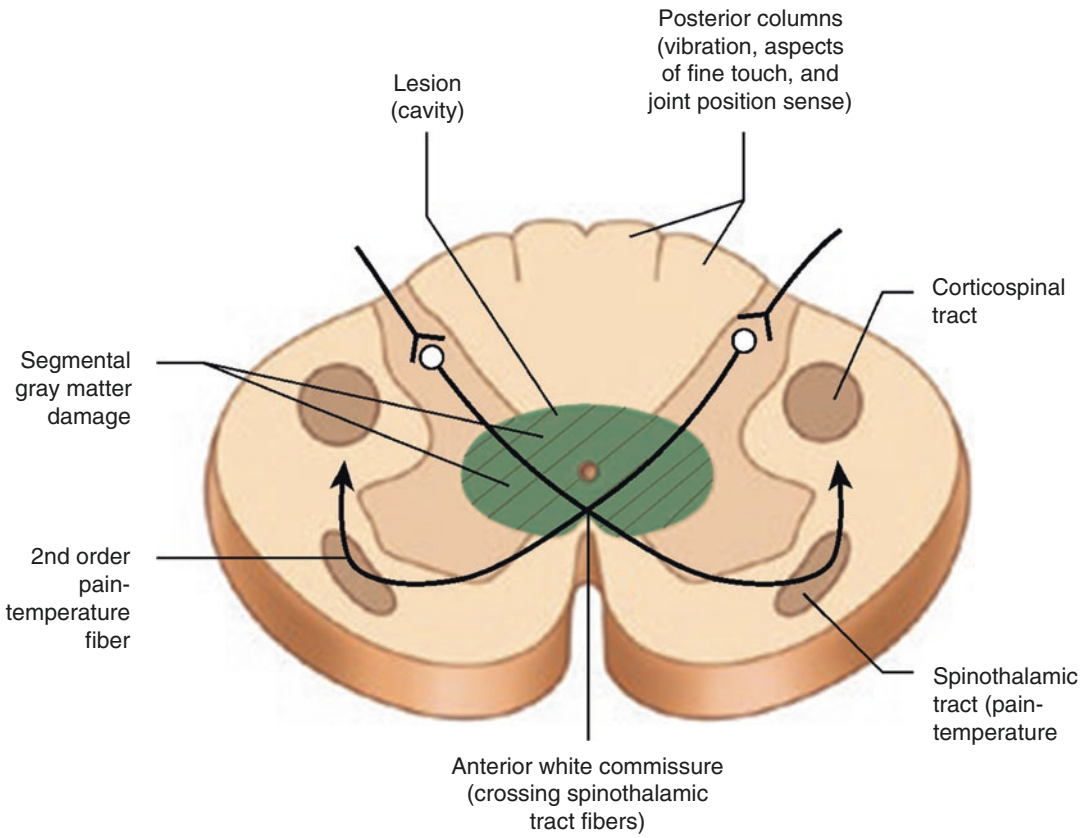

Fig. 17.1 Central cord syndrome. The lesion (a central cavity) involves the anterior white commissure (just ventral to the central canal) through which the second-order fibers of the pain-temperature pathways cross

sensory and motor deficits are disproportionately severe in the upper compared with lower extremities. Lower motor neuron type motor deficits occur at the level of the lesion due to involvement of anterior horn cells, whereas upper motor neuron type deficits occur due to corticospinal tract involvement below the level of the lesion (Kunam et al. 2018) (Table 17.2).

According to a study, difference of at least 10 points of key muscles' motor score between the upper and lower extremities supports the diagnostic criterion of a central cord syndrome (van Middendorp et al. 2010). Fine motor function of the hand is usually most severely affected and recovers poorly. Sacral segmental function has fairly good prognosis for recovery to ambulatory status. Patients younger than 50 years of age tend to have a better prognosis for independent ambulation and return of bowel and bladder function. The recovery pattern typically begins with recovery of strength and sensation in the lower extremities, followed by recovery of the bowel and bladder, and finally proximal and then distal strength and sensation recovery in the upper extremities (McKinley et al. 2007; Nowak et al. 2009).

17.2.2 Brown–Séquard Syndrome (Unilateral Cord Syndrome)

The Brown–Séquard syndrome, which was first described by the neurologist Charles Edouard Brown–Séquard in 1851, often results from a traumatic cause, mostly motor vehicle accidents, penetrating injuries including stabbing or gunshot wound and assaults with spinal cord hemisection resulting in damage to the lateral

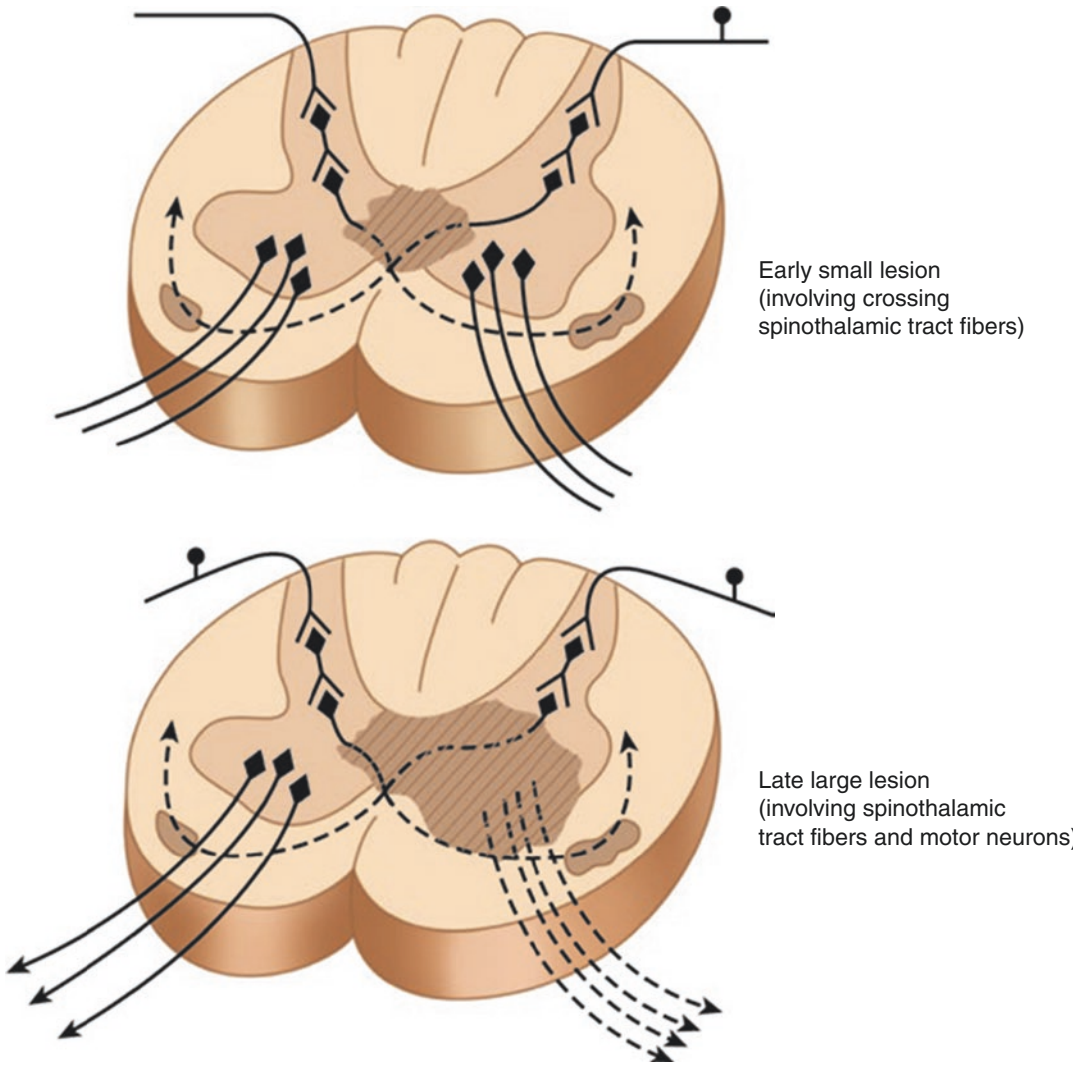

Fig. 17.2 Differences in the structures involved depending on the size of the central canal lesion

corticospinal tract, dorsal columns, and spinothalamic tract. Closed injuries are mainly unilateral facet dislocations or other rotational deformities and tumor compression or spinal stenosis (McKinley et al. 2007). Spinal cord ischemia in the cervical spinal cord can cause unilateral spinal cord injury (Goldsmith et al. 1998).

A Brown–Séquard lesion is characterized by ipsilateral weakness due to an interruption of the ipsilateral corticospinal tract and loss of both vibration and position sense below the level of injury and ataxia due to the ipsilateral posterior column damage. In addition, there is a loss of temperature and pain sensation below the level of the lesion on the contralateral side. Since pain and temperature fibers extend rostrally a few segments through the Lissauer's tract before crossing the midline to enter the lateral spinothalamic tract, the loss of pain and temperature sensory modalities extends rostrally on the contralateral side to a segmental level that is a few segments below the level of the lesion (Fig. 17.3). The signs and symptoms depend on the site of injury, which may also involve the cervical or sympathetic thoracic trunk, resulting in Horner's syndrome. Overall, the symptoms depend on which

Fig. 17.3 Drawing of the areas affected by the clinical features in Brown–Séquard syndrome. These features show ipsilateral spastic paralysis (UMN type involving the CST); ipsilateral loss of proprioception and vibration sensations involving the dorsal columns; and contralateral loss of pain and temperature sensations involving the STT. The loss of contralateral pain and temperature sensations (blue) starts two to three segments below the level of the motor deficit because STT fibers ascend two to three segments before crossing to the opposite side. A small segmental ipsilateral region of combined LMN deficit and complete sensory deficit (arrow, red) is present at the level of the lesion. UMN, upper motor neuron; CST, corticospinal tract; STT, spinothalamic tract; LMN, lower motor neuron

part of the spinal cord is affected (Shams and Arain 2021). As the spinothalamic tracts ascend ipsilaterally for one or two spinal cord segments before crossing to join the opposite side spinothalamic tract, the sensory level on the opposite side is often one to two segments lower than the site of the lesion.

Brown–Séquard syndrome is uncommon and occurs in 2–4% of acute spinal cord injuries, and most commonly occurs after cervical spinal cord

injury (Hayes et al. 2000; McKinley et al. 2007). A pure hemisection is unusual, leading more frequently to clinical examination with some features of the Brown–Séquard and central cord syndrome. Some refer to this variation as Brown–Séquard plus syndrome, which refers to relatively ipsilateral hemiplegia with a relative contralateral hemianalgesia (Roth et al. 1991). Brown–Séquard syndrome has the best prognosis for the recovery of the incomplete spinal cord injury syndrome; 90% of patients have been observed to be independent ambulatory at discharge from rehabilitation.

17.2.3 Conus Medullaris and Cauda Equina Syndrome

Traumatic injuries to the thoracolumbar spine can result in conus medullaris or cauda equina syndrome. The injuries of cauda equina and conus medullaris are generally described together because they are generally clinically indistinguishable and often manifest as combined injuries. The clinical symptoms of patients with conus medullaris or cauda equina syndrome include the following: low back pain, lower limb weakness, perineum or saddle anesthesia, and bladder and/or bowel dysfunction. Lower limb weakness associated with cauda equina syndrome is predominantly asymmetrical in patients with an incomplete injury. The conus medullaris or cauda equina syndromes are assumed to be separate clinical entities, but there is no clear definition of neurological symptoms and level of injury (Brouwers et al. 2017). In practice, both conus medullaris and cauda equina lesions are often combined as "conus-cauda lesion" (Brouwers et al. 2017).

The spinal cord portion immediately rostral to the conus medullaris is called the epiconus. Anatomically, cauda equina is defined as the bundle of the spinal roots below the tip of the conus medullaris around the filum terminale (Fig. 17.4). Unlike the cervical and thoracic spinal cord and the respective surrounding spine, the conus medullaris is condensed to spinal cord segments to less than two vertebral heights. In adults, the

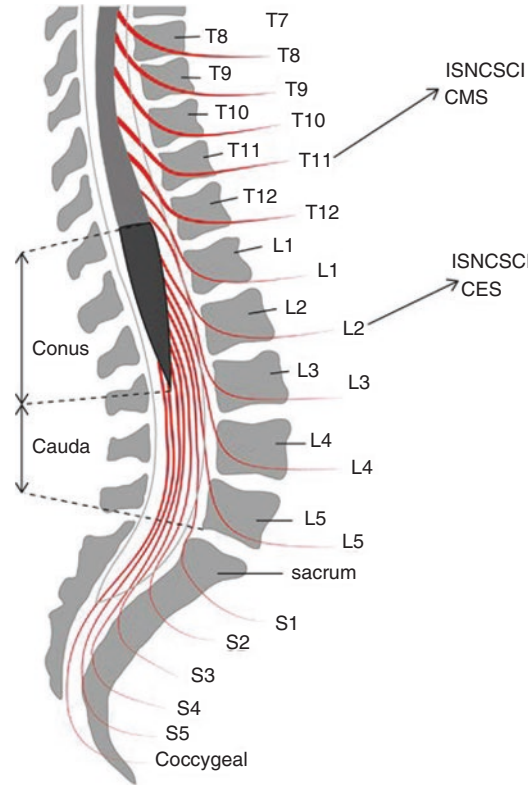

Fig. 17.4 Schematic presentation of the conus medullaris and cauda equina. ISNCSCI, International Standards for Neurological Classification of Spinal Cord Injury; CMS, conus medullaris syndrome; CES, cauda equina syndrome. From Brouwers et al. (2017), with permission

conus medullaris extends from the T12/L1 intervertebral disk space caudal to the middle third of the L2 vertebral body or L1/L2 intervertebral disk space. Within this short distance, almost ten spinal cord segments (L1–S5) are concentrated in the conus medullaris, with no close spatial relationship to their respective vertebrae. Almost all lumbar cord segments are typically facing the T12 vertebral body, and almost all of the sacral segments are opposite the L1 vertebra. The lumbar sympathetic, sacral parasympathetic, and lumbar/sacral somatic nerves all originate in the conus medullaris (Kingwell et al. 2008) (Table 17.3) .

17.2.3.1 Conus Medullaris Syndrome

The conus medullaris comprises both upper and lower motor neurons, while the cauda equina consists entirely of lower motor neurons. Conus

Table 17.3 Summary of complete epiconus injuries, conus medullaris syndrome, and cauda equina syndrome

Neurological syndrome	Neurological level of injury	Clinical examination	Bladder, bowel, sexual function
Epiconus	Above T12	Conus segments intact, UMN syndrome, BCR and AR preserved, muscle tone increased	Bladder and bowel dysfunction, UMN type; sexual dysfunction (in men preserved reflexogenic erections, loss of psychogenic erection)
Conus medullaris	T12–L1 to S4–5	Complete damage of conus medullaris; UMN syndrome; reflexes abolished; muscle tone flaccid with atrophy	Bladder-bowel dysfunction, LMN type; sexual dysfunction (in men loss of reflexogenic erection, psychogenic erection preserved)
Cauda equina	Below L2	LMN syndrome; Motor: variable L/E weakness, diminished tone Sensory: variable sensory deficit; Reflexes: dependent on level of injury	Bladder-bowel dysfunction, LMN type; sexual dysfunction (in men loss of reflexogenic erection, psychogenic erection preserved)

Adapted from Kingwell et al. (2008)

medullaris syndrome may initially be clinically similar to the cauda equina syndrome. If the neurological level of lesion is high, conus medullaris syndrome may be suspected. It is usually caused by damage to the sacral spinal cord in the conus medullaris in association with a fracture of the thoracolumbar junction, disk herniation in the lower thoracic and upper lumbar spine, trauma resulting in a compression or burst fracture with retropulsed fragments causing cord compression, intramedullary tumor (metastasis or primary tumor), infection (i.e., epidural abscess), spinal dural arteriovenous fistulas, and cord infarction. Conus medullaris injury is often accompanied by symptoms of upper motor neuron injury and lower motor neuron injury due to nerve root damage around the conus medullaris. In many cases, it is difficult to distinguish conus medullaris syndrome from cauda equina syndrome. If the damaged area is epiconus, it is considered a spinal cord injury, which is a symptom of upper motor neuron injury with retention of sacral reflexes. Depending on the level of the lesion, injuries to the conus medullaris tend to have a mixed picture of upper and lower motor neuron lesions with initial flaccid paralysis of the legs, bladder, anal sphincter, and variable lower extremity hypesthesia and saddle anesthesia (Table 17.1). The sacral segments may occasionally preserve the reflexes, i.e., bulbocavernosus and anal reflex, with higher lesions of the conus medullaris (ASIA 2019).

17.2.3.2 Cauda Equina Syndrome

Cauda equina syndrome is caused by the lumbosacral nerve root injuries below the level of the conus medullaris within the lumbosacral spinal canal, and it is not a true spinal cord injury because the spinal cord itself may be spared. Injury to the nerve roots causes classically lower motor neuron lesions, resulting in flaccid paralysis of the lower extremities and areflexic bladder and bowel. Therefore, there is no bulbocavernosus reflex and anal reflex, and there is no difference in the damage priority of the sensory type. It is believed that the regenerative capacity in the lower motor neuron lesions is superior to the upper motor neuron lesions and therefore the functional outcome of cauda equina syndrome could be better than the functional outcome of conus medullaris syndrome (Radcliff et al. 2011; Tator 1998). If the spinal fracture results in a combination of the conus medullaris and cauda equina lesions, it cannot be clinically distinguished from cauda equina syndrome and conus medullaris injury accompanied with injuries of the surrounding nerve roots (Fig. 17.5).

In general, cauda equina lesions are considered to have a much better prognosis for neurological recovery compared with spinal cord injuries because the lower motor neuron is inherently more resilient to trauma and has greater regenerative capacity than the axonal tracts of the central nervous system. However, the sacral nerve roots

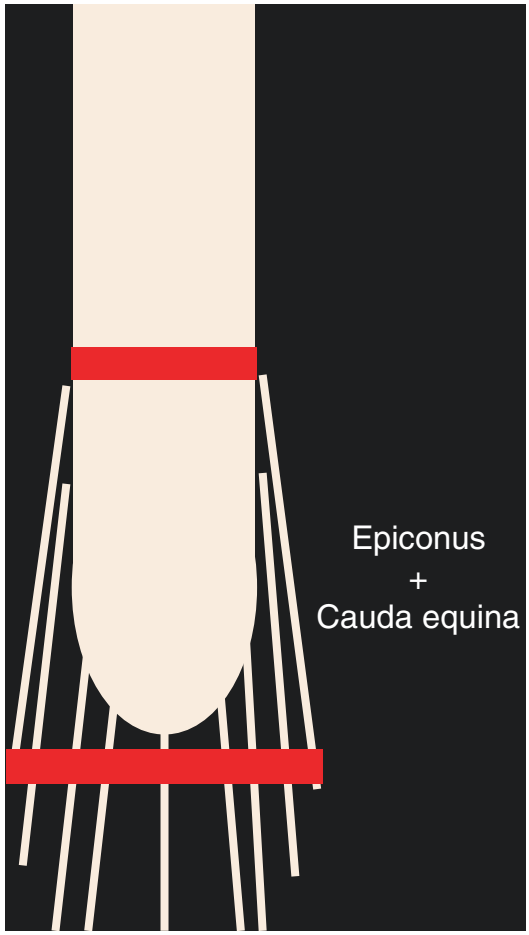

Fig. 17.5 Cauda equina syndrome and conus medullaris syndrome are clinically indistinguishable if there is accompanying damage of cauda equina and conus medullaris

that provide bowel and bladder function and perineal sensation can be very delicate and difficult to recover. Unlike other syndromes classified as an incomplete syndrome of spinal cord injuries, cauda equina syndrome is a peripheral nerve injury caused by multiple nerve root injuries. It is, therefore, to be expected that recovery by nerve regeneration is likely to be favorable. On the other hand, the nerve roots constituting the cauda equina are in the absence of the epineurium in the spinal canal, and the length of each nerve root in the spinal canal is long, and the neural or perineural blood flow is poor compared to the other nerve roots. These anatomical disadvantages may contribute to poor neural regeneration.

17.2.4 Anterior Cord Syndrome

Lesions that affect the anterior two-thirds of the spinal cord and spare the posterior columns cause anterior cord syndrome. The most common cause of anterior cord syndrome, also known as anterior spinal artery syndrome, is ischemia or infarction of the spinal cord (Kunam et al. 2018). Anterior cord syndrome is most commonly associated with occlusion of the anterior spinal artery or Adamkiewicz artery (Diaz and Morales 2016). The major cause of anterior cord syndrome is ischemia of the anterior spinal artery. The most common cause of anterior cord syndrome is iatrogenic, namely thoracic and thoracoabdominal aortic aneurysm repair or aortic clamping. Several factors during surgery can contribute to ischemia of the spinal cord, including hypotension, clamping of the aorta, increased spinal canal pressure, and occlusion of arteries feeding the cord (Piffaretti et al. 2014). Aortic dissection is a rare cause of spinal cord ischemia due to occlusion of branch vessels of the aorta, including radicular arteries that help to feed the anterior spinal artery (Joo and Cummings 2000). Anterior cord syndrome may also follow after surgeries at the distal aorta and proximal iliac arteries using aortic counter-pulsation devices and occasionally retroperitoneal hematomas or abscesses. Similarly, survivors of cardiac arrest and significant hypotensive episodes may have a midthoracic anterior cord ischemic syndrome because the vasculature near the T6 segment is particularly susceptible to distal field ischemia. Anterior cord syndrome often tends to be compressed directly from bone fragments of a burst fracture, posteriorly extruded disk material, or the lower vertebral body in a fracture dislocation. In general, the prognosis of recovery is less favorable and the practical possibility of a functional motor recovery is only 10–20% (Pouw et al. 2010). Among all of the incomplete spinal cord syndromes, anterior cord syndrome is associated with the worst prognosis.

Anterior cord syndrome affects the anterior two-thirds of the spinal cord, including the segmental anterior horn cells, spinothalamic tracts, and corticospinal tracts. The clinical presentation

is determined by the neuronal structures and the tracts involved. This mainly involves a loss of function of the corticospinal and spinothalamic tracts leading to segmental flaccid motor paralysis at the segment of the level of injury and spastic paralysis, as well as the impaired sensation of pin prick below the level of injury with a relatively preserved proprioception sensation, and orthostatic hypotension, bladder and bowel dysfunction, and sexual dysfunction due to involvement of the autonomic center. Bilateral sensory deficits begin two to three segments below the level of lesion, as the spinothalamic tracts ascend at least two or three segments before crossing to the opposite side at the anterior commissure (Kunam et al. 2018). There are various degrees of functional preservation of the posterior column, that is, preservation of proprioception, deep touch, vibratory sensation, and two-point discrimination (Pouw et al. 2010).

Because the incidence of the incomplete spinal cord injuries listed below is low, they are not classified as a clinical syndrome in the ISNCSCI. However, posterior cord syndrome, subacute combined degenerative myelopathy, and cruciate paralysis are also typical incomplete spinal cord injuries.

T2 hyperintensities on MRI in the region of the anterior horns are the hallmark finding. These hyperintensities on the sagittal view appear as thin "pencil-like" lesions that extend vertically over several spinal segments. On the axial view, these hyperintensities appear as two bright dots, one within each anterior horn, that resemble "owl's eyes" in appearance (Pearl and Dubensky 2021).

17.2.5 Posterior Cord Syndrome

The posterior cord syndrome is rare, less than 1% of all spinal cord injuries (Hayes et al. 2000), and can be caused by posterior impingement of the cord, such as from depressed laminar fractures or a posterior epidural hematoma, and infrequently affected in metabolic and toxic spinal cord disease, such as subacute combined degeneration due to vitamin B12 deficiency. Other causes of the posterior cord syndrome include multiple sclerosis, tabes dorsalis, degenerative cervical myelopathy, AIDS-related myelopathy, and epidural or intradural extramedullary tumors (Kunam et al. 2018). Trauma is an uncommon cause of posterior cord syndrome (McKinley et al. 2007). Posterior spinal cord infarction can be associated with unilateral posterior cord syndrome and is rare compared with anterior spinal cord infarction due to a rich vascular pill plexus and paired posterior spinal arteries (Kamin and Garstang 2008; Rubin and Rabinstein 2013).

This syndrome shows a posterior column dysfunction such as loss of proprioception, including deep touch, position, and vibratory sensation, and typically sensory ataxia, while other sensory and motor functions are preserved. Three sensory inputs are required for normal balance: vestibular, visual, and proprioception. Removal of visual inputs and a lack of proprioception due to posterior column involvement result in sensory ataxia and positive Romberg sign. Large lesions can also affect the lateral corticospinal tract and autonomic tracts to the sacral cord. Involvement of these tracts causes weakness and spasticity when the corticospinal tract is involved, bowel and bladder incontinence, erectile dysfunction, and orthostatic hypotension when the autonomic tract is involved (Kunam et al. 2018).

17.2.6 Subacute Combined Degeneration Myelopathy (Posterolateral Column Syndrome)

Involvement of the posterior and lateral columns of the spinal cord will lead to a pattern of sensory loss that predominantly involves the modalities of position and vibration sense and a motor syndrome of spastic paralysis that reflects the involvement of the corticospinal tract (Fig. 17.6). This clinical syndrome is characterized by bilateral corticospinal tract pattern weakness below the level of lesion with decreased vibratory and position sense but sparing pain and temperature sensation (Cho and Bhattacharyya 2018). Symptoms or signs resulting from subacute com-

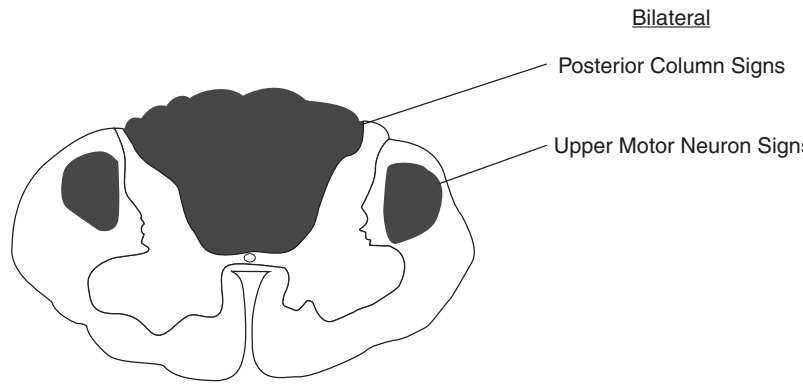

Fig. 17.6 Posterolateral column syndrome

bined degeneration myelopathy resulting from a deficiency of vitamin B_{12} or copper are gait disturbance, hypesthesia, dysesthesia, impaired vibration and position sense, autonomic dysfunction with constipation, erectile dysfunction, and urinary frequency, and mild motor dysfunction with pyramidal signs (Beck 1991; Saperstein and Barohn 2002). Other known causes are HIV-associated vacuolar myelopathy, adrenomyeloneuropathy, methotrexate toxicity, and spinal dural arteriovenous fistular. Causes of adenosylcobalamin deficiency, which is required as a cofactor for the conversion of methylmalonyl coenzyme A (CoA) to succinyl CoA, include atrophic gastritis with consecutive cobalamin malabsorption, gastric surgery, acid reduction therapy, parasitic infestation by fish tapeworm, hereditary enzymatic defect, and rarely strict vegetarianism. Adenosylcobalamin deficiency can accumulate methylmalonyl CoA and reduce normal myelin synthesis (Beck 1991).

Usually, the symptoms of lesions in the posterior column of the spinal cord are first manifested, and the lesion becomes larger due to damage to the corticospinal tract. Therefore, the initial symptom is the abnormality of proprioceptive sensation such as sensory ataxia and posture abnormality with a positive Romberg sign due to the posterior column injury, while pain and temperature sensation remain intact because of preservation of the spinothalamic tract. Symptoms such as spasticity due to damage to the corticospinal tract appear later. Characteristically, the symptoms of subacute combined degenerative myelopathy invariably appear as early symptoms of sensory decrease and numbness in the lower extremity, followed by weakness and gait disorders. On rare occasions, there are cases of upper extremity symptoms, and usually do not lead to voiding difficulties.

The most common laboratory abnormality is macrocytic anemia. The most commonly used screening test is serum cobalamin analysis, but it has low sensitivity and specificity. Serum methylmalonic acid and plasma total homocysteine are good monitoring tools and should be measured annually. On MRI, a signal change with high intensity of the posterior and lateral columns of the spinal cord and spinal cord atrophy can be observed (Bassi et al. 1999). A cobalamin deficiency can promote concomitant neuropathic changes in the peripheral nerves (Saperstein and Barohn 2002).

For an immediate effect of a subacute combined degeneration myelopathy associated with a vitamin B12 deficiency, vitamin B12 (cobalamin) 1000 μg should initially be administered intramuscularly. After that, 8–10 injections over 3 months followed by monthly injections are recommended. Since 1.2% of the oral dose of cobalamin is absorbed regardless of the intrinsic factor, 1000 μg of oral cobalamin can also be used as a replacement in the event of malabsorption (Carmel 2008). Mean corpuscular volume (MCV) normalizes within 8 weeks after cobalamin replacement (once daily for 4 weeks, then once weekly for 1 year, then once per month) (Carmel 2008). Neurological symptoms begin to improve as early as 1 week and continue to improve until 3 months after cobalamin replace-

ment. Nerve conduction velocities and median nerve SEP normalize. MR detected signal changes in the spinal cord might disappear over time (Hemmer et al. 1998).

17.2.7 Cruciate Paralysis

Cruciate paralysis (Bell's cruciate paralysis, cervicomedullary syndrome) causes paralysis of both upper extremities without weakness in the legs due to an injury to the upper portion of the pyramidal decussation (Bell 1970). It is believed that the basis for the clinical presentation is due to midline damage of the rostral portion of the pyramidal decussation, which would selectively injure the fibers of the corticospinal tract that serve hand and arm function (Levi et al. 1996). Cruciate paralysis can occur after the cervicomedullary junction is injured by trauma, odontoid fracture, tuberculosis, or cervical spine injury (Pappas et al. 1991). In the decussation of the lateral corticospinal tract at the medullary pyramid, located at the anterior surface of the lower end of the medulla oblongata, fibers that are functionally associated with the arm movement are more rostral and medial to those associated with leg movement (Fig. 17.7). Wallenberg (1901) reported the complex anatomy at the cervicomedullary junction, including the illustration that fibers serving function to the arms decussate more rostrally than those subserving function to the legs. The pyramidal decussation extends over a longitudinal distance that spans the cervicomedullary junction to the C2 level. The motor tract of the upper extremities crosses ventrally and rostrally to the fibers supplying the lower extremities between the medulla and the C2 region (Fig. 17.8). This observation suggested a somatotopic organization of these fibers at the cervicomedullary junction. However, there is some debate about explanation for cruciate paralysis. So far, there is no evidence of the presence of a somatotopically organized corticospinal tract at the cervicomedullary junction (Benglis and Levi 2010). In an anatomical study in monkeys, there was no definite anatomical evidence for a differential decussation of the fore-limb and hind-limb fibers, and the fore-limb and hind-limb fibers appeared to be completely intermingled and decussated together in the pyramidal tract. Thus, this study suggests that two alternative explanations for cruciate paralysis: (1) selective damage to neural areas involving the internuncial cells, the central ray area, and the cuneate nucleus, or (2) injury to the anterior corticospinal tract (Pappas et al. 1991). It is known that lesion

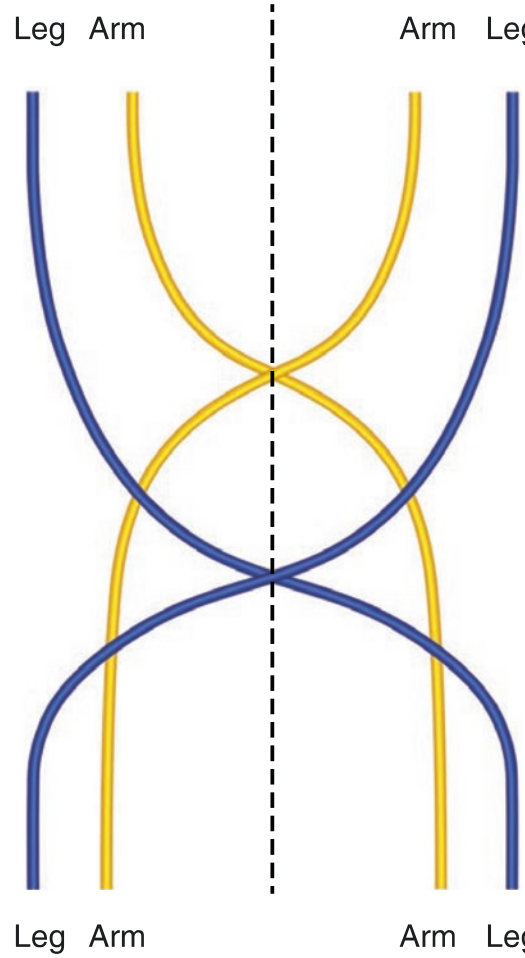

Fig. 17.7 At the decussation of the pyramids in the lower Medulla, the arm fibers lie medial to the leg fibers. Arm fibers decussate first and come to lie in the medial portion of the corticospinal tract in the upper cervical spinal cord. Leg fibers decussate more caudally and come to lie in the lateral portion of the lateral corticospinal tract. Adapted from Campbell (2013)

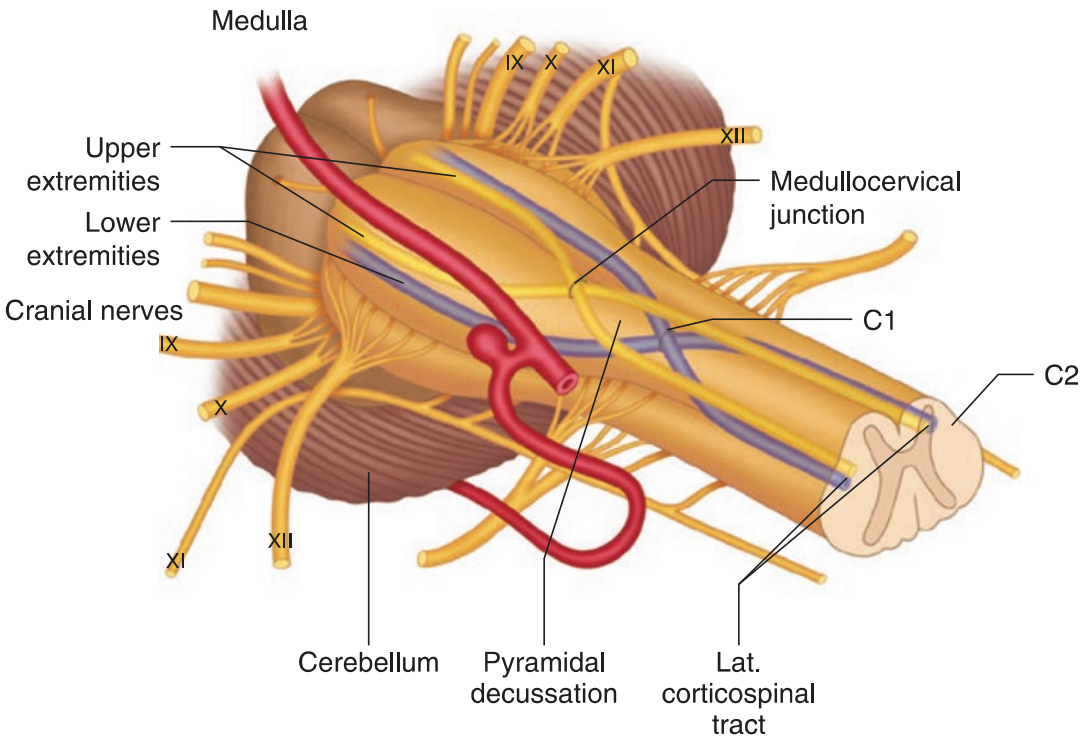

Fig. 17.8 The cervicomedullary junction showing longitudinal expanse of the pyramidal decussation. The ventral and medial arm fibers decussate rostral to the leg fibers. Characteristic spinal cord lamination of the arm and leg fibers is reached at the C2 vertebral level. Adapted from Dumitru and Lang (1986)

of the pyramidal decussation causes a variety of clinical syndromes that depend on both the level of damage and its relationship to the midline (Coppola 1973). It has been reported that the midline lesions of the pyramidal decussation may result in flaccid tetraplegia, paraplegia, and cruciate paralysis (Benglis and Levi 2010; Hopkins et al. 2016; Inamasu et al. 2001).

Acute midline injuries of the anterior aspect of the junction of the medullar oblongata and upper cervical cord may result in differential damage to the fibers of the pyramidal tract (Benglis and Levi 2010; Hopkins et al. 2016). Initial clinical presentations of cruciate paralysis are confusing with central cord syndrome or cervical syringomyelia. Since upper extremity weakness is more severe than lower extremity weakness, symptoms and signs of cruciate paralysis are likely to be central cord syndrome and therefore discrimination is required. Table 17.4 summarizes the differences between the central cord syndrome and cruciate paralysis. Lesions that cause cruciate paralysis must be superficial and minimal, as extensive lower medullary injuries would cause massive neurological deficits and death. The prognosis for the possible recovery of full function in the upper extremities in cruciate paralysis is therefore good (Inamasu et al. 2001).

17.2.8 Anterior Horn Syndrome

Anterior horn syndrome shows motor weakness of the lower motor neuron lesion type, while all sensory functions are normal. This is a syndrome that is distinguished from the anterior cord syndrome. Although poliomyelitis is a typical example of anterior horn syndrome, it rarely occurs today, and postpolio syndrome can be seen in patients with poliomyelitis. In addition to poliomyelitis, diseases that show the pattern of anterior horn syndrome are as follows: spinal

Table 17.4 Central cord syndrome vs. cruciate paralysis with arms weaker than legs

	Central cord syndrome	Cruciate paralysis
Site of lesions	Mid to lower cervical Anterior horn cells Lateral corticospinal tract (medial part)	Lower medulla and upper cervical, anterior aspect Corticospinal decussation caudal to the pyramids
Clinical manifestations	Arms weaker than legs Flaccid arms acutely Legs normal or variably weak Lower motor neuron deficit in upper limbs persists	Arms weaker than legs Flaccid arms acutely Legs normal or variably weak Upper motor neuron deficit in upper limbs develops ± Trigeminal sensory deficit ± Cranial nerve dysfunction (9th, 10th, or 11th cranial nerve)
Prognosis for neurologic recovery	Variable	Usually good

Adapted from Benzel and Tator (1995)

muscular atrophy, progressive muscular atrophy (lower motor neuron lesion, a restricted form of amyotrophic lateral sclerosis), spinal and bulbar muscular atrophy (Kennedy disease), Hirayama disease, monomeric amyotrophy, West Nile virus myelitis, and very rare cases of HIV infection (Cho and Bhattacharyya 2018).

References

American Spinal Injury Association (ASIA). International standards for neurological classification of spinal cord injury. 7th ed. updated 2015. Atlanta: ASIA; 2015.

American Spinal Injury Association (ASIA). International standards for neurological classification of spinal cord injury. 8th ed. revised 2019. Richmond: ASIA; 2019.

Armand J. The origin, course and termination of corticospinal fibers in various mammals. Prog Brain Res. 1982;57:329–60.

Bassi SS, Bulundwe KK, Greeff GP, et al. MRI of the spinal cord in myelopathy complicating vitamin B12 deficiency: two additional cases and a review of the literature. Neuroradiology. 1999;41:271–4.

Beck WS. Diagnosis of megaloblastic anemia. Ann Rev Med. 1991;42:311–22.

Bell HS. Paralysis of both arms from injury of the upper portion of the pyramidal decussation: "cruciate paralysis". J Neurosurg. 1970;33:376–80.

Benglis D, Levi AD. Neurologic findings of craniovertebral junction disease. Neurosurgery. 2010;66(3 Suppl):13–21.

Benzel EC, Tator CH, editors. Contemporary management of spinal cord injury. American Association of Neurological Surgeons: Park Ridge, IL; 1995.

Brouwers E, van de Meent H, Curt A, et al. Definitions of traumatic conus medullaris and cauda equina syndrome: a systematic literature review. Spinal Cord. 2017;55:886–90.

Campbell WW. Dejong's the neurologic examination. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2013.

Carmel R. How I treat cobalamin (vitamin B12) deficiency. Blood. 2008;112:2214–21.

Cho TA, Bhattacharyya S. Approach to myelopathy. Continuum (Minneap Minn). 2018;24(2, Spinal Cord Disorders):386–406.

Coppola AR. "Cruciate paralysis": a complication of surgery. South Med J. 1973;66:684.

Diaz E, Morales H. Spinal cord anatomy and clinical syndromes. Semin Ultrasound CT MR. 2016;37:360–71.

Dumitru D, Lang JE. Cruciate paralysis. Case report. J Neurosurg. 1986;65:108–10.

Goldsmith P, Rowe D, Jager R, et al. Focal vertebral artery dissection causing Brown-Sequard's syndrome. J Neurol Neurosurg Psychiatry. 1998;64:415–6.

Hayes KC, Hsieh JT, Wolfe DL, et al. Classifying incomplete spinal cord injury syndromes: algorithms based on the international standards for neurological and functional classification of spinal cord injury patients. Arch Phys Med Rehabil. 2000;81:644–52.

Hemmer B, Glocker FX, Schumacher M, et al. Subacute combined degeneration: clinical, electrophysiological, and magnetic resonance imaging findings. J Neurol Neurosurg Psychiatry. 1998;65:822–7.

Hopkins B, Khanna R, Dahdaleh NS. Revisiting cruciate paralysis: a case report and systematic review. J Craniovertebr Junction Spine. 2016;7:265–72.

Inamasu J, Hori S, Ohsuga F, et al. Selective paralysis of the upper extremities after odontoid fracture: acute central cord syndrome or cruciate paralysis? Clin Neurol Neurosurg. 2001;103:238–41.

Jimenez O, Marcillo A, Levi AD. A histopathological analysis of the human cervical spinal cord in patients with acute traumatic central cord syndrome. Spinal Cord. 2000;38:532–7.

Joo JB, Cummings AJ. Acute thoracoabdominal aortic dissection presenting as painless, transient paralysis of the lower extremities: a case report. J Emerg Med. 2000;19:333–7.

Kamin S, Garstang S. Vascular disease of the spinal cord. Top Spinal Cord Inj Rehabil. 2008;14:42–52.
Kingwell SP, Curt A, Dvorak MF. Factors affecting neurological outcome in traumatic conus medullar is and caudal equine injuries. Neurosurg Focus. 2008;25:E7.
Kunam VK, Velayudhan V, Chaudhry ZA, et al. Incomplete cord syndromes: clinical and imaging review. Radiographics. 2018;38:1201–22.
Levi AD, Tator CH, Bunge RP. Clinical syndromes associated with disproportionate weakness of the upper versus the lower extremities after cervical spinal cord injury. Neurosurgery. 1996;38:179–83; discussion 83-5.
McKinley W, Santos K, Meade M, et al. Incidence and outcomes of spinal cord injury clinical syndromes. J Spinal Cord Med. 2007;30:215–24.
Molliqaj G, Payer M, Schaller K, et al. Acute traumatic central cord syndrome: a comprehensive review. Neurochirurgie. 2014;60:5–11.
Morse SD. Acute central cervical spinal cord syndrome. Ann Emerg Med. 1982;11:436–9.
Nowak DD, Lee JK, Gelb DE, et al. Central cord syndrome. J Am Acad Orthop Surg. 2009;17:756–65.
Pappas CT, Gibson AR, Sonntag VK. Decussation of hindlimb and fore-limb fibers in the monkey corticospinal tract: relevance to cruciate paralysis. J Neurosurg. 1991;75:935–40.
Pearl NA, Dubensky L. Anterior cord syndrome. 2020 Aug 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
Piffaretti G, Bonardelli S, Bellosta R, et al. Spinal cord ischemia after simultaneous and sequential treatment of multilevel aortic disease. J Thorac Cardiovasc Surg. 2014;148:1435–42. e1.
Pouw MH, van Middendorp JJ, van Kampen A, et al. Diagnostic criteria of traumatic central cord syndrome. Part 1: a systematic review of clinical descriptors and scores. Spinal Cord. 2010;48:652–6.
Radcliff KE, Kepler CK, Delasotta LA, et al. Current management review of thoracolumbar cord syndromes. Spine J. 2011;11:884–92.
Roth EJ, Park T, Pang T, et al. Traumatic cervical Brown-Sequard and Brown-Sequard-plus syndromes: the spectrum of presentations and outcomes. Paraplegia. 1991;29:582–9.
Rubin MN, Rabinstein AA. Vascular diseases of the spinal cord. Neurol Clin. 2013;31:153–81.
Saperstein DS, Barohn RJ. Peripheral neuropathy due to cobalamin deficiency. Curr Treat Options Neurol. 2002;4:197–201.
Schneider RC, Cherry G, Pantek H. The syndrome of acute central cervical spinal cord injury; with special reference to the mechanisms involved in hyperextension injuries of cervical spine. J Neurosurg. 1954;11:546–77.
Shams S, Arain A. Brown Sequard Syndrome. 2020 Sep 14. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
Sweeney PJ. Clinical evaluation of cervical radiculopathy and myelopathy. Neuroimaging Clin N Am. 1995;5:321–7.
Tator CH. Biology of neurological recovery and functional restoration after spinal cord injury. Neurosurgery. 1998;42:696–707; discussion 707–8.
van Middendorp JJ, Pouw MH, Hayes KC, et al. Diagnostic criteria of traumatic central cord syndrome. Part 2: a questionnaire survey among spinal specialists. Spinal Cord. 2010;48:657–63.
Wallenberg A. Wallenberg syndrome: acute ischemic stroke of the posterior inferior cerebellar artery (in German). Arch Psychiatr. 1901;34:923–59.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.
Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. Oxford: Oxford University Press; 2001.
Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.
Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.
Mancall EL, Brock DG, editors. Gray's clinical neuroanatomy. The anatomic basis for clinical neuroscience. Elsevier Saunders: Philadelphia; 2011.
Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia: Elsevier; 2016.
Passias PG, editor. Cervical myelopathy. Philadelphia: Jaypee Brothers Medical Publishers (P) Ltd; 2016.
Thron AK. Vascular anatomy of the spinal cord. In: Radioanatomy as the key to diagnosis and treatment. 2nd ed. Switzerland: Springer; 2016.
Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.
Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part I. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976.
Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part II. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976.

18 Neural Tube Defects and Abnormalities in Neurulation

Neurulation is usually described as the developmental process that results in the rolling up of a flat layer of epithelial cells into an elongated tube, which is the process of neural tube formation that will become the spinal cord and brain, occurs during days 18–27 (Colas and Schoenwolf 2001). Rostral to Hensen's node, the ectoderm that covers the notochordal process is initially thickened to form the neural plate. The edges of the neural plate are heaped to create the neural folds and the midline neural groove. Changes occur first in the middorsal region of the embryo, the site of the future cervical cord, and continue to caudal. Here, fusion of the opposing neural folds and subsequent formation of the neural tube occurs at the hindbrain–spinal cord junction. This event requires several days and must be coordinated simultaneously at the rostral and caudal ends. Closure of the neural tube takes 4–6 days. After closure of the neural folds, both ends temporarily remain open and are called neuropores (O'rahilly and Müller 2002). Closure of the neural groove begins initially at the region of the third or fourth somite, the future cervicomedullary junction, and continues both rostrally and caudally at the same time. Rostrally and caudally, the cavity of the developing neural tube communicates via the rostral and caudal neuropores with the amniotic cavity.

At days 24–25, the neural tube completes its rostral closure at the anterior neuropore within a few hours, which becomes the site of the lamina terminalis for the development of the brain vesicle. On days 26–27, caudal closure of the neural tube occurs at the posterior neuropore, corresponding to the L1/L2 segment of the spinal cord. The closure of the neural tube in human embryos is generally described as a continuous process that begins at the level of the future cervical region, and proceeds both rostrally and caudally. This process of neural tube closure and extension of the spinal cord to S4/S5 is called *primary neurulation*. Primary neurulation leads to the formation of all spinal cord segments and ganglia. The more caudal cord segments do not develop by neurulation but later by the process of canalization. Unlikely more rostral elements of the spinal cord, the conus medullaris and the film terminals form through the process of secondary neurulation. *Secondary neurulation* is the continuing formation of the sacrocaudal part of the spinal cord without direct involvement of the surface ectoderm, i.e., without the intermediate phase of a neural plate (O'Rahilly and Müller 2006). The rostral neuropore closes completely at about 30 days within a few hours, and caudal neuropore about 1 day later. An opening in the central canal of the tube, the posterior neuropore, is normally closed by this time. The median and lateral hinge points are necessary for proper folding and closing of the neural tube, and a number of neural tube closure defects along the embryo can lead to abnormalities in the spinal cord. Depending on the position of the defect, it can range from

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anencephaly to craniorachischisis, lumbosacral spina bifida, or spinal dysraphism and encephalocele (Copp and Greene 2013; Greene and Vopp 2014). At the cranial and spinal level, four main types of neural tube defects are found: (1) the neural plate remains open (anencephaly and myeloschisis, respectively); (2) the neural tube is exteriorized (encephalomeningocele and myelomeningocele); (3) only meninges are exteriorized (cranial and spinal meningoceles); and (4) only a skeletal defect is evident (cranium bifidum occultum and spina bifida occulta) (ten Donkelaar et al. 2014a; O'Rahilly and Müller 2002). For details on neurulation in human development, please refer to Chap. 2.

18.1 Spina Bifida and Myelomeningocele

Spinal dysraphism refers to a congenital neural tube defect caused by failure of fusion of the midline mesenchymal, bony, and neural structures as common features. Four main types of spina bifida occur, characterized by the following: (1) the neural plate remaining open (myeloschisis or myelocele); (2) the neural plate or tube being exteriorized (myelomeningocele), almost always associated with a Chiari II malformation; (3) only meninges protruding (meningocele); and (4) merely a skeletal defect being evident (spina bifida occulta) (ten Donkelaar et al. 2014a) (Fig. 18.1). Myeloceles (myeloschisis) and myelomeningoceles are the two commonest forms of spina bifida aperta, and appear to result from deranged neurulation. In both myeloceles and myelomeningoceles, epithelial cells may grow inward from the skin around the midline defect to cover the membranes and even the neural tissue. Failure of the caudal end of the neural tube to close can result in a severe form of spina bifida called myelomingocele involving both spinal cord and meninges, which accounts for more than 90% of open spinal dysraphisms and is associated with neurological defects (Liptak and Dosa 2010). Myelomeningocele occurs mainly in the lumbar region and is almost always accompanied by the Chiari II malformation (ten Donkelaar et al. 2014a). Spina bifida occulta is a defect in one or more vertebral arches occurring without herniation of neural or meningeal structures through the mesenchymal defect.

18.1.1 Epidemiology

Incidence of myelomeningocele appears to be decreasing not only in the United States but worldwide. Possible causes include increased folic acid intake in women of childbearing age, mandatory fortification of cereal products, as well as an extensive screening and voluntary cessation. In the United States, the rate of myelomeningocele is estimated at just under 2/1000 births, although there are some geographical variations.

Myelomeningocele and other neural tube defects are due to failure of neural tube closure during the third and fourth weeks of gestation. Genetic and environmental factors are believed to be involved. People with a family history are at increased risk. Most children with myelomeningocele are born in families without children already affected, but the risk of recurrence increases by 2–5% in a child affected and 10–15% in two affected children. If a parent has spina bifida, the risk of having a child of the same condition is 4%. The etiology of myelomeningocele is related to several environmental factors, including folic acid deficiency, exposure to certain drugs during early pregnancy including carbamazepine and valproate, occupational exposure to certain solvents, and maternal diabetes.

18.1.2 Prevention

It is recommended that all women who may become pregnant take 0.4 mg of folic acid daily. Women who have already had an affected pregnancy should take higher amounts from 1 month before pregnancy until the end of the first trimester of pregnancy. Prenatal screening includes the serum α-fetoprotein test in the mother between

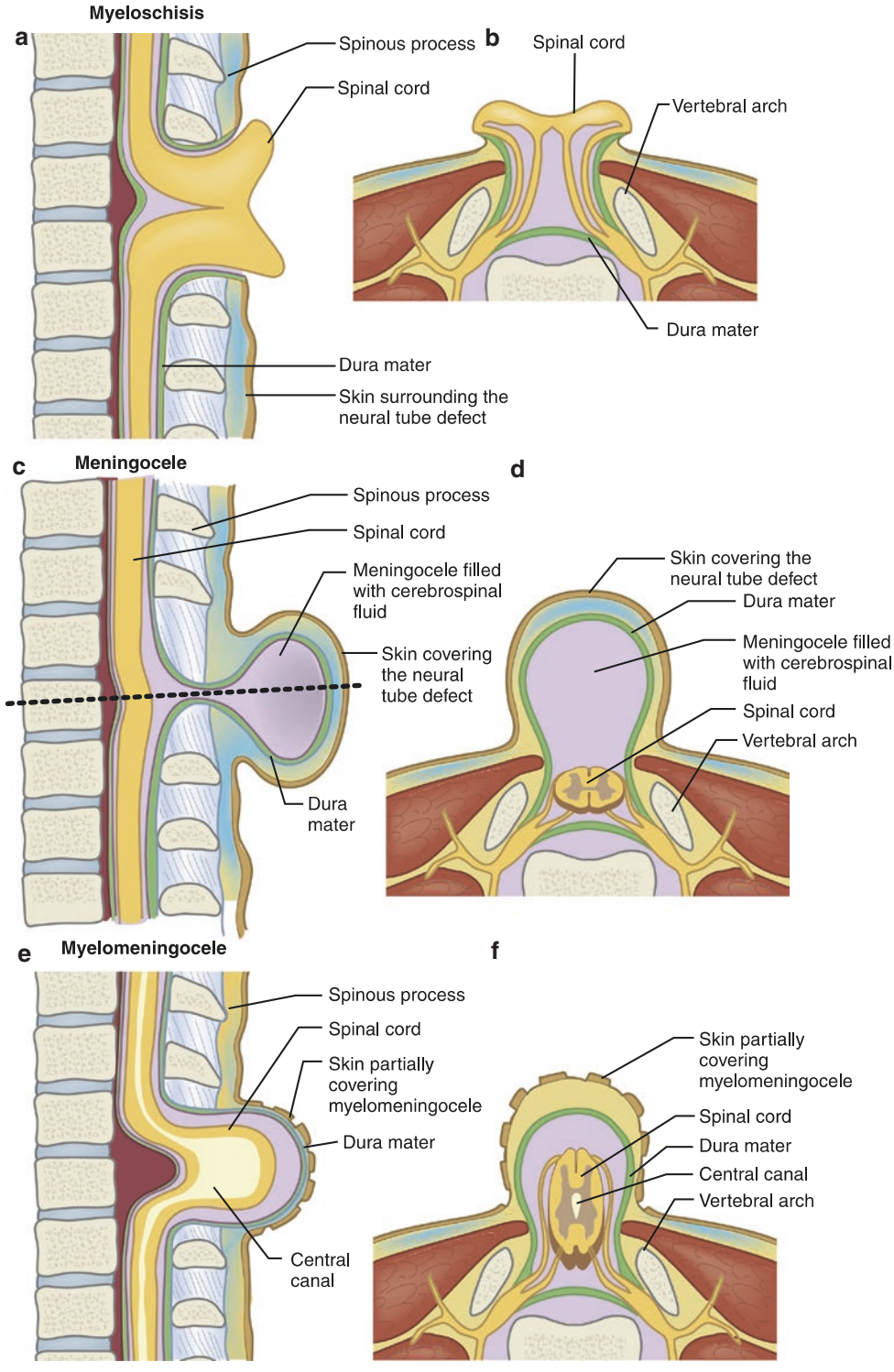

Fig. 18.1 Spinal neural tube defects. Myeloschisis, sagittal (**a**) and axial (**b**); meningocele, sagittal (**c**) and sagittal (**d**); myelomeningocele, sagittal (**e**) and axial (**f**). From Sundar et al. (2022), with permission

the 16th and 18th weeks of gestation. A high-level ultrasound can confirm the diagnosis in most cases (Shaer et al. 2007). In a small percentage, where it is impossible to obtain good images to make a definitive diagnosis, amniocentesis can be used to test the levels of α-fetoprotein in the amniotic fluid. Once the diagnosis is made, genetic counseling and a discussion of management options should be made.

18.1.3 Clinical Presentation

Myelomeningocele has a direct or indirect effect on many body systems (Liptak and Dosa 2010). The most common site of primary neural defect is the lumbosacral spine, at approximately 70%. To prevent infection, defects should be closed early within 72 h of delivery (Hudgins and Gilreath 2004). Associated neurological problems include hydrocephalus, hydromyelia or syringomyelia, tethered cord syndrome, and Chiari II malformation. Neurological deficits depend on the site of the defect and include motor, sensory, bowel, and bladder dysfunction. Deficits associated with primary myelomeningocele are static at birth and no longer progress (Roy et al. 2011; Sandler 2010; Yamada et al. 2004a, b).

18.1.4 Transition to Adult

About 80% of people with myelomeningocele survive to adulthood. Persistent problems in adulthood include late neurological changes, overuse musculoskeletal injuries, pathological fractures, and persistent urological complications (Liptak and El Samra 2010; Liptak et al. 2013). Interest in relationships with sexual and reproductive health is important from adolescence. Sexually active women with myelomeningocele should take 4 mg daily with a higher dose of folic acid than recommended. Problems related to employment and independent living generally need to be resolved. Regular preventive healthcare and management of unrelated medical issues must be integrated into ongoing primary care.

18.2 Chiari Malformation

18.2.1 Classification

Chiari malformations are abnormalities of the development of the hindbrain characterized by a displacement of the caudal part of the cerebellum and, in some cases, the lower brainstem in the cervical spinal canal by the foramen magnum (Table 18.1). They are classified according to the parts of the hindbrain protruding into the spinal canal and the associated anatomic anomalies. The type I Chiari malformation is accompanied by a herniation of the cerebellar tonsils below the foramen magnum (Fig. 18.2) and displaced into the upper cervical canal, and is the most common form. Syringomyelia is present in more than 30% of type I Chiari malformations. Type II malformation is also known as Arnold-Chiari malformation. Type II involves displacement and deformation of both the cerebellum vermis, pons, medulla, and an elongated fourth ventricle displaced caudal wards into the cervical canal (ten Donkelaar et al. 2014a). Type II is due to a space conflict between the hypoplastic basicraniocervical mesoderm and the developing hindbrain and spinal cord (Hori 1998). Type II Chiari malformation is usually associated with myelomeningocele. Hydrocephalus is more common with type II malformation than type I malformation (Fig. 18.3). While it is possible that disturbance of the cerebrospinal fluid (CSF) flow and abnormalities in CSF pressure may be the cause of syringomyelia, the exact mechanism underlying syringomyelia is not clear. The syrinx is often located in the mid-cervical region but can extend caudally or rostrally (Sekula et al. 2011). Type III is very rare and includes an occipitocervical or high cervical bony defect with herniation of cerebellum into the encephalocele. Type IV is a form of cerebellar hypoplasia.

18.2.2 Clinical Presentation

Type I Chiari malformation may remain asymptomatic. Insidious symptoms may appear in adolescence or adulthood. The clinical evolution is

Table 18.1 Chiari pathological classification and new radiological variants

Chiari	Description	Association
I	Herniation of the cerebellar tonsils 5 mm below the foramen magnum	Association with craniosynostosis, skull base anomalies, and craniocephalic mismatch
II	Herniation of the cerebellar vermis and fourth ventricle Low-lying tentorium with low torcula Occipital lobe often posterior to cerebellum	Associated with myelomeningocele, defect, hydrocephalus, syringomyelia, and neurological deficits
III	Cerebellum, brainstem, fourth ventricular herniation with occipital or occipito-cervical meningoencephalocele	Most serious form of Chiari malformation. Hydrocephalus may be present. Severe neurological deficits, incompatible with survival
IV	Cerebellar hypoplasia, fourth ventricle communicates with cisterna magna, no hindbrain hernia	Dandy-Walker-type malformation
Proposed new variants		
0	Patients with headaches and other symptoms of Chiari malformation or syringomyelia and no tonsillar hernia or tonsillar hernia less than 3 mm	Abnormal CSF flow at the posterior fossa or foramen magnum as the suspected cause for syringomyelia
1.5	A Chiari is seen in combination with brainstem herniation through the foramen magnum	Obex below the foramen magnum. Flat medulla oblongata. Mean backward angulation of the odontoid process in relation to the C2 body was 84°. Fifty percent have syringomyelia. Patients may not respond well to posterior fossa decompressive surgery especially if syringomyelia is present

From Flint and Rusbridge (eds) (2014), with permission

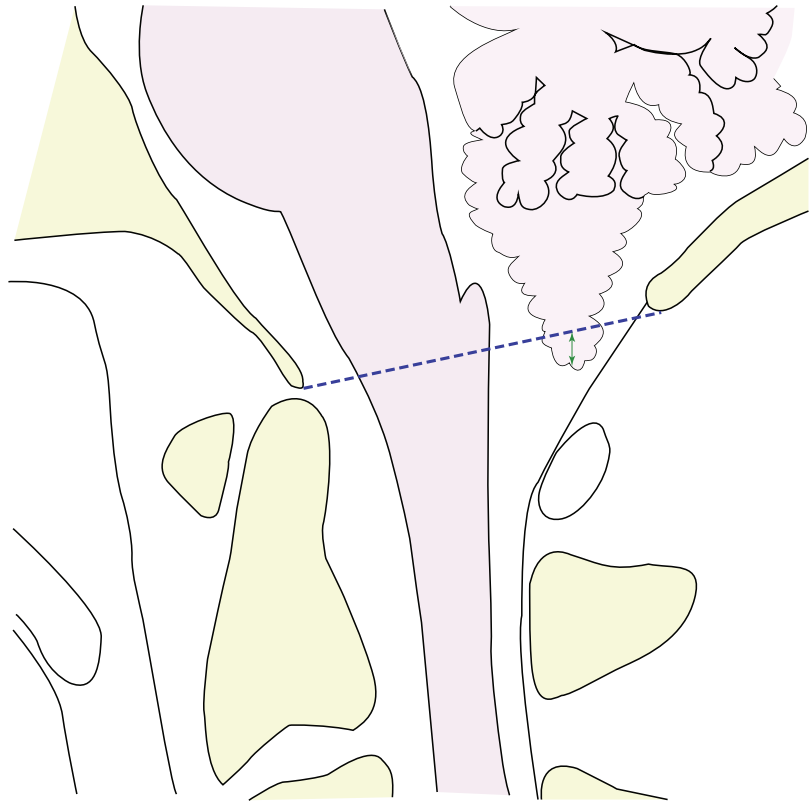

Fig. 18.2 Cerebellar tonsillar herniation. Cerebellar tonsillar position is the vertical distance (green arrows) from the tip of the cerebellar tonsils to a line drawn between the anterior and posterior rims of the foramen magnum (McRae line, dotted blue line). It is normal for the tonsils to be above the McRae line

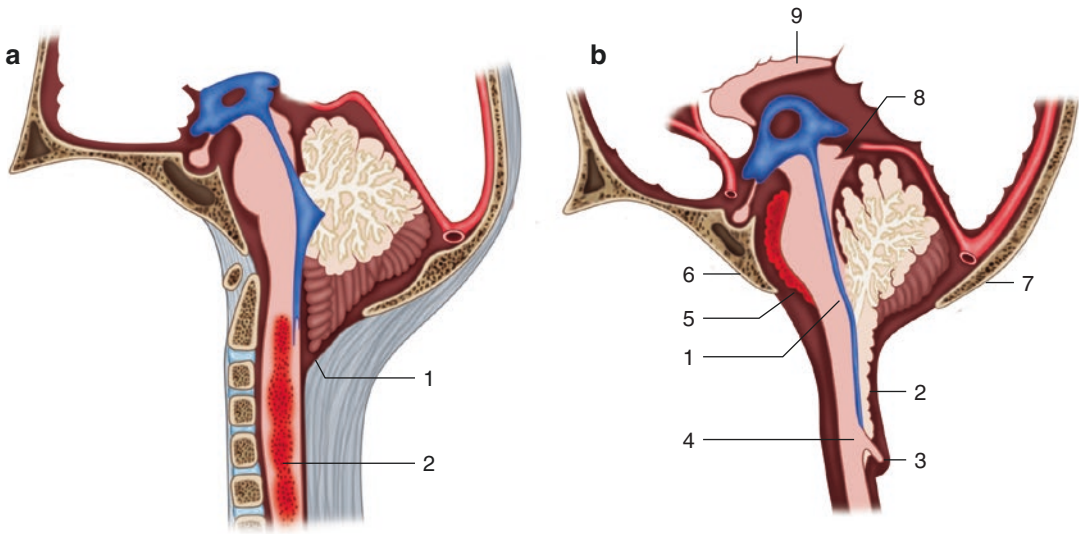

Fig. 18.3 A Chiari I (**a**) and a Chiari II (**b**) malformation. (**a**) Pointed, low-lying tonsils (1) and syringomyelia (2) are found. (**b**) An elongated, tube-like fourth ventricle (1), an inferior displaced vermis (2), a medullary spur (3), and a medullary kink (4) are found. The cerebellar hemispheres "creep" around the brain stem (5). Moreover, there is a concave clivus (6), a low-lying confluens sinuum (7), "beaked" colliculi (8), and partial callosal agenesis (9). From ten Donkelaar et al. (2014), with permission

variable and unpredictable. Type II malformations are often present in infancy or early childhood and are one of the leading causes of death in infancy or in childhood with myelomeningoceles.

In type I Chiari malformation, neck pain and occipital headache are common initial symptoms and may be exacerbated by activity, stooping, Valsalva maneuver, and sneezing or coughing. A Chiari malformation can occur even without syrinx, probably due to compression or stretching of cervical roots. Painful or burning pain in the neck, shoulder, and arm, often asymmetrical and often on the edge of sensory impairment, is common in patients with syringomyelia (Saletti et al. 2011). The classic presentation of syringomyelia is a dissociated sensory loss of pain and temperature sensation with preserved touch and vibration in a cape distribution on the neck, shoulders, and arms. In most cases, it begins asymmetrically and can cause injuries or burns to the hand due to impaired sensation. The extension of syrinx in gray matter can lead to muscle weakness and loss of reflexes in the upper extremities. As a result, deformation of the hand by the claw hand deformity can occur. The gradual expansion of the syrinx and the compression of the spinal cord of the white matter can lead to spastic paralysis of the legs, bladder and bowel dysfunction, and Horner's syndrome. Horner's syndrome is due to lesions involving descending sympathetic pathways or cells in the T1 and T2 intermediolateral column.

Syringobulbia due to extension of the syrinx in the brainstem with involvement of the cranial nerve can cause dysarthria, dysphagia, nystagmus, dizziness, and tongue atrophy. When two disorders coexist, it may be difficult to isolate symptoms and signs caused by the Chiari malformation, such as nystagmus, ataxia, vertigo, dizziness, and head and neck pain, from the symptoms by the syrinx (Saletti et al. 2011). Children with syringomyelia often develop progressive scoliosis, although this rarely occurs in adults because of skeletal maturity. In some cases, craniovertebral abnormalities may occur, for example, Klippel-Feil anomaly with fusion of C2 and C3 vertebrae and a short neck and a low hairline on examination (deSouza et al. 2011).

18.2.3 Diagnosis

The diagnosis of Chiari malformation is confirmed by MRI, which shows displacement of the cerebellum. The entire spinal cord must be imaged to identify and define the extent of associated syringomyelia. The signal from the syrinx is generally similar to that of CSF unless it is loculated and contains proteinaceous material or blood degradation material.

18.2.4 Management

For symptomatic patients, surgical decompression of the posterior fossa for the Chiari tonsillar herniation with suboccipital craniectomy, with or without duraplasty and cervical laminectomy, is indicated. The syrinx shunt, although often unpredictable, may improve or stabilize the neurological deficit in some patients, and the additional benefit of this procedure is unclear. If hydrocephalus is present, a shunt should be placed before treating syrinx (Dicianno et al. 2008).

18.3 Caudal Dysgenesis

Diseases of the caudal spinal cord are known to result from disturbed canalization and retroprogressive differentiation disorders, which include the tight filum terminale syndrome, lipoma of the filum terminale, terminal syringomyelia, caudal spinal anomalies, anterior sacral meningocele, and sacrococcygeal teratoma (Naidich et al. 1996). Tight filum terminale syndrome is caused by failure of complete involution of the spinal cord. Lipoma of the filum terminale results from the persistence of caudal cells that differentiate into fat cells, found in 4–6% of normal adults. The progressive expansion of the terminal ventricle leads to terminal syringomyelia, which affects up to 30% of patients with occult spinal dysraphism. Caudal spinal anomalies are associated with anorectal and urogenital malformations, such as the OEIS complex (omphalocele, exstrophy of the bladder, imperforate anus, and spinal anomalies) and the caudal regression syndrome, for which the common term caudal dysgenesis can be used. Anterior sacral meningoceles are diverticula of the thecal sac that protrude anteriorly into the retroperitoneal retrorectal space (Naidich et al. 1996; ten Donkelaar et al. 2014a).

18.4 Ascensus Medullae

Until the 11th gestational week, the length of the spinal cord corresponds to that of the vertebral column. Then, the “ascensus” begins, the filum terminale is formed and the lower spinal nerves show a progressive inclination, which is caused by the shift between the spinal cord and the vertebral column. It ascends to lumbar levels due to the disproportional growth of the spinal cord and the vertebral column. Finally, the lower spinal roots form the cauda equina. In newborns, the spinal cord terminates at the level of L3 vertebra, and in adults it usually ends at the level of L1 or L3 vertebra (Fig. 18.4).

Developmental disorders of abnormal “ascensus” can lead to a tethered spinal cord. Tethered cord syndrome is usually reserved for lumbosacral defects in which there are variable combinations of thickening of the filum terminale, low or dilated conus medullaris, spinal lipoma, dermoid cyst, split cord, hydromyelia, and sacral agenesis. Neurological symptoms associated with tethered cord syndrome increase in severity with age and patients are often treated by untethering the spinal cord (ten Donkelaar et al. 2014b).

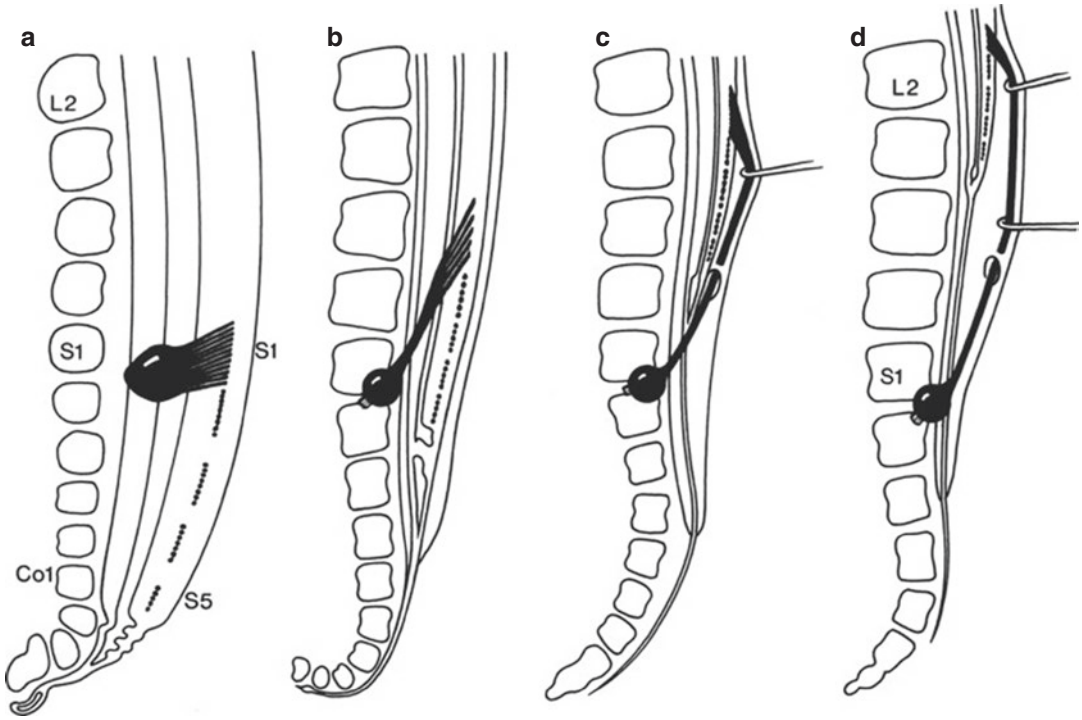

Fig. 18.4 Ascensus medullae: (**a**–**d**) four successive stages in the development of the caudal end of the human spinal cord showing the formation of the filum terminale and the progressive obliquity of the first sacral root. From ten Donkelaar et al. (2014b), with permission

References

Colas JF, Schoenwolf GC. Towards a cellular and molecular understanding of neurulation. Dev Dyn. 2001;221:117–45.

Copp AJ, Greene ND. Neural tube defects-disorders of neurulation and related embryologic processes. Wiley Interdiscip Rev Dev Biol. 2013;2:213–37.

deSouza RM, Zador Z, Frim DM. Chiari malformation type I: related conditions. Neurol Res. 2011;33:278–84.

Dicianno BE, Kurowski BG, Yang JM, et al. Rehabilitation and medical management of the adult with spina bifida. Am J Phys Med Rehabil. 2008;87:1027–50.

Greene ND, Vopp AJ. Neural tube defects. Annu Rev Neurosci. 2014;37:221–42.

Hori A. Developmental anomalies of the spinal cord. Neuropathology. 1998;18:433–43.

Hudgins RJ, Gilreath CL. Tethered spinal cord following repair of myelomeningocele. Neurosurg Focus. 2004;16:E7.

Liptak GS, Dosa NP. Myelomeningocele. Pediatr Rev. 2010;31:443–50.

Liptak GS, El Samra A. Optimizing health care for children with spina bifida. Dev Disabil Res Rev. 2010;16:66–75.

Liptak GS, Garver K, Dosa NP. Spina bifida grown up. J Dev Behav Pediatr. 2013;34:206–15.

Naidich TP, Zimmerman RA, McLone DG, et al. Congenital anomalies of the spine and spinal cord. In: Atlas SW, editor. Magnetic resonance imaging of the brain and spine. 2nd ed. New York: Lippincott-Raven; 1996.

O'rahilly R, Müller F. The two sites of fusion of the neural folds and the two neuropores in the human embryo. Teratology. 2002;65:162–70.

O'Rahilly R, Müller F. The embryonic human brain: an atlas of developmental stages. 3rd ed. Hoboken: Wiley; 2006.

Roy AK, Slimack NP, Ganju A. Idiopathic syringomyelia: retrospective case series, comprehensive review, and update on management. Neurosurg Focus. 2011;31:E15.

Saletti V, Esposito S, Frittoli M, et al. Neurological pictures in paediatric Chiari I malformation. Neurol Sci. 2011;32(Suppl 3):S295–8.

Sandler AD. Children with spina bifida: key clinical issues. Pediatr Clin N Am. 2010;57:879–92.
Sekula RF Jr, Arnone GD, Crocker C, et al. The pathogenesis of Chiari I malformation and syringomyelia. Neurol Res. 2011;33:232–9.
Shaer CM, Chescheir N, Schulkin J. Myelomeningocele: a review of the epidemiology, genetics, risk factors for conception, prenatal diagnosis, and prognosis for affected individuals. Obstet Gynecol Surv. 2007;62:471–9.
Sundar SJ, Volovetz J, Recinos VM. Spinal cord dysraphism and myelodysplasia. In: Steinmetz MP, Berven SH, Benzel EC, editors. Benzel's spine surgery. 15th ed. Philadelphia: Elsevier; 2022.
ten Donkelaar HJ, Bekker M, Renier WO, et al. Neurulation and neural tube defects. In: In: ten Donkelaar HJ, Lammens M, Hori A., editor. Clinical neuroembryology: development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014a.
ten Donkelaar HJ, Itoh K, Horn A. Development and developmental disorders of the spinal cord. In: ten Donkelaar HJ, Lammens M, Hori A, editors. Clinical neuroembryology: development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014b.
Yamada S, Siddiqi J, Won DJ, Kido DK, et al. Symptomatic protocols for adult tethered cord syndrome. Neurol Res. 2004a;27:741–4.
Yamada S, Won DJ, Yamaga SM. Pathophysiology of tethered cord syndrome: correlation with symptomatology. Neurosurg Focus. 2004b;16:E6.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.
Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.
Crossman A, Neary D. Neuroanatomy: an illustrated colour test. 5th ed. Philadelphia: Elsevier; 2015.
Felten DL, O'Banion MK, Maida MS. Netter's atlas of neuroscience. 3rd ed. London: Elsevier; 2016.
Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.
Mai JK, Paxinos G, editors. The human nervous system. 3rd ed. London: Elsevier; 2011.
Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.
Noback CR, Strominger NL, Demarest RJ, et al. The human nervous system: structure and function. 6th ed. Totoma: Humana Press; 2005.
ten Donkelaar HJ, Lammens M, Hori A. Clinical neuroembryology: development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014.
Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.
Vogel LC, Zebracki K, Betz RR, et al., editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.

19 Cauda Equina and Conus Medullaris Injuries

The length of the spinal cord corresponds to that of the vertebral column up to the 11th gestational week. Then, the "ascensus" begins, the filum terminale is formed, and the lower spinal nerves show a progressive obliquity, which is caused by the shift between the spinal cord and the vertebral column. It ascends to lumbar levels due to the disproportional growth of the spinal cord and the vertebral column, forming the cauda equina. In newborns, the spinal cord terminates at the level of L3 vertebra, and in adults, it usually ends at the level of L1 or L3 vertebra. The most common location for the termination of the conus medullaris is the L1–L2 disc space. No clear anatomical landmark defines the rostral extent of the conus medullaris. The part of the spinal cord that is immediately rostral to the conus medullaris is called the epiconus. The conus medullaris is condensed to less than two vertebral heights. The conus medullaris is located from the T12–L1 intervertebral disc space to the L1–L2 intervertebral disc space. Within this short distance, approximately ten spinal cord segments, L1–S5, are concentrated in the conus medullaris and are not in close spatial relationship to the respective vertebrae (Kapetanakis et al. 2017). The spinal cord begins to taper at the T12–L1 disc space, and the L1–L5 nerve roots form a peripheral rim. Only 10–15% of the spinal cord (conus medullaris) remain uncovered by the nerve roots at this level. The lumbar sympathetic, sacral parasympathetic, and lumbar and sacral somatic nerves also originate from the conus medullaris (Kingwell et al. 2008).

Caudally, at the L1–L2 disc space, the lumbar and sacral nerve roots are oriented lateral to medial, L2 roots most lateral and S4–S5 roots most medial, and the dorsal and ventral roots move together. Anatomically, the cauda equina is defined as a bundle of the spinal roots that is located below the tip of the conus medullaris around the filum terminale (De Vloo et al. 2016) (Fig. 19.1). During development, the bony structures of the vertebrae grow from the rostral to the caudal regions, and the spinal cord segments of the lumbar and sacral spinal nerve roots are located above the position of the corresponding intervertebral foramen emerging from the spinal canal. The nerve roots of L2–S5 and coccygeal nerve travel long down to the corresponding intervertebral foramen, resulting in a bundle of multiple lumbar and sacral spinal nerve roots on both sides (Tarulli 2015). The cauda equina includes ascending and descending L2–L5 segments, S1–S5 segments, and coccygeal segments, all within the thecal sac before and after entering and exiting the conus medullaris and their respective neural foramen. The lumbosacral nerve roots belonging to the cauda equina regulated the motor nerves of the myotomes of L2–S2, the sensory nerves corresponding to L2–S3 in the legs, and the bladder function through the pelvic nerve from S2–S4, the external urethral sphincter control through the pudendal nerve from S2–S4, the

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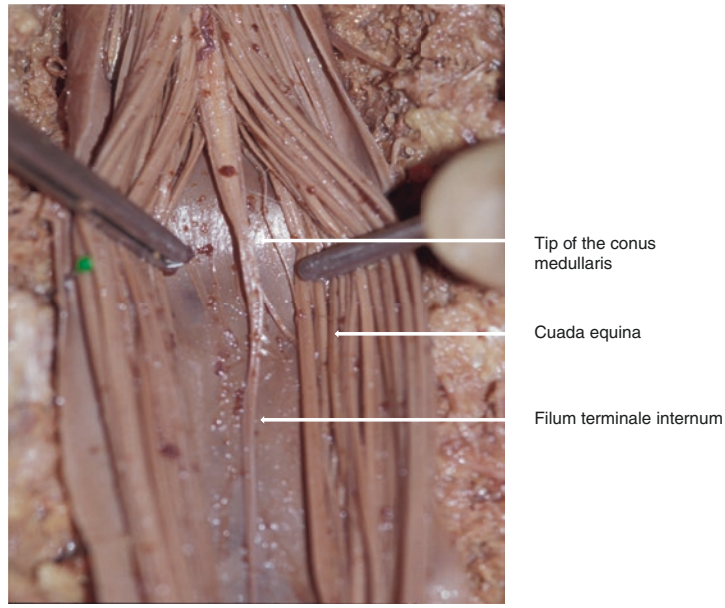

Fig. 19.1 Cauda equina, conus medullaris, filum terminale

sensory perception of the perineum, and the external genital area through by the pudendal nerves of S2–S4 (Chuang et al. 2001; Goodman 2018).

The neurological structures associated with traumatic cauda equina and conus medullaris injuries, which are resulted from the thoracolumbar spine injuries, differ significantly from those structures that are injured in cervical and thoracic spinal cord injuries. As the thoracolumbar spine is also where the distal spinal cord or epiconus, conus medullaris, and cauda equina are in close proximity, management decisions and prognosis should consider the unique variation in the injured neuroanatomical structures (Kingwell et al. 2008). It is unlikely that the cervical and the majority of the thoracic spine where the spinal column level and the neurological segment are in close proximity, in the thoracolumbar region, there is a profound disparity between the spinal column level and the spinal cord segment. Injuries of the cauda equina and conus medullaris are generally clinically not clearly distinguishable and are often described together, since they often occur as combined injuries (Kingwell et al. 2008). The clinical features and presentation of the epiconus, conus medullaris, and cauda equina lesions are summarized in Table 19.1.

The pure cauda equina syndrome (lesion) resulted from damage of the nerve roots traveling caudal to the conus medullaris to their neuroforaminal exits leaving the spinal canal has a typical neurological level of injury below L2 with more asymmetrical sensorimotor deficit affecting the L5 and S1 myotomes predominantly. There is an atonic bladder with flaccid sphincter tone, which is often indistinguishable from a neurogenic bladder/bowel dysfunction in conus medullaris syndrome (Hoang and Havton 2006; Kingwell et al. 2008; Lawson et al. 2014). Lesions on the conus medullaris, which damage the conus medullaris itself, lead to a neurological level of injury between T12 and S4–S5, that usually shows symmetrical sensorimotor deficits, flaccid muscle tonicity, and areflexic bladder with flaccid anal sphincter. All muscles of the lower extremity and sensory function up to the dermatomes of the lowest sacral segment may be affected. However, conus medullaris syndrome may present with upper motor neuron lesion signs in the lower extremities when the upper conus medullaris is injured (Kennedy et al. 1999; Kingwell et al. 2008). The epiconus lesion is above the T12 vertebral level and is present as upper motor neuron type spinal cord injury over time. Regarding the neurological level of injury,

Table 19.1 Clinical features of the epiconus, conus medullaris, and cauda equina lesions

Neurological syndrome	Neurological level of injury	Clinical examination	Bladder, bowel, sexual function
Epiconus	Above T12	UMN lesion type Intact conus medullaris segment Preserved lower sacral reflexes (BCR, anal reflex) Increased leg muscle tonicity	UMNL type bladder and bowel dysfunction Preserved reflexogenic erection, loss of psychogenic erection
Conus medullaris	T12-L1 to S4-5	LMN lesion type Damage of conus medullaris Absent lower limb and sacral reflexes, but can preserve in high conus lesion More often symmetrical motor weakness Leg muscle flaccidity with atrophy Saddle pattern sensory abnormality Less favorable recovery	LMNL type bladder and bowel dysfunction Loss of reflexogenic erection, preserved psychogenic erection
Cauda equina	Below L2	LML lesion type Reflexes depending on level of injury Variable motor weakness, relatively asymmetrical over conus medullaris lesion Variable sensory deficit More favorable recovery	LMNL type bladder and bowel dysfunction Loss of reflexogenic erection, preserved psychogenic erection

Adapted from Kingwell et al. (2008)

the neurological level of injury above T10 tends to show upper motor neuron type syndrome, while the neurological level of injury below T12 presents as flaccid paralysis in the lower extremities. The neurological lesion between T10 and L1 represents a mixed zone with signs of upper and lower motor neuron lesion according to the segments (McCarthy et al. 2007).

19.1 Cauda Equina Lesion

The clinical manifestations of a cauda equina lesion are variable and can cause pain, weakness, sensory loss, and bladder and bowel impairment. Understanding these potential clinical features and understanding the limits of clinical examination are critical in establishing a diagnosis of cauda equina syndrome. The term cauda equina syndrome is only used when there is impairment of the bladder, bowel, or sexual function in conjunction with sensory loss in the saddle or perineal areas (Goodman 2018; Lavy et al. 2009). The potential for other symptoms, such as back pain, lower limb sensory loss, lower limb weakness, and abnormal lower limb reflexes, is recognized but is not required for the diagnosis of cauda equina syndrome.

19.1.1 Development and Anatomical Features of the Cauda Equina

The ventral and dorsal roots beneath the conus medullaris around the filum terminale form the cauda equina. The most common location of the distal end of the conus medullaris is the L1–L2 intervertebral disc, which is usually located between the T12–L1 disc space and the middle of the L2 vertebral body. However, it should be considered that there are large differences in the location from the T11–T12 intervertebral disc space to the L4 vertebra body. Development of the cauda equina begins shortly after the postsomite phase, at the beginning of the third month of 3 months of gestation. This is the time when the developing spinal cord fills the entire spinal canal to the coccyx (Orendácová et al. 2001). The bones and cartilage of the vertebrae then grow faster than the spinal cord (Hertzler 2nd et al. 2010). The difference in growth rate between the spinal canal and the spinal cord leads to a gradual

increase in the obliquity of the nerve roots, with the exception of the upper cervical vertebrae. The lumbar and sacral nerve roots run almost vertically in the subarachnoidal space and reach the corresponding intervertebral foramen. The nerve root bundle running in the vertical direction in the lower part of the conus medullaris forms a cauda equina (Lavy et al. 2009).

MRI and contrast-enhanced CT make it possible to visualize the cauda equina nerve roots at each disc level in the thecal sac. For example, the nerve roots show a crescentic pattern at the level of the L5–S1 intervertebral disc. The nerve roots are visible in the thecal sac, with the S1 root anterior and lateral. At the L4–L5 intervertebral level, the L5 root is situated anterolaterally, displacing the S1 root. The lower sacral roots are positioned posteriorly (Orendácová et al. 2001; Ridley et al. 2018) (Fig. 19.2). The axial images of the upper lumbar region, the more nerve roots are displayed on the image, fill the thecal sac, and the arrangement of the nerve roots appears complicated. However, the arrangement pattern of the nerve roots, ventral roots, and dorsal roots is the same

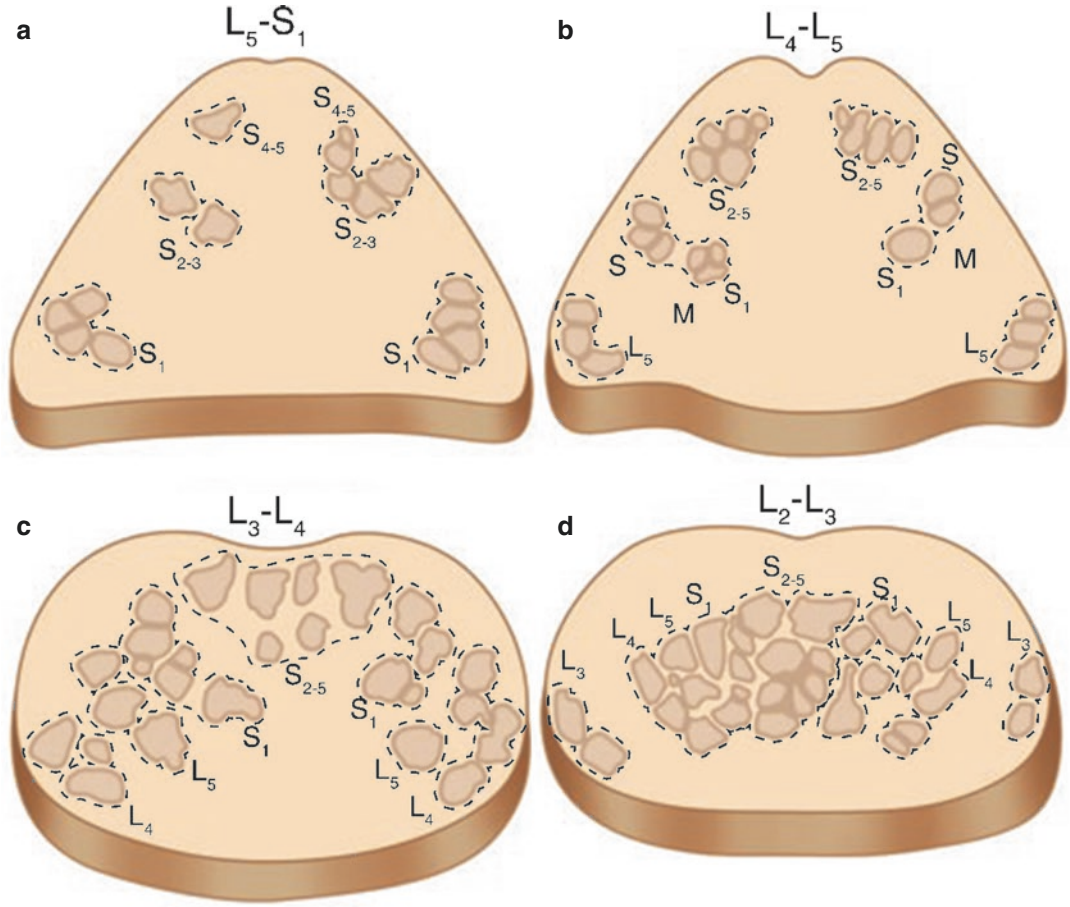

Fig. 19.2 Anatomical diagrams of the cauda equina on CT scans and MRI. (**a**) L5-S1 intervertebral level. The S1 root is anterior and lateral. (**b**) L4-L5 intervertebral level. The L5 root is anterolateral and displaces the S1 root. The lower sacral roots are positioned dorsally. (**c**) L3-L4 intervertebral level. Although the anatomy is more crowded, the motor bundles (M) of the L4, L5, and S1 nerve roots are visible anterior and medial to their corresponding multifascicular sensory bundles (S). (**d**) L2-L3 intervertebral level. The roots occupy most of the thecal sac at this level, with the motor bundle anterior to its sensory bundle of each root. From Orendácová et al. (2001), with permission

(Cohen et al. 1991; Wall et al. 1990). The area of the ventral roots is half of the dorsal roots. Although there are differences depending on the individual, the S1 nerve root has the largest ventral and dorsal root (Mauffrey et al. 2008; McNamee et al. 2013; Monajati et al. 1987).

19.1.2 Arterial Vasculature of the Cauda Equina

Although the vascular anatomy of the caudal spinal structure has many similarities with the other segmental levels, this elongation forms the basis of the characteristic vascular anatomy in this region. The arterial supply to the extradural cauda equina nerve roots can be divided into the L1–L4 region and L5 to sacrococcygeal region. In the L1–L4 region, the corresponding lumbar arteries form the radicular artery of the cauda equina as in any other segment level. The arterial supply to the L1–L4 region is similar to the cervical and thoracic spinal nerve root arterial anatomy. In the L5 and sacrococcygeal region, the arterial supply also follows the segmental distribution. However, the rich anastomosis in this area gives wide diversity to the vascular pattern in this area. The arterial supply to the cauda equina nerve roots depends on the hemodynamic balance between the middle sacral, iliolumbar, and lateral sacral arteries (Namba 2016) (Fig. 19.3).

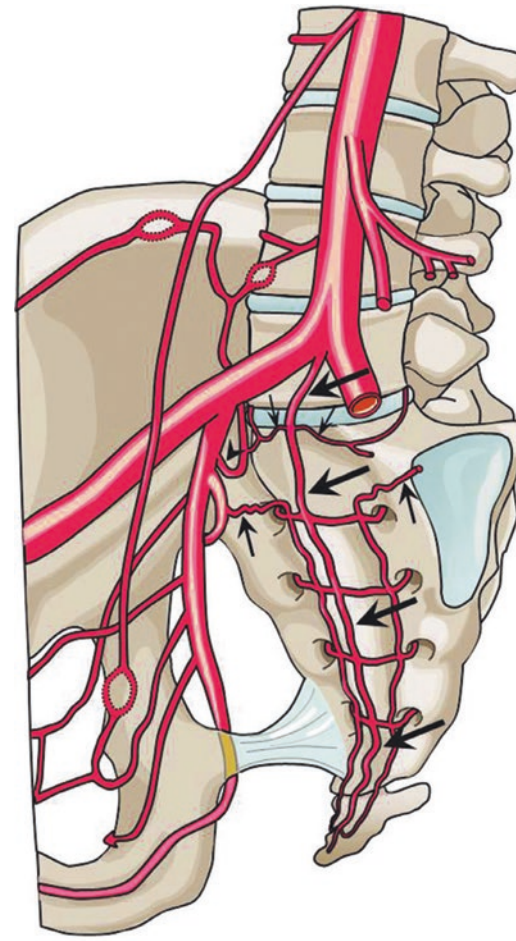

Fig. 19.3 Extradural arterial supply to the lumbosacral and coccygeal spinal structures. The middle sacral artery (large arrows) gives rise to a pair of the lowest lumbar artery (small arrows), which is the L5 segmental artery. A branch of the iliolumbar artery (arrowhead) may also supply the L5 region. The size of this vessel is inversely proportional to the development of the lowest lumbar artery. The spinal structures within the sacral vertebral body are usually supplied by the branches of the lateral sacral arteries (arrows), which run medial to the anterior sacral foramen. The branches of the sacral artery form numerous anastomoses with the lateral branches of the medial sacral artery. From Namba (2016)

The anterior and posterior radicular arteries penetrate the superolateral aspect of the dural sheath of each lumbar and sacral spinal nerve just proximal to its dorsal root ganglion. They run continuously along the respective anterior and posterior nerve filaments of the cauda equina to connect arteries on the surface of the spinal cord. The anterior radicular arteries run cranially and eventually connect with either the anterior spinal artery or the adjacent vasa corona. In a similar way, the posterior radicular arteries are connected cranially with the posterior spinal artery or the vasa corona (Fig. 19.4). In the anterior roots of the lumbosacral region of the spinal cord, the one or two anterior medullary feeder arteries (radiculomedullary) carried the afferent flow to the anterior spinal artery. From the plexus of the vasa corona, the emerging anterior root fibers received true radicular arteries, which supplied a proximal one-third of each root. The distal two-thirds are then supplied by radicular arteries ascending from the respective segmental sources to anastomose with their superior complement. In the posterior roots, the distinction between the medullary

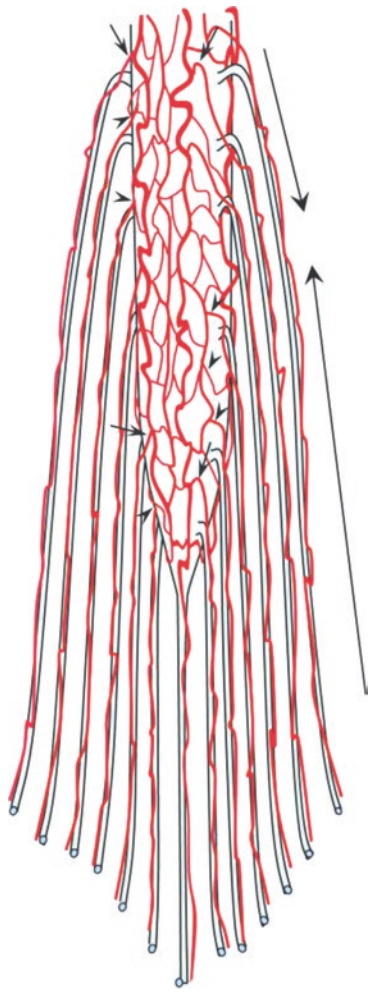

Fig. 19.4 Arterial anatomy of the cauda equina and conus medullaris. On the right side, the arteries of the anterior roots are shown, whereas on the left side, the arteries of the posterior roots are shown. Note the multiple anastomoses among the radicular artery and the spinal cord arteries (arrows) or the vasa corona (arrowheads). The long arrows on the right indicate that the proximal one-third of the root is supplied from the radicular artery arising from the arterial plexus of the spinal cord and the distal two-thirds from the segmental radicular artery. From Namba (2016)

(radiculopial) and radicular arteries was less pronounced. Radiculopial arteries, however, were more numerous in the posterior roots but were seldom the caliber of the anterior vessels (Namba 2016) (Fig. 19.5). The arterial supply to filum terminale is derived from the artery of the filum, the caudal extension of the anterior spinal artery. In very rare cases, both the anterior spinal artery and the branch of the lateral sacral artery may supply the filum terminale (Jin et al. 2010).

19.1.3 Etiology

Cauda equina syndrome can occur with spinal trauma, but there are several nontraumatic causes of cauda equina syndrome, including herniated lumbosacral discs, spinal stenosis, and spinal neoplasms (ependymoma, nerve sheath tumor, metastases). The most common cause is midline lumbar disc herniation. The most common site of a herniated disc associated with the cauda equina syndrome is the L4–L5 level (Bagley and Gokaslan 2004; Özgen et al. 2004; Podnar 2007a). Subdural hematoma of the spine is a rare cause of cauda equina syndrome and can occur after spinal and epidural anaesthetic procedures. Vascular disorders of the aorta, including aortic dissection and thrombosis of an abdominal aortic aneurysm, should be considered in the differential diagnosis of cauda equina syndrome. While aortic vascular disease most likely results in ischemia to the lower spinal cord, several cases in the literature ascribe neurologic impairment to cauda equina syndrome (He et al. 2015).

19.1.4 Pathophysiology

The nerve roots that form the cauda equina can be particularly susceptible to a mechanical compression injury or chemical or inflammatory irritation due to a relative lack of protective connective tissue covering the nerve roots. Unlike the peripheral nerves, which are covered by the epineurium, perineurium, and endoneurium, nerve roots of the cauda equina only have endoneurium. In the cauda equina, the layers equivalent to the perineurium and epineurium are the cerebrospinal fluid and the dura sac, respectively. This relative lack of protection makes the nerve roots of the cauda equina particularly susceptible to traumatic injury (Spector et al. 2008). In addition to the primary compressive injury, secondary injury mechanisms may include nerve root

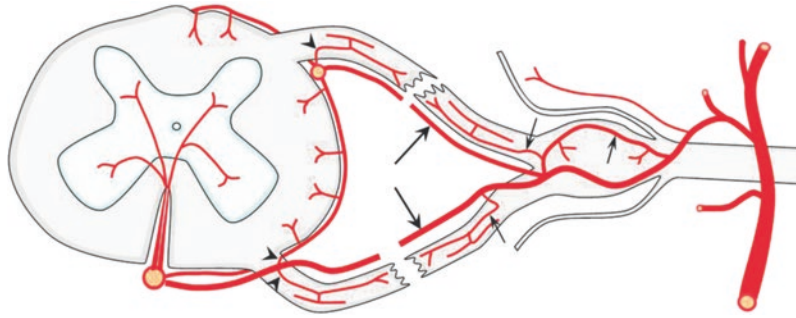

Fig. 19.5 Arterial structures of the spinal nerve roots that can be applicable to all segmental levels. The radiculomedullary and radiculopial arteries (arrows) run along their respective nerve roots to supply the spinal cord. The segmental arteries give rise to the distal radicular arteries for supplying the distal part of the roots (small arrows). The anterior and posterior spinal arteries or the vasa corona give rise to the radicular arteries in the proximal nerve roots (arrowheads). From Namba (2016)

ischemia. Mechanical compression of the nerve roots also affects the nutrition of the nerve roots, causing venous congestion and interfere with the axonal flow. Some patients may be susceptible to a cauda equina injury if they have a congenitally narrowed spinal canal or if they have acquired spinal stenosis as a result of a combination of degenerative changes of the disc and the facet joints and thickening of the ligamentum flavum (McKinley et al. 2008).

19.1.5 Clinical Features

The cauda equina injury/lesion is necessary to distinguish polyneuropathy, polyradiculoneuropathy, or myelopathy. Specific clinical features suggestive of a cauda equina lesion are: (1) no neurologic symptoms in the upper limbs, including normal upper extremity strength, reflexes, and sensory functions; (2) no thoracic sensory level; (3) absent or hyporeactive lower limb reflexes; (4) abnormal sensations in the lower limbs, perineal, or saddle area; and (5) flaccid lower limb weakness (Goodman 2018). The motor, sensory, and reflex functions of the lumbosacral nerve roots of the cauda equina are summarized in Table 19.2. If the spinal fracture is accompanied by a conus medullaris and a cauda equina injury, a distinction between the cauda equina syndrome and conus medullaris syndrome with lesions of the lumbosacral roots surrounding the conus medullaris is not clinically possible (Goodman 2018) (Fig. 19.6). Only 10–15% around the conus medullaris are not covered by the nerve roots.

The neurological symptoms are therefore determined whether the injured area is the epiconus or the distal part of the spinal cord, or conus medullaris or cauda equina, and the symptoms depend on the affected roots of the cauda equina (Harrop et al. 2004). T12–L1 fractures can be a common injury impact of the cauda equina and/or conus medullaris lesion, but it is difficult to determine cauda equina or conus medullaris in relation to the vertebral fracture site (Kostuik 2004). In terms of extreme anatomical features, the spinal cord, which corresponds to vertebrae T12 and L1, comprises all ten spinal cord segments of the lumbar and sacral spinal cord segments. If T12 and L1 fractures injure the corresponding spinal cord, destruction of the conus medullaris and damage to the lumbosacral nerve roots surrounding the conus medullaris may occur (Findlay and Macfarlane 2009; Fraser et al. 2009; Podnar 2007b).

Clinical presentation of the cauda equina lesion is usually caused by multiple lumbosacral nerve root lesions, but symptoms are determined by the involvement of the nerve roots and the degree of injury. Depending on the area of injury, cauda equina lesion may be divided into upper

Table 19.2 Motor, sensory, and reflex function of the lumbosacral nerve roots of the cauda equina

Nerve root	Motor	Sensory	Reflexes
L2	Hip flexion, hip adduction	Proximal thigh	Hip adductor reflex
L3	Knee extension, hip adduction	Lower thigh	Knee jerk
L4	Ankle extension	Anteromedial lower leg	Knee jerk
L5	Toe extension	Anterolateral lower leg, foot dorsum	Tibialis posterior reflex
S1	Ankle and toe flexion, knee flexion	Posterior lower leg	Ankle jerk, medial hamstring reflex
S2	Ankle and toe flexion, knee flexion	Posterior thigh	Lateral hamstring reflex
S3	None	Posterior buttock, perineal region	Bulbocavernosus reflex (?)
S4-5	External anal sphincter, external urethral sphincter	Perianal area	Bulbocavernosus reflex, anal reflex

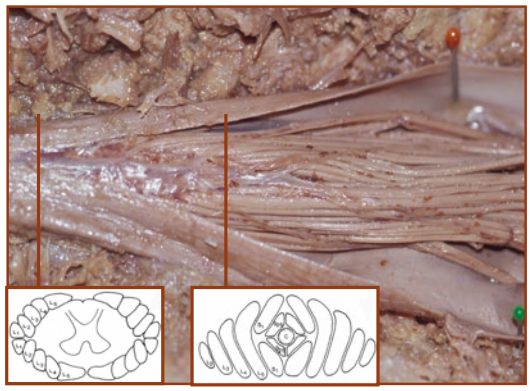

Fig. 19.6 The relationship between the conus medullaris and nerve roots surrounding the conus medullaris and arrangement pattern of the nerve roots

(L2–L4), middle (L5–S1), lower (S2–S5), and unilateral injuries. Depending on the severity of the injury, it can be classified as complete and incomplete injuries and, depending on the timing of symptom presentation, as rapid and slow injuries. Due to the anatomical features of the nerve roots orientation described above, injury to the proximal or middle nerve roots of the cauda equina is more likely to be caused by damage to the anterior spinal canal, such as herniated disc herniation (Namba 2016). On the other hand, in case of damage to the posterior column in the three-column theory or hypertrophy of the ligamentum flavum, it is easy to cause a symptom resulting from damage to the lower sacral nerve roots, such as urinary and bowel dysfunction.

Patients may experience urinary retention or incontinence, acute onset of low back pain with variable radiation to the legs, variable leg weakness, and perineal hypesthesia or anesthesia. Bowel dysfunction can range from constipation to incontinence, but is not always obvious in patients with acute symptoms associated with loss of rectal sensation. Some patients may have a much more insidious clinical presentation, including numbness, tingling, or urinary symptoms. They may experience abnormal perianal sensations when wiping with toilet paper. Particularly patients with no incontinence are not always reported bladder dysfunction, but there may be a large amount of postvoid residual urine. In a cauda equina lesion with urinary dysfunction, detrusor function may recover later than lower extremity reflexes and bulbocavernosus reflex when the somatic and autonomic nerve functions are restored over time (New 2009). In the early phase of injury, it is not possible to distinguish between cauda equina and conus medullaris lesions if damage to the epiconus region is accompanied by damage to adjacent lumbosacral nerve roots (Parke et al. 1981) (Fig. 19.7). Impairment of sexual function may occur, and genital sensory disorders can reduce the penile sensation or the sensation during sexual activity. Some of these patients may have long-standing history of lumbar disc disease associated with back pain. Patients with

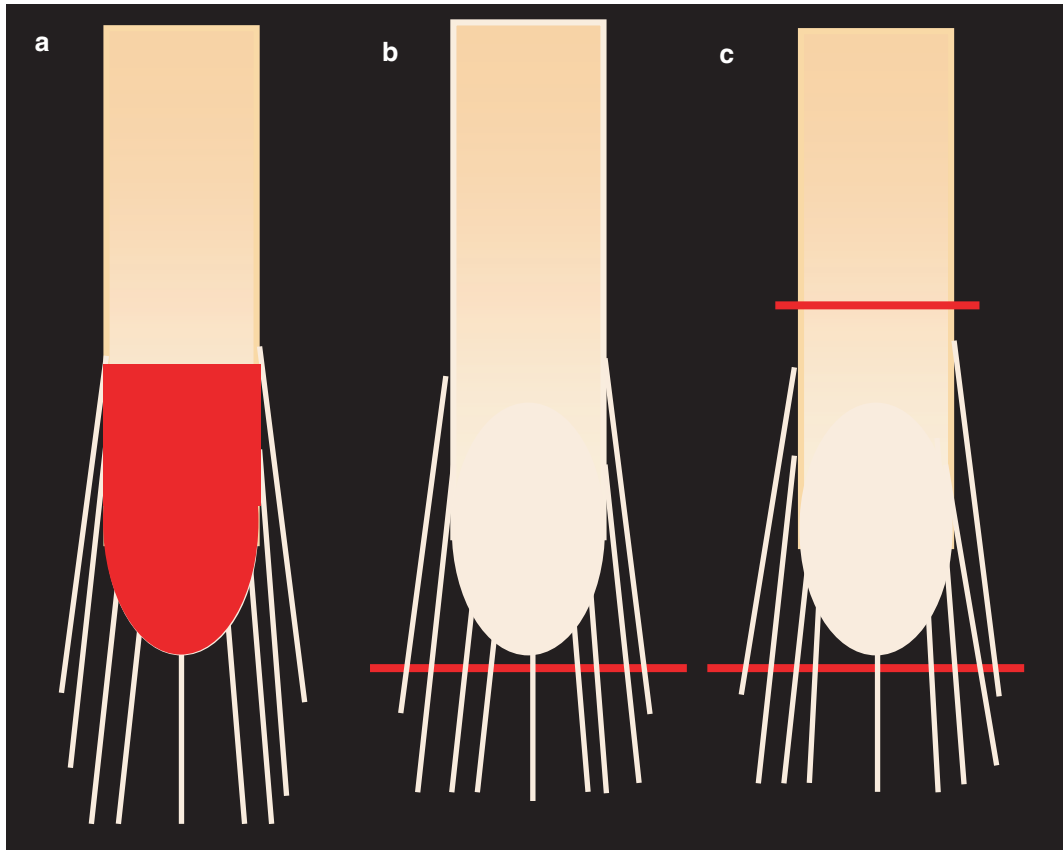

Fig. 19.7 In the early injury phase, it is not clinically possible to distinguish between (**a**) intraconal lesion or conus damage, (**b**) cauda equina lesion, and (**c**) combined lesion of epiconus and cauda equina (or surrounding lumbosacral nerve roots)

preexisting lumbar spinal stenosis often have a history of neurogenic claudication with walking or prolonged standing.

19.1.6 Physical Examination

A full neurological assessment for the cauda equina syndrome should be carefully performed to establish if any dermatomal sensory loss, myotomal weakness or reflex change is present and should be included light touch and pinprick sensation of the perianal areas, deep anal pressure, voluntary anal contraction, anal reflex, and bulbocavernosus reflex. Motor examination may show variable weakness and loss of reflexes in the legs. A digital rectal examination, such as perianal sensation and sphincter tone, is essential component of the physical examination in a patient suspected with cauda equina lesion (Greenhalgh et al. 2018).

The anal reflex and bulbocavernosus reflex are mediated by the sacral nerve roots. This differs from a sustained voluntary contraction of the anal sphincter, which represents intact rectal muscle tone and implies intact sacral efferent innervation. The anal reflex is a superficial reflex elicited by painful stimulation of the perirectal region and leads to an involuntary contraction of the anus. Voluntary anal contraction must be distinguished from the anal reflex, which is a sacral reflex arc. The bulbocavernosus reflex is elicited by applying pressure to the glans penis or clitoris or by traction on a Foley catheter, which triggers anal

Table 19.3 Reflexes in epiconus, conus medullaris, and cauda equina lesions

Reflex	Epiconus lesion	Conus medullaris lesion	Cauda equina lesion
Lower extremity DTRs	May be absent initially (spinal shock) but hyperreflexic	Absent	Depending on level of injury (cranial levels will have DTR)
Anal reflex, bulbocavernosus reflex	May be absent initially and recur after spinal shock resolves	Absent	Absent/dependent on location of injury

DTR deep tendon reflex, BCR bulbocavernosus reflex
From Radcliff et al. (2011), with permission

sphincter contraction as a normal response (Radcliff et al. 2011). Complete loss of pinprick, light touch, and pressure sensation is a late finding associated with poor neurologic recovery (Spector et al. 2008). The results of the reflexes in the epiconus, conus medullaris, and cauda equina lesions are shown in Table 19.3.

19.1.7 Management

The goal of treatment for all traumatic spinal cord injuries is to preserve neurologic function and restore spinal stability. Surgical decompression is often indicated with anterior or posterior decompression, and nonsurgical management has a relatively limited role. A progressive neurologic deficit, significant deformity, or spinal instability is indication of surgical intervention. Thoracolumbar fractures typically involve anterior compression of the neural elements due to retropulsion of bony elements. The most appropriate treatment for incomplete conus medullaris and/or cauda equina lesions in a medically suitable patient with persistent neural compression is surgical decompression (Kim et al. 1999). There is still controversy about the degree of canal compromise, the extent of decompression, and treatment technique toward neurologic recovery. However, an early surgical decompression is often recommended to maximize the potential for neurologic recovery. An anterior approach provides direct visualization and decompression of the neural elements and allows little or no manipulation of the dura or neural elements (Radcliff et al. 2011). Surgical approaches are similar for the cauda equina and conus medullaris injuries.

Despite extensive study, the value of timing of surgical intervention has no consensus. In general, decompression should not be delayed and should be performed within 24–48 h (Chau et al. 2014). Studies have found improved respiratory outcomes, shorter intensive care unit stay, decreased mortality, fewer ventilator days, and shorter hospitalization in patients who underwent early surgery (Chipman et al. 2004; Radcliff et al. 2011; Frangen et al. 2010). More care should be taken to avoid further damage to the nerve roots. After surgery, a comprehensive rehabilitation program may be indicated to treat residual impairments and functional deficits in mobility and activities of daily living and to treat accompanying neurogenic bladder, bowel, and sexual dysfunction.

19.1.8 Prognosis

The prognosis of acute cauda equina lesion with emergent treatment is generally considered good. Urinary incontinence as a clinical presentation in cauda equina syndrome is not good prognostic sign. Patients with incomplete cauda equina syndrome without urinary impairment such as urinary retention or incontinence have a better prognosis for recovery than those with the problems. Recovery may last up 1 year or longer after surgery (Jensen 2004). Prognostic factors for the conus medullaris and cauda equina lesions are shown in Table 19.4.

19.2 Conus Medullaris Lesion

Conus medullaris syndrome is difficult to define and characterize because it is an injury of the region between the spinal cord and nerve roots; its presentation is variable because of injury of the long tracts, cell bodies (anterior horn cells),

Table 19.4 Prognostic factors for conus medullaris and cauda equina lesions

Prognosis	Conus medullaris lesion	Cauda equina lesion
Better	• Earlier surgical decompression (<48 h of symptoms) • Intact sacral pin prick sensation for good recovery of bladder function • Intact bulbocavernosus reflex	• Earlier surgical decompression (<48 h of symptoms) • Younger age • Urinary retention
Poor	• Surgical decompression after 48 h of symptoms • Hemorrhage within spinal column on MRI	• Preoperative history of chronic back pain • History of preinjury rectal dysfunction • Incomplete urinary retention • Bilateral sciatica versus unilateral sciatica • Lower extremity pain

From Radcliff et al. (2011), with permission

and nerve roots (Radcliff et al. 2011). The neurological features of the conus medullaris lesion including upper motor neuron lesion or lower motor neuron lesion and features of bladder and bowel dysfunction are determined depending on whether conus medullaris and nerve root injury with obliquity surrounding the conus medullaris are accompanied, or the intramedullary lesion only of the conus medullaris, or the epiconus lesion. An isolated conus medullaris injury from thoracolumbar fractures without elements of concomitant cauda equina dysfunction is rare. Other causes of conus medullaris lesion include infection, iatrogenic compression, penetrating trauma, and falls. An example of an iatrogenic cause of conus medullaris lesion is direct contusion from epidural anesthesia or spinal implant (Radcliff et al. 2011). With respect to spinal cord injuries and cauda equina injuries, little information is available about conus medullaris lesion. There are no definitive diagnostic clinical signs and symptoms. The clinical presentation is usually bilateral.

19.3 Cauda Equina Vs. Vonus Medullaris Lesions

The conus medullaris and cauda equina lesions (syndromes) are believed to be separate clinical entities, but there is no clear definition of neurological symptoms and level of injury. From a purely anatomical point of view, the conus medullaris and the cauda equina are separate structures, but clinical differentiation between incomplete conus medullaris lesion and cauda equina lesion is difficult on the basis of neurological examination alone. The conus medullaris comprises both upper and lower motor neurons, while the cauda equina consists only of lower motor neurons (Radcliff et al. 2011). The conus medullaris lesion is difficult to define and characterize because it is an injury in the region between the spinal cord and nerve roots; its presentation is variable due to injury of the long tracts, cell bodies (anterior horn cells), and nerve roots. It is assumed that the regenerative capacity of lower motor neuron lesions is superior to upper motor neuron lesions and, therefore, the functional outcome of cauda equina lesion might be better than the functional outcome of conus medullaris lesion (Tator 1998). Conus medullaris and cauda equina lesions are often combined as a "conus–cauda lesion," although the outcome between these two lesions may differ. A clear definition of both lesions is necessary to determine functional outcomes, guide treatment decision-making and predict complications (van Middendorp et al. 2010).

Neurological examination depends on the location of the lesion and the relative involvement of the conus medullaris and cauda equina. The clinical symptoms of patients with conus medullaris or cauda equina lesion are: low back pain, lower extremity weakness, perineum or saddle anesthesia, and bladder and/or bowel dysfunction (Brouwers et al. 2017). The classic description of conus medullaris lesion is symmetric saddle anesthesia, paralytic bladder incontinence, bowel incontinence, and mild lower extremity weakness (Radcliff et al. 2011). Lesions of the conus medullaris (conus medullaris itself) typically cause an impaired sensa-

tion of the sacral dermatomes, flaccid anal sphincter with loss of anal and bulbocavernosus reflexes, and sometimes weakness of the lower extremity muscles (Brouwers et al. 2017). Depending on the level of lesion, this type of injury may manifest with a mixed picture of upper motor neuron and lower motor neuron signs (Pavlakis et al. 1983). For example, higher lesions of the conus medullaris may preserve the bulbocavernosus reflex and anal reflex that are generally absent with lower lesions. These can be referred to as an epiconus lesion when the lesion is strictly defined. Lower extremity weakness associated with cauda equina lesion is predominantly asymmetrical in patients with incomplete injury (Fraser et al. 2009; Podnar 2007a; Wagner and Jagoda 1997). Involvement of cauda equina results in asymmetrical weakness and atrophy, flaccid paralysis of the lower extremities, radicular sensory loss, and impaired sphincters. In some cases, it may be difficult to clinically distinguish a cauda equina injury from a conus medullaris injury (Wostrack et al. 2014). The differences in clinical features between the cauda equina lesion and conus medullaris lesion are summarized in Table 19.5.

Table 19.5 Differentiation of the clinical features between cauda equina lesion and conus medullaris lesion

Symptoms, signs	Cauda equina lesion	Conus medullaris lesion
Symmetry	Often asymmetrical	More often symmetrical
Stretch reflexes	Depressed reflexes according to involved roots	Usually preserved
Sensory loss	According to involved roots	Saddle pattern
BCR, anal reflex	Usually absent	Preserved in high conus injury or epiconus lesion
Pain	Common	Less common
Bladder activity	Usually absent	Preserved in high conus injury or epiconus lesion
Recovery	More likely	Less likely

BCR bulbocavernosus reflex

References

Bagley CA, Gokaslan ZL. Cauda equina syndrome caused by primary and metastatic neoplasms. Neurosurg Focus. 2004;16:E3.

Brouwers E, van de Meent H, Curt A, et al. Definitions of traumatic conus medullaris and cauda equina syndrome: a systematic literature review. Spinal Cord. 2017;55:886–90.

Chau AM, Xu LL, Pelzer NR, et al. Timing of surgical intervention in cauda equina syndrome: a systematic critical review. World Neurosurg. 2014;81:640–50.

Chipman JG, Deuser WE, Beilman GJ. Early surgery for thoracolumbar spine injuries decreases complications. J Trauma. 2004;56:52–7.

Chuang TY, Cheng H, Chan RC, et al. Neurourologic findings in patients with traumatic thoracolumbar vertebra junction lesions. Arch Phys Med Rehabil. 2001;82:375–9.

Cohen MS, Wall EJ, Kerber CW, et al. The anatomy of the cauda equina on CT scans and MRI. J Bone Joint Surg Br. 1991;73:381–4.

De Vloo P, Monea AG, Sciot R, et al. The filum terminale: a cadaver study of anatomy, histology, and elastic properties. World Neurosurg. 2016;90:565–73.

Findlay G, Macfarlane R. Cauda equina syndrome. J Neurosurg Spine. 2009;11:90–1.

Frangen TM, Ruppert S, Muhr G, et al. The beneficial effects of early stabilization of thoracic spine fractures depend on trauma severity. J Trauma. 2010;68:1208–12.

Fraser S, Roberts L, Murphy E. Cauda equina syndrome: a literature review of its definition and clinical presentation. Arch Phys Med Rehabil. 2009;90:1964–8.

Goodman BP. Disorders of the cauda equina. Continuum (Minneap Minn). 2018;24:584–602.

Greenhalgh S, Finucane L, Mercer C, et al. Assessment and management of cauda equina syndrome. Musculoskelet Sci Pract. 2018;37:69–74.

Harrop JS, Hunt GE Jr, Vaccaro AR. Conus medullaris and cauda equina syndrome as a result of traumatic injuries: management principles. Neurosurg Focus. 2004;16:E4.

He F, Xing T, Yu F, et al. Cauda equina syndrome: an uncommon symptom of aortic diseases. Int J Clin Exp Med. 2015;8:10760–6.

Hertzler DA 2nd, DePowell JJ, Stevenson CB, et al. Tethered cord syndrome: a review of the literature from embryology to adult presentation. Neurosurg Focus. 2010;29:E1.

Hoang TX, Havton LA. Novel repair strategies to restore bladder function following cauda equina/conus medullaris injuries. Prog Brain Res. 2006;152:195–204.

Jensen RL. Cauda equina syndrome as a postoperative complication of lumbar spine surgery. Neurosurg Focus. 2004;16:E7.

Jin YJ, Kim KJ, Kwon OK, et al. Perimedullary arteriovenous fistula of the filum terminale: case report. Neurosurgery. 2010;66:E219–20.
Kapetanakis S, Chaniotakis C, Kazakos C, et al. Cauda equina syndrome due to lumbar disc herniation: a review of literature. Folia Med (Plovdiv). 2017;59:377–86.
Kennedy JG, Soffe KE, McGrath A, et al. Predictors of outcome in cauda equina syndrome. Eur Spine J. 1999;8:317–22.
Kim NH, Lee HM, Chun IM. Neurologic injury and recovery in patients with burst fracture of the thoracolumbar spine. Spine (Phila Pa 1976). 1999;24:290–3. discussion 294
Kingwell SP, Curt A, Dvorak MF. Factors affecting neurological outcome in traumatic conus medullaris and cauda equina injuries. Neurosurg Focus. 2008; 25:E7.
Kostuik JP. Medicolegal consequences of cauda equina syndrome: an overview. Neurosurg Focus. 2004;16:E8.
Lavy C, James A, Wilson-MacDonald J, et al. Cauda equina syndrome. BMJ. 2009;338:b936.
Lawson BK, Jenne JW, Koebbe CJ. Cauda equina and conus medullaris avulsion with herniation after midlumbar Chance fracture. Spine J. 2014;14:1060–2.
Mauffrey C, Randhawa K, Lewis C, et al. Cauda equina syndrome: an anatomically driven review. Br J Hosp Med (Lond). 2008;69:344–7.
McCarthy MJ, Aylott CE, Grevitt MP, et al. Cauda equina syndrome: factors affecting long-term functional and sphincteric outcome. Spine (Phila Pa 1976). 2007;32:207–16.
McKinley W, Graham S, Lee K, et al. Cervical and lumbar spinal stenosis associated with myelopathy and cauda equina syndrome. Top Spinal Cord Inj Rehabil. 2008;14:10–8.
McNamee J, Flynn P, O'Leary S, et al. Imaging in cauda equina syndrome - a pictorial review. Ulster Med J. 2013;82:100–8.
Monajati A, Wayne WS, Rauschning W, et al. MR of the cauda equina. AJNR Am J Neuroradiol. 1987;8:893–900.
Namba K. Vascular anatomy of the cauda equina and its implication on the vascular lesions in the caudal spinal structure. Neurol Med Chir (Tokyo). 2016;56:310–6.
New PW. Cauda equina syndrome. Specialist Rehabil BMJ. 2009;338:b1725.
Özgen S, Baykan N, Dogan IV, et al. Cauda equina syndrome after induction of spinal anesthesia. Neurosurg Focus. 2004;16:e5.
Orendácová J, Cízková D, Kafka J, et al. Cauda equina syndrome. Prog Neurobiol. 2001;64:613–37.
Parke WW, Gammell K, Rothman RH. Arterial vascularization of the cauda equina. J Bone Joint Surg Am. 1981;63:53–62.
Pavlakis AJ, Siroky MB, Goldstein I, et al. Neurourologic findings in conus medullaris and cauda equina injury. Arch Neurol. 1983;40:570–3.
Podnar S. Epidemiology of cauda equina and conus medullaris lesions. Muscle Nerve. 2007a;35:529–31.
Podnar S. Saddle sensation is preserved in a few patients with cauda equina or conus medullaris lesions. Eur J Neurol. 2007b;14:48–53.
Radcliff KE, Kepler CK, Delasotta LA, et al. Current management review of thoracolumbar cord syndromes. Spine J. 2011;11:884–92.
Ridley LJ, Han J, Ridley WE, et al. Cauda equina: normal anatomy. J Med Imaging Radiat Oncol. 2018;62(Suppl 1):123.
Spector LR, Madigan L, Rhyne A, et al. Cauda equina syndrome. J Am Acad Orthop Surg. 2008;16:471–9.
Tarulli AW. Disorders of the cauda equina. Continuum (Minneap Minn). 2015;21:146–58.
Tator CH. Biology of neurological recovery and functional restoration after spinal cord injury. Neurosurgery. 1998;42:696–707. discussion 707-8
van Middendorp JJ, Audigé L, Hanson B, et al. What should an ideal spinal injury classification system consist of? a methodological review and conceptual proposal for future classifications. Eur Spine J. 2010;19:1238–49.
Wagner R, Jagoda A. Spinal cord syndromes. Emerg Med Clin North Am. 1997;15:699–711.
Wall EJ, Cohen MS, Massie JB, et al. Cauda equina anatomy. I: Intrathecal nerve root organization. Spine (Phila Pa 1976). 1990;15:1244–7.
Wostrack M, Shiban E, Obermueller T, et al. Conus medullaris and cauda equina tumors: clinical presentation, prognosis, and outcome after surgical treatment: clinical article. J Neurosurg Spine. 2014;20:335–43.

Recommended Additional Reading

Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.
Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.
Eagler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker Inc.; 1998.
Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.

Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.

Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia: Elsevier; 2016.

Patestas MA, Gartner LP. A text book of neuroanatomy. Oxford: Blackwell Publishing; 2006.

Thron AK. Vascular anatomy of the spinal cord. Neurological investigations and clinical syndromes. New York: Springer; 1988.

Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.

Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, third series, vol. 109. London: Elsevier; 2012.

Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part I. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976a.

Vinken PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part II. Handbook of clinical neurology, vol. 25. Oxford: North-Holland Publishing Company; 1976b.

Syringomyelia and Chiari Malformations

20

The term syringomyelia was introduced by the French pathologist and clinician Charles-Prosper Ollivier d'Angers in 1827 and has its origins in the Greek *syrinx*, which means "cavity of tubular shape," and *myelos*, which means "narrow" (Flint and Rusbridge 2014; Klekamp 2002). Since its introduction, the term has been used to describe several types of intramedullary cysts, including proteinaceous cysts, terminal ventricles, and hydromyelia. In particular, hydromyelia refers to the dilatation of the central canal that is lined with ependymal cells, and syringomyelia refers to a cystic cavity in the spinal cord separate from the central canal that is not lined by ependymal cells. This distinction is of little practical importance as both entities appear similar in imaging. Syringomyelia is a neurologic condition caused by the presence of a fluid-filled cavity in the central canal or parenchyma of the spinal cord that expands in the spinal cord (Barnett and Jousse 1976; Greitz 2006). Syringomyelia is not a disease in itself, but a manifestation of other pathological processes such as obstruction of cerebrospinal fluid (CSF) circulation in the spinal canal, tethering of the spinal cord, or an intramedullary tumor. Syringomyelia can be classified into the following four categories based on etiology: hindbrain-related, posttraumatic/inflammatory, tumor-associated, and idiopathic. Syringomyelia is typically seen in association with type I Chiari malformation. Other causes include spinal cord tumors, trauma, and posttraumatic or infectious adhesive arachnoiditis. Syringomyelia can occur in patients following spinal cord injuries, that is, posttraumatic syringomyelia. The mammalian spinal cord responds quickly and aggressively to traumatic injuries. Petechial or flame-shaped hemorrhages will occur at or near the site of the spinal cord injury within minutes. Extensive necrosis of the spinal cord occurs within a few days and by the end of the third week cavities form in the injured spinal cord and, in some cases, scarring of the connective tissue (Rigamonti et al. 1978).

The expanding syrinx insidiously damages the spinal cord and causes dissociated sensory deficit, pain, weakness, and stiffness of the trunk, shoulders, arms, or legs. Sweating, sexual function, and bladder and bowel control may also be disturbed (Roy et al. 2011). Initial neurological presentation appears as central cord syndrome. The increased use of magnetic resonance imaging (MRI) has led to increased detection of syringomyelia. The natural history of patients with syringomyelia is variable and unpredictable. The clinical course progresses over months or even years, with the early rapid deterioration that gradually slows down (Bogdanov and Mendelevich 2002). This chapter focuses on posttraumatic syringomyelia and the syringomyelia associated with Chiari malformation.

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20.1 Posttraumatic Syringomyelia

After spinal cord injuries, many patients present with fluid-filled cysts or microcysts on MRI that are not syringomyelia but rather myelomalacia. Formation of intramedullary cysts may be due to dilated central canal or expanding posttraumatic microcysts as a result of myelomalacia. More than a quarter of people with spinal cord injuries develop syringes, and many of these people have progressive neurological deficits due to cyst enlargement (Brodbelt and Stoodley 2003). The mechanism of initial cyst formation and progressive enlargement is unknown, and the abundance of etiological theories and management practices proves that even the basic mechanisms of cyst formation and enlargement have not been understood, despite arachnoiditis and persisting spinal cord compression with disturbance of CSF flow appear to be important etiological factors. Recognition of posttraumatic syringomyelia depends on the physician's vigilance in recognizing the importance of new symptoms occurring after spinal cord injury and the availability and utilization of imaging techniques.

20.1.1 Epidemiology

In a Japanese study, half the patient with syringomyelia had a Chiari malformation (51.2%), while about 20% had spinal cord trauma (11%) or arachnoiditis (6%) (Moriwaka et al. 1995). The incidence and duration of symptom onset of posttraumatic syringomyelia after trauma are quite variable (Ko et al. 2012). If all patients suffering a spinal injury are investigated between 1 and 30 years after injury, a syrinx is found in 21–28% and some cystic change in the spinal cord in 30–50% (Backe et al. 1991; Brodbelt and Stoodley 2003; Wang et al. 1996). Since MRI is available, clinically silent and early symptomatic posttraumatic syringomyelia has been identified. According to a report, current imaging techniques and careful examination of patients showed the incidence of 22% (Vannemreddy et al. 2002). In contrast, symptomatic syringomyelia is reported in only 1–9% of the population with spinal injuries (Wang et al. 1996). However, the clinical manifestation of posttraumatic syringomyelia is the same in both sexes. The incidence of posttraumatic syringomyelia is higher in men because of the higher frequency of spinal cord injury in males (Edgar and Quail 1994). The incidence of this complication was higher in patients with paraplegia than in patients with tetraplegia after high cervical injury (paraplegia:tetraplegia, 9:1) (Griffiths and McCormick 1981). There was no difference in the incidence of posttraumatic syringomyelia in patients with a complete neurological deficit at admission compared to patients with incomplete injuries. The interval between time of injury and the onset of neurological deterioration varies from 2 months to many years (Umbach and Heilporn 1991; Yarkony et al. 1994).

20.1.2 Pathogenesis

Many theories have been proposed to explain the pathogenesis of posttraumatic syringomyelia, but it is generally accepted that development and propagation of the syrinx is related to partial or complete obstruction of normal cerebrospinal fluid flow in the subarachnoid space (Klekamp et al. 1997; Williams et al. 1981). However, the pathogenesis of posttraumatic syrinx formation and route and source of fluid flow is still not fully understood (Brodbelt and Stoodley 2003). Information from clinical observations, the development of new imaging studies, and information from animal studies provided clues to understanding the mechanisms of syrinx development. An incomplete understanding of the underlying mechanisms of syrinx formation has prevented the development of effective therapies for posttraumatic syringomyelia.

The cavity may be formed by liquefaction of the initial hematoma of the spinal cord or the traumatized cord itself (Umbach and Heilporn 1991). Absorption of a hematoma can leave a cystic cavity that forms the basis of the subsequent syrinx. In particular, posttraumatic syringes are often found in the vascular watershed regions within the cord. This suggests that ischemia due

to the primary injury or subsequent arachnoiditis may play a role in the initiation syrinx by forming small cystic cavities from infarction (Brodbelt and Stoodley 2003; Edgar and Quail 1994; Milhorat et al. 1995). Another possible mechanism of initial cyst formation is the coalescence of extracellular fluid. This theory is supported by the detection of spinal cord edema on imaging studies prior to syrinx formation (Fischbein et al. 1999; Milhorat et al. 1995).

The pulsatile action of the CSF and its sloshing within the cavity due to changes in pressure in the spinal cord may cause a subsequent enlargement of the cavity in the spinal cord and its upward and downward progression (Williams 1980). In addition to the obstruction of CSF flow, the hydrodynamics of CSF can contribute to the influx of water transfer into the syrinx. In the "slosh-and-suck" theory, activities such as the Valsalva maneuver, coughing, and sneezing cause a forced expiratory effort by the closed glottis. This increase in intraspinal pressure produces rapid fluid movement inside the cord (slosh), followed by the opening of cord tissue at the periphery of the cavity (suck). These effects promote the development of syrinx dilation in patients with posttraumatic syringomyelia (Williams et al. 1981; Williams 1990, 1992) (Fig. 20.1).

The injured spinal cord may adhere to the overlying dura at the level of injury caused by focal arachnoiditis. As the spine is repeatedly moved over the fixed cord, the cord at the site of adherence is stretched and compressed circumferentially to increase pressure within the cyst cavity, causing it to disrupt into adjacent cord tissue along the line with least resistance. After adhesion in the subarachnoid space, more CSF enters the spinal cord. A complete subarachnoidal block can produce a pressure difference above and below the site of cord adherence. Impairment of CSF flow in a narrow or occluded subarach-

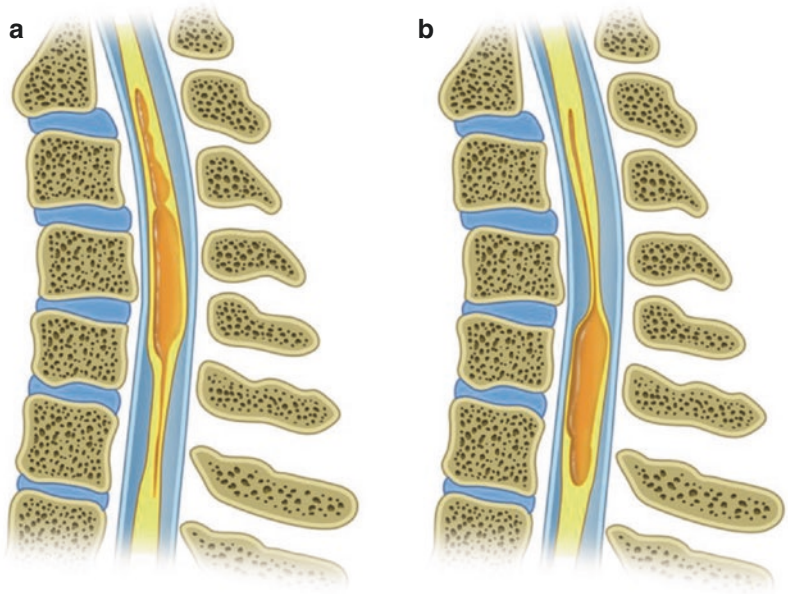

Fig. 20.1 Proposed mechanism for cord filling and propagation of the cavity (slosh-and-suck theory). The upward movement of CSF (**a**), which can occur during coughing, for example, produces compression of the lower part of the syrinx and an upward surge of fluid in the cavity that may cut the cephalad in the soft gray matter within the cord. The upward surge of CSF is more energetic than the returning pulsation. The dropping back of the lesion and the involved cord after the coughing can create a pressure differential and encourage fluid to pass through the permeable walls of the cord into the cord cavity (**b**). From Williams (1990), with permission

noid space can lead to water accumulation and syrinx development (Shields et al. 2012). Subarachnoid adhesion due to arachnoiditis or vertebral fracture following spinal cord injuries can aggravate cavity formation. It significantly affects the free propagation of the CSF pulse wave in the spinal canal (Greitz 2006). This fixed type of subarachnoid obstruction significantly decreases the pulsatile volume and pressure conduction to the distal CSF spaces. During systole, the CSF pulse pressure is increased above the obstruction and decreased below the obstruction, generating a pressure gradient. The cyst will gradually increase under the constant combined effect of filling and suction effects during each pulsation (Greitz 2006; Shields et al. 2012) (Fig. 20.2).

In posttraumatic syringomyelia, CSF flow obstruction can be caused by scarring of the arachnoid membrane at or around the trauma level and by narrowing of the spinal canal due to posttraumatic stenosis or kyphosis. Posttraumatic cord tethering can also contribute to the development of the syrinx (Falci et al. 2009; Klekamp 2012c). The presence of uncorrected kyphosis and stenosis correlate with syrinx formation and

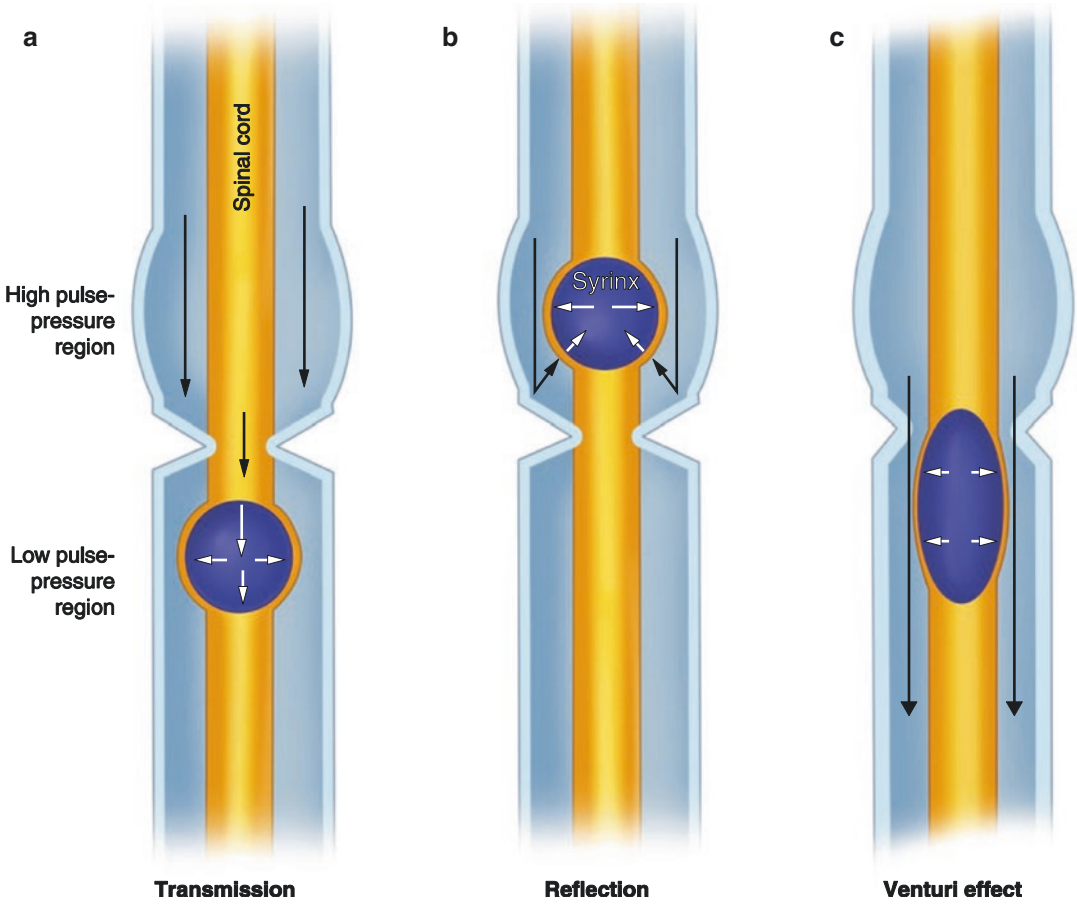

Fig. 20.2 Posttraumatic syringomyelia. Subarachnoid adhesions or vertebral fractures cause a fixed type of subarachnoid obstruction that decreases the systolic pressure transmission to the distal CSF spaces. (**a**) The systolic CSF pulse pressure (black arrows) is instead transmitted through the spinal cord at the obstruction distending the cord below the obstruction (white arrows). (**b**) Part of the systolic CSF pulse pressure is simultaneously reflected into the cord at the obstruction distending the cord just above the obstruction. (**c**) At partial subarachnoid obstruction, the systolic CSF flow jet (black arrows with tails) causes a Venturi effect or a suction effect on the spinal cord that distends the cord at the obstruction. From Greitz (2006), with permission

symptom severity. The syrinx starts at the level of obstruction and expands from there. If the syrinx expands in a rostral direction, the obstruction is found at the caudal end of the syrinx and vice versa (Klekamp 2012c).

20.1.3 Classification

Milhorat et al. (Milhorat 2000; Milhorat et al. 1995) established a disease-based classification system for syringomyelia according to pathological and MRI findings with the aim of making MRI interpretation and diagnosis easier and at the same time providing guidelines for optimal treatment. Within this classification, there are four categories which are classified as follows on the basis of pathological findings: (1) dilations of the central canal that are anatomically continuous with the fourth ventricle (communicating central canal syringomyelia); (2) dilations of the central canal that do not communicate with the fourth ventricle (noncommunicating central canal syringomyelia); and (3) noncommunicating extracanalicular syringes that originate in the spinal cord parenchyma and do not communicate with the central canal or fourth ventricle (primary parenchymal cavitations). These lesions are distinguished from two other types of cavitation: (1) atrophic syringes occurring with myelomalacia (syringomyelia ex vacuo); and (2) neoplastic cysts (Milhorat 2000).

Communicating central canal syringes are central canal dilatations in continuity with the fourth ventricle and are often associated with hydrocephalus. Communicating syringes are caused by obstructions of the CSF pathways distal to the fourth ventricle outlets. On histological examination, communicating syringes appear as simple dilations of the central canal, lines whole or partially by ependyma. The length of the cavity is defined caudally by central canal stenosis (Milhorat 2000). *Noncommunicating central canal syringes* are associated with Chiari I malformations, cervical spinal stenosis, spinal arachnoiditis, tethered cord, and basilar invagination (Brodbelt and Stoodley 2003; Milhorat et al. 1995). Dilations of the central canal that do not communicate with the fourth ventricle are associated with obstructions of the CSF pathways at or below the foramen magnum. On histological examination, noncommunicating syringes appear as isolated cavities that are defined rostrally and caudally by central spinal canal stenosis (Milhorat 2000). *Noncommunicating extracanalicular syringes (primary parenchymal cavitations)* are associated with spinal trauma, infarction, hemorrhage, or transverse myelitis. These lesions consist of tubular cavitations of the spinal cord that originate in the parenchyma and do not communicate with the central canal or fourth ventricle. A distinguishing feature of this type of syringomyelia is its association with conditions that injure the spinal cord tissue (Milhorat 2000). Most extracanalicular syringes are located in the watershed areas of the spinal cord, dorsal, and lateral to the central canal. Posttraumatic syringes are usually juxtaposed to the injury site and extend rostral in 81% of cases, caudal in 4%, and in bidirectionally in 15% of cases. Up to 17% of posttraumatic syringes extend more than ten levels (Edgar and Quail 1994; Milhorat et al. 1995). *Atrophic cavitations* associated with spinal cord atrophy can lead to the formation of microcysts, intramedullary clefts, and localized dilations of the central spinal canal. Atrophic cavitations presumably do not propagate due to the lack of a filling mechanism and are caused by the loss of parenchymal tissue (syringomyelia ex vacuo).

In *neoplastic cavitations*, syrinx-like cavities can be formed by the cystic degeneration of intramedullary tumors such as astrocytomas, ependymomas, and other less common neoplasms. The necrotic process begins centrally and tends to extend rostrally or caudally from the poles of the tumor. Neoplastic cysts contain proteinaceous fluid that is quite different from CSF (Milhorat 2000).

Table 20.1 provides the five syringomyelias and causative factors that belong to each category, and Fig. 20.3 schematically shows the relationship between the fourth ventricle, central canal, and syrinx of each syringomyelia.

Table 20.1 Anatomical classification of syringomyelia adapted from Milhorat (2000)

I. Communicating syringomyelia Central canal dilatation a. Communicating hydrocephalus (posthemorrhagic, postmeningitic) b. Complex hindbrain malformation (Chiari II, encephalocele) c. Dandy-Walker cyst
II. Noncommunicating syringomyelia Central canal and parenchymal dilatations (Canalicular) a. Chiari I malformations b. Basilar invagination c. Spinal arachnoiditis (posttraumatic, postmeningitic) d. Extramedullary compression (spondylosis, tumors, cysts) e. Tethered cord f. Acquired tonsillar herniation (hydrocephalus, intracranial mass lesion, craniosynostosis) Primary parenchymal cavitations (Extracanalicular) a. Spinal cord trauma b. Ischemia, infarction c. Intramedullary hemorrhage d. transverse myelitis
III. Atrophic cavitations (Syringomyelia ex vacuo)
IV. Neoplastic cavitations

From Sharma et al. (2006), with permission

20.1.4 Clinical Presentation

Posttraumatic syringomyelia is clinically characterized by the insidious progression of pain and loss of sensory motor function that may develop many years after traumatic spinal cord injury. Development of posttraumatic syringomyelia varied between 2 and 3 months and 34 years following spinal cord injuries. In a comprehensive study of posttraumatic syringomyelia, the time from injury to the diagnosis of posttraumatic syringomyelia ranged from 9 months to 30 years (mean 9.4 years). The diagnosis was delayed up to 17 years (mean 2.3 years) after the appearance of the first symptom of posttraumatic syringomyelia (Schurch et al. 1996). The diagnosis of patients with this disorder is often not recognized or misdiagnosed for many years (Hilton and Henderson 2003).

The symptoms of posttraumatic syringomyelia vary widely. Common initial symptoms of posttraumatic syringomyelia include increased pain at the level of injury associated with progressive ascending weakness and numbness

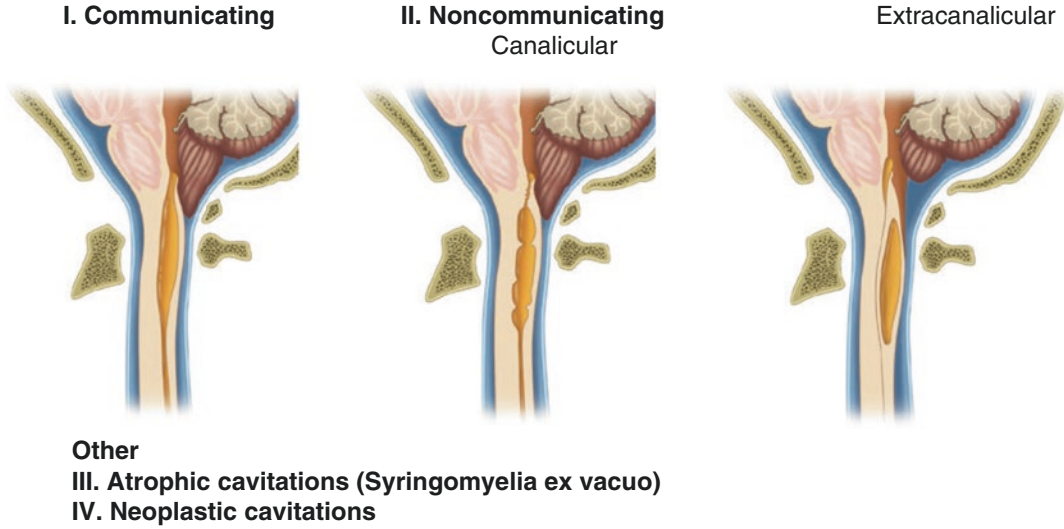

Fig. 20.3 Anatomical classification of syringomyelia by Milhorat. Communicating syringes are associated with obstruction of the outlets of the fourth ventricle and often hydrocephalus. The syrinx communicates directly with the fourth ventricle via the central canal. Noncommunicating canalicular syringes start as dilatations of the central canal that do not communicate with the fourth ventricle, but may then rupture into the spinal cord. These are more common with chronic posterior fossa abnormalities such as the Chiari I malformation. Noncommunicating extracanalicular syringes form as a cavity separate to the central canal, and are the most common type occurring after spinal cord trauma. From Brodbelt and Stoodley (2003), with permission

above the level of injury (Kramer and Levine 1997). The pain is often at or above the level of injury and may be mild or severe, constant or intermittent. Coughing, sneezing, straining, or sitting make the pain worse (Schurch et al. 1996). In most patients, sensory loss starts at the level of the injury and moves upwards, often insidiously. The speed and direction of progression of the sensory deficit vary from patient to patient, and some patients taking years, but sometimes progress rapidly within hours. Dissociated sensory loss of pain and temperature and preserved sensation for light touch or proprioception occur when the cyst is formed at the base of the posterior horn of the gray matter in the spinal cord, interrupting the crossing fibers of the spinothalamic tract just anterior to the central canal. Sometimes both deep and superficial sensations are lost, as shown by the development of Charcot joints in these patients. Motor involvement is an unusual initial presentation. The onset of weakness is usually subtle and insidious (Barnett and Jousse 1976). However, as the syrinx grows, the ventral horn of the gray matter may be involved (see Fig. 17.2). Patients generally report a gradual loss of motor function above the level of the previous injury. There is now evidence that spasticity in people with spinal cord injury with a syrinx is worse than those without syringes (Edgar and Quail 1994; Schurch et al. 1996).

In addition to the sensorimotor symptoms, there is often a painless joint deformity, a decrease in reflex micturition, and autonomic dysfunctional symptoms. Dysautonomic features may also be identified, such as emerging orthostatic hypotension, autonomic dysreflexia, and hyperhidrosis. When the syrinx extends into the upper cervical segments, trigeminal symptoms and Horner's sign may occur. If the lesion involves the brainstem causing syringobulbia, symptoms include hiccups, nystagmus, recurrent laryngeal nerve palsy, hypoglossal nerve palsy, or death. All symptoms associated with syringomyelia can be exacerbated by coughing, sneezing, or body movement. The insidious progression of posttraumatic syringomyelia can be devastating when added to the already compromised neurological function after spinal cord injury (Barnett and Jousse 1976).

20.1.5 Diagnosis

Diagnosis of posttraumatic syringomyelia is often delayed because the presence of a spinal cord injury precedes a subtle deterioration of neurological signs and symptoms. The patient may notice the ascending progression of sensorimotor symptoms above the neurological deficit caused by the spinal cord injury. Symptoms of posttraumatic syringomyelia are initially minimal and consist of subtle sensory or motor symptoms above the level of injury. Paraplegic patients using a wheelchair after spinal cord injury may complain of difficulty in mobilizing the chair due to progressive arm weakness. Serial quantitative measurements of strength, including pinch, grip, or hand myometry, are useful for monitoring the progression of weakness in addition to periodic neurological examination based on International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI).

Physicians should be aware of the possibility of posttraumatic syringomyelia and perform early imaging studies to confirm this diagnosis. Imaging studies, especially MRI, are the preferred method for the diagnosis and monitoring of posttraumatic syringomyelia. MRI provides a clear diagnosis of posttraumatic syringomyelia. MRI shows that syringes are often asymmetrical, loculated, or multiple, and this information can be helpful in surgical planning. Due to partial volume effects, MRI may not be able to sufficiently detect cavities within small spinal cords or in patients with scoliosis or other bony deformities (Brodbelt and Stoodley 2003). Cardiac-gated cine MRI by pulsatile movements of the syrinx and related structures is used to study spinal CSF flow to determine areas of flow obstruction corresponding to arachnoid pathology (Fujimoto et al. 2004; Klekamp 2012c). CISS (constructive interference in steady state) sequences can be used to demonstrate the syrinx and to detect the arachnoid webs, scars, and cysts, which are less susceptible to CSF flow artifacts (Hirai et al. 2000). The severity of syringomyelia can be assessed by measuring the cross-sectional area of syringes and calculating the percentage of the cross-sectional area of the spinal cord occupied by the cyst.

20.1.6 Management

Posttraumatic syringomyelia remains difficult to treat. The generally accepted treatment of choice is surgical drainage of the syrinx, but there is no current consensus on the optimum method of drainage (Carroll and Brackenridge 2005). Despite reports of neurological recovery following surgery, 5- and 10-year follow-up studies demonstrate deterioration or stabilization only in up to 80% of cases, regardless of the method of treatment or achievement of radiological improvement (Brodbelt and Stoodley 2003; Sgouros and Williams 1995). Surgical options to re-establishing cerebrospinal fluid flow in the subarachnoid space include correction of deformity or compression, various shunting procedures, arachnolysis with or without duraplasty, and cord transection (Klekamp 2012b). In a systemic review of surgical management for posttraumatic syringomyelia, the literature does not provide strong evidence for the superiority of one surgical technique over the others. However, the consensus panel gave a weak recommendation that spinal cord untethering with expansile duraplasty is the preferred first-line surgical technique (Bonfield et al. 2010). A recent review shows that there is no satisfactory standard treatment for syringomyelia, even when posttraumatic syringomyelia is diagnosed early in its evolution. No clear consensus on the recommended treatment exists (Kleindienst et al. 2020). Posttraumatic syringomyelia remains a neurosurgical challenge that is diagnosed even at the beginning of its course.

20.2 Chiari Malformations

20.2.1 Classification

Chiari malformations are abnormalities of the hindbrain development characterized by displacement of the caudal part of the cerebellum and, in some cases, of the lower brainstem in the cervical spinal canal by the foramen magnum. They are classified according to the parts of the hindbrain that protrude into the spinal canal and its associated anatomic abnormalities (Table 20.2). In patients with Chiari malformations, CSF flow can be compromised by cerebellar tonsils filling the space of the cisterna magna,

Table 20.2 Pathological classification and new radiological variants of Chiari malformations

Chiari	Description	Association
I	Herniation of the cerebellar tonsils 5 mm below the foramen magnum	Association with craniosynostosis, skull base anomalies, and craniocephalic mismatch
II (Arnold-Chiari)	Herniation of the cerebellar vermis and fourth ventricle Low-lying tentorium with low torcula occipital lobe often posterior to cerebellum	Associated with myelomeningocele, defect, hydrocephalus, syringomyelia, and neurological deficits
III	Cerebellum, brainstem, fourth ventricular herniation with occipital or occipitocervical meningoencephalocele	Most serious form of Chiari malformation. Hydrocephalus may be present. Severe neurological deficits, incompatible with survival
IV	Cerebellar hypoplasia, fourth ventricle communicates with cisterna magna, no hindbrain hernia	Dandy-Walker-type malformation
Proposed new variants		
0	Patients with headaches and other symptoms of Chiari malformation or syringomyelia and no tonsillar hernia or tonsillar hernia less than 3 mm	Abnormal CSF flow at the posterior fossa or foramen magnum as the suspected cause for syringomyelia
1.5	A Chiari is seen in combination with brainstem herniation through the foramen magnum	Obex below the foramen magnum. Flat medulla oblongata. Mean backward angulation of the odontoid process in relation to the C2 body was 84°. Fifty percent have syringomyelia. Patients may not respond well to posterior fossa decompressive surgery, especially if syringomyelia is present.

From Flint and Rusbridge (2014), with permission

arachnoid scarring in the foramen magnum area, and obstruction of the foramen of Magendie (Klekamp 2012c).

Type I Chiari malformation is accompanied by a herniation of the cerebellar tonsils below the foramen magnum and constitutes the common form. Syringomyelia is present in more than 30% of type I Chiari malformation. Type I Chiari malformation is characterized by caudal descent of the cerebellar tonsils (≥5 mm) through the foramen magnum. It is associated with arachnoidal adhesions between the cerebellar tonsils and hydromyelia or syringomyelia. Although it is possible that the cerebrospinal fluid flow disorder and cerebrospinal fluid pressure abnormalities are the cause of syringomyelia, the exact mechanism underlying syringomyelia is not clear. The syrinx is often located in the mid-cervical region but may extend caudally or rostrally (Sekula Jr. et al. 2011). Kinking of the lower medulla is common. However, herniation of the medulla itself through the foramen magnum is rare (McVige et al. 2014). Type II Chiari malformation is associated with a more extensive pathology throughout the craniospinal axis. It is usually associated with meningomyelocele and hydrocephalus (Liptak and Dosa 2010). In addition to herniation of the cerebellar tonsils, the cerebellar vermis, fourth ventricle, and medulla also protrude through the foramen magnum. The clinical relevance of the attempt to differentiate hindbrain malformation into Chiari I and II based on poorly defined anatomical criteria has not been established. Chiari II malformation is defined as cerebellar descending in the presence of a neural tube defect, regardless of associated abnormalities or age of onset. In some cases, there may be some confusion in the distinction between Chiari I and II malformations. Kinking of the cervicomedullary junction and caudal dislocation of the medulla were used to diagnose Chiari II malformations in adults without neural tube defect (Eisenstat et al. 1989). Chiari III anomaly is a caudal displacement of the cerebellum and brainstem into a high cervical or suboccipital meningocele. A Chiari IV malformation is caused by cerebellar hypoplasia without cerebellar herniation. Also, see Chap. 18.

20.2.2 Pathogenesis of Chiari I Malformation and Syringomyelia

All the signs and symptoms of Chiari I malformation are present in adulthood. Cerebellar herniation through the foramen magnum results from changes in normal CSF dynamics resulting from the posterior fossa. It has long been thought that change in CSF flow due to tonsillar herniation contributes to the formation of syringomyelia (Sekula Jr. et al. 2011).

The mechanism of altered CSF dynamics contributes to the formation and expansion of syrinx. It is purely speculative and subject to much controversy. The hydrodynamic theory suggested that syringomyelia was caused by the expansion of the central canal of the spinal cord, and the cavitation was caused by excessive ventricular pulsations. Due to obstruction at the foramina of Luschka and Magendie, the water hammer effect of the choroid plexus-driven CSF caused dilatation, hydromyelia, and syringomyelia (Rufener et al. 2011). The cranial-spinal pressure dissociation theory suggested that obstruction of cranial CSF flow down into the spinal subarachnoid space occurs at the foramen magnum following tonsillar herniation. Thus, a cranial-spinal pressure gradient was created, which caused CSF to flow from the fourth ventricle into the central canal, eventually leading to the formation of the syrinx (Fig. 20.4). The pressure gradient forced CSF into the central canal, resulting in a further expansion of syrinx (suck effect). The hydrodynamic theory suggests arterial pulse pressure acting from the inside of the neural axis to generate a syrinx, while the cranial-spinal pressure dissociation theory suggests a relatively long intrathoracic venous pulsation initially acting on the syrinx cavity from outside (slosh) and then from inside (suck). There are many arguments for these hypotheses, alone, or in various combinations. Many of the arguments discussed were strongly criticized because the human central canal was regarded as vestigial and its obliteration occurred in childhood (de Souza et al. 2011). Although the progressive degree of stenosis develops with age, a large autopsy series has shown that most adults maintain a patent central

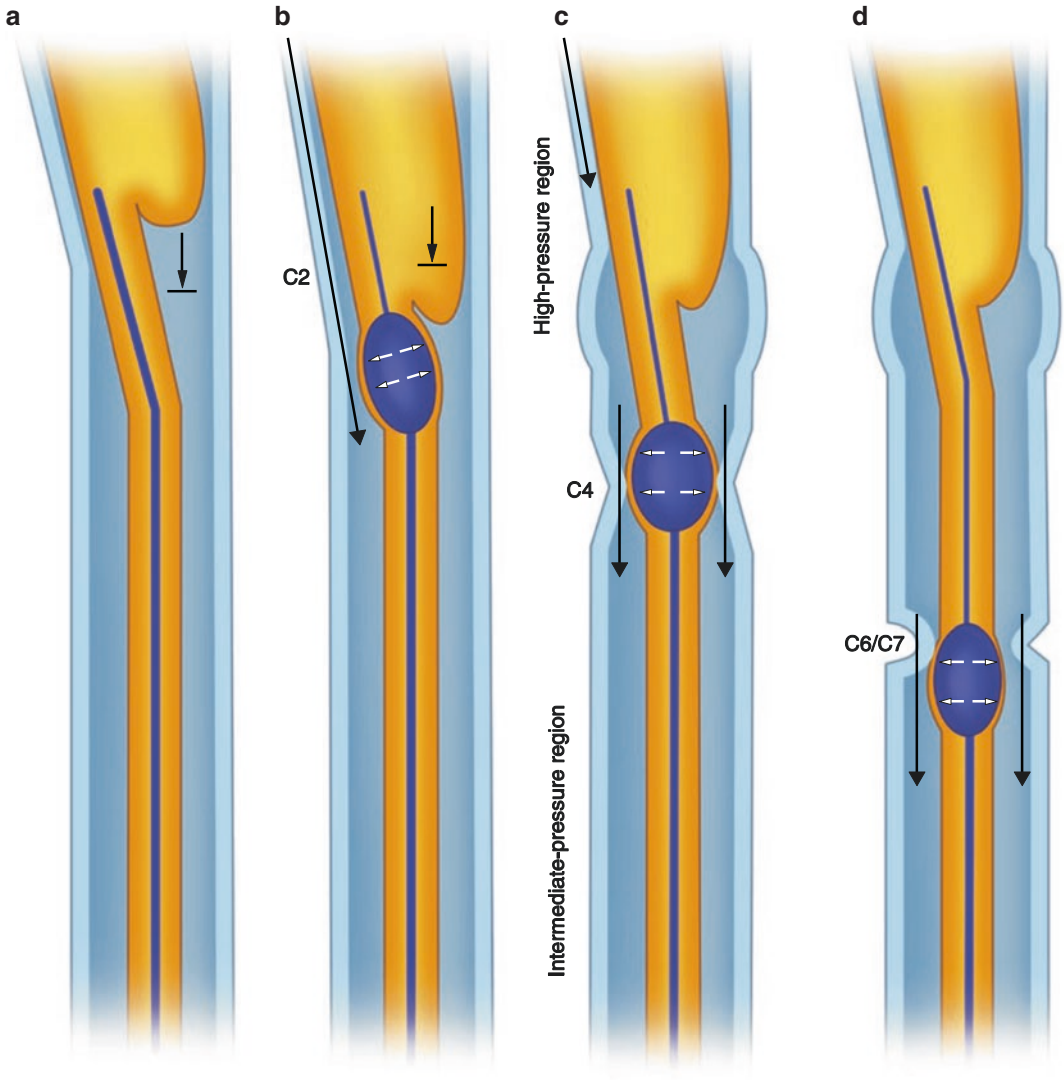

Fig. 20.4 Syringomyelia associated with Chiari 1 malformation. In Chiari malformations, the increased intracranial pulse pressure and downward motion of the cerebellar tonsils increases the systolic pressure transmission to the distal CSF spaces. In this way, a shock-like CSF pressure wave is created that explains the extended Venturi effect in the spinal canal. (**a**) Pre-systolic phase of the cervical spinal canal. (**b**) When the spinal canal is wide, the systolic CSF flow jet at the foramen magnum (black arrow with tail) causes a Venturi effect or a suction effect on the spinal cord, which distends the cord and central canal just below the obstructing cerebellar tonsils (white arrows). (**c**) When the subarachnoid space is narrowed, e.g., by the cervical intumescence, the pressure differences between the cord and CSF are rapidly leveled out in the high-pressure region above the subarachnoid impediment. However, at the intumescence of cervical cord, the Venturi effect or the suction effect of the systolic CSF flow jet is unrestricted. Therefore, syringomyelia often develops at this level. (**d**) When a bulging disc is present, syringomyelia develops just below that level. From Greitz (2006), with permission

canal in the upper cervical region throughout life (Milhorat et al. 1994). Therefore, it is still appropriate to consider a patent central canal in the pathogenesis of syringomyelia associated with Chiari malformation (Klekamp 2012a; Levy et al. 1983).

The normal pattern of CSF flow is closely related to the cardiac cycle. The pulsation in the basal cisterns is caused by the expansion of the cerebral hemispheres and is much larger than the concordant pulsations within the ventricular system (DuBoulay et al. 1974). Caudal CSF pulsa-

tion in the cisterns is greatest in systole, but cranial pulsation is greatest in diastole. The flow direction at the foramen magnum and at C2 during the very early phase of systole (within the first 100 msec) is in a cranial direction. In normal subjects, despite this pulsatile movement of the cerebral hemispheres and CSF, the brainstem and cerebellum do not move within the posterior fossa (Battle et al. 2011). However, in patients with Chiari malformation, pulsatile movements of the cerebellar tonsils during the systole appear downward into the upper cervical spinal canal, followed by retraction during diastole, resulting in obstruction of CSF flow at the craniocervical junction (DuBoulay et al. 1974). In Chiari I malformations, the velocity and the duration of caudal CSF flow at the foramen of Magendie and foramen magnum are reduced. During middle-to-late systole, the flow direction through the foramen magnum tends to be cranially directed, unlike the caudal flow seen in normal individuals.

20.2.3 Clinical Presentation

The Chiari I malformation may remain asymptomatic. The clinical evolution is variable and unpredictable. Type II malformations are often present in infancy or early childhood and are one of the leading causes of death in infancy or in childhood with myelomeningoceles. Insidious symptoms of Chiari I malformation may appear in adolescence or adulthood. The majority of patients with Chiari I malformation develop symptoms between the third and fifth decades, and later only 5%. It has been reported that syringomyelia is associated with symptomatic Chiari I in 40–80.5% of cases (Milhorat et al. 1999). Asymptomatic Chiari I patients likely have a much lower incidence of syringomyelia (Sekula Jr. et al. 2011). The syrinx is most commonly affected in the cervical spinal cord, usually in the upper cervical region. When there is thoracic cord involvement, it extends from a cervical origin, except in very rare cases. Women may have a higher incidence than men. Ten to twenty percent of children with meningomyelocele show symptoms associated with dysfunction of the cranial nerve, cerebellum, or brainstem. If the neural tube defect is at or above L3, the incidence is higher (Blegvad et al. 2014; Dicianno et al. 2008).

In Chiari I malformation, neck pain and occipital headache are common initial symptoms and can be exacerbated by activity, stooping, Valsalva maneuver, and sneezing or coughing. Symptoms of Chiari I malformation can occur even without syrinx, probably due to compression or stretching of cervical roots. Patients with syringomyelia often experience painful or burning pain in the neck, shoulder, and arm that are often asymmetrical (Saletti et al. 2011). The classic presentation of syringomyelia is a dissociated sensory loss of pain and temperature sensation with preserved touch and vibration in a cape distribution on the neck, shoulders, and arms. In most cases, it starts asymmetrically and can cause injuries or burns to the hand due to impaired sensation. As a result, claw hand deformation can occur. The extension of the syrinx in gray matter can lead to muscle weakness and loss of reflexes in the upper extremities.

Classic Chiari headache is described as a dull or throbbing occipital or suboccipital discomfort aggravated by sudden changes of intracranial pressure caused by increased intrathoracic pressure or postural changes of the head (Klekamp 2012a). The gradual expansion of the syrinx and the compression of the spinal cord of the white matter can lead to spastic paralysis of the legs, bladder and bowel dysfunction, and a Horner's syndrome. Horner's syndrome is due to lesions involving descending sympathetic pathways or cells in the T1 and T2 intermediolateral column. The typical clinical findings of Chiari I malformations can also be related to cerebellar, bulbar, or spinal cord dysfunction. Syringobulbia due to the extension of the syrinx in the brainstem with involvement of the cranial nerve can cause dysarthria, dysphagia, nystagmus, dizziness, and tongue atrophy. When two disorders coexist, it can be difficult to isolate symptoms and signs caused by the Chiari malformation, such as nystagmus, ataxia, vertigo, dizziness, and head and neck pain, from the symptoms by the syrinx (Saletti et al. 2011). The more common clinical presentations are listed in Table 20.3.

Children with syringomyelia often develop progressive scoliosis, although this is rare in adults due to skeletal maturity. In some cases, craniovertebral abnormalities may occur, such as Klippel-Feil anomaly with fusion of C2 and C3 vertebrae and a short neck and a low hairline on examination (de Souza et al. 2011).

Table 20.3 Presenting symptoms and signs in Chiari malformation with or without syringomyelia

Clinical findings in Chiari I malformation without syringomyelia	Clinical findings in Chiari I malformation with syringomyelia
Headache, neck pain	Extremity numbness
Nystagmus	Extremity weakness
Extremity weakness	Extremity pain
Hyperreflexia, spasticity	Gait disturbance
Gait disturbance	Spasticity, hyperreflexia
Ataxia	Headache, neck pain
Dysphagia	Nystagmus
Dysarthria	Bladder/bowel dysfunction
Sleep apnea	Decreased facial sensation
	Neuropathic joint
	Scoliosis

20.2.4 Management

Chiari I malformation can be treated with medical and surgical management. Initially, medical management is performed through pharmacotherapy, physical therapy, and therapeutic injections. Since headaches are the most common presenting symptom of Chiari I malformation, they are usually treated based on the presenting phenotype. The decision for surgery is based on a combination of the clinical presentation, imaging and/or physiologic studies such as somatosensory evoked potentials, brainstem evoked potentials, swallow evaluations, and sleep studies. When surgery is required, most neurosurgeons prefer suboccipital craniectomy with cervical laminectomy with or without duroplasty as the primary surgical treatment. After Chiari decompression, postoperative CT is usually done within the first 24 h to document adequate decompression and to detect any hemorrhage, hydrocephalus, or pneumocephalus (McVige and Leonardo 2014). Figure 20.5 is a flow chart for clinical management of Chiari I malformation.

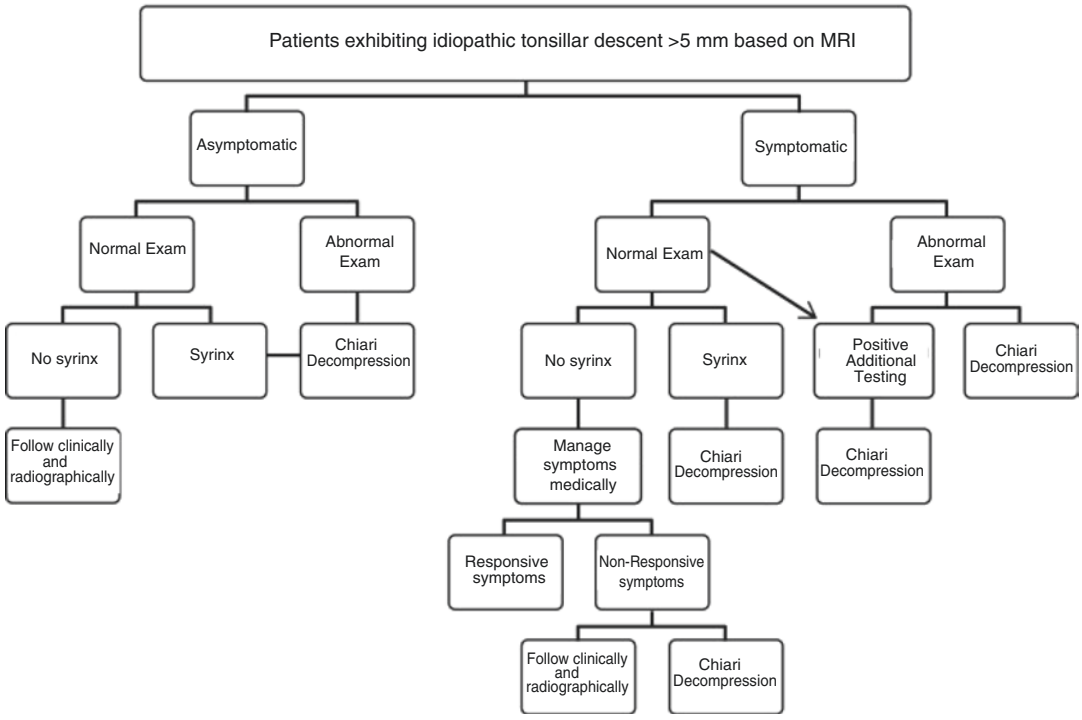

Fig. 20.5 Flow chart for clinical management of Chiari I malformation. From McVige and Leonardo (2014), with permission

References

Backe HA, Betz RR, Mesgarzadeh M, et al. Post-traumatic spinal cord cysts evaluated by magnetic resonance imaging. Paraplegia. 1991;29:607–12.

Barnett HJM, Jousse AT. Posttraumatic syringomyelia (cystic myelopathy). In: Vinken PJ, Bruyn GW, Braakman R, editors. Injuries of the spine and spinal cord. Amsterdam: North-Holland Publishing Company; 1976.

Blegvad C, Grotenhuis JA, Juhler M. Syringomyelia: a practical, clinical concept for classification. Acta Neurochir. 2014;156:2127–38.

Bogdanov EI, Mendelevich EG. Syrinx size and duration of symptoms predict the pace of progressive myelopathy: retrospective analysis of 103 unoperated cases with craniocervical junction malformations and syringomyelia. Clin Neurol Neurosurg. 2002;104:90–7.

Bonfield CM, Levi AD, Arnold PM, et al. Surgical management of post-traumatic syringomyelia. Spine (Phila Pa 1976). 2010;35(21 Suppl):S245–58.

Brodbelt AR, Stoodley MA. Post-traumatic syringomyelia: a review. J Clin Neurosci. 2003;10:401–8.

de Souza RM, Zador Z, Frim DM. Chiari malformation type I: related conditions. Neurol Res. 2011;33:278–84.

Dicianno BE, Kurowski BG, Yang JM, et al. Rehabilitation and medical management of the adult with spina bifida. Am J Phys Med Rehabil. 2008;87:1027–50.

DuBoulay GH, Shah SH, Currie JC, et al. The mechanism of hydromyelia in Chiari type I malformation. Br J Radiol. 1974;47:579–87.

Edgar R, Quail P. Progressive post-traumatic cystic and non-cystic myelopathy. Br J Neurosurg. 1994;8:7–22.

Eisenstat DDR, Bernstein M, Fleming JFR, et al. Chiari malformation in adults: a review of 40 cases. Can J Neurol Sci. 1989;13:221–8.

Falci SP, Indeck C, Lammertse DP. Posttraumatic spinal cord tethering and syringomyelia: surgical treatment and long-term outcome. J Neurosurg Spine. 2009;11:445–60.

Fischbein NJ, Dillon WP, Cobbs C, et al. The "presyrinx" state: a reversible myelopathic condition that may precede syringomyelia. AJNR Am J Neuroradiol. 1999;20:7–20.

Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.

Fujimoto S, Mizuno R, Saito Y, et al. Clinical application of wave intensity for the treatment of essential hypertension. Heart Vessel. 2004;19:19–22.

Greitz D. Unraveling the riddle of syringomyelia. Neurosurg Rev. 2006;29:251–63. discussion 264

Griffiths ER, McCormick CC. Post-traumatic syringomyelia (cystic myelopathy). Paraplegia. 1981;19:81–9.

Hilton EL, Henderson LJ. Neurosurgical considerations in posttraumatic syringomyelia. AORN J. 2003;77:135–9. 141-4

Hirai T, Korogi Y, Shigematsu Y, et al. Evaluation of syringomyelia with three-dimentional constructive interference in a steady state (CISS) sequence. J Magn Reson Imaging. 2000;11:120–6.

Kleindienst A, Laut FM, Roeckelein V, et al. Treatment of posttraumatic syringomyelia: evidence from a systematic review. Acta Neurochir. 2020;162:2541–56.

Klekamp J. The pathophysiology of syringomyelia - historical overview and current concept. Acta Neurochir. 2002;144:649–64.

Klekamp J. Surgical treatment of Chiari I malformation-analysis of intraoperative findings, complications, and outcome for 371 foramen magnum decompressions. Neurosurgery. 2012a;71:365–80.

Klekamp J. Treatment of posttraumatic syringomyelia. J Neurosurg Spine. 2012b;17:199–211.

Klekamp J. Treatment of syringomyelia related to non-traumatic arachnoid pathologies of the spinal canal. Neurosurgery. 2012c;72:376–89.

Klekamp J, Batzdorf U, Samii M, et al. Treatment of syringomyelia associated with arachnoid scarring caused by arachnoiditis or trauma. J Neurosurg. 1997;86:233–40.

Ko HY, Kim W, Kim SY, et al. Factors associated with early onset post-traumatic syringomyelia. Spinal Cord. 2012;50:695–8.

Kramer KM, Levine AM. Posttraumatic syringomyelia: a review of 21 cases. Clin Orthop Relat Res. 1997;334:190–9.

Levy WJ, Mason L, Hahn JF. Chiari malformation presenting in adults: a surgical experience in 127 cases. Neurosurgery. 1983;12:377–90.

Liptak GS, Dosa NP. Myelomeningocele. Pediatr Rev. 2010;31:443–50.

McVige JW, Leonardo J. Imaging of Chiari type I malformation and syringohydromyelia. Neurol Clin. 2014;32:95–126.

Milhorat TH. Classification of syringomyelia. Neurosurg Focus. 2000;8:E1.

Milhorat TH, Capocelli AL Jr, Anzil AP, et al. Pathological basis of spinal cord cavitation in syringomyelia: analysis of 105 autopsy cases. J Neurosurg. 1995;82:802–12.

Milhorat TH, Chou MW, Trinidad EM, et al. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery. 1999;44:1005–17.

Milhorat TH, Kotzen RM, Anzil AP. Stenosis of the central canal of spinal cord in main: incidence and pathological findings in 232 autopsy series. J Neurosurg. 1994;80:716–22.

Moriwaka F, Tashiro K, Tachibana S, et al. Epidemiology of syringomyelia in Japan—the nationwide survey. Rinsho Shinkeigaku. 1995;35:1395–7. Japanese

Rigamonti DD, Wrathall JR, Kao CC. Lysosomal autolysis of contused spinal cords. Program Soc Neurosci. 1978;4:570.

Roy AK, Slimack NP, Ganju A. Idiopathic syringomyelia: retrospective case series, comprehensive review, and update on management. Neurosurg Focus. 2011;31:E15.

Rufener S, Ibrahim M, Parmar HA. Imaging of congenital spine and spinal cord malformations. Neuroimaging Clin N Am. 2011;21:659–76.
Saletti V, Esposito S, Frittoli M, et al. Neurological pictures in paediatric Chiari I malformation. Neurol Sci. 2011;32(Suppl 3):S295–8.
Schurch B, Wichmann W, Rossier AB. Post-traumatic syringomyelia (cystic myelopathy): a prospective study of 449 patients with spinal cord injury. J Neurol Neurosurg Psychiatry. 1996;60:61–7.
Sekula RF Jr, Arnone GD, Crocker C, et al. The pathogenesis of Chiari I malformation and syringomyelia. Neurol Res. 2011;33:232–9.
Sgouros S, Williams B. A critical appraisal of drainage in syringomyelia. J Neurosurg. 1995;82:1–10.
Sharma M, Coppa N, Sandhu GA. Syringomyelia: a review. Sem Spine Surg. 2006;18:180–4.
Shields CB, Zhang YP, Shields LB. Post-traumatic syringomyelia: CSF hydrodynamic changes following spinal cord injury are the driving force in the development of PTSM. Handb Clin Neurol. 2012;109:355–67.
Umbach I, Heilporn A. Review article: post-spinal cord injury syringomyelia. Paraplegia. 1991;29:219–21.
Vannemreddy SS, Rowed DW, Bharatwal N. Posttraumatic syringomyelia: predisposing factors. Br J Neurochir (Wien). 2002;55:295–302.
Wang D, Bodley R, Sett P, et al. A clinical magnetic resonance imaging study of the traumatised spinal cord more than 20 years following injury. Paraplegia. 1996;34:65–81.
Williams B. On the pathogenesis of syringomyelia: a review. J Royal Soc Med. 1980;73:798–806.
Williams B. Post-traumatic syringomyelia, an update. Paraplegia. 1990;28:296–313.
Williams B. Pathogenesis of post-traumatic syringomyelia. Br J Neurosurg. 1992;6:517–20.
Williams B, Terry AF, Jones HWF, et al. Syringomyelia as a sequel to traumatic paraplegia. Paraplegia. 1981;19:67–80.
Yarkony GM, Sheffler LR, Smith J, et al. Early onset post-traumatic cystic myelopathy complicating spinal cord injury. Arch Phys Med Rehabil. 1994;75:102–5.

Recommended Additional Reading

Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies. 1st ed. New York: Oxford University Press; 2001.
Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Cohen-Adad J, Wheeler-Kingshott CAM, editors. Quantitative MRI of the spinal cord. New York: Elsevier; 2014.
Eagler GL, Cole J, Merton, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker, Inc.; 1998.
Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.
Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.
Mancall E, editor. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.
ten Donkelaar HJ, Lammens M, Hori A. Clinical neuroembryology: development and developmental disorders of the human central nervous system. 2nd ed. Heidelberg: Springer; 2014.
Verhaagen J, McDonald III JW, editors, Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology. 3rd series, vol. 109. London: Elsevier; 2012.
Vogel LC, Zebracki K, Betz RR, et al., editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.
Weidner N, Rupp R, Taney KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.

21 Autonomic Nervous System Dysfunction After Spinal Cord Injuries

The term *autonomic* comes from *auto*, the meaning of self, and *nomos* stands for law. The autonomic nervous system is largely responsible for regulating internal organs, adapting them to the needs of the movement, and maintaining the normal internal environment of the body. The autonomic nervous system performs by itself, mostly unconsciously and according to its own internal laws, the maintenance of essential internal homeostatic activities such as temperature, blood pressure, control of digestion, and other functions (Banister and Mathias 1992; Krassioukov and Weaver 1996). The target organs or tissues of the autonomic nervous system are the visceral muscle and the glandular epithelium. The main difference between the somatic and visceral organs of the nervous system is the speed of reaction. The visceral system with slow-acting smooth muscle tends to respond slowly to the internal stimuli, with the exception of pain responses. In contrast, skeletal muscle tends to respond rapidly to stimuli (Krassioukov and Weaver 1996). Most of the autonomic functions have involuntary activity, except when activating micturition, etc.

The autonomic nervous system is a component of the nervous system that has a major role in maintaining homeostasis and adaptive responses to external or internal stressors. It innervates all organs of the body, including the eye, the skin, and the cardiovascular, respiratory, gastrointestinal, and genitourinary systems, and functionally interacts with the endocrine, pain, and motor systems. The system regulates circulation, bowel function, urogenital system, temperature control, and sweating. In addition, the autonomic nervous system controls blood flow to skeletal muscle, kidneys, splanchnic circulation, and skin. Impaired regulation of the autonomic nervous system caused by spinal cord injury leads to many of the clinical problems that occur in individuals with spinal cord injuries, including altered cardiovascular and thermoregulatory function and manifestations of end-organ dysfunction such as neurogenic bowel and bladder (Garstang and Miller-Smith 2007). When normal autonomic control is disrupted, the local sign of the reflexes is lost, and mass reflexes appear. A spinal cord injury disrupts the connections between higher centers and the spinal cord and leads not only to the somatic motor and sensory deficits but also to autonomic dysfunctions.

People with spinal cord injury may have other presentations of autonomic dysfunction such as baseline hypotension, orthostatic hypotension, disturbed temperature regulation, decreased sweating, etc. (Garstang and Miller-Smith 2007). Hypotension and bradycardia last 2–6 weeks and are accompanied by arrhythmias, which occur primarily in the acute setting. Orthostatic hypotension occurs acutely but is clinically more relevant during the post-acute phase during rehabilitation when mobilization occurs. However, some patients have long-term

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orthostasis. These disabilities can cause life-threatening symptoms. In particular, high thoracic or cervical spinal cord injury often causes episodic hypertension associated with autonomic dysreflexia as a result of massive sympathetic discharges and deregulated sympathetic outflow (Hou and Rabchevsky 2014). Pulmonary effects of disruption of sympathetic innervation in individuals with tetraplegia are also important in the period immediately after injury. Chronic manifestations of autonomic dysfunction include impaired temperature regulation and impaired cardiovascular function and responses to exercise.

This chapter describes the anatomy of the autonomic nervous system, the general assessment of the autonomic function based on ISAFSCI (second ed.), specific tests that require a special device to assess the autonomic function, and the effects on autonomic nervous system after spinal cord injuries.

21.1 Anatomy of Autonomic Nervous System

The autonomic nervous system is divided into two main parts: the sympathetic nervous system and the parasympathetic nervous system (Fig. 21.1). Most organs of the autonomic nervous system are innervated by sympathetic and parasympathetic nerves, but the adrenal medulla, kidney, spleen, and most blood vessels have only sympathetic innervation. The enteric nervous system, also considered a division of the autonomic nervous system, is not directly disrupted after spinal cord injury. The enteric nervous system consists of neurons located in ganglia within the walls of the gut that are involved in local reflexes (Idiaquez et al. 2018).

The sympathetic and parasympathetic systems of the autonomic nervous system have two neurons between the central nervous system and target organs: preganglionic and postganglionic neurons. The preganglionic neurons located in the spinal cord or the gray matter of the brain constitute the first neuron. The preganglionic fibers (axons) are myelinated B fibers. The preganglionic fibers synapse on the second neuron (postsynaptic or postganglionic or ganglionic neuron). The preganglionic neurons receive and integrate two types of information, inputs from primary visceral afferents that trigger autonomic reflexes and descending inputs from central autonomic areas that initiate responses to stress, emotion, and other behavioral states. The postganglionic axons are unmyelinated C fibers (Krassioukov and Weaver 1996). Both the preganglionic and the postganglionic fibers frequently travel in components of the peripheral nervous system (spinal nerves, cranial nerves) and are intermingled with afferents and somatic motor fibers of peripheral nerves. The descending autonomic pathways from the brain travel into the spinal cord and terminate at the preganglionic sympathetic and parasympathetic neurons in the spinal cord that are located at T1–L2 and S2–S4, respectively. The target organs and corresponding spinal cord segments of the sympathetic and parasympathetic innervation are listed in Table 21.1.

21.1.1 Sympathetic Nervous System

The sympathetic preganglionic neurons are located in the intermediolateral cell column of the T1–L2 spinal cord segments. This is often referred to as the thoracolumbar system (division). The axons of the sympathetic preganglionic neurons travel within the ventral roots of the spinal cord or cranial nerves and the white rami communicans. They synapse with rostrally or caudally located paravertebral postganglionic neurons or bypass of the paravertebral postganglionic neuron to synapse on prevertebral ganglia. The preganglionic sympathetic neurons control visceral function via projections to two types of ganglia: the paravertebral sympathetic ganglia (sympathetic chain ganglia) and prevertebral sympathetic ganglia (the celiac, superior mesenteric ganglia, and inferior mesenteric ganglia) (Figs. 21.1 and 21.2). Postganglionic fibers innervate the corresponding target organs through

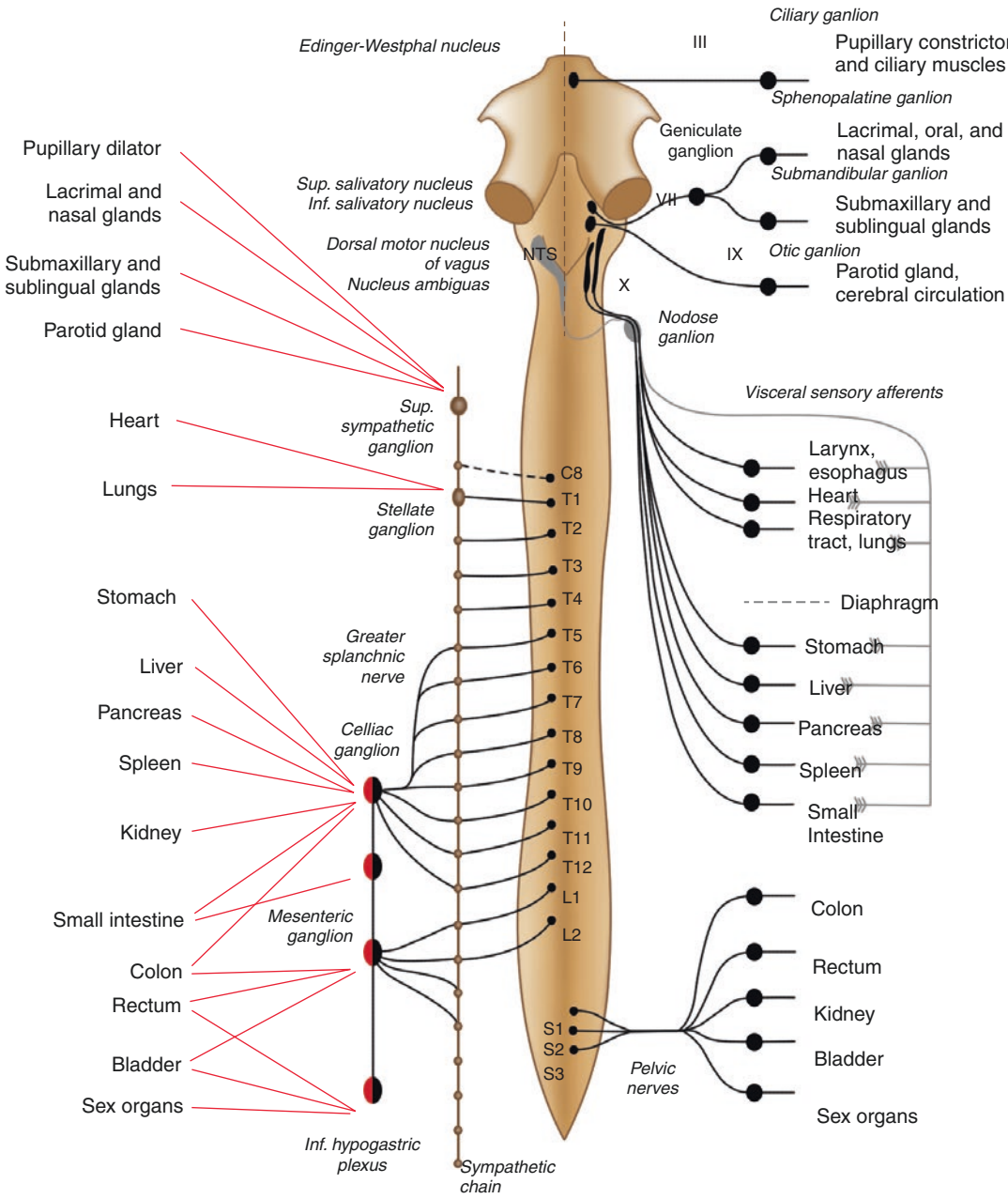

Fig. 21.1 The sympathetic (thoracolumbar) (left) division and the parasympathetic (craniosacral) (right) division of the autonomic nervous system. NTS, nucleus of the tractus solitarius in the brainstem. Adapted from Wehrwein et al. (2016)

the peripheral nerves (Krassioukov 2009). There are 11 paravertebral ganglia in the thoracic region and four lumbar and four sacral paravertebral ganglia (Garstang and Miller-Smith 2007). The paravertebral ganglia form a sympathetic trunk (chain) that looks like a string of beads on each side of the vertebral column and contain the ganglion neurons that innervate the terminal effec-

Table 21.1 Autonomic innervation of human major organ/systems

Organ/system	Sympathetic (T1–L2)	Parasympathetic (Vagus and S2–S4)	Somatic/motor
Heart	T1–T5	Vagus nerve (CN X)	None
Blood vessels Upper body Lower body	T1–T5 T6–L2	Blood vessels in certain organs: salivary glands, GI glands (CN X), genital erectile tissue (S2-S4)	None
Broncho-pulmonary	T1–T5	Vague nerve (CN X)	C3-C8
Sweat glands Face Upper limbs Trunk Lower limbs	T1–L2 T1–T4 T2–T8 T4–T12 T12–L2	None None None None None	None
Lower urinary tract Detrusor Bladder neck/internal urethral sphincter External urethral sphincter	T10–L2 T10–L2 None	S2–S4 None none	None None S2–S4
Gastrointestinal tract Esophagus to splenic flexure Splenic flexure to rectum/internal anal sphincter External anal sphincter	T1–L2 T1–L2 T10–L2	Vague nerve (CN X) S2–S4 S2–S4	None None S2–S4
Genitalia and reproductive organs Vagina Female reproductive organs Penis Male reproductive organs	T10–L2 T10–L2 T10–L2 T10–L2	S2–S4 S2–S4 S2–S4 S2–S4	S1-S4 S1-S4 S1-S4 S1-S4

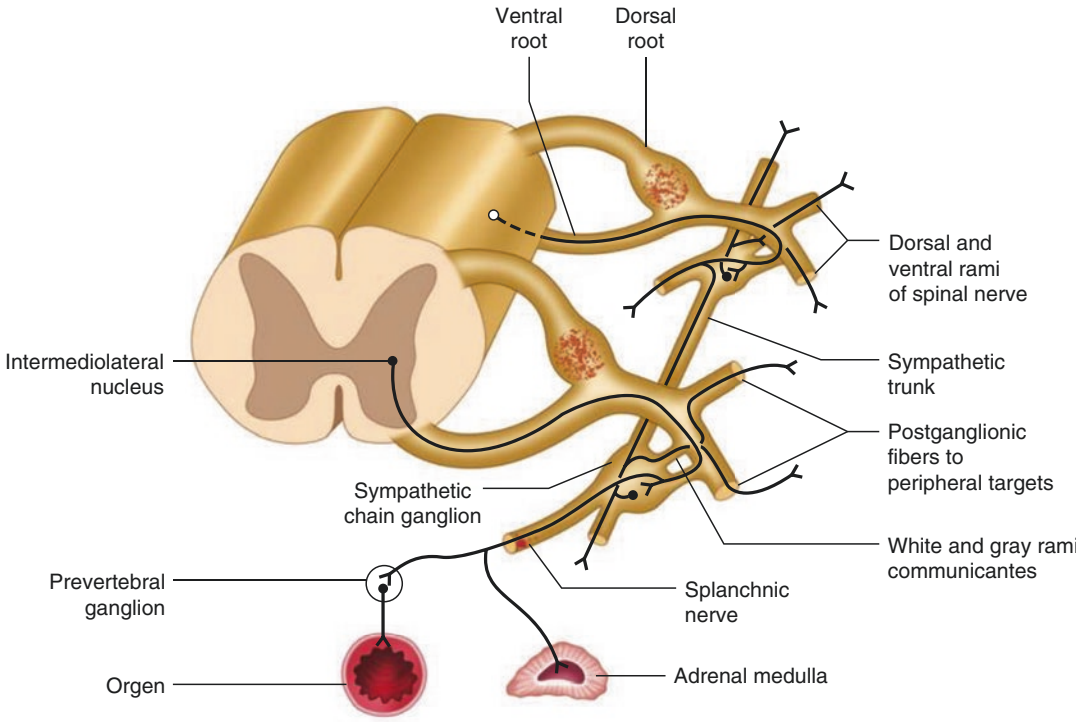

Fig. 21.2 The sympathetic chain, composed of sympathetic preganglionic and postganglionic axons. From Krassioukov and Weaver (1996), with permission

tors, including the eye and cerebral blood vessels, skin, and thoracic and abdominal, visceral including the heart, lungs, and gastrointestinal tract. The prevertebral ganglia lie close to the abdominal arteries and anterior to the spinal column, innervate all visceral and blood vessels of the abdomen and pelvis, including the rectum, bladder, and genital organs (Benarroch 2020). The name of the ganglia is named by the adjacent vessels, namely two celiac ganglia, the superior mesenteric ganglion and the inferior mesenteric ganglion.

Above the diaphragm, all sympathetic preganglionic fibers form a synapse in the sympathetic chain. In the cervical region, there are several paravertebral ganglia, namely the superior cervical ganglion, the middle cervical ganglion, and the stellate ganglion (which consists of the inferior cervical ganglion and first thoracic ganglion). The adrenal medulla is a unique organ that receives direct innervation by the preganglionic fibers from the spinal cord.

21.1.2 Parasympathetic Nervous System

The parasympathetic preganglionic neurons develop in the segments of the spinal cord S2–S4 and the brain stem (four cranial nerve nuclei of III, VII, IX, X). The parasympathetic nervous system is called the craniosacral system (division) of the autonomic nervous system because of the parasympathetic preganglionic neurons in the brainstem and sacral spinal cord (Garstang and Miller-Smith 2007). The cranial parasympathetic neurons occupy the general visceral efferent column of the brainstem and provide inputs from that area carried by cranial nerves to local ganglia that innervate effectors in the head and neck, thorax, and abdomen. The sacral parasympathetic neurons located in the sacral parasympathetic nucleus at the S2–S4 segments emerge with the ventral roots to form the principal motor component of the nerves, synapsing with short postganglionic neurons in the walls of the

bladder, descending colon and rectum, and the genital organs. The parasympathetic postganglionic neurons locate close to the organ being innervated. The parasympathetic preganglionic fibers travel a long distance to reach the terminal ganglia. The parasympathetic preganglionic fibers reach the terminal ganglia, which are near or within the visceral organ. The parasympathetic postganglionic fibers, after synapsis with the parasympathetic ganglia near the target organs, are short (Krassioukov and Weaver 1996) (Fig. 21.3). There is no parasympathetic innervation of the peripheral vasculature except in the pelvic organs and potentially the brain (Wecht et al. 2021).

21.2 Neurotransmitters

On the basis of the neurotransmitter that they release, autonomic fibers are classified as cholinergic and adrenergic. Autonomic preganglionic fibers release neurotransmitters at the synapses within the ganglia and at the contact point with a visceral organ. In the sympathetic and parasympathetic nervous system, the neurotransmitter for ganglion transmission of stimulation from preganglionic fibers to ganglionic neurons is acetylcholine, i.e., cholinergic. The neurotransmitter of the sympathetic ganglia and parasympathetic ganglia is acetylcholine. However, the neurotransmitters released between the ganglion

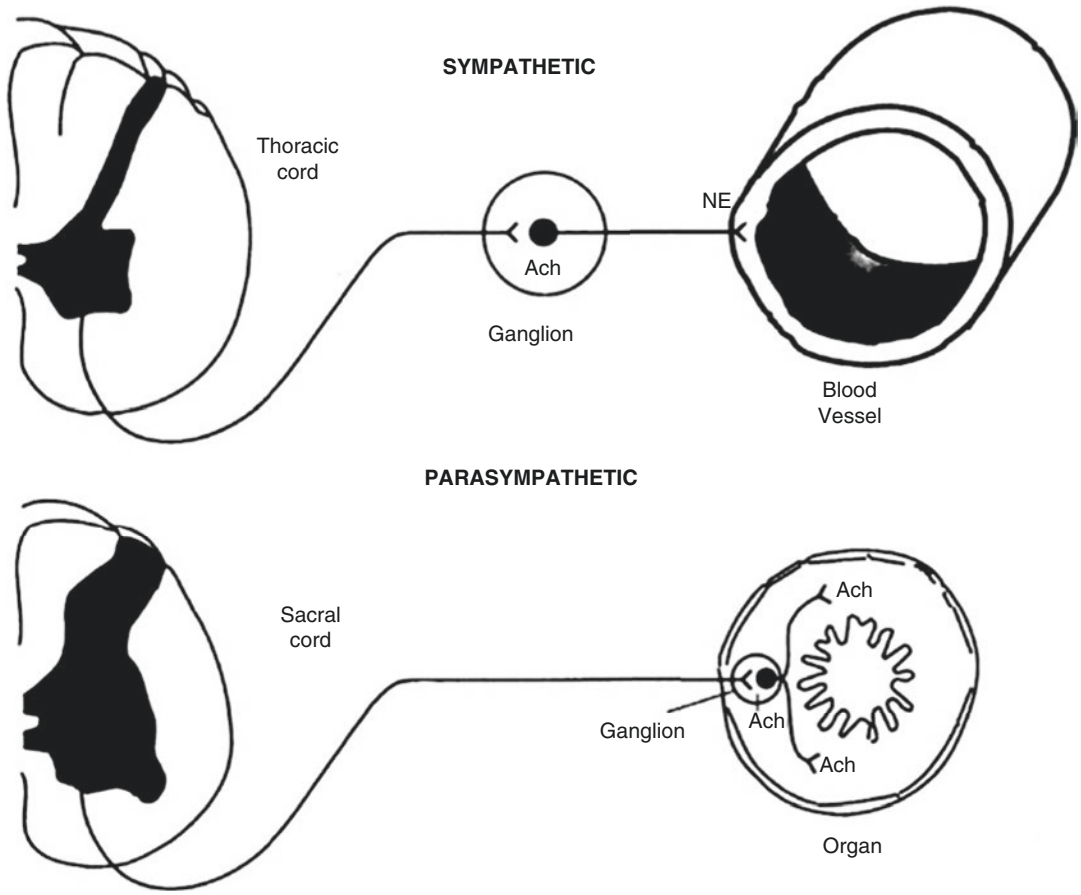

Fig. 21.3 A comparison of the location of ganglia and lengths of preganglionic and postganglionic fibers in the sympathetic and parasympathetic nervous systems. From Krassioukov and Weaver (1996)

fibers and the target organ are different. In the sympathetic nervous system, the effector organs receive the adrenergic postganglionic fibers, and the neurotransmitter is norepinephrine; the exception is sympathetic ganglion neurons innervating the sweat glands, which are cholinergic. In the parasympathetic nervous system, acetylcholine is a neurotransmitter in the neuroeffector junction of the target organ (Krassioukov and Weaver 1996). In summary, sympathetic preganglionic neurons are affected by acetylcholine, and postganglionic neurons are affected by norepinephrine, except for the sudomotor fiber, which is controlled by acetylcholine. On the other hand, parasympathetic preganglionic neurons are located in the third, seventh, ninth, and tenth cranial nerves and the S2–S4 spinal cord segments, and both preganglionic neurons and postganglionic neurons are regulated by acetylcholine.

In the cardiovascular system and upper gastrointestinal system, the tenth cranial nerve goes to the S-A node of the heart and the intrinsic nervous system of the intestine. There is no parasympathetic nerve innervation of the peripheral blood vessels, except the vascular system in the pelvic organs affected by the parasympathetic nervous system of S2–S4. The sweat glands are controlled by sympathetic nerves similar to blood vessels, and the upper part of the body is affected by T1–T5 and the lower part of the body by spinal sympathetic neurons of T5–L2 (Quinton 1983). There are two exceptions in the sympathetic innervation of target organs: the adrenal medulla is innervated directly by preganglionic cholinergic fibers; the sweat glands receive postganglionic cholinergic fibers, which are similar to innervation to target organs by the parasympathetic nervous system.

The effect of acetylcholine and norepinephrine is determined by the type of postsynaptic receptor in the organs. There are two types of acetylcholine receptors: nicotinic receptors and muscarinic receptors. The effect of norepinephrine (and/or epinephrine) is determined by two types of postsynaptic receptors, α receptors and β receptors. Two major subtypes of α receptors are α_1 receptor and α_2 receptor. The α_1 receptors are generally excitatory and postsynaptic receptors, while α_2 receptors are presynaptic receptors and are involved in feedback regulation. The α_1 receptors mediate excitation of the smooth muscle in blood vessels, iris (pupil dilator), vas deferens, bladder neck, and internal sphincter of the rectum. The α_2 receptors are less common than α_1 receptors. They are found in the wall of the gastrointestinal tract. The α_2 receptors are located mostly in presynaptic terminals, and their main effect is presynaptic inhibition of the release of norepinephrine from sympathetic terminals (inhibitory autoreceptors) or other neurotransmitters from parasympathetic or afferent terminals (Benarroch 2020).

Subtypes of the β receptors are defined as the β_1 and β_2 receptors. The β_1 receptors are prominent in the heart (increase in heart rate and myocardial contractility), in the saliva glands (increase in secretion), in the adipose tissue, and in the kidney (where they promote renin secretion). The β_2 receptors are found in the vascular smooth muscle of skeletal muscle, in the walls of the gastrointestinal tract and bladder, and in the bronchioles. The activation of β2-receptors in these tissue leads to relaxation or dilatation (Benarroch 2020). Almost all visceral organs receive innervation from both sympathetic and parasympathetic nervous systems, with the exception of most blood vessels that are only sympathetically innervated.

The effects of acetylcholine on target organs are primarily mediated by muscarinic receptors, including excitatory M1-like (M1 and M3 subtypes) and inhibitory M2 receptors. Muscarinic receptors are located in all of the effector organs of the parasympathetic nervous system: in the heart, gastrointestinal tract, bronchioles, bladder, and male sex organs. These receptors also are found in certain effector organs of the sympathetic nervous system, specifically, in sweat glands (Svorc 2018). The M3 subtype mediates most of the excitatory effects of acetylcholine on the visceral targets of parasympathetic neurons, including smooth muscle contraction, exocrine gland secretion, and endothelial synthesis of nitric oxide. The M3 receptors also mediate the excitatory action of cholinergic sympathetic neu-

Table 21.2 Sympathetic and parasympathetic effects

	Sympathetic			Parasympathetic		
Target	Effect	Neurotransmitter	Receptor	Effect	Neurotransmitter	Receptor
Heart	Stimulation	NE	β1	Inhibition	Ach	M2
Vessels	Constriction	NE	α1	Dilation	NO	
	Dilation	NO				
	Dilation	Epi	β			
Pupil	Dilatation	NE	α1	Constriction	Ach	M3
Sweat gland	Stimulation	Ach	M3			
Salivary gland	Variable			Stimulation	Ach	M3
Bronchi	Relaxation	Epi	β	Constriction	Ach	M3
GI motility	Inhibition	NE	α2, β	Stimulation	Ach	M3
				Inhibition	NO	
GI secretion				Stimulation	NO, VIP	
Bladder detrusor	Inhibition	NE	β	Stimulation	Ach	M3
Bladder neck	Contraction	NE	α1	Relaxation	NO	
Sexual organs	Ejaculation	NE	α1	Erection	NO	

Ach acetylcholine, Epi epinephrine, NE norepinephrine, NO nitric oxide, VIP vasoactive intestinal polypeptide

rons on the sweat gland. The M2 receptors mediate the inhibitory effects of the vagus by decreasing the automatism of the sinus node and atrioventricular conduction (Benarroch 2020). The effects of neurotransmitters on target organs are summarized in Table 21.2.

21.3 Evaluation of Autonomic Function

In general, evaluation of autonomic function is indirect because it depends on the results of end-organ activities, such as heart rate, blood pressure, sudomotor activity, etc. (Nance and Hoy 1996). The presence, distribution, and pattern of autonomic dysfunction facilitates diagnosis, indicates prognosis, and permits monitoring over time. Grading the severity of autonomic dysfunction allows detection of disease progression. Many methods evaluating the autonomic nervous system have been described. Some of them are used in clinical practice, while others are mainly used in scientific studies. This section describes some methods of evaluating the autonomic nervous system, with an emphasis on those useful in diagnosis and treatment of cardiovascular dysfunctions. Several factors influence the autonomic function, such as body position, emotional state, ingested food and medication, and other substances. Given the complexity of the autonomic system, there is no single test that accurately reflects the function of the autonomic nervous system (Zygmunt and Stanczyk 2010). Caffeine and nicotine should be withheld for at least 3–4 h before testing, alcohol for 8 h. If possible, sympathomimetic drugs should be discontinued 24–48 h before the test, and anticholinergics for 48 h (Jaradeh and Prieto 2003).

Most of the tests are based on the evaluation of the cardiovascular reflexes triggered by performing specific provocative maneuvers. Stimuli that increase blood pressure, such as isometric exercise or cold pressor test, activate mainly sympathetic outflow. In addition, blood pressure responses to orthostatic testing and Valsalva maneuver largely reflect sympathetic activity. Changes in heart rate during orthostatic testing and Valsalva maneuver as well as during deep breathing reflect parasympathetic modulation (Zygmunt and Stanczyk 2010).

21.3.1 International Standards to Document Autonomic Function Following Spinal Cord Injury

An international collaboration between the American Spinal Injury Association (ASIA) and

the International Spinal Cord Society (ISCoS) has been initiated to develop international standards for the documentation of the remaining autonomic functions after spinal cord injury (Alexander et al. 2009), which to be the first edition of the International Standards to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) in 2012 (ASIA 2012; Krassioukov et al. 2012). The second edition, designed to more effectively determine the level and severity of injury to autonomic nervous system after spinal cord injury and to tract changes over time and in response to therapeutic interventions, was published in 2021 (Wecht et al. 2021). Figures 21.4 and 21.5 show the ISAFSCI general autonomic function assessment form and sacral autonomic function assessment form (second ed.) (Wecht et al. 2021).

The following instructions are recommended for performing assessments based on ISAFSCI on individuals with spinal cord injuries: The patient must be otherwise healthy and have no current illness or infection, including, but not limited to, urinary tract infections and pressure injuries.; The patient should avoid caffeine, a large meal, heavy exertion or exercise, nicotine products, cannabis, and alcohol for at least 4 h prior to administration of the ISAFSCI.; Upon arrival, patients should be asked to empty their bladder and indicate the time of their last bowel movement.; All tight clothing or pressure garments (e.g., abdominal binders, compression stockings) should be removed before the test.; The patient should be placed in a quiet, dimly lit, thermo-neutral private room for a period of about 10 min prior to beginning the ISAFSCI assessment. Ideally, the room temperature should be maintained at 23 °C, with relatively humidity between 25% and 35% (Wecht et al. 2021).

21.3.2 Cardiovascular Automatic Tests

21.3.2.1 Heart Rate Variability

The beat-to-beat variation is evaluated by the time-domain and the frequency-domain analysis. The time-domain analysis used the duration of each R-R interval (msec). The beat-to beat variation of the R-R interval can be analyzed as a complex waveform, expressed in cycles/sec or Hz. Time-domain analysis derives from direct R-R interval measurements or the differences between successive R-R intervals. Most often, it is calculated over a full 24-h ECG recording. Sometimes, they are calculated over shorter recording, e.g., 5-min (Zygmunt and Stanczyk 2010). In frequency-domain analysis, the relative power of contributing frequencies is identified by fast Fourier transformation (FFT). Sympathetic activity was attributed to the power density in the low-frequency range. The ratio of the amplitude of the low-frequency to the high-frequency power density has been suggested to indicate the balance between sympathetic and parasympathetic activity (Nance and Hoy 1996).

21.3.2.2 Automatic Challenge Tests

Various maneuvers are adapted to activate the sympathetic or parasympathetic nervous system. For the routine assessment of cardiovascular autonomic function, the Valsalva maneuver, active standing, and especially deep breathing are considered to be the most valuable tests. The tests that primarily analyze parasympathetic heart rate control are the Valsalva maneuver, deep breathing, and active standing. Active standing can also be used to monitor sympathetic blood pressure control. The many other tests that activate sympathetic or parasympathetic tone include the cold pressor test, the cold face test, squatting, coughing, and mental arithmetic (Hilz and Dütsch 2006; Low 2003).

Deep Breathing

Inspiration reduces intrathoracic pressure, increases right heart filling, and increases right ventricular stroke volume, left heart filling, left ventricle stroke volume, cardiac output, and blood pressure. This test is based on the phenomenon of respiratory arrhythmia. The patient breathes six times/min, allowing 5 s for inspiration and 5 s for expiration. The difference between the average of the largest accelerations during inspiration and the average of the largest decelerations during expiration is calculated. It

Cardiovascular	Scoring	Condition	Definitions	Score
Heart Rate	**Normal (2)**		61-99 bpm	
Supine _____ mmHg	**Altered (1)**	Bradycardia	≤ 60 bpm	
		Tachycardia	≥ 100 bpm	
		Arrhythmias §		
Seated _____ mmHg	**Not Tested (NT): indicate reason**			
Systolic BP	**Normal (2)**		91-139 mmHg	
Supine _____ mmHg	**Altered (1)**	Supine Hypotension	SBP ≤ 90 bpm	
		Orthostatic Hypotension	Fall ≥ 20 mmHg within 10 minutes*	
		Neurogenic Shock	within 30 days of injury; heart rate ≤ 60 bpm; SBP ≤ 90 mmHg	
		Autonomic Dysreflexia**	increase in SBP > 20mmHg above baseline	
Seated _____ mmHg		Supine Hypertension	≥ 140 mmHg	
	Not Tested (NT): indicate reason			
Diastolic BP	**Normal (2)**		61-89 mmHg	
Supine _____ mmHg	**Altered (1)**	Supine Hypotension	≤ 60 mmHg	
		Orthostatic Hypotension	Fall ≥ 10 mmHg within 10 minutes*	
		Supine Hypertension	≥ 90 mmHg	
Seated _____ mmHg	**Not Tested (NT): indicate reason**			

*§ define the arrlrythmia; *within 3 minutes, but delayed orthostatic hypotension; within 10 minutes, may be more common in the SCI population. ** self-report ** within the past 7-days". *** unanticipated i.e., not in response to know intervention (e.g., medication).*

Thermoregulation Core Body Temp	Scoring	Condition	Definitions	Score
	Normal (2)	Normal	36.4-37.6 °C (97.5-99.7 °F)	
	Altered (1)	Subnormal	35.1-36.3 °C (95.1-97.4 °F)	
		Elevated	37.7-37.9 °C (99.8-100.3 °F)	
		Hypothermia	≤35°C (≤95°F)	
		Hyperthermia	≥38.0°C (≥100.4°F)	
	Not Tested (NT): indicate reason			

*** Under ambient conditions: 20-25°C(68-77°F); 30-50% relative humidity; wearing single-layer, indoor garments; after 10-minutes of rest; no acute illness or infection*

Sudomotor*	Scoring	Condition	Definitions	Score
	Normal (2)	Normal sweating	Sweating on all skin surfaces	
	Altered (1)	Hypohidrosis	Diminished sweating above NLI Diminished sweating above NLI	
		Hyperhidrosis	Excessive sweating above NLI Excessive sweating above NLI	
	Absent (0)	Anhidrosis	No sweating above or below NLI	
	Not Tested (NT): indicate reason			

** Record sweating responses to high ambient heat or exercise only. Do not record sweating associated with AD, OH, or mental stress.*

Broncho-pulmonary System	Findings	Condition	Definitions	Score
	Normal (2)			
	Altered (1)	Invasive ventilation	24 hours/day	
		Partial invasive ventilatory support	< 24 hours/day	
		Impaired voluntary respiration not requiring ventilatory support	Continuous Positive Airway Pressure (CPAP) for sleep apnea	
	Not Tested (NT): indicate reason			
Forced Vital Capacity (FVC) *	**supine _____seated _____ abdominal binder: YES_____ NO_____ ml_____; kg_____; ml/kg_____**			

Fig. 21.4 General autonomic function assessment form of the ISAFSCI (2nd ed.). From Wecht et al. (2021)

should not be less than 10–15 beats per min. The expiratory-inspiratory ratio (E: I ratio), which is the ratio of the longest R-R interval during expiration and the shortest R-R interval during inspiration from 5 cycles, can also be determined. The E: I ratio in young persons should be higher than 1.2.

Isometric Handgrip (Sustained Handgrip)

Isometric contraction of hand muscles will elevate systolic and diastolic blood pressure for the duration of the contraction. An increase in diastolic blood pressure is a result of heart rate acceleration without an increase of peripheral vascular resistance. Isometric handgrip is per-

Bladeer Emptying	Method Frequency Timing Voluntarily	Yes _____ No _____		
System/Organ	**Scoring**	**Anticipated Function (based on ISNCSCI)**	**Anticipated Functional Score**	**Patient Reported Score**
Awareness bladder fullness	Normal (2)	Any level injury with normal sensation in the T11-L2 and S3-S5 dermatomes		
	Altered (1)	Any level injury with partial preservation of sensation in the T11-L2 and/or S3-S5 dermatomes		
	Absent (0)	NLI at or above T9 no sensation below		
	Not Tested (NT): indicate reason			
Ability to prevent bladder leakage	Normal (2)	Individuals with normal sensation and more function in the S3-S5 dermatomes		
	Altered (1)	Individuals with partial sensation and motor function in the S3-S5 dermatomes		
	Absent (0)	No motor function at the S3-5 dermatomes		
	Not Tested (NT): indicate reason			
Bowel Emptying	Method Frequency Timing Voluntarily	**Yes** _____ **No** _____		
System/Organ	**Scoring**	**Anticipated Function (based on ISNCSCI)**	**Anticipated Functional Score**	**Patient Reported Score**
Awareness bladder fullness	Normal (2)	Normal sensetion and motor function in the S3-S5 dermatomes		
	Altered (1)	Partial preservation of sensation or motor function in the S3-S5 dermatomes		
	Absent (0)	No sensation or motor function in the S3-5 dermatomes		
	Not Tested (NT): indicate reason			

Fig. 21.5 Sacral autonomic function assessment form of the ISAFSCI (2nd ed.). From Wecht et al. (2021)

Ability to prevent bladder leakage	Normal (2)	Individuals with normal sansation and motor function in the S3-S5 dermatomes		
	Altered (1)	Individuals with partial sensation and motor function in the S3-S5 dermatomes		
	Absent (0)	No motor function at the S3-5 dermatomes		
	Not Tested (NT): indicate reason			
System/Organ	**Scoring**	**Anticipated Function (based on ISNCSCI)**	**Anticipated Functional Score**	**Patient Reported Score**
Psychogenic arousal	Normal (2)	Normal sensation and relex motor function at T11-L2		
	Altered (1)	Partial sensation and motor reflex function at T11-1.2		
	Absent (0)	No sensation or reflex motor function at T11-L2		
	Not Tested (NT): indicate reason			
Reflex genital arousal	Normal (2)	Normal sensation and reflex function at S3-5		
	Altered (1)	Partial sensation and motor reflex function at S3-5		
	Absent (0)	No sensation or motor function at S3-5		
	Not Tested (NT): indicate reason			
Orgasm	Normal (2)	Intact S3-5 sensation and or motor function with any degree of preserved sacral reflexes		
	Altered (1)	No S3-5 sensation or motor function and preserved saeral reflexes		
	Absent (0)	No S3-5 sensation or motor function and absent sacral reflexes		
	Not Tested (NT): indicate reason			
Ejaculation	Normal (2)	Normal T11-12 sensation and sacral reflexes		
	Altered (1)	Diminished sensation at T11-12 dermatomes and normal sacral reflexes		
	Absent (0)	No sensation at T11-12 dermatomes and absent sacral reflexes		
	Not Tested (NT): indicate reason			

Fig. 21.5 (continued)

formed by isometric pressing of a handgrip dynamometer at approximately one-third of the maximum contraction strength for 3–5 min. During isometric grip, blood pressure measurements are taken at the other arm at 1 min intervals. Normally, diastolic blood pressure at the

end of the effort is at least 16 mmHg higher than before the maneuver. A diastolic pressure increase by only 10 mmHg or less is abnormal.

Valsalva Maneuver

The Valsalva maneuver is a voluntary and sudden increase in intrathoracic and intraabdominal pressure against resistance. The standard of the test method is to blow into a mouthpiece and maintain a pressure of 40 mmHg for 15 s after 15–20 min of rest. Valsalva maneuver evaluates function of baroreceptors. The effect of the Valsalva maneuver can be divided into four phases (Table 21.3). Phase I consists of an increase in left ventricular stroke volume and an increase in blood pressure. An increase in intrathoracic pressure leads to the transient increase in blood pressure by activating baroreceptors and leads to a slight bradycardia. In phase II, there is a decrease of venous return and stroke volume, a decrease in blood pressure with compensatory tachycardia. Phase III begins after the Valsalva maneuver strain ends. There is a further transient decrease in arterial blood pressure and an increase in heart rate. In phase IV, the heart rate decreases due to activation of parasympathetic nerve; the arterial blood pressure abruptly rises above the initial values, and bradycardia occurs (Lindqvist 1990; Nishimura and Tajik 1986). Several indices can be calculated based on changes in hemodynamic parameters. Valsalva ratio is the most important of them and is derived from the longest R-R interval in phase IV divided by the shortest R-R interval in phase II and at the very beginning of phase III. Its value below 1.21 is considered abnormal. Valsalva ratio reflects parasympathetic activity, while changes in blood pressure are a measure of sympathetic function. The Valsalva ratio is used as an index of the baroreflex-mediated bradycardia and is calculated as the ratio of the highest heart rate during expiration and the lowest heart rate during the first 20 s after the expiratory strain. A Valsalva ratio below 1.10 is abnormal (Hilz and Dütsch 2006).

Cold Pressor Test

The cold pressor test is a well-established provocative test of autonomic vascular regulation. The normal response to a brief cold stimulus includes vasoconstriction in the digits, increased heart rate, and increased blood pressure. It is thought that the cold pressor test is a test of sympathetic function, because immersion of a hand in ice water is associated with a marked increase in muscle sympathetic nerve activity in the leg, and a beta-blocker can abolish the heart rate response to the stimulus. Immersion of hands or feet (or one upper limb or one lower limb) for approximately 60–90 s in cold water (0–4 °C) should, due to activation of afferent pain and temperature fibers from the skin as well as emotional arousal, lead to sympathetic activation and increase in blood pressure and heart rate (Hilz and Dütsch 2006; Zygmunt and Stanczyk 2010).

Table 21.3 Phases and mechanisms of the Valsalva maneuver

Phase	Phase event	Mechanism
I	Maneuver start Brief (1–3 s) increase in BP	Mechanical compression of great vessels
II_{early}	BP ↓	↓ Venous return counteracted by vagal release
II_{late}	BP recovery, HR ↑	Peripheral sympathetic vasoconstriction; continued vagal release
III	Pressure release	Brief (1–3 s) fall in BP Release of mechanical compression
IV	Sustained BP overshoot	Maintained vasomotor and cardiac sympathetic activation HR peak then nadir and normalization of cardiac output

Adapted from Weimer (2010)
BP blood pressure, HR heart rate

The impulses pass through the spinothalamic tract to several brain areas and result in sympathetically mediated heart rate acceleration, peripheral vasoconstriction, and an increase in blood pressure (Hilz and Dütsch 2006). An increase in diastolic blood pressure is calculated, and it should normally exceed 15 mmHg.

Diving Reflex Test or Cold Face Test

Diving reflex, a modification of the cold pressor test, takes place after immersion of the face in water with breath holding, as regardless of water temperature, it leads to bradycardia. Heart rate decreases by approximately 40 beats per min, while blood pressure increases by approximately 25 mmHg. The cold face test is a modification of the diving reflex and consists of the application of cold compresses (1–2 °C) to the forehead and maxillary region of the subject's face for 60–180 s. The cold face test is more comfortable than the diving reflex (Hilz and Dütsch 2006).

21.3.3 Orthostatic Challenge Tests

21.3.3.1 Active Orthostasis

Active orthostasis is the intentional induction of hypotension in a patient who voluntarily moves from the supine position to the sitting or standing position. Venous pooling in the lower extremities from the thorax and abdomen results in a decrease in cardiac venous return and filling pressure of the heart. The resulting reduction in cardiac output leads to reflex activation of the sympathetic nervous system. When the sympathetic function is impaired, venous constriction is insufficient to maintain the venous return to the heart properly. Orthostatic challenge causes an early cardiovascular response that occurs within the first 30 s. There is an immediate response with an abrupt decrease in systolic and diastolic blood pressures and a visible acceleration in heart rate within the first 30 s. During the upright position, 300–900 mL of blood is redistributed from central blood vessels to the lower extremity. The early circulatory stabilization occurs after 1–2 min of orthostasis. Finally, there is a response to prolonged orthostasis lasting for more than 5 min (Hilz and Dütsch 2006; Zygmunt and Stanczyk 2010). There is the early phase of stabilization during 1–2 min of standing after an initial response to active standing. This phase shows an increase in diastolic blood pressure by approximately 10 mmHg and a sympathetic heart rate increase by 10 per min. A decrease in systolic blood pressure by more than 20 mmHg and by more than 10 mmHg for diastolic blood pressure is considered abnormal. Active standing is the best test to diagnosis orthostatic hypotension (Hilz and Dütsch 2006).

21.3.3.2 Head-Up Tilt Test

The head-up tilt (HUT) test evaluates adaptation to orthostasis and subsequent changes in hemodynamic parameters after passive tilting on a special motorized table. Cardiovascular changes during head-up tilt are more gradual than during active standing. There is no biphasic response of heart rate and blood pressure, but a gradual increase in diastolic blood pressure and heart rate and no major change in systolic blood pressure. The head-up tilt test is a suitable diagnostic tool for the assessment of autonomic regulation during long-duration orthostatic challenges (Hilz and Dütsch 2006). A provocative tilt test is performed on an automated tilt test table that allows a consistent slow tilt to 60–80°. The 60° tilt angle seems optimal because at this point, 90% of the gravitational blood volume displacement occurs in comparison to a fully upright position. It should be done in the morning after the overnight fast or several hours after a meal. In the first phase, the patient remains supine for a period of about 15–30 min. ECG and blood pressure recordings are obtained before the test and during 30–45 min of tilting.

21.3.4 Testing of Sudomotor Function

The cholinergic part of the autonomic nervous system can be assessed based on the reaction of the sweat glands to various stimuli conducted by cholinergic postganglionic sympathetic fibers.

21.3.4.1 Thermoregulatory Sweat Test

Perspiration of the anterior surface of the body is induced by controlling ambient air temperature, humidity, and the patient's skin temperature. Sweat secretion after raising body temperature by 1–1.4 °C (but not above 38 °C) is measured. The subject is exposed to infrared heat lamps at a temperature of 45–50 °C, relative humidity of 45–50%, and a skin temperature of 39–40 °C. The peak response of sweat glands occurs after 35–45 min. Cutaneous perspiration is monitored by the application of a moisture-sensitive powder (quinizarin or alizarin red). Normal subjects should demonstrate generalized perspiration.

21.3.4.2 Sympathetic Skin Response

With regard to the sympathetic skin response (SSR) recording, it is possible to analyze the sympathetic outflow to the sweat gland in the hands, feet, and perineal areas (Ellaway et al. 2010). The SSR shows how the connection from the brain to the sympathetic nervous system is maintained in the thoracolumbar spinal cord (T1–L2). The SSR measures electrical potentials from electrodes situated on the palms of the hands and soles of the feet, which reflect sympathetic cholinergic activity of sweat glands. Depending on the neurological level of spinal cord injury and completeness, the SSR may be completely or partially defective. In complete cervical spinal cord injury, SSR in the hands, feet, and perineum is usually absent, but these responses are preserved in lesions below L2 (Cariga et al. 2002; Curt et al. 1996; Rodic et al. 2000). It has been shown that the absence of SSR is associated with the autonomic reflex disorder (Curt et al. 1997, 1996).

21.3.4.3 Quantitative Sudomotor Axon Reflex Test (QSART)

There are two types of human sweat glands, apocrine and eccrine. A complete complement of eccrine sweat glands exists at birth and gradually decreases with age. It is innervated mainly by sympathetic cholinergic nerve fibers. The sweat glands are very complicated. It is adrenergic in utero and switches adrenergic action to the cholinergic innervation during development. The main role of sweat glands is temperature regulation. Men have the same number of glands as women, but the volume of each gland is several times.

The quantitative sudomotor axon reflex test is a quantified assessment of the peripheral sweating mechanism. Acetylcholine is administered into the subcutaneous tissue by iontophoresis. Measurements of the QSART are the latency of the initial sweat response and quantity of sweat produced in $\mu L/cm^2$. The latency of the response is normally 1–2 min, and sweating returns to baseline within 5 min after stopping the stimulation (Fig. 21.6). The normal test indicates the integrity of the postganglionic sympathetic ganglion (Banister and Mathias 1992).

21.4 Autonomic Nervous System Dysfunction in Spinal Cord Injury

Spinal cord injury results in a decrease or loss of autonomic control that is directly related to the level of injury. Clinical disorders known to be due to disorders of the sympathetic nervous system in spinal cord injuries include low resting blood pressure, orthostatic hypotension, autonomic dysreflexia, reflex bradycardia and cardiac arrest, limited cardiovascular responses to exercise, lack of temperature regulation, abnormal reactions to hypoglycemia, and bladder, bowel, and sexual dysfunction. This problem of sympathetic nervous system dysfunction following a spinal cord injury is due to loss of supraspinal facilitatory and inhibitory control. A spinal cord injury above the mid-thoracic level is important for the development of clinical sympathetic dysfunction. The level of spinal cord injury required for the development of clinical sequelae is T6, although autonomic dysreflexia appears in spinal cord injury between T6 and T8. A spinal cord injury above the T6 significantly reduces sympathetic outflow to the splanchnic vascular bed and the blood vessels of the lower extremities. Alpha-receptors in sympathetically denervated blood vessels become hyperresponsive or denervation supersensitivity states.

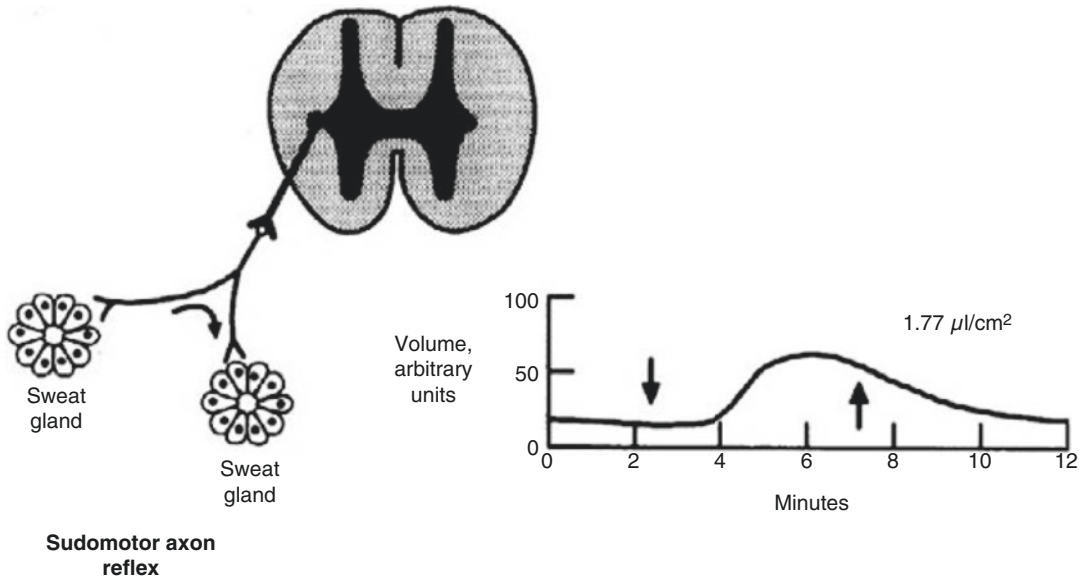

Fig. 21.6 QSART. Stimulus of nerve terminals by acetylcholine iontophoresis results in activation of postganglionic sympathetic sudomotor fibers, acetylcholine release and activation of a new population of sweat glands. From Baruah et al. (2017), with permission

Decreased sympathetic efferent activity below the level of spinal cord injury in a patient with high-level spinal cord injury has been associated with numerous clinical findings, including low resting blood pressure, orthostatic hypotension, abnormal response to hypoglycemia, and bradycardia. The resting catecholamine levels in individuals with cervical spinal cord injuries were lower than normal compared to normal control and paraplegic control subjects, which indicates a decrease in sympathetic nervous system activity at rest (Mathias et al. 1976). As long as there is no stimulation below the level of spinal cord injury, catecholamines and their metabolites are usually in the low normal range. Although resting plasma levels of catecholamine, particularly noradrenaline, decrease in patients with spinal cord injury, peripheral vascular alpha-adrenergic receptors may become hypersensitized below the level of spinal cord injury due to possible unregulatory or denervation supersensitivity mechanism.

21.4.1 Cardiovascular Dysfunction

The heart receives both sympathetic and parasympathetic innervation, while the vasculature receives only sympathetic innervation. The vagal nerve innervates the atria, nodes, and Purkinje fibers through local cardiac ganglia. Vagal stimulation to the SA node causes tonic restraint in firing rate, decreasing heart rate, conduction velocity, and to a lesser extent contractility (Wecht et al. 2021). Blood pressure is determined by cardiac output and total peripheral resistance. Cardiac output is the product of heart rate and stroke volume. Stroke volume is directly related to the cardiac venous return. Heart rate and blood pressure are affected by the sympathetic and parasympathetic nervous systems. Spinal cord injury can disrupt the sympathetic fibers from the thoracic and lumbar spinal cords depending on the level of injury. However, parasympathetic vagal nerve fibers from the brainstem are usually spared.

Many of the major cardiovascular functions are associated with segmental outflow from several levels, such as the outflow to the heart or the splanchnic outflow. Table 21.4 shows spinal cord segments and corresponding ganglia of sympathetic control of blood vessels. Descending sympathetic input from the supraspinal center travels through the cervical spinal cord and synapse via spinal interneurons with

Table 21.4 Spinal cord segments and corresponding ganglia of blood vessel control

CNS or spinal cord segments	ANS	Ganglion	Nerve	Target organs
Dorsal motor nucleus of CN X	Parasympathetic	Not applicable	Vagus nerve, cardiac nerve	Heart, lungs, abdominal viscera, ascending and transverse colon
T1–T4	Sympathetic	Middle cervical and stellate	Cardiac nerves	Heart, lungs
T3–L3 (mainly T5-T9)	Sympathetic	Superior mesenteric	Lesser splanchnic nerve	Adrenal medulla
T5–T11	Sympathetic	Celiac and superior mesenteric	Greater and lesser splanchnic nerves	Abdominal viscera, ascending and transverse colon
L1–L3	Sympathetic	Inferior mesenteric	Lumbar splanchnic nerves	Descending colon and rectum, kidney, bladder, uterus, external genitalia
S2–S4	Parasympathetic	Not applicable	Pelvic splanchnic nerves	Descending colon and rectum, bladder, uterus, external genitalia

the sympathetic preganglionic neurons starting at T1. The sympathetic innervation of the heart, including the myocardium, SA, and AV nodes, ranges from T1 to T4. Injuries between T1 and T4 have partial innervation of the heart, and injuries below T4 have complete innervation of the heart. If the level of injury is below T4, normal cardiac responses are maintained, but the vascular tone and blood pressure control are still under local regulation. Since the parasympathetic innervation to the heart is via the vagus nerve, which does not travel in the spinal cord, the only supraspinal control of cardiac responses is parasympathetic (Garstang and Miller-Smith 2007).

The sympathetic outflow to the splanchnic organs occurs mainly from T5 to T9 via the greater splanchnic nerve to the celiac ganglion (although there are splanchnic efferents from T5 to L2). This outflow regulates most of the blood flow in the splanchnic circulation. Injuries below T5 have some ability to regulate splanchnic flow, with more control with distal levels of injury. Lesion to the spinal cord above this outflow impedes the ability of the splanchnic beds to vasodilate, causing blood to pool in the splanchnic circulation. This lack of compensatory response to an elevation in blood pressure is part of the pathogenesis of autonomic dysreflexia that occurs in persons with spinal cord injury above T6. The sympathetic efferents to the adrenal medulla range from T3 to L3, but the major outflow is T5 to T9. This innervation allows control of the release of epinephrine from the adrenal medulla, which is part of the normal response to exercise or stress. Therefore, injuries above T9 will have an impaired adrenal response to exercise (Garstang and Miller-Smith 2007). Sweat glands receive a dual innervation from both cholinergic and adrenergic fibers. However, cholinergic stimulation triggers the largest response. The spinal segments T2–T4 supply sweat glands on the head and neck, T2–T8 to glands of the upper limbs, T6–T10 to the trunk, and T11–L2 to the lower extremities (Garstang and Miller-Smith 2007; Quinton 1983).

21.4.1.1 Hypotension and Orthostatic Hypotension

Hypotension can be present in the acute and/or chronic phase of spinal cord injury. Decreased blood pressure in the acute phase of spinal cord injury is considered secondary to a decrease in sympathetic activity below the neurological level injury. Hypotension is associated with the impaired vascular tone, reduced circulating catecholamines, and impaired venous return. In the later stages of spinal cord injury, both resting systolic and diastolic blood pressure in tetraplegics remain lower than normal subjects. Orthostatic hypotension is defined as a symptomatic or asymptomatic decrease in systolic blood pressure $\geq$20 mmHg and/or diastolic blood pressure $\geq$10 mmHg within 3 min of changing from a supine to an upright position (Freeman et al. 2011).

The mean arterial pressure (MAP) in the supine position of the normal person is approximately 93 mmHg, while 57 mmHg in person with cervical spinal cord injuries (Mathias et al. 1979a). In the acute phase of spinal cord injury, MAP should be between 85 and 90 mmHg or higher to prevent neurological deterioration (Hadley et al. 2002). The duration of blood pressure support after the injury is not clear, but it is recommended to maintain adequate blood pressure for about 5–7 days. If the mean arterial pressure is less than 85 mmHg, a β-agonist should be used and the use of α-agonists considered. They usually use dopamine or norepinephrine, which can work with α- and β-agonists. Overdose of the fluid should be avoided.

Patients with cervical spinal cord injury often have a systolic blood pressure of 90 mmHg and diastolic 60–70 mmHg or much lower (Rosner et al. 1984). It is not uncommon for a patient to have a sitting systolic blood pressure of 60–80 mmHg. Some people experience dizziness and syncope. Others are asymptomatic. As the blood is diverted to the gastrointestinal system for digestion, meals can make symptoms worse. Treatment is rarely required unless orthostatic hypotension is a clinical problem. Treatment includes thigh-high compression stockings and

abdominal binder. Caregivers should sit the spinal cord injured person slowly from the recumbent position. If these strategies are unsuccessful, midodrine, fludrocortisone, ephedrine, or pseudoephedrine may be considered.

21.4.1.2 Supine Hypertension or Supine Hypotension

Supine hypertension is defined as a systolic blood pressure in the supine position ≥140 mmHg and /or a diastolic pressure in the supine position ≥90 mmHg. Supine hypotension is defined as a systolic blood pressure in the supine ≤90 mmHg and/or a diastolic blood pressure in the supine ≤60 mmHg.

21.4.1.3 Bradycardia

The result of a decrease in sympathetic activity in the acute phase after high-level spinal cord injury is reflex bradycardia. Tracheal suction in the acute phase of spinal cord injury can cause reflex bradycardia and cardiac arrest due to a vasovagal reflex. In normal person, tracheal stimulation causes hypertension and tachycardia associated with changes in efferent sympathetic discharge (Corbett et al. 1969). Efferent cardiac parasympathetic nerve pathways remain intact in tetraplegic patient despite reduced sympathetic activity, which may make the patients susceptible to vagal overactivity by tracheal stimulation, leading to bradycardia and in extreme cases, cardiac arrest.

Bradycardia is a heart rate less than 60 beats/min, and tachycardia is defined as more than 100 beats/min. In some cases, there are severe bradycardias below 45. It usually tends to recover slowly after 4 days of injury. Bradycardia may continue for 2–6 weeks after injury. In the early stages of spinal cord injury, almost all tetraplegics experience hypotension and bradycardia with a systolic blood pressure less than 90 mmHg and heart rate below 50. In patients with tetraplegics, vagus nerve stimulation during bronchial suctioning may exacerbate bradycardia and cause sinus arrest. Use small amounts of isoproterenol if treatment is needed. In case of bradycardia, administer atropine 10 min before airway suctioning. In patients with symptomatic bradycardia, administer atropine 0.4–0.6 mg intravenously. Dopamine may be administered intravenously at a dose of 2–10 μg/kg/min or epinephrine 0.01–0.1 μg/kg/min. If the bradycardia persists, 200–300 mg of aminophylline is injected, followed by 100 mg three times daily for 2–3 months. In rare cases, a temporary pacemaker is inserted.

21.4.1.4 Autonomic Dysreflexia

Autonomic dysreflexia is a syndrome characterized by a sudden increase in systolic and diastolic blood pressure in response to noxious stimuli below the level of injury. Autonomic dysreflexia commonly occurs in spinal cord lesions above the major sympathetic splanchnic outflow. In general, autonomic dysreflexia is associated with injuries at or above the T6 level. However, it is reported as low as T8–T10 (Erickson 1980). Autonomic dysreflexia is defined by an increase in systolic blood pressure more than 20 mmHg above baseline, which may or may not be associated with symptoms including headache, flushing, piloerection, stuffy nose, sweating above the level of the lesion, and dysrhythmia (ASIA 2012; Consortium for Spinal Cord Medicine 2001). Untreated autonomic dysreflexia can lead to intracerebral hemorrhage and death. It is often associated with bradycardia (Colachis III 1992). However, tachycardia and other cardiac rhythm disturbances can occur. Other symptoms include sweating or flushing above the level of injury, pallor below the level of injury, sudden bilateral headache, nasal congestion, anxiety, and rarely visual impairment. Many people with spinal cord injuries may not show symptoms when they have an episode of autonomic dysreflexia, a term known as “silent” autonomic dysreflexia that can be fatal (Wan and Krassioukov 2014).

Autonomic dysreflexia occurs after the period of spinal shock has resolved. An individual must have an undamaged spinal cord below the level of injury to develop autonomic dysreflexia. A strong afferent stimulus, a noxious stimulus below the neurological level, travels into the spinal cord and causes reflex sympathetic constriction of the vascular structure. This can increase preload and resulting hypertension. The elevated blood pressure is detected by the carotid baroreceptor, resulting in increased vagal tone. This usually

leads to bradycardia. However, heart rate is influenced by the opposing effects of sympathetic and parasympathetic nervous systems. Therefore, tachycardia is also possible. In undamaged persons, this reflex vasoconstriction is regulated by the higher centers of the brainstem, subcortical and cortical centers. However, this adjustment is absent or compromised in patients with spinal cord injury.

Clinical symptoms range from mild symptoms to acute life-threatening conditions. The mild episodes of autonomic dysreflexia can occur frequently throughout the day and generally have little effect, but excessive sweating and repeated headaches can cause severe morbidity. The classic syndrome of autonomic dysreflexia includes paroxysmal elevation of systolic and diastolic blood pressures, bradycardia, severe headache, piloerection, and sweating. Cold distal extremities are due to a marked decrease in peripheral blood flow. Above the level of spinal cord injury, vasodilatation presenting as flushing in the face, neck, and upper chest, hyperhidrosis, elevated skin temperature, and nasal congestion appear. Headache is the result of pain-sensitive intracranial arterial dilatation, but is not correlated with the severity of hypertension. More serious complications associated with severe hypertension can lead to myocardial infarction or intracerebral hemorrhage with resulting neurological presentations, especially autonomic dysreflexia during labor in pregnant women with spinal cord injury above T6.

Prevention of autonomic dysreflexia is the most important treatment. To manage autonomic dysreflexia, it is important to identify the cause of afferent stimulus and to eliminate or reduce the cause of the stimulus. Individuals should be placed with the head up and feet down or in a sitting position to induce a venous pool and reduce preload. Blood pressure should be monitored every 5 min. If systolic blood pressure exceeds 150 mmHg and the precipitating cause cannot be easily treated, medical therapy should be given. Topical or sublingual nitrates are appropriate choices. Topical nitroglycerin has a rapid onset and must be applied above the level of the lesion. If hypotension occurs, the nitropaste should be wiped away, and the individual should be placed in a recumbent position and the leg elevated. If dysreflexia cannot be controlled, admission to an intensive care unit for intravenous nitroglycerin or nitroprusside should be considered. Sublingual administration of nifedipine is related to stroke and should not be used. However, oral nifedipine is considered.

Chronic autonomic dysreflexia occurs in some individuals. Successful management requires recognition and treatment of precipitating conditions (i.e., bladder spasticity, pressure injuries, etc.). There are a number of drugs that can be used to manage chronic autonomic dysreflexia. However, medication can lower baseline blood pressure and cause orthostatic hypotension.

21.4.2 Abnormal Response to Hypoglycemia

Hypoglycemia in people without spinal cord injury results in a marked increase in plasma adrenaline levels and a slight increase in plasma noradrenaline levels (Mathias et al. 1979b). Clinical manifestations of hypoglycemia include anxiety, tremulousness, hunger, sweating, tachycardia, and a rise in systolic blood pressure. Insulin-induced hypoglycemia does not increase plasma adrenaline or noradrenaline level in tetraplegia, resulting in no symptom other than sedation and low systolic blood pressure. Unlike normal subjects, there is a reduction in both systolic and diastolic blood pressure during hypoglycemia (Mathias et al. 1979b). This is accompanied by a rise in heart rate. This indicates that patients with tetraplegia do not have sympathetic response to hypoglycemia, that is, the usual neuroglycopenic symptoms associated with hypoglycemia do not occur in the tetraplegics.

21.4.3 Impairment of Gastric Motility

Bowel function requires coordinated activity between the somatic, autonomic, and enteric ner-

vous systems. The vagus nerve innervates the splenic flexure of the colon. The inferior splanchnic nerve carries pelvic parasympathetic fibers from S2 to S4 of the spinal cord to the distal bowel (splenic flexure, left colon, and rectum). The Auerbach's myenteric plexus with unmyelinated fibers and postganglionic parasympathetic cell bodies primarily coordinates motility, while the Meissner's submucosal plexus transmits local sensory and motor responses (Inskip et al. 2009). The internal anal sphincter is a continuation of the circular muscle layer of the rectum under the reflex control of the enteric nervous system and S2–S4 segments of the spinal cord. The external anal sphincter and pelvic floor are supplied by the mixed motor and sensory somatic pudendal nerve, which provide voluntary control. There is also evidence of sympathetic control of the external anal sphincter (Krogh and Christensen 2009; Wecht et al. 2021). Postganglionic parasympathetic neurons increase smooth muscle activity (via acetylcholine). The sympathetic innervation comes from the spinal segments T10–L1, which is mainly postganglionic and indirectly inhibits muscle and secretory activity through noradrenergic modulation of activity in both Meissner's and Auerbach's plexuses.

Gastric motility in people without spinal cord injury is influenced by activity of the sympathetic nervous system. The increase in sympathetic tone is generally associated with decreased antroduodenal motility and increased pyloric sphincter tone. Gastroduodenal motility is relatively normal in people with spinal cord injuries. The gastric emptying time is similar to that of normal controls (Krogh and Christensen 2009). The splanchnic sympathetic activity is also relatively normal in patients with spinal cord injury, unless there is no autonomic dysreflexia.

21.4.4 Disorder of Temperature Regulation

Maintaining normal body temperature requires an intact autonomic nervous system and a neuroendocrine system. Temperature regulation is highly dependent on an intact sympathetic nervous system. The sympathetic nervous system in high-level spinal cord injuries is hypoactive below the level of injury, cannot adequately respond to changes in environmental temperatures, and is, therefore, at significant risk of developing problems regulating body temperature appropriately. The higher the level of spinal cord lesion, the greater the potential degree of temperature dysregulation (Mathias and Frankel 1992).

Temperature regulation is controlled by the hypothalamus. When the core temperature drops, the homeostasis mechanism causes shivering. In addition, blood flow to the extremities is reduced. As the core body temperature rises, a normal homeostatic reaction increases sweating and directs blood to the limbs (Quinton 1983). In spinal cord injuries, this normal regulatory mechanism can be compromised by an abnormality in the autonomic nervous system. Hyperthermia and hypothermia usually occur in people with spinal cord injuries. Other causes of fever should be ruled out before the patient concluded that the patient has hyperthermia secondary to dysautonomia (i.e., quad fever). In some cases, hyperthermia and hypothermia are secondary to ambient temperature (poikilothermia) and can be corrected by adjusting the thermostat. People with temperature regulation disorders need a home and van with good air conditioning system.

People with tetraplegia are vulnerable to hypothermia when exposed to cold conditions because they lack the ability to shiver and cannot constrict cutaneous blood vessels. A hypothermic condition is usually considered when the central body temperature is below 35 °C. Shivering provides protection against hypothermia (Johnson 1976). Shivering causes heat, but it depends on skeletal muscle activation. This is not possible in tetraplegics because most of the skeletal muscles are no longer under the supraspinal control (Mathias and Frankel 1992). Severe hypothermia can occur particularly soon after acute spinal cord injury. This may be due to cutaneous vasodi-

latation in the acute stage and the resulting loss of heat (Johnson 1976). Over time, these effects may be partially alleviated by the development of peripheral alpha-adrenergic hypersensitivity below the level of injury. Hyperthermia can occur in high-level spinal cord injury when the ambient temperature rises or the internal temperature increases in response to infection. Vasodilatation may occur but is no longer under supraspinal control. More important is the loss of sweating in response to thermal stress. Sweating normally results in heat loss through evaporation and depends on a rise in central or core temperature and subsequent activation of sudomotor fibers in the sympathetic nervous system. The hypoactivity of the sympathetic nervous system leads to impairment of sudomotor activity in response to a thermal stress with subsequent thermoregulatory problems.

References

Alexander MS, Biering-Sorensen F, Bodner D, et al. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord. 2009;47:36–43.

American Spinal Injury Association. International standards to document remaining autonomic function after spinal cord injury. 1st ed. Atlanta: American Spinal Injury Association; 2012.

Banister R, Mathias C, editors. Autonomic failure: a textbook of clinical disorders of the autonomic nervous system. 3rd ed. Oxford: Oxford University Press; 1992. p. 839–81.

Baruah S, Deepika A, Shukla D, et al. Demonstration of autonomic dysfunction in traumatic brachial plexus injury using quantitative sudomotor axon reflex test: preliminary results. Neurol India. 2017;65:1317–21.

Benarroch EE. Physiology and pathophysiology of the autonomic nervous system. Continuum (Minneap Minn). 2020;26:12–24.

Cariga P, Catley M, Mathias CJ, et al. Organisation of the sympathetic skin response in spinal cord injury. J Neurol Neurosurg Psychiatry. 2002;72:256–360.

Colachis SC III. Autonomic hyperreflexia with spinal cord injury. J Am Paraplegia Soc. 1992;15:171–86.

Consortium for Spinal Cord Medicine. Acute management of autonomic dysreflexia. 2nd ed. Washington, DC: Paralyzed Veterans of America; 2001.

Corbett JL, Kerr JH, Prys-Roberts C. Cardiovascular responses to aspiration of secretions from the respiratory tract in man. J Physiol. 1969;201:51P–2P.

Curt A, Nitsche B, Rodic B, et al. Assessment of autonomic dysreflexia in patients with spinal cord injury. J Neurol Neurosurg Psychiatry. 1997;62:473–7.

Curt A, Weinhardt C, Diez V. Significance of sympathetic skin response in assessment of autonomic failure in patients with spinal cord injury. J Auton Nerv Syst. 1996;61:175–80.

Ellaway PH, Kuppuswamy A, Nicotra A, et al. Sweat production and the sympathetic skin response: improving the clinical assessment of autonomic function. Auton Neurosci. 2010;155:109–14.

Erickson RP. Autonomic hyperreflexia: pathophysiology and medical management. Arch Phys Med Rehabil. 1980;610:431–40.

Freeman R, Wieling W, Axelrod FB, et al. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. Clin Auton Res. 2011;21:69–72.

Garstang SV, Miller-Smith SA. Autonomic nervous system dysfunction after spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:275–96.

Hadley MN, Walters BC, Grabb PA, et al. Blood pressure management after acute spinal cord injury. Neurosurgery. 2002;50(3 Suppl):S58–62.

Hilz MJ, Dütsch M. Quantitative studies of autonomic function. Muscle Nerve. 2006;33:6–20.

Hou S, Rabchevsky AG. Autonomic consequences of spinal cord injury. Compr Physiol. 2014;4:1419–53.

Idiaquez J, Benarroch E, Nogues M, editors. Evaluation and management of autonomic disorders: a case-based practical guide. Cham: Springer; 2018.

Inskip JA, Ramer LM, Ramer MS, et al. Autonomic assessment of animals with spinal cord injury: tools, techniques and translation. Spinal Cord. 2009;47:2–35.

Jaradeh SS, Prieto TE. Evaluation of the autonomic nervous system. Phys Med Rehabil Clin N Am. 2003;14:287–305.

Johnson RH. Temperature regulation in spinal cord injuries. In: Vincent PJ, Bruyn GW, editors. Injuries of the spine and spinal cord. Part II. Handbook of clinical neurology, vol. 26. Oxford: North-Holland Publishing Company; 1976.

Krassioukov A. Autonomic function following cervical spinal cord injury. Respir Physiol Neurobiol. 2009;169:157–64.

Krassioukov A, Biering-Sørensen F, Donovan W, et al. International standards to document remaining autonomic function after spinal cord injury. J Spinal Cord Med. 2012;35:201–10.

Krassioukov AV, Weaver LC. Anatomy of the autonomic nervous system. Phys Med Rehabil State Art Rev. 1996;10:1–14.

Krogh K, Christensen P. Neurogenic colorectal and pelvic floor dysfunction. Best Pract Res Clin Gastroenterol. 2009;23:531–43.

Lindqvist A. Noninvasive methods to study autonomic nervous control of circulation. Acta Physiol Scand Suppl. 1990;588:1–107.
Low PA. Testing the autonomic nervous system. Semin Neurol. 2003;23:407–21.
Mathias CJ, Christensen NJ, Corbett JL, et al. Plasma catecholamines during paroxysmal neurogenic hypertension in quadriplegic man. Circ Res. 1976;39:204–8.
Mathias CJ, Christensen NJ, Frankel HL, et al. Cardiovascular control in recently injured tetraplegics in spinal shock. Q J Med. 1979a;48:273–87.
Mathias CJ, Frankel HL. Autonomic disturbance in spinal cord lesion. In: Bannister R, Mathias CJ, editors. Autonomic failure. 3rd ed. Oxford: Oxford University Press; 1992. p. 839–88.
Mathias CJ, Frankel HL, Turner RC, et al. Physiological responses to insuline hypoglycemia in spinal man. Spinal Cord. 1979b;17:319–26.
Nance PW, Hoy CSG. Assessment of the autonomic nervous system. Phys Med Rehabil State Art Rev. 1996;10:15–35.
Nishimura RA, Tajik AJ. The Valsalva maneuver and response revisited. Mayo Clin Proc. 1986;61:211–7.
Rodic B, Curt A, Dietz V, et al. Bladder neck incompetence in patients with spinal cord injury: significance of sympathetic skin response. J Urol. 2000;163:1223–7.
Rosner MJ, Elias Z, Coley I. New principles of resuscitation for brain and spinal injury. N C Med J. 1984;45:701–8.
Quinton P. Sweating and its disorders. Annu Rev Med. 1983;34:429–52.
Svorc P. Introductory chapter: autonomic nervous system - what we know about it, Autonomic nervous system, Svorc P, IntechOpen; 2018. https://doi.org/10.5772/intechopen.81026. Available from https://www.intechopen.com/books/autonomic-nervous-system/introductory-chapter-autonomic-nervous-system-what-we-know-about-it
Wecht JM, Krassioukov AV, Alexander M, et al. International Standards to document Autonomic Function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.
Wehrwein EA, Orer HS, Barman SM. Overview of the anatomy, physiology, and pharmacology of the autonomic nervous system. Compr Physiol. 2016;6:1239–78.
Weimer LH. Autonomic testing: common techniques and clinical applications. Neurologist. 2010;16:215–22.
Zygmunt A, Stanczyk J. Methods of evaluation of autonomic nervous system function. Arch Med Sci. 2010;6:11–8.

Recommended Additional Reading

Buijs RM, Swaab DF. editors. Autonomic nervous system. Handbook of clinical neurology, 3rd series, vol. 117. London: Elsevier; 2013.
Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation Phys Med Rehabil Clin N Am. Philadelphia, PA: Elsevier; 2014.
Cardinali DP. Autonomic nervous system. Basic and clinical aspects. Cham: Springer; 2018.
Colombo J, Arora R, DePace NL, et al. Clinical autonomic dysfunction. Measurement, indications, therapies, and outcomes. New York: Springer; 2015.
Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.
Iwase S, Hayano J, Orimo S, editors. Clinical assessment of the autonomic nervous system. Japan: Springer; 2017.
Low PA, Benarroch ED, editors. Clinical autonomic disorders. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
Mai JK, Paxinos G. The human nervous system. 3rd ed. London: Elsevier; 2012.
Mancall E. Gray's clinical neuroanatomy: the anatomic basis for clinical neuroscience. Philadelphia: Elsevier; 2011.
Noback CR, Strominger NL, Demarest RJ, et al., editors. The human nervous system: structure and function. 6th ed. Totowa: Humana Press; 2005.
Patestas MA, Gartner LP. A text book of neuroanatomy. Oxford: Blackwell Publishing; 2006.
Robertson D, Bigaaioni I, Burnstock G, et al. Primer on the autonomic nervous system. 3rd ed. London: Elsevier; 2011.
Struhal W, Lahrmann H, Fanciulli A, et al., editors. Bedside approach to autonomic disorders. A clinical tutor. Cham: Springer; 2017.
Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.
Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.
Vodusek DB, Boller F. Neurology of sexual and bladder disorders. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 130. London: Elsevier; 2015.
Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury. Progress in brain research. Vol. 152. New York: Elsevier; 2006.

Cardiovascular Dysfunctions Following Spinal Cord Injuries

22

After spinal cord injuries, any and all of the ascending and descending tracts involving in motor, sensory, and autonomic function can be damaged to various degrees. Impairment secondary to loss of autonomic function can be profound and greatly impact an individual's ability to live well with spinal cord injury. This includes the control of heart rate, blood pressure, sweating, pulmonary secretory and bronchodilatory function, control of bladder and bowel function, and sexual function (Krassioukov 2009). Cardiovascular dysfunction is a major cause of morbidity and mortality in people with spinal cord injuries. In the past, respiratory and renal complications were the most prevalent comorbidities in people with spinal cord injuries. Cardiovascular disease has gradually emerged as the main cause of mortality in chronic spinal cord injuries (Garshick et al. 2005). Spinal cord injuries disrupt autonomic pathways and therefore affect cardiovascular homeostasis (Furlan and Fehlings 2008). Cardiovascular dysfunction increases with higher levels of injury and greater severity of the lesions (Helkowski et al. 2003). People with high-level spinal cord injury are predisposed to dramatic fluctuations in arterial blood pressure during orthostatic hypotension and autonomic dysreflexia (Hubli et al. 2015). Most people with spinal cord injuries have transient episodes of instability in blood pressure and cardiovascular responses.

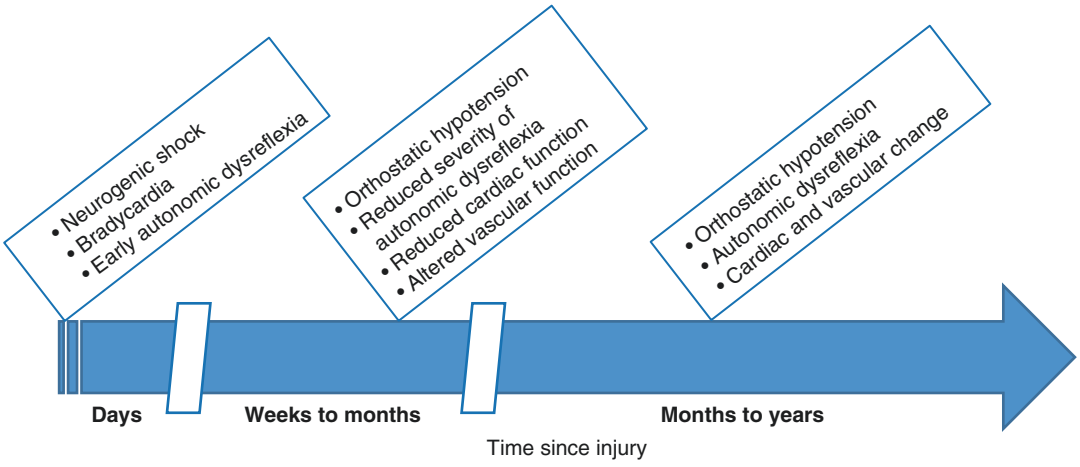

Fig. 22.1 Timeline of changes in cardiovascular function after spinal cord injuries. Adapted from Phillips and Krassioukov (2015)

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Immediately after spinal cord injury, major cardiovascular abnormalities occur as a neurogenic shock (Yue et al. 2017).

After attenuation of neurogenic shock, new cardiovascular problems associated with instability of blood pressure, including orthostatic hypotension and autonomic dysreflexia, occur (Bauman et al. 2012) (Fig. 22.1). The most frequent cardiovascular complications in the acute phase of the traumatic spinal cord injuries are bradyarrhythmia, hypotension, increased vasovagal reflexes, ventricular and supraventricular ectopic beats, venous stasis, and vasodilation. Cardiovascular complications in the early stages of complete cervical spinal cord injury can be life-threatening. Although some of these conditions may improve in the weeks following spinal cord injury, cardiovascular control usually does not return to normal. In the chronic phase, orthostatic hypotension, alteration of the arterial pressure and the regulation of the body temperature as well as changes of the blood volume and cardiovascular diseases as metabolic disorders occur. Nearly all risk factors pf cardiovascular diseases tend to be more prevalent in people with spinal cord injuries. Disordered control of blood pressure following spinal cord injury has important consequences, as patients with spinal cord injuries have an increased risk of developing heart disease and stroke (Yekutiel et al. 1989), and cardiovascular dysfunction is currently a leading cause of death in people with spinal cord injuries (Bauman and Spungen 2008; Dyson-Hudson and Nash 2009; Garshick et al. 2005). Knowledge of cardiovascular alterations is critical to the management and rehabilitation of patients with spinal cord injuries (Calvo-Infante et al. 2018).

22.1 Cardiovascular Consequences as Autonomic Dysfunction

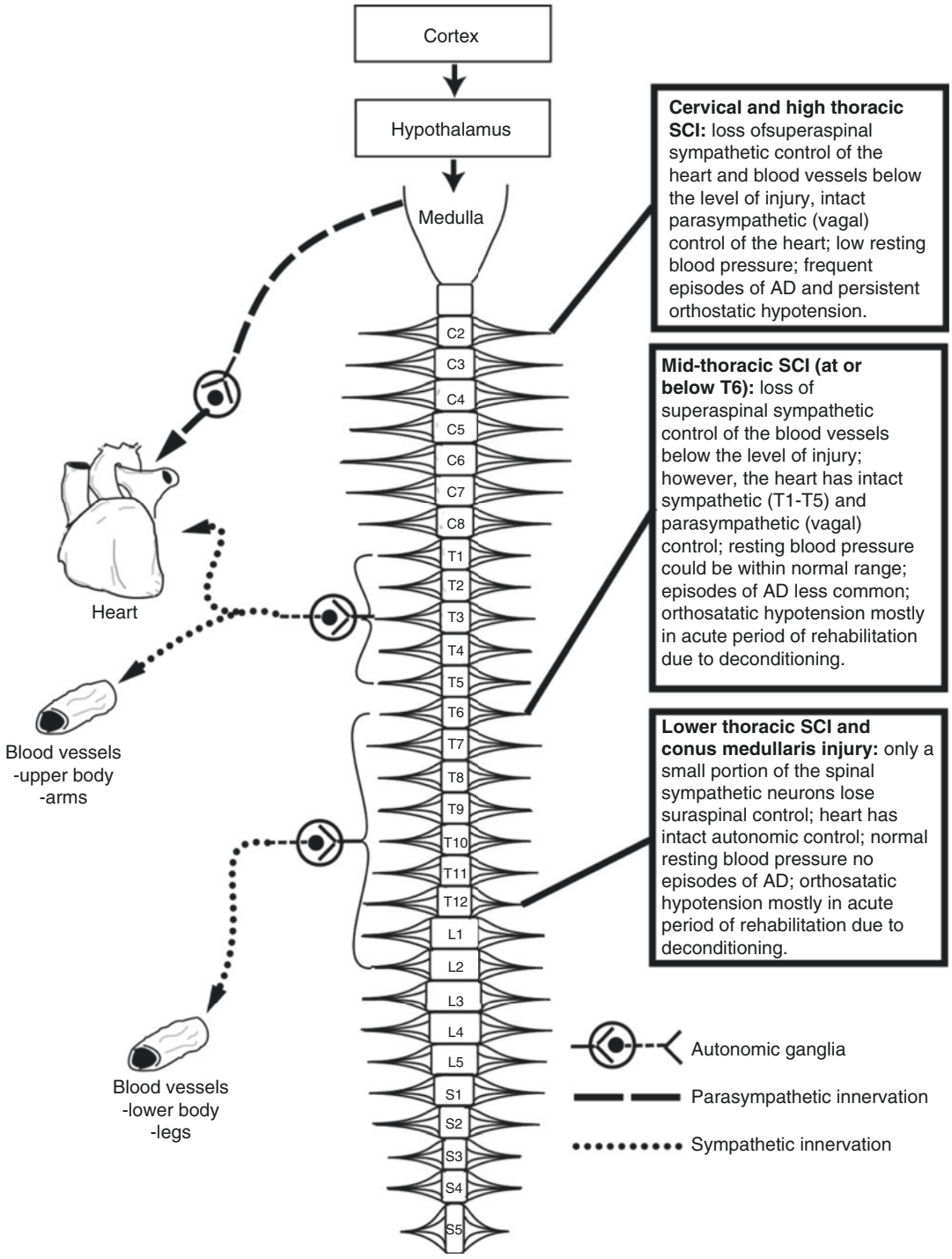
Severe hypotension and bradycardia occur in the acute phase following a high spinal cord injury. These are classic clinical presentations as neurogenic shock. One hundred percent of people with cervical spinal cord injury experience severe hypotension in the acute phase following spinal cord injury (Krassioukov and Claydon 2006). Bradycardia has been reported in 64–77% of patients with cervical spinal cord injury (Piepmeier et al. 1985). When spinal cord injury occurs in the midthoracic region or caudal region, bradycardia is generally less severe, secondary to the partial preservation of supraspinal influences on cardiac sympathetic neurons. These cardiovascular disturbances in all cases of the acute phase of spinal cord injuries resolve spontaneously 2–6 weeks after injury. The effect on the cardiovascular system depends on the extent of damage to the spinal or central component of the autonomic nervous system. Cardiac changes following spinal cord injury are caused by loss of supraspinal sympathetic control, which correspond to relatively increased parasympathetic and decreased sympathetic activity (Biering-Sørensen et al. 2018) (Fig. 22.2).

22.1.1 Pathophysiology of Cardiovascular Consequences as Autonomic Dysfunction

Sympathetic division has its cells of origin in preganglionic cell bodies located in the intermediolateral gray columns of the spinal cord, segments

Fig. 22.2 Schematic diagram of autonomic control of cardiovascular systems and possible cardiovascular outcomes following spinal cord injury. The cerebral cortex and hypothalamus provide excitatory and inhibitory inputs to the various nuclei within the medulla oblongata involved in cardiovascular control. The parasympathetic control of the heart exits at the level of the brain stem via the vagus nerve (CN X). The preganglionic fibers of the vagus nerve then synapse with postganglionic parasympathetic neurons in ganglia on or near the target organ. Descending sympathetic input from the rostroventralateral medulla (RVLM) provide tonic control to spinal sympathetic preganglionic neurons (SPNs) involved in cardiovascular control. SPNs are found within the lateral horn of the spinal cord in segments T1–L2 and exit the spinal cord via the ventral root. They then synapse with postganglionic neurons located in the sympathetic chain (paravertebral ganglia). Finally, the sympathetic postganglionic neurons synapse with the target organs (heart and blood vessels). From Biering-Sørensen et al. (2018), with permission

T1–L2. These preganglionic fibers terminate in the paravertebral ganglia, segmented along the anterolateral surfaces of the vertebral column (sympathetic trunks) and prevertebral ganglia located outside of the sympathetic trunk. These ganglia give rise to postganglionic sympathetic fibers that travel to target organs. Sympathetic neurons innervate all the chambers of the heart, the arteries, and the veins. Although blood vessels receive predominately sympathetic innerva-



tion (with the exception of cerebral vasculature and genital erectile tissue cavernous bodies), the heart receives innervation from both divisions of the autonomic system: sympathetic and parasympathetic. Although the heart's rhythmic contractions occur spontaneously, the rate and rhythm of the contractions, as well as the force of the contractions (i.e., the contractility), can be adjusted by autonomic nervous system or hormonal influences. Increases in sympathetic activity lead to tachycardia, cardiac contractility, and vasoconstriction with increased blood pressure.

The parasympathetic division has its cells of origin in preganglionic neurons located in the brainstem and sacral spinal cords (S2–S4). The cranial outflow involved in cardiovascular control occurs from preganglionic cell bodies located in the nucleus ambiguus of the medulla and dorsal motor nucleus, which send fibers to cranial nerves IX and X (Teasell et al. 2000). These fibers do not pass through the spinal cord and therefore are not affected by spinal cord injury. As a result, parasympathetic mechanisms that slow the heart rate are largely preserved in people with spinal cord injuries. Vagal cardiovascular responses are limited to reducing heart rate and cardiac contractility, and it is generally accepted that it does not extend to the vasculature itself, except in specific regions, including blood vessels of the salivary glands, gastrointestinal glands, genital erectile tissue, and potentially the cerebrovasculature (Kano et al. 1991; Krassioukov and Claydon 2006; Suzuki et al. 1990). The sacral outflow originates from preganglionic cell bodies in the intermediolateral gray matter of S2–S4 spinal cord segments and terminates in the ganglia in the wall of the pelvic viscera. Postganglionic fibers originate from the visceral ganglia and terminate at their respective target organs. Activation of the parasympathetic nervous system is generally limited to reducing heart rate and cardiac contractility, and it is generally accepted that it does not extend to the vasculature itself, except in specific areas such as blood vessels of the salivary glands, gastrointestinal glands, genital erectile tissues, and potentially the cerebral vasculature (Kano et al. 1991; Krassioukov and Claydon 2006).

The heart and blood vessels above the diaphragm are supplied by the sympathetic innervation of preganglionic cell bodies in the thoracic cord segments T1–T7, while the vasculature below the diaphragm, including the splanchnic bed, is supplied by T5 and lower thoracic cord segments. As a result, injury to the spinal cord above the T1 interrupts the transmission of information from the brain to sympathetic neurons controlling cardiovascular function. The parasympathetic nervous system is spared from spinal cord injuries. Due to the spared parasympathetic nervous system, patients with acute cervical spinal cord injury are subject to hypotension, bradycardia, and asystole during vagal tone interventions such as tracheal suction (Mathias 1976).

The response of a patient with spinal cord injury to cardiovascular problems may occur with the level of lesion of spinal cord injury. The major cranial parasympathetic source passes through the vagus nerve, which leaves the central nervous system through the brainstem. Thus, the vagal supply is spared in spinal cord injuries. Injury above T1 results in a loss of excitatory and inhibitory input for all preganglionic sympathetic neurons. The heart and blood vessels above the diaphragm are largely innervated by the thoracic cord segments T1–T7. If more segments of the thoracic cord are spared, the cardiovascular system will be less affected. Patients injured in the lower thoracic or lumbar spinal cord have intact autonomic innervation in their heart and vasculature, and their responses to underlying cardiovascular disease and pharmacologic interventions are generally similar to those of individuals without spinal cord injury. In cervical and high thoracic injuries, an interruption to the sympathetic outflow results in cardiovascular dysfunction, but parasympathetic influences remain intact. The risk of heart disease is almost three times higher in patients with spinal cord injury, while the risk of stroke is almost four times higher than in those without spinal cord injury due to abnormal sympathetic outflow (Cragg et al. 2013).

Alterations in autonomic function are clinically often due to changes in spinal sympathetic control that lead to unstable blood pressure, including hypotension, bradycardia, orthostatic hypotension, autonomic dysreflexia, and atrioventricular block (ASIA 2012; Krassioukov and Claydon 2006; Krassioukov 2009). In addition to autonomic abnormalities, there are indirect effects such as reduced physical activity, impaired metabolic function, and other spinal cord injury-related

cardiovascular function. Other autonomic dysfunctional effects on the bladder, the bowel, sexual function, sweating, and thermoregulation are non-cardiovascular presentations of autonomic impairment. Approximately 500 mL of blood shift from the heart and brain to the blood vessels of the intestines and legs with changing posture from the supine to the upright position (Sjostrand 1953). Central baroreceptors detect the decrease in blood volume in upright position and respond by decreasing vagal tone to the heart and increasing peripheral sympathetic activity. The increase in sympathetic activity induces an increased heart rate and peripheral vasoconstriction to maintain stable arterial blood pressure (Phillips et al. 2012). Although the baroreceptors detect a decrease in the central blood volume during orthostasis, impaired descending sympathetic pathways in spinal cord injuries decrease vasoconstriction ability and lead to an abnormal compensatory response of blood pressure when the body position changes (Krassioukov et al. 2009a, b).

Without adequate resting sympathetic tone, a number of secondary mechanisms, particularly hormonal mechanisms, attempt to maintain blood pressure. It is important that the renin-angiotensin-aldosterone system can accomplish this through the direct pressor effects of angiotensin II and the salt-retaining effects of aldosterone. Drugs that interfere with the system, such as the angiotensin-converting enzyme inhibitor captopril, significantly lower supine blood pressure in tetraplegics. Small doses of diuretics, which cause salt loss and lower intravascular fluid volume, can lead to a marked fall in supine blood pressure (Sutters et al. 1992). The practical significance of these observations for people with high spinal cord lesions is that a period of recumbency will often accentuate orthostatic hypotension, a problem that can be reduced or prevented by head-up tilt.

22.1.2 Neurogenic Shock

In the acute phase, especially after cervical cord injury, patients have clinically severe hypotension and persistent bradycardia, which are common components of the phenomenon known as neurogenic shock (Krassioukov and Claydon 2006). Neurogenic shock is considered distributive and refers to the loss of vasomotor tone and the instability that subsequently occurs due to an imbalance in the autonomic nervous system (Hagen 2015; Ruiz et al. 2018). Loss of sympathetic tone leads to unopposed parasympathetic control, which is manifested by refractory hypotension and bradycardia (Hagen 2015). Neurogenic shock, which often occurs concurrently with spinal shock, is clinically recognized by bradyarrhythmias, atrioventricular conduction block and hypotension, which reflect dysfunction of the autonomic nervous system (Krassioukov and Claydon 2006; Piepmeier et al. 1985). Neurogenic shock is most commonly defined as a systolic blood pressure of $\leq$100 mmHg and heat rate $\leq$80 bpm (Biering-Sørensen et al. 2018). The incidence of neurogenic shock in newly injured individuals with cervical cord lesions was almost 25% and 19% for the thoracic spinal cord lesions, and neurogenic shock was associated with significantly longer Intensive Care Unit and hospital stays (Mallek et al. 2012; Ruiz et al. 2018). Neurogenic shock occurs most commonly after an acute injury above T6, while a spinal cord injury lower than T6 is regarded as rarely associated with neurogenic shock (Hagen 2015).

Significant hypotension, systolic blood pressure <90 mmHg in the supine position, was reported in all individuals with severe cervical cord lesion during the initial period, and half of the patients with them required vasopressor therapy to maintain arterial pressure (Glenn and Bergman 1997). Bradycardia has been reported in 64–77% of patients with cervical spinal cord injuries. Persistent bradycardia (<60 bpm) was reported in all patients and marked bradycardia (<45 bpm) in 71% of individuals with severe cervical spinal cord injuries during the acute phase (Lehmann et al. 1987). The most severe and frequent episodes of bradycardia occur within the first 5 weeks. Bradycardia is less of a problem when the injury is in the upper thoracic spinal cord or is less severe because cardiac sympathetic neurons remain under brainstem control and maintain a more balanced vagal and sympathetic influence (Furlan et al. 2003; Lehmann et al. 1987).

In the current management guidelines, the mean arterial pressure should be maintained

above 85–90 mmHg for the first 5–7 days (Ryken et al. 2013). The first thing to do in treating neurogenic shock is to ensure restored intravascular volume. If needed, hypotension can be treated with vasopressors. These include norepinephrine, epinephrine, dopamine, phenylephrine and simultaneous use of atropine in patients with significant bradycardia (Consortium for Spinal Cord Medicine 2008). Enteral pseudoephedrine has also been used successfully as adjunctive therapy (Wood et al. 2013).

22.1.3 Bradycardia

Cardiovascular instability, including severe bradycardia, often occurs immediately after a high cervical spinal cord injury due to the acute withdrawal of sympathetic tone to the heart and vascular system and may even be life-threatening (Piepmeier et al. 1985). Peripheral sympathetic denervation leads to arterial dilatation and pooling of the blood in the venous compartment. Disruption of cardiac sympathetic innervation (T1–T4) promotes bradycardia and decreases myocardial contractility. In addition, parasympathetic innervation of the heart from the vagus nerve remains intact and can lead to bradycardia. Less commonly, the cardiac arrest has been described (Yue et al. 2017).

Bradycardia during the early days following spinal cord injury results from sympathetic pathway disruption, which results in an autonomic nervous system imbalance with markedly reduced or absent sympathetic activity and a relative predominance of parasympathetic activity. The severity of bradycardia is directly related to the level and completeness of spinal cord injury. While sinus bradycardia is the most common cardiac rhythm problem in the acute stage, other cardiac rhythm abnormalities have also been reported, including atrioventricular blocks and cardiac arrest (Sadaka and Veremakis 2012). Other factors can contribute to the occurrence of bradycardia and cardiovascular instability in tetraplegia. Induction of reflex bradycardia and sinus arrest by upper airway stimulation during tracheal suction or bronchial toilet, leading to an increase in the unopposed vagal stimulation, is common in patients with acute cervical spinal cord injury. Hypoxia also stimulates a vagal response by activating the carotid body chemoreceptor, and the normally counteracting sympathetic response is compromised in spinal cord injury (Phillips et al. 2012).

Hypotension and bradycardia are most profound within 3–5 days after cervical spinal cord injury, but they usually resolve within the first 2–6 weeks after injury and rarely last longer than 2 months. Although bradycardia returns to normal, relative bradycardia and hypotension are common in chronic tetraplegia. An associated abnormality with bradycardia including a junctional escape rhythm and atrioventricular block may also be present (Franga et al. 2006). Mild bradycardia is usually asymptomatic. With heart rate below 40–50/min, the patient may experience fatigue or dizziness. In more severe cases, syncope may occur.

Bradycardias can be prevented by pretreatment with atropine 10–15 min prior to tracheal suction and by hyperventilation just before suction, thereby preventing hypoxia and activation of arterial chemoreflexes. In general, asymptomatic bradycardia is not treated because it tends to recover after an acute injury. Pharmacological management of symptomatic bradycardia includes 0.4–0.6 mg atropine intravenously, every 4 h, for short-term therapy. High doses of atropine up to 0.04 mg/kg may be required to achieve the desired effect. Atropine is generally recommended as a first-line treatment for symptomatic bradycardia following cervical spinal cord injury. Acute episodes of bradycardia and hypotension can occur suddenly without warning in the first few hours and in the first days after injury, so that atropine should always be available at the bedside. Atropine improves conduction through the atrioventricular node by decreasing vagal tone via muscarinic receptor blockade (Sadaka and Veremakis 2012) (Table 22.1).

Another drug commonly used for intravenous medications includes sympathomimetic agents such as dopamine or epinephrine, which increase heart rate through action on β1-receptors in the

Table 22.1 Therapeutic modalities for bradycardia secondary to cervical spinal cord injuries

Modality	Administration route	Mechanism of action
Atropine	IV	Reduces vagal tone by muscarinic receptor blockade
Dopamine	IV infusion	Beta1 receptor on the heart
Epinephrine	IV infusion	Beta1 receptors on the heart
Aminophylline	IV	Inhibition of PDR enzyme thus increasing c-AMP with subsequent rise in catecholamines
Theophylline	Enteral or parenteral	Inhibition of PDE enzyme thus increasing c-AMP with subsequent rise in catecholamines
Propantheline	Enteral	Postganglionic parasympathetic acetylcholine receptor blocker
Permanent pacemaker	Invasive	

From Sadaka and Veremakis (2012), with permission

heart. Continuous infusion of dopamine at a rate 2–10 μg/kg/min or epinephrine 0.01–0.1 μg/kg/min was also used in the acute setting (McMahon et al. 2009). Complications include tachyarrhythmia, angina pain, palpitations, vasoconstriction, nausea, vomiting, and headache. The methylxanthine agents including aminophylline and theophylline have been used effectively for the management of refractory symptomatic bradycardia when other agents have failed (Weant et al. 2007; Whitman et al. 2008). Aminophylline has been used effectively to treat refractory bradycardia when other agents have failed. Aminophylline is administered as an initial loading dose (oral or intravenous) of 200–300 mg, followed by maintenance doses of 100 mg three times a day for 8–12 weeks (Sadaka et al. 2010). One of the obvious advantages of these drugs is that they can be administered on a fixed schedule as an enteral preparation. It has recently been reported that methylxanthines are specifically used as an effective first-line treatment for bradycardia associated with cervical spinal cord injury. When intermittent boluses of atropine or continuous infusion of sympathomimetics fail to prevent recurrent symptomatic bradycardia, temporary or permanent cardiac pacemaker is used as the next therapeutic alternative (Moerman et al. 2011).

Particular attention should be given to other potential exacerbating factors, including rapid changes in positioning, prolonged recumbency, adverse drug effects, underlying infection, and hypovolemia. Before moving the patient from the supine position, abdominal binder, thigh-high stockings, and elastic bandages to the lower extremities should be applied. These measures decrease venous pooling in the lower extremities and splanchnic vasculature. The patient can be moved slowly, from a supine position to a relatively upright position.

22.1.4 Orthostatic Hypotension

Orthostatic hypotension is very common in individuals with spinal cord injury. Orthostatic hypotension is most common and severe in the acute phase of spinal cord injury but also can be observed in the chronic phase. Episodes of orthostatic hypotension are characterized by drastic decreases in blood pressure when a person assumes the upright posture (Davidson and Phillips 2017). Orthostatic hypotension is defined as a decrease in systolic blood pressure of 20 mmHg or more or a decrease in diastolic blood pressure of 10 mmHg or more when an upright posture from the supine position regardless of the presence of symptoms (Kaufmann 1996). The disruption of the sympathoexcitatory pathways following spinal cord injury impairs the ability of the arterial baroreflex to efficiently produce vasoconstriction and maintain blood pressure. Although the cardiovagal baroreflex is impaired after spinal cord injury, the sympathetic nervous system is primarily responsible for maintaining blood pressure during an orthostatic challenge. It must be noted that the cardiovagal effect on heart rate affects blood pressure stability dur-

ing the first 2–3 s after an orthostatic challenge (Ogoh et al. 2006; Phillips et al. 2012).

Orthostatic hypotension occurs in 74% of individuals with spinal cord injury. Symptoms of orthostatic hypotension in people with spinal cord injuries are similar to those in healthy people and include fatigue or weakness, lightheadedness, dizziness, blurred vision, dyspnea, and restlessness. Orthostatic hypotension does not always cause presyncopal symptoms, and asymptomatic orthostatic hypotension occurs in 41% of patients (Claydon and Krassioukov 2006). In chronic spinal cord injury, asymptomatic decrease in blood pressure, indicative of orthostatic hypotension, occurs in up to 50% of patients with cervical spinal cord injury and 20% of thoracic patients. Presyncopal symptoms present in one-third and one-fifth of individuals with orthostatic hypotension, respectively (Claydon and Krassioukov 2006). Symptoms associated with orthostatic hypotension gradually decrease after the first few weeks of the rehabilitation period and seem to be helped by repeated postural challenges. This adaptation may occur because of an improved ability of the cerebrovascular circulation to autoregulate in the presence of extremely low perfusion pressure.

Episodes of orthostatic hypotension can cause syncope, nausea, fatigue, and dizziness and can have a significant impact on rehabilitation. One of the first clinical problems when a patient begins rehabilitation after spinal cord injury and increases physical activity is orthostatic hypotension. Long-term orthostatic hypotension can increase the risk of stroke after spinal cord injury. Resting hypotension also plays a role in cognitive dysfunction. Orthostatic hypotension results from low venous return secondary to blood pooling in the vasculature caudal to the level of injury and low arterial vascular tone. There is low resting catecholamine after cervical spinal cord injury and no effective increase with central supraspinal sympathetic activation by upright tilt (Claydon and Krassioukov 2006). Other factors contributing to orthostatic hypotension following spinal cord injury include reduced plasma volumes caused by hyponatremia (Frisbie and Steele 1997), insufficient increases of the efficacy of the renin-angiotensin system for maintaining blood pressure, and potential cardiac deconditioning (Groothuis et al. 2010).

Treatment of orthostatic hypotension as well as autonomic dysreflexia is very important in the clinical setting because of relevant clinical consequences such as myocardial infarction, stroke, cognitive decline, and orthostatic intolerance. Numerous pharmacological and non-pharmacological interventions are possible to manage these two conditions. However, prevention is the first line of treatment for orthostatic hypotension and autonomic dysreflexia after spinal cord injury. Patients with spinal cord injuries may experience episodes of orthostatic hypotension on a daily basis. Most activities in patients with spinal cord injuries are performed in seated or upright position in the wheelchair, which can lead to orthostatic instability. Initial and simplest prevention strategies for orthostatic hypotension include appropriate fluid intake, avoiding diuretics and large meals, compression stockings or bandages, and semi-upright sleep position. Pharmacological intervention may be required. These drugs include increasing vascular tone with alpha-agonist midodrine hydrochloride and/or volume expansion with fludrocortisone. Midodrine 10 mg can prevent early symptoms of orthostatic hypotension by maintaining cerebral blood flow and helps prevent presyncopal symptoms by maintaining perfusion of the brainstem (Krassioukov et al. 2009a).

22.1.5 Autonomic Dysreflexia

In general, the resting arterial blood pressure in individuals with cervical and high thoracic spinal cord injuries is lower than in healthy subjects. However, the majority of these people also have life-threatening episodes of hypertension during autonomic dysreflexia, sometimes every day. Episodes of autonomic dysreflexia are characterized by paroxysmal increase in systolic blood pressure of at least 20 mmHg in individuals of spinal cord injury at or above T6 spinal cord segment and may or may not be accompanied by a bradycardia (Krassioukov et al. 2021; Lee et al.

Table 22.2 Definition of autonomic dysreflexia

Age	Definition
Adult	Systolic rise >20 mmHg
Adolescents	Systolic rise >15–20 mmHg
Children	Systolic rise >15 mmHg

1995) (Table 22.2). Compensatory bradycardia is often seen in autonomic dysreflexia due to a baroreceptor-mediated parasympathetic (vagal) response, although tachycardia can also be observed (Claydon et al. 2006a, b). The level and completeness of the injury are the critical determinants for the presence of autonomic dysreflexia which is three times more common in complete vs. incomplete tetraplegics (Curt et al. 1997; West et al. 2013). Among complete tetraplegics, the clinical presentation of autonomic dysreflexia is variable and ranges from uncomfortable symptoms to life-threatening crises. Autonomic dysreflexia occurs in response to peripheral painful or non-painful visceral or somatic stimulation below the level of injury (Eltorai and Schmit 2001; Krassioukov et al. 2009a, b). Vasoconstriction, hypertensive crisis, and other manifestations of sympathetic overactivity seen in autonomic dysreflexia are mediated via postganglionic release of norepinephrine with α-adrenergic activation of vascular smooth muscle (Eldahan and Rabchevsky 2018). Autonomic dysreflexia is reported to occur in 50–90% of people with cervical and high thoracic spinal cord injury. Episodes of autonomic dysreflexia can occur in both the acute and chronic phases of spinal cord injuries. Autonomic dysreflexia occurs three times more often in people with complete vs. incomplete tetraplegia (Curt et al. 1997). In fact, systolic blood pressure can exceed 300 mmHg during autonomic dysreflexia (Wan and Krassioukov 2014). In the chronic phase of spinal cord injuries, the majority of people with high-level spinal cord injuries above the T5 level experience episodes of autonomic dysreflexia that occur up to 41 times per day, on average 11 times per day (Hubli et al. 2015).

The most common stimuli that cause autonomic dysreflexia are bladder and bowel distention. Any stimuli below the level such as pressure ulcer, tight shoe or pants, indwelling catheter, catheterization, urinary tract infection, bladder percussion, and instrumental procedures such as urodynamic study, cystoscopy, muscular electrical stimulation, and vibration or electrostimulation for ejaculation can contribute to autonomic dysreflexia (Kirshblum et al. 2002; Yoon et al. 2018). The intensity of autonomic dysreflexia varies from silent to severe. Many episodes of autonomic dysreflexia are asymptomatic, with elevated blood pressure and sweating or piloerection (Kirshblum et al. 2002). Mild episodes of autonomic dysreflexia occur intermittently through the days in response to a variety of stimuli, but they can often not be noticed and have little consequence. Severe autonomic dysreflexia has important clinical significance. Episodes of autonomic dysreflexia often show a throbbing headache and flushing above the level of injury. With recurrent episodes of dysreflexia, headache may become a particularly severe symptom despite modest elevation in blood pressure. Without treatment, autonomic dysreflexia can be life-threatening complications such as cerebral hemorrhage, seizure, cardiac arrhythmia, retinal detachment, and death (Myers et al. 2007; Partida et al. 2016).

To effectively prevent autonomic dysreflexia, patients, caregivers, and family members should be educated about proper management of the bladder, bowel, and skin as triggers from these organs. The first approach to autonomic dysreflexia treatment is recognition of symptoms and elimination of trigger stimuli. Pharmacological intervention is necessary if autonomic dysreflexia does not respond to non-pharmacological managements, such as elimination of noxious stimuli and head elevation. Pharmacological intervention is required if blood pressure continues above 150 mmHg. The most commonly used drugs are nifedipine (a short-acting calcium channel blocker), captopril (angiotensin-converting enzyme), or nitroglycerine (vasodilator). These drugs have been shown to aggravate low resting blood pressure (Krassioukov et al. 2009b; Ryken et al. 2013). Prazosin 1 mg effectively reduces recurrent episodes of autonomic dysreflexia without affecting resting blood pressure (Phillips et al. 2015). Botulinum toxin A can reduce the

frequency and severity of autonomic dysreflexia secondary to detrusor overactivity. As a rule, 200 U of botulinum toxin A (diluted in 10 mL saline to 20 U/mL) are injected into the detrusor muscle at 20 sites (10 U per site) with sparing the trigon.

22.1.6 Low Resting Blood Pressure

In addition to hypotension in the acute phase after spinal cord injuries, i.e., neurogenic shock, people with cervical and high thoracic spinal cord injuries often have significantly lower resting arterial blood pressure than in healthy individuals (West et al. 2012). Low resting blood pressure after spinal cord injuries is also associated with a number of other conditions, including exacerbated dizziness, development of syncope, poor mood, lethargy, and fatigue (Claydon et al. 2006a, b; Davidson and Phillips 2017; Wecht and Bauman 2013). Asymptomatic systolic blood pressures around 90 mmHg are common in tetraplegia. Therefore, it is important to identify the person's baseline blood pressure to determine whether a low value is truly pathological and to guide treatment endpoints with fluids or pressors (Ong et al. 2020). Decreased blood pressure in the acute phase of spinal cord injury is considered secondary to a decrease in sympathetic activity below the neurological level injury. Hypotension is associated with the impaired vascular tone, reduced circulating catecholamines, and impaired venous return. Hypotension in acute cervical spinal cord injury improves over the weeks, but relatively low blood pressure can continue lifelong.

The mean arterial pressure (MAP) in the supine position of the normal person is approximately 93 mmHg (70–100 mmHg), while 57 mmHg in person with cervical spinal cord injuries (Mathias et al. 1979). Patients with cervical spinal cord injury often have a systolic blood pressure of 90 mmHg and diastolic 60–70 mmHg or much lower (Rosner et al. 1984). It is not uncommon for a patient to have a sitting systolic blood pressure of 60–80 mmHg. The extent and severity of hypotension correlate well with the level of injury and severity of spinal cord injury (Mathias and Bannister 2002; West et al. 2012). Impairment of cerebrovascular and cognitive function in the spinal cord injuries such as dizziness, syncope, lethargy, poor mood, and fatigue has been shown to be associated with low resting blood pressure (Phillips et al. 2014a, 2014b). Most individuals are asymptomatic despite these low blood pressures. The improvements of the symptoms of hypotension may be partially associated with greater tolerance of low cerebral perfusion pressure, possibly cerebral autoregulation.

22.2 Cardiovascular Consequences as Metabolic Disorder

Cardiovascular morbidity is high compared to ambulatory subjects, and coronary artery disease tends to occur earlier in people with spinal cord injuries than in ambulatory populations. A major factor in the increased risk of cardiovascular disease in people with spinal cord injuries is that risk factors such as hyperlipidemia, diabetes, and obesity are comparatively high in people with spinal cord injuries. Another factor contributing to the high cardiovascular morbidity and mortality associated with spinal cord injuries is the sedentary lifestyle and the decreased physical function associated with loss of motor function. Tetraplegics are associated with an excess 16% risk of all cardiovascular diseases (coronary artery disease, hypertension, cerebrovascular disease, valvular disease, and dysrhythmias), a fivefold risk of cerebrovascular disease, but 70% less coronary heart disease compared with paraplegics. Complete injury is associated with a 44% greater risk of overall cardiovascular disease (Groah et al. 2001). Measuring lipid and lipoprotein levels is a prerequisite for risk assessment of cardiovascular disease as well as a clinical tool that defines the urgency for therapeutic lifestyle intervention. Therapeutic lifestyle intervention is warranted in a high percentage of young, healthy, community-dwelling people with paraplegia. Early detection and treatment of cardiovascular

Table 22.3 Risk enhancers for cardiovascular disease

Risk enhancer	Remarks
Family history of premature ASCVD	
Persistently elevated LDL-C	LDL-C ≥ 160 mg/dL (≥4.1 mmol/L)
Chronic kidney disease	eGFR 15–59 mL/min/1.73 m^2 with or without albuminemia
Metabolic syndrome	elevated blood pressure, elevated glucose, increased waist circumference, elevated triglycerides (>150 mg/dL, nonfasting), and low HDL-C (<40 mg/dL in men, <50 mg/dL in women)
Conditions specific to women	Preeclampsia, premature menopause
Inflammatory diseases	Rheumatoid arthritis, psoriasis, HIV
Ethnicity	e.g., South Asian ancestry
Lipid/ biomarkers	Persistently elevated triglycerides ≥175 mg/dL (≥2.0 mmol/L)
In selected individuals if measured	hs-CRP ≥2.0 mg/L Lp(a) levels ≥50 mg/dL or ≥ 125 nmol/L apoB ≥130 mg/dL Ankle-brachial index (ABI) <0.9

From Arnett et al. (2019) and Grundy et al. (2019)
apoB apolipoprotein B, ASCVD atherosclerotic cardiovascular disease, HIV human immunodeficiency virus, hsCRP high sensitive C-reactive protein, LDL-C low density lipoprotein cholesterol, Lp(a) lipoprotein (a)

disease are an emerging clinical challenge in this population (Myers et al. 2007). Risk-enhancing factors for cardiovascular disease are summarized in Table 22.3 (Arnett et al. 2019; Grundy et al. 2019).

22.3 Deep Venous Thrombosis

The most common peripheral vascular disorder in patients with spinal cord injuries is deep vein thrombosis. Deep vein thrombosis is emphasized as a major clinical problem in patients with spinal cord injuries due to their high prevalence, high morbidity and mortality rates, changes in clinical symptoms in the lower extremities, and availability of effective prophylactic and therapeutic strategies (Dhall et al. 2013; Watson 1968). The prevalence of deep vein thrombosis in patients with spinal cord injury is 12–100%. Variability of this wide range of prevalence rates is influenced by time after spinal cord injury, the associated risk factors, the diagnostic modalities, and the presence of prevention and prevention modalities. The incidence of deep vein thrombosis and pulmonary embolism is high in the first 3 months after a spinal cord injury, thus emphasizing the prophylaxis of this period reasonably (Dhall et al. 2013). In patients with spinal cord injuries, the loss of an active calf muscle pump in the paralyzed limbs significantly reduces blood flow. As a result, the sluggishness of venous return is further exacerbated by the hypercoagulability associated with spinal cord injury. In combination with the pressure that the bed exerts on the calf muscles, this sluggishness causes the bedridden spinal cord injured patient to be at high risk of developing deep vein thrombosis (Teasell et al. 2009).

22.4 Peripheral Arterial Disease

The prevalence of peripheral arterial disease in patients with spinal cord injuries has not been well studied. Patients with spinal cord injury tend to have the same arterial disorders as the general population, but neurologic deficits can make diagnosis difficult because they do not have the main symptom of intermittent claudication. Symptoms of advanced limb ischemia, such as rest pain or numbness, may not be evident in patients with spinal cord injury. The diseases can initially be detected as gangrenous changes or other signs of advanced disease. Pallor and reduced peripheral arterial pulses may be the only signs of arterial disease of the lower extremities in patients with spinal cord injuries (Lee 1991).

Thoracic aortic aneurysms or dissecting aneurysm, surgical trauma to the aorta, and intercostal artery ligation can lead to neurologic deficits due to emboli in the spinal cord, but these additional neurological deficits can be masked in tetraplegics. Although the abdominal aortic aneurysm

presents with abdominal and back pain, the relevant clinical presentations are not evident in patients with spinal cord injuries.

22.4.1 Assessment and Management of Peripheral Arterial Disease

As part of the regular examination of patients with spinal cord injuries, a routine examination of peripheral arterial pulses and feet for ischemic lesions should be performed. However, people with spinal cord injuries can have skin discoloration and cold temperature in the feet without evidence of significant peripheral vascular disease, and it can be difficult to palpate foot arterial pulses because of dependent leg edema associated with spinal cord injuries. Since the limitations of history and physical assessment of arterial disease in patients with spinal cord injuries, vascular examinations may be needed to diagnose, assess disease severity, and follow-up. Specific arterial testing includes continuous wave Doppler, segmental pressures, transcutaneous oximetry, and imaging studies (Lee 1991).

Continuous wave Doppler or duplex scanning detects blood movement. In the normal arteries, the pulsatile waveform is generally triphasic. Mild stenosis can attenuate the signal. When the severity worsens, the signal becomes monophasic (Lee 1991). Segmental pressures can be measured by sequentially inflating and deflating the pneumatic cuffs around the limb or digit. The most commonly reported segmental pressure is an ankle-brachial index (ABI) (Grew et al. 2000). ABIs above 1.0 are regarded as normal, mild disease is between 1.0 and 0.8, moderate disease is between 0.8 and 0.5, and severe disease is considered to be less than 0.5. ABI can be used as a useful screening tool for peripheral arterial disease in patients with spinal cord injuries. As is common in diabetics, this measurement cannot be used if vessel walls are not compressible due to calcification (Lee 1991). Transcutaneous oximetry is used to evaluate skin blood flow using oxygen-sensitive electrodes. This measurement is also useful for determining the adequacy of skin perfusion for healing of an amputation site or pressure injury wound. Generally, values above 40 mmHg are adequate, but values below 20 mmHg are insufficient. Imaging techniques such as real-time 2D sonography, computed tomography, and magnetic resonance angiography are increasingly being used instead of invasive angiography (Groah et al. 2011).

Reduction in risk factors such as smoking, diabetes, and hyperlipidemia are key elements of management (Lavis et al. 2007). Ischemic heart disease is a common comorbidity in patients with peripheral vascular disease and a common cause of death in these patients; primary and secondary prevention of ischemic heart disease is indicated (Goldberg 2009; Groah et al. 2011). Because there are no symptoms in patients with spinal cord injuries, revascularization of the limb may not be an issue to relieve claudication (Goldberg 2009). Arterial reconstruction for the occlusive disease may be difficult due to small and atrophic arteries in patients with spinal cord injuries.

References

American Spinal Injury Association (ASIA). International standards to document remaining autonomic function after spinal cord injury. 1st ed. American Spinal Injury Association: Atlanta; 2012.

Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;74:1376–414.

Bauman WA, Korsten MA, Radulovic M, et al. 31st g. Heiner Sell lectureship: secondary medical consequences of spinal cord injury. Top Spinal Cord Inj Rehabil. 2012;18:354–78.

Bauman WA, Spungen AM. Coronary heart disease in individuals with spinal cord injury: assessment of risk factors. Spinal Cord. 2008;46:466–76.

Biering-Sørensen F, Biering-Sørensen T, Liu N, et al. Alterations in cardiac autonomic control in spinal cord injury. Auton Neurosci. 2018;209:4–18.

Calvo-Infante R, Narvaez-Rojas A, Padilla-Zambrano H, et al. Cardiovascular complications associated with spinal cord injury. J Acute Dis. 2018;7:139–44.

Claydon VE, Elliott SL, Sheel AW, et al. Cardiovascular responses to vibrostimulation for sperm retrieval in men with spinal cord injury. J Spinal Cord Med. 2006a;29:207–16.

Claydon VE, Krassioukov AV. Orthostatic hypotension and autonomic pathways after spinal cord injury. J Neurotrauma. 2006;23:1713–25.

Claydon VE, Steeves JD, Krassioukov A. Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord. 2006b;44:341–51.

Consortium for Spinal Cord Medicine. Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. J Spinal Cord Med. 2008;31:403–79.

Cragg JJ, Noonan VK, Krassioukov A, et al. Cardiovascular disease and spinal cord injury: results from a national population health survey. Neurology. 2013;81:723–8.

Curt A, Nitsche B, Rodic B, et al. Assessment of autonomic dysreflexia in patients with spinal cord injury. J Neurol Neurosurg Psychiatry. 1997;62:473–7.

Davidson R, Phillips A. Cardiovascular physiology and responses to sexual activity in individuals living with spinal cord injury. Top Spinal Cord Inj Rehabil. 2017;23:11–9.

Dhall SS, Hadley MN, Aarabi B, et al. Deep venous thrombosis and thromboembolism in patients with cervical spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):244–54.

Dyson-Hudson T, Nash M. Guideline-driven assessment of cardiovascular disease and related risks after spinal cord injury. Top Spinal Cord Inj Rehabil. 2009;14:32–45.

Eldahan KC, Rabchevsky AG. Autonomic dysreflexia after spinal cord injury: systemic pathophysiology and methods of management. Auton Neurosci. 2018;209:59–70.

Eltorai IM, Schmit JK. Emergencies in chronic spinal cord injury patients. Jackson Heights, NY: Eastern Paralyzed Veterans Association; 2001.

Franga DL, Hawkins ML, Medeiros RS, et al. Recurrent asystole resulting from high cervical spinal cord injuries. Am Surg. 2006;72:525–9.

Frisbie JH, Steele DJ. Postural hypotension and abnormalities of salt and water metabolism in myelopathy patients. Spinal Cord. 1997;35:303–7.

Furlan JC, Fehlings MG. Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis, and management. Neurosurg Focus. 2008;25:E13.

Furlan JC, Fehlings MG, Shannon P, et al. Descending vasomotor pathways in humans: correlation between axonal preservation and cardiovascular dysfunction after spinal cord injury. J Neurotrauma. 2003;20:1351–63.

Garshick E, Kelley A, Cohen SA, et al. A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord. 2005;43:408–16.

Glenn MB, Bergman SB. Cardiovascular changes following spinal cord injury. Top Spinal Cord Inj Rehabil. 1997;2:47–53.

Goldberg R. Guideline-driven intervention on SCI-associated dyslipidemia, metabolic syndrome, and glucose intolerance using pharmacological agents. Top Spinal Cord Inj Rehabil. 2009;14:46–57.

Grew M, Kirshblum SC, Wood K, et al. The ankle brachial index in chronic spinal cord injury: a pilot study. J Spinal Cord Med. 2000;23:284–8.

Groah S, Hosier H, Ward E, et al. Cardiometabolic risk clustering and atherosclerosis: is there a link in spinal cord injury? Top Spinal Cord Inj Rehabil. 2011;16:1–13.

Groah SL, Weitzenkamp D, Sett P, et al. The relationship between neurological level of injury and symptomatic cardiovascular disease risk in the aging spinal injured. Spinal Cord. 2001;39:310–7.

Groothuis J, Thijssen D, Rongen GA, et al. Angiotensin II contributes to the increased baseline leg vascular resistance in spinal cord-injured individuals. J Hypertens. 2010;28:2094–101.

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139:e1082–143.

Hagen EM. Acute complications of spinal cord injuries. World J Orthop. 2015;6:17–2.

Helkowski WM, Ditunno JF Jr, Boninger M. Autonomic dysreflexia: incidence in persons with neurologically complete and incomplete tetraplegia. J Spinal Cord Med. 2003;26:244–7.

Hubli M, Gee CM, Krassioukov AV. Refined assessment of blood pressure instability after spinal cord injury. Am J Hypertens. 2015;28:173–81.

Kano M, Moskowitz MA, Yokota M. Parasympathetic denervation of rat pial vessels significantly increases infarction volume following middle cerebral artery occlusion. J Cereb Blood Flow Metab. 1991;11:628–37.

Kaufmann H. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. Clin Auton Res. 1996;6:125–6.

Kirshblum SC, House JG, O'Connor KC. Silent autonomic dysreflexia during a routine bowel program in persons with traumatic spinal cord injury: a preliminary study. Arch Phys Med Rehabil. 2002;83:1774–6.

Krassioukov A. Autonomic function following cervical spinal cord injury. Respir Physiol Neurobiol. 2009;169:157–64.

Krassioukov A, Claydon VE. The clinical problems in cardiovascular control following spinal cord injury: an overview. Prog Brain Res. 2006;152:223–9.

Krassioukov A, Eng JJ, Warburton DE, et al. A systematic review of the management of orthostatic hypotension after spinal cord injury. Arch Phys Med Rehabil. 2009a;90:876–85.

Krassioukov A, Linsenmeyer TA, Beck LA, et al. Evaluation and management of autonomic dysreflexia and other autonomic dysfunctions: preventing the

highs and lows: management of blood pressure, sweating, and temperature dysfunction. Top Spinal Cord Inj Rehabil. 2021;27:225–90.

Krassioukov A, Warburton DE, Teasell R, et al. A systematic review of the management of autonomic dysreflexia after spinal cord injury. Arch Phys Med Rehabil. 2009b;90:682–95.

Lavis TD, Scelza WM, Bockenek WL. Cardiovascular health and fitness in persons with spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:317–31.

Lee BY, Karmakar MG, Herz BL, et al. Autonomic dysreflexia revisited. J Spinal Cord Med. 1995;18:75–87.

Lehmann KG, Lane JG, Piepmeier JM, et al. Cardiovascular abnormalities accompanying acute spinal cord injury in humans: incidence, time course and severity. J Am Coll Cardiol. 1987;10:46–52.

Mallek JT, Inaba K, Branco BC, et al. The incidence of neurogenic shock after spinal cord injury in patients admitted to a high-volume level I trauma center. Am Surg. 2012;78:623–6.

Mathias CJ. Bradycardia and cardiac arrest during tracheal suction-mechanisms in tetraplegic patients. Eur J Intensive Care Med. 1976;2:147–56.

Mathias CJ, Bannister R. Autonomic disturbances in spinal cord lesions. In: Weaver LC, Polosa C, editors. Autonomic failure: a textbook of clinical disorders of the autonomic nervous system. 4th ed. New York: Oxford University Press; 2002.

Mathias CJ, Christensen NJ, Frankel HL, et al. Cardiovascular control in recently injured tetraplegics in spinal shock. Q J Med. 1979;48:273–87.

McMahon D, Tutt M, Cook AM. Pharmacological management of hemodynamic complications following spinal cord injury. Orthopedics. 2009;32:331.

Moerman JR, Christie B 3rd, Sykes LN, et al. Early cardiac pacemaker placement for life-threatening bradycardia in traumatic spinal cord injury. J Trauma. 2011;70:1485–8.

Myers J, Lee M, Kiratli J. Cardiovascular disease in spinal cord injury: an overview of prevalence, risk, evaluation, and management. Am J Phys Med Rehabil. 2007;86:142–52.

Ogoh S, Yoshiga CC, Secher NH, et al. Carotid-cardiac baroreflex function does not influence blood pressure regulation during head-up tilt in humans. J Physiol Sci. 2006;56:227–33.

Ong B, Wilson JR, Henzel MK. Management of the patient with chronic spinal cord injury. Med Clin North Am. 2020;104:263–78.

Partida E, Mironets E, Hou S, et al. Cardiovascular dysfunction following spinal cord injury. Neural Regen Res. 2016;11:189–94.

Phillips AA, Krassioukov AV. Contemporary cardiovascular concerns after spinal cord injury: mechanisms, maladaptations, and management. J Neurotrauma. 2015;32:1927–42.

Phillips AA, Krassioukov AV, Ainslie P, et al. Baroreflex function following spinal cord injury. J Neurotrauma. 2012;29:2432–45.

Phillips AA, Krassioukov AV, Ainslie PN, et al. Perturbed and spontaneous regional cerebral blood flow responses to changes in blood pressure after high level spinal cord injury: the effect of midodrine. J Appl Physiol. 2014a;116:645–53.

Phillips AA, Warburton DE, Ainslie PN, et al. Regional neurovascular coupling and cognitive performance in those with low blood pressure secondary to high-level spinal cord injury: improved by alpha-1 agonist midodrine hydrochloride. J Cereb Blood Flow Metab. 2014b;34:794–801.

Phillips AA, Elliott SL, Zheng MM, et al. Selective alpha adrenergic antagonist reduces severity of transient hypertension during sexual stimulation after spinal cord injury. J Neurotrauma. 2015;32:392–6.

Piepmeier JM, Lehmann KB, Lane JG. Cardiovascular instability following acute cervical spinal cord trauma. Cent Nerv Syst Trauma. 1985;2:153–60.

Rosner MJ, Elias Z, Coley I. New principles of resuscitation for brain and spinal injury. N C Med J. 1984;45:701–8.

Ruiz I, Squair J, Phillips A, et al. Incidence and natural progression of neurogenic shock after traumatic spinal cord injury. J Neurotrauma. 2018;35:461–6.

Ryken TC, Hurlbert RJ, Hadley MN, et al. The acute cardiopulmonary management of patients with cervical spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):84–92.

Sadaka F, Veremakis C. Bradycardia secondary to cervical spinal cord injury. In: Breijo-Marquez FR, editor. Cardiac arrhythmias. London: IntechOpen; 2012. Available from: https://www.intechopen.com/books/cardiac-arrhythmias-new-considerations/bradycardia-secondary-to-cervical-spinal-cord-injury.

Sadaka F, Naydenov SK, Ponzillo JJ. Theophylline for bradycardia secondary to cervical spinal cord injury. Neurocrit Care. 2010;13:389–92.

Sjostrand T. Volume and distribution of blood and their significance in regulating the circulation. Physiol Rev. 1953;33:202–28.

Sutters M, Wakefield C, O'Neil K, et al. The cardiovascular, endocrine and renal response of tetraplegic and paraplegic subjects to dietary sodium restriction. J Physiol. 1992;457:515–23.

Suzuki N, Hardebo JE, Kåhrström J, et al. Neuropeptide Y co-exists with vasoactive intestinal polypeptide and acetylcholine in parasympathetic cerebrovascular nerves originating in the sphenopalatine, otic, and internal carotid ganglia of the rat. Neuroscience. 1990;36:507–19.

Teasell RW, Arnold JM, Krassioukov A, et al. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil. 2000;81:506–16.

Teasell RW, Hsieh JT, Aubut JA, et al. Spinal cord injury rehabilitation evidence review research team. Venous thromboembolism after spinal cord injury. Arch Phys Med Rehabil. 2009;90:232–45.

Wan D, Krassioukov AV. Life-threatening outcomes associated with autonomic dysreflexia: a clinical review. J Spinal Cord Med. 2014;37:2–10.

Watson N. Venous thrombosis and pulmonary embolism in spinal cord injury. Paraplegia. 1968;6:13–21.

Weant KA, Kilpatrick M, Jaikumar S. Aminophylline for the treatment of symptomatic bradycardia and asystole secondary to cervical spine injury. Neurocrit Care. 2007;7:250–2.

Wecht JM, Bauman WA. Decentralized cardiovascular autonomic control and cognitive deficits in persons with spinal cord injury. J Spinal Cord Med. 2013;36:74–81.

West CR, Bellantoni A, Krassioukov AV. Cardiovascular function in individuals with incomplete spinal cord injury: a systematic review. Top Spinal Cord Inj Rehabil. 2013;19:267–78.

West CR, Mills P, Krassioukov AV. Influence of the neurological level of spinal cord injury on cardiovascular outcomes in humans: a meta-analysis. Spinal Cord. 2012;50:484–92.

Whitman CB, Schroeder WS, Ploch PJ, et al. Efficacy of aminophylline for treatment of recurrent symptomatic bradycardia after spinal cord injury. Pharmacotherapy. 2008;28:131–5.

Wood GC, Boucher AB, Johnson JL, et al. Effectiveness of pseudoephedrine as adjunctive therapy for neurogenic shock after acute spinal cord injury: a case series. J Am Coll Clin Pharm. 2013;34:89–93.

Yekutiel M, Brooks ME, Ohry A, et al. The prevalence of hypertension, ischaemic heart disease and diabetes in traumatic spinal cord injured patients and amputees. Paraplegia. 1989;27:58–62.

Yoon JA, Shin YB, Shin MJ, et al. Cardiovascular monitoring during video urodynamic studies in persons with spinal cord injury. Am J Phys Med Rehabil. 2018;97:1–6.

Yue JK, Winkler EA, Rick JW, et al. Update on critical care for acute spinal cord injury in the setting of polytrauma. Neurosurg Focus. 2017;43:E19.

Recommended Additional Reading

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Crossman A, Neary D. Neuroanatomy: an illustrated colour text. 5th ed. Philadelphia: Elsevier; 2015.

Eltorai IM, Schmit JK, editors. Emergencies in chronic spinal cord injury patients. New York: Eastern Paralyzed Veterans Association; 2001.

Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston: Butterworth-Heinemann; 1996.

Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.

Robertson D, Bigaaioni I, Burnstock G, et al. Primer on the autonomic nervous system. 3rd ed. London: Elsevier; 2011.

Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia: Elsevier; 2016.

Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, progress in brain research, vol. 152. New York: Elsevier; 2006.

23 Respiratory Dysfunction and Management in Spinal Cord Injuries

Spinal cord injuries result in multiple effects on the respiratory system, which unfortunately lead to significant disabilities and/or respiratory failure in people with spinal cord injuries. Respiratory disorders can develop as a result of the wide variety of functional impairments that can occur in these diverse conditions and are considered as a leading cause of mortality for many patients with spinal cord injuries. A spinal cord injury is characterized by profound respiratory compromise caused by the level of loss of motor, sensory, and autonomic control associated with the injury. Patients are most vulnerable to respiratory illness in the first year after injury but continue to suffer from respiratory complications throughout life (Berlowitz et al. 2016). Pulmonary complications are the leading cause of morbidity and death both in the short and long term after a spinal cord injury. It is estimated that up to 84% of patients with high cervical spinal cord injuries (C1–C4) and 60% with low cervical injuries (C5–C8) suffer from respiratory compromise (Berney et al. 2011). Survival rates in population with spinal cord injuries have improved considerably, but respiratory complications remain a major problem (Shavelle et al. 2006). Spinal cord injury has a significant effect on lung function. Respiratory complications pose a serious threat to patients with spinal cord injuries, and death from respiratory disease is a leading cause of mortality. Atelectasis is the most common overall respiratory complication overall, followed by pneumonia and respiratory failure, regardless of the level of injury. Other pulmonary complications after spinal cord injuries include pulmonary edema due to excess fluid resuscitation in the acute phase and pulmonary embolism, which can occur in up to 4.5% of patients in the first 3 months. Pneumonia is a leading cause of death after spinal cord injuries, while atelectasis, ventilatory failure, and pulmonary embolism are common causes of morbidity (Ball 2001; Jia et al. 2013).

These respiratory problems cannot be recognized as quickly in patients with spinal cord injuries as in normally innervated individuals. Pulmonary complications are more common in patients with spinal cord injury with higher level lesions, reduced spirometry (FEV1 and FVC), impaired gas exchange (lower PaO_2), and advanced age. A high spinal cord injury above the fifth cervical segmental level usually results in a severe impairment of respiratory function. To minimize morbidity and mortality, people with tetraplegia need continuous preventive measures, careful surveillance, prompt diagnosis, and appropriate treatment of respiratory complications. Considering the morbidity of the respiratory system that results from spinal cord injuries, it is imperative to have a thorough understanding of the physiologic effects of spinal cord injuries. Then we can better understand how to evaluate and interpret the physiologic tests that have been developed. Although some effects on the respiratory system are more obvious, such as muscle

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weakness and decreased flows, others can occur secondarily and can lead to deleterious results which are seen as poor cough, swallowing dysfunction, skeletal and chest wall abnormalities, and sleep-disordered breathing (Gartman 2018). If a patient survives an acute stage of respiratory distress, chronic problems that may lead to a complication of the respiratory system may occur. It is important for the clinician to understand the muscles and normal mechanics of respiration before evaluating the respiratory status of the patient and establishing treatment goals.

Paralysis of the muscle required for breathing, mainly the diaphragm muscle, results in a significant loss of vital capacity and may require partial or complete mechanical ventilation. Approximately 10% of all patients with spinal cord injuries require temporary noninvasive or invasive ventilation during initial and acute treatment. Six percent of this group requires permanent mechanical ventilation because of the unsuccessful weaning of the mechanical ventilation. Diagnostic procedures and treatments of neurogenic respiratory dysfunctions are complex interventions that a full team of well-trained, comprehensive professionals must perform. These include lifetime medical care for patients with neurogenic respiratory dysfunction as an inpatient or outpatient and appropriate application and education in noninvasive or invasive ventilation, weaning from mechanical ventilation. With advances in technology and patient care, permanent or temporary ventilation can now be applied and managed at home. Comorbidities affecting respiratory care should be properly managed (Bach and Tilton 1994).

23.1 Respiratory Anatomy

23.1.1 Respiratory Muscles

Respiratory muscles have a distinct endurance that is different from the skeletal muscles. Respiratory muscles are controlled voluntarily and involuntarily. Although the inspiratory muscles are important for proper ventilation, the expiratory muscles are needed to overcome airway resistance and generate the force and volume required for proper coughing and airway removal of secretions including mucus and aspirated materials. Respiratory muscles include the diaphragm, abdominal muscles, intercostal muscles, and inspiratory accessory muscles (Fig. 23.1). The most important inspiratory muscle for breathing is the diaphragm. The higher the diaphragm position before the diaphragm contracts, the more the diaphragmatic pressure is increased by Laplace's law and the larger the area of the zone of apposition, which is the border with the lower rib, is favorable for breathing. When the diaphragm is lowered during inspiration, the force is transmitted to the zone of apposition by the abdominal pressure to inflate the lower rib cage. Unlike the action of the diaphragm, the intercostal muscles and the scalene muscles expand the upper ribs when contracted. Innervation of the respiratory muscles is as follows: diaphragm C3–C5, mainly C4 (phrenic nerve); intercostal muscles T1–T11 (intercostal nerves), accessory muscles (trapezius, sternocleidomastoid cranial nerve XI and C2–C4 and scalene C4–C8), and abdominals T6–T12 (Fig. 23.2). A cervical spinal cord injury damages all or most of the expiratory muscle functions. The diaphragm is usually completely innervated with lesions below C5, which preserves the inspiratory function. However, expiratory forces remain reduced so that coughing may be ineffective. Accessory muscles involved in inspiration and expiration contribute to structural changes in the thoracic cage during periods of intense exercise or respiratory distress. The accessory respiratory muscles are shown schematically in Fig. 23.3.

The intercostal muscles form two thin layers that each covers the intercostal spaces. The outer layer, the external intercostals, extends from the tubercles of the ribs dorsally to the costochondral junctions ventrally. The fibers of this layer are oriented obliquely, in the caudal-ventral direction, from the rib above to the rib below. In contrast, the inner layer, the internal intercostals, extends from the sternocostal junctions to near the tubercles of the ribs, and its fibers extend in the caudal-dorsal direction from the rib above to the rib below. The functions of the intercostal muscles involving respiration are determined by their typical origin and the insertion of the muscles between the ribs. The external intercostal muscles originate on ribs 1–11 and insert on ribs

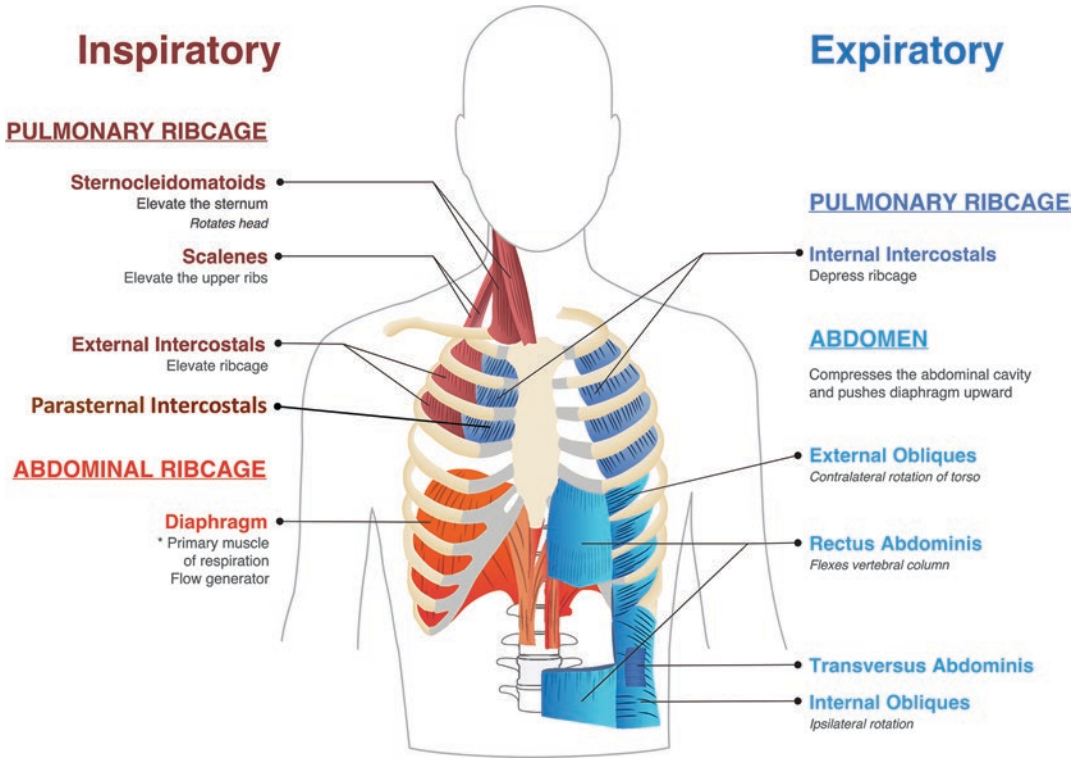


Fig. 23.1 Major contributing respiratory muscles and their function. Inspiratory (red) and expiratory (blue) respiratory muscles, categorized by their respective compartments: pulmonary ribcage, abdominal ribcage, and abdomen. The medial parasternal part of the internal intercostal muscles forms parasternal intercostal muscles and acts as inspiratory muscles. The primary respiratory action and non-respiratory action (italicized) are listed below each muscle or muscle group. From Welch et al. (2019), with permission

2–12. Each external intercostal muscle arises from the lower border of a rib and insert into the upper border of the rib below, directed obliquely downward, forward, and medially. The external intercostal muscles are thicker than the internal intercostal muscles. The muscles involve in quiet and forced inhalation. The internal intercostal muscles originate on the upper border of a rib and insert on the lower border of the rib above. The fibers are directed obliquely in a direction opposite to the external intercostal muscles. The internal intercostal muscles are only used in forceful exhalation such as coughing or during exercise, not in quiet breathing (Fig. 23.4). Ventrally, between the sternum and the chondrocostal junctions, the external intercostals are replaced by a fibrous aponeurosis, the anterior intercostal membrane, and the only muscle fibers are those of the internal intercostals. This portion of the internal intercostals differs from the interosseous portion by both in its location and in its function and is conventionally referred to as the "*parasternal intercostals*" (Fig. 23.1). Although the external intercostal muscle does not extend to the ventral region of the rib cage, the parasternal intercostals are covered on their inner surface by a thin muscle called the *triangularis sterni* or *transversus thoracis*. This muscle is usually not considered among the intercostal muscles (De Troyer et al. 2005). The parasternal intercostals in humans have an inspiratory effect in every interspace, and the triangularis sterni has an expiratory effect (De Troyer et al. 2005).

23.1.2 Inspiratory Muscles

The inspiration is mainly due to the action of the diaphragm and the external intercostal muscles and paraspinal intercostals (the inter cartilaginous portion of the internal intercostals), and secondly to the contribution of the inspiratory accessory mus-

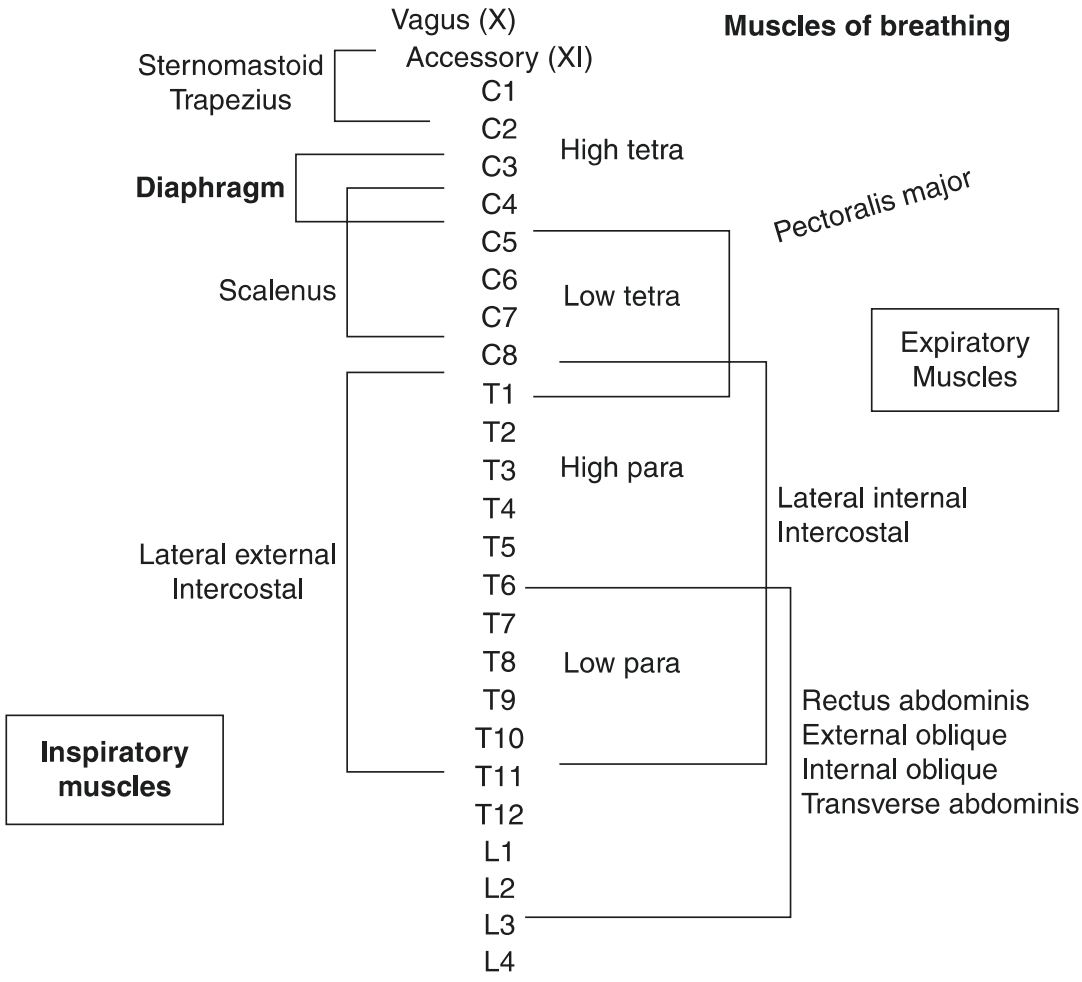
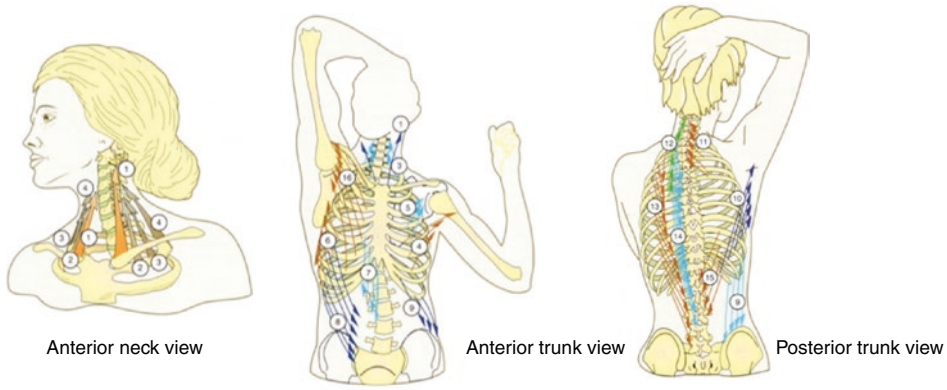


Fig. 23.2 Overview of the affected inspiratory and expiratory muscles in relation to the neurological level of injury

cles. The expansion of the rib cage and abdominal wall are prominent features of the inspiratory phase of the breathing cycle. The expansion of the abdominal wall is produced by the action of the diaphragm. When the diaphragm is activated, its muscle fibers shorten and its dome, which essentially corresponds to the central tendon, moves in the caudal direction, pushing the abdominal viscera caudally and pushing the abdominal wall outward (De Troyer et al. 2005). The normal expansion of the rib cage during inspiration is mainly produced by the intercostal muscles and the scalenes.

The diaphragm and external intercostal muscles are the "active" muscles in normal inspiration. However, with a compromised respiratory system, the patient uses the accessory muscles of inspiration to assist with ventilation. The use of the accessory muscles in quiet inspiration is a clear indicator of the difficulty in breathing. The scalene muscles are a group of 3 muscles of the anterior, middle, and posterior scalene. The scalene muscles originate from the transverse processes of C2–C7 and insert into the first (anterior and middle scalene) and second ribs (posterior scalene). The middle scalene is the largest and longest of the three scalene muscles. It is inserted into the upper surface of the first rib. Because of their insertions into the upper ribs, the scalene muscles elevate the upper ribs and act as inspiratory muscles. Therefore, the scalene muscles can be considered as one of the primary inspiratory muscles (Fig. 23.5). The sternocleidomastoid



Accessory inspiratory muscles
(1) sternocleidomastoids and (2–4) scalenes (anterior, middle, and posterior) in the anterior neck view; (4, 16) pectoralis major, (5) Pectoralis minor, and (6) lower fibers of serratus anterior in the anterior trunk view; (10) latissimus dorsi, (11) serratus posterior superior, and (12) iliocostalis cervicis in the posterior trunk view

Accessory expiratory muscles
(7) rectus abdominalis, (8) external oblique, and (9) internal oblique in the anterior trunk view; (13) iliocostalis thoracis, (14) longissimus, and (15) serratus posterior posterior inferior in the posterior trunk view

Fig. 23.3 Accessory inspiratory and expiratory muscles. From Kapandji (2008), with permission

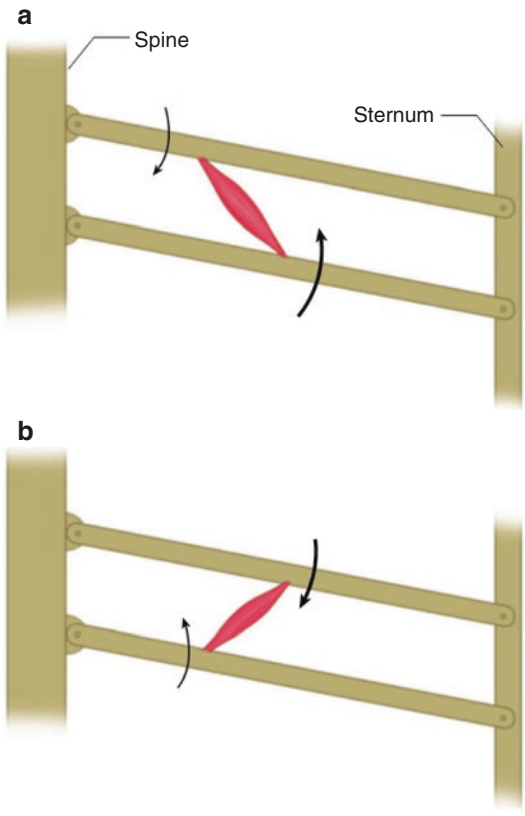


Fig. 23.4 Diagram of the actions of the intercostal muscles. (**a**) When the external intercostal contracts, the torque acting on the lower ribs is greater than that acting on the upper rib. (**b**) The torque acting on the upper rib is greater than that acting on the lower rib with contraction of the external intercostal muscles

muscle is derived from the manubrium of the sternum and the clavicle and is inserted at the mastoid process of the temporal bone. The primary actions of the muscles are rotation of the head to the opposite and flexion of the neck. Because of the origin and insertion sites of the muscle, fixation of the head and neck movement by using functionally reversed origin and insertion can function more effectively as an accessory inspiratory muscle. The sternocleidomastoid muscle is likely to be shortened or atrophied because it is a muscle across two or more joints.

23.1.3 Expiratory Muscles

Expiration and coughing are mainly performed by contraction of abdominal muscles and assisted by internal intercostal muscles. Normally, expiration is a passive process by passive movement of the diaphragm during quiet breathing, unless the active contraction of the respiratory muscles is required for coughing, sneezing, or expelling secretions. Abdominal muscles are important for enhancing contractions and the expulsive force required to cough effectively and clear secretion. In complete tetraplegia, abdominal muscle function is absent, and when the diaphragm relaxes during expiration, the flaccid chest wall moves outward, limiting the expiratory reserve volumes to less than 20% of nor-

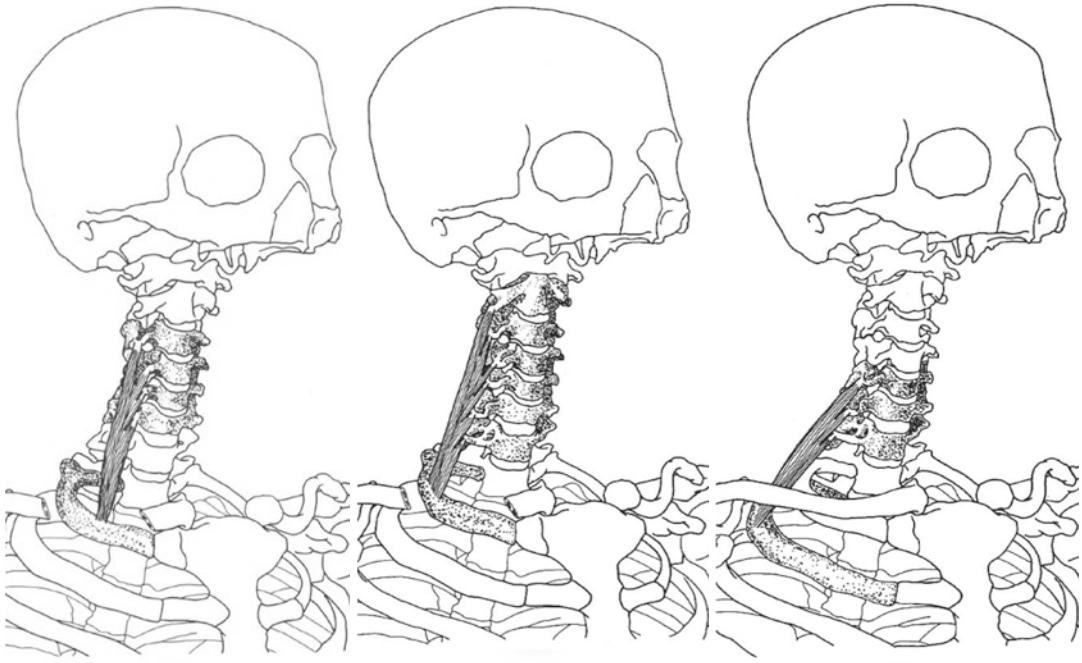


Fig. 23.5 The scalene muscles (anterior, middle, and posterior). The scalene muscles originate from the transverse processes of C2–C7 and insert into the first (anterior and middle scalene) and second ribs (posterior scalene). The middle scalene is the largest and longest of the three scalene muscles. It is inserted into the upper surface of the first rib

mal (Berlly and Shem 2007). Forced expiration is even severely impaired during wakefulness and sleep, since abdominal musculature is also flaccid. The internal intercostal muscles involve assisting this function with forced expiration by the abdominal muscles. During forced expiration, the diaphragm is pushed up into the thoracic cavity by contraction of the abdominal muscles. The ribs become depressed by contraction of the internal intercostal muscles and decrease the lateral and anteroposterior diameter of the thorax. Some muscles of the accessory muscles (clavicular head of the pectoralis major, serratus posterior) assist the expiration; their function is determined by the origin and the insertion of the muscles.

23.2 Pathophysiology

In patients with tetraplegia, the initial compliance of the thoracic cavity decreases, and compliance of the abdomen increases. This is because of stiffness, decreased movement of the joints between the ribs, vertebrae, and sternum, restricted lung volume expansion, and weakness and decreased tension of the abdominal muscles. Abdominal compliance decreases when abdominal spasticity occurs. In the early stages of spinal cord injury, respiratory dysfunction depends largely on the level of injury, but after spinal shock, the paralysis of the intercostal muscles also changes from flaccidity to spasticity, resulting in a stiff thoracic wall. These changes mainly affect the improvement of inspiratory function. In other words, paradoxical breathing with the collapse of the upper thorax and the expansion and protrusion of the abdomen during the early phase of injury is not present, which increases the vital capacity. Over time, as the spasticity of the intercostal muscles and abdomen occurs, the vital capacity becomes double.

Respiratory dysfunction in patients with upper cervical cord injuries is summarized as respiratory muscle paralysis, decreased vital capacity, decreased coughing function, decreased compliance of the lung and thorax, and increased oxygen demand in respiration. In addition, lesions above T6 affect the sympathetic nervous system with an unopposed parasympathetic activity leading to bronchial reactivity. Increased bronchial activity leads to an increase in nasal resistance, which

may contribute to obstructive sleep apnea (OSA) in people with high cervical injuries (Daoud et al. 2020). In restrictive lung disease such as spinal cord injuries, saturation of arterial blood due to respiratory failure precedes hypercapnia rather than hypoxia. In tetraplegia and upper lesion paraplegia, impairment of the muscles involved in the exhalation, including the abdominal muscles, is greater than that of the muscles involved in the inspiration, so that the forced vital capacity (FVC) decreases more than the decrease in the total lung volume (TLV). It is easy to develop atelectasis because of a significant reduction in coughing and stagnation of pulmonary secretions (Schilero et al. 2018; Schilero et al. 2009).

Patients with upper cervical spinal cord injuries can also improve pulmonary function as the respiratory muscles recover over the years after spinal cord injury. The prognosis for pulmonary function is closely related to the neurological level of injury and injury severity. In spinal cord injuries C6–C8, FVC increases by 9% when the neurological level of injury goes down by one segment. FVC of incomplete injury is about 10% higher than that of complete injury. There is a 1% increase in FVC when the level of injury goes down by one segment. However, the difference in FVC between a complete injury and an incomplete injury is not significant.

Different neurological levels of spinal cord injuries result in different functional impairments of the diaphragm, the intercostal muscles, accessory respiratory muscles, and abdominal muscles. The anatomical levels of injury determine the potential degree of respiratory complications and damage to the respiratory muscles. Respiratory dysfunction in patients with spinal cord injury is due to impaired ventilation and coughing. Inadequate coughing induces mucus retention, and decreased sympathetic function and relative parasympathetic predominance contribute to increased bronchial mucus secretion and bronchoconstriction. These increase the risk for atelectasis and pulmonary infection and ultimately increase the mortality rate significantly. If the spontaneous breathing function in patients with upper cervical cord injuries, FVC is approximately 50% of normal predicted values.

Upper cervical cord lesions, C3 or higher lesions, cause ventilatory failure due to diaphragm weakness. The accessory muscles at C3 are still functioning and can produce a small tidal volume (60–300 mL), but are not retained by fatigue. Individuals with complete injury at the C2 level or above may have apnea. The accessory respiratory muscles can be hypertrophied to elevate the sternum and expand the upper rib cage to create larger tidal volumes as possible as they can.

In patients with C4–C8 spinal cord injury, the function of the diaphragm is partially or normally spared, and loss of vital capacity is mainly due to the reduction of expiratory reserve volume. Respiratory function in these patients is strongly dependent on the position. Respiration is easier, and vital capacity is larger in the supine position because the diaphragm has a more favorable mechanical advantage from the descent of the diaphragm. Abdominal binders in the sitting position in tetraplegic patients help to minimize postural worsening and decrease in vital capacity. Paradoxical respiration may be seen (upper chest caves in as abdomen expands) during the early phase of spinal cord injury. Vital capacity may double in 3–6 months, as paradoxical respiration decreases with the development of intercostal and abdominal spasticity. Thoracic cord lesion causes a less severe decrease in lung volumes and inspiratory respiratory muscle strength. Respiratory problems in thoracic cord lesions are mainly due to the absence or weakness of the expiratory muscles and ineffective coughing and retained secretion, resulting in mucus plugging and pneumonia.

Tracheostomy, vocal cord paralysis, cervical orthoses, and anterior cervical spinal surgery may cause swallowing impairment that may result in aspiration. Other problems such as abdominal distention due to paralytic ileus may cause additional respiratory impairment in the acute phase of spinal cord injury.

23.2.1 Respiratory Muscle Weakness

Restriction in lung function is defined as a decrease in total lung capacity. Lung volume measurement is often not practical for patients with spinal cord injury, but many simple, reliable, and reproducible parameters can be used to assess the severity of respiratory impairment. Measurements of respiratory muscle strength are important to assess over time in patients with spinal cord injuries. The most

commonly used measurement is vital capacity, which is a global assessment of respiratory muscle capacity that includes both inspiratory and expiratory muscle function. Vital capacity in supine can be very helpful in assessing diaphragm weakness. A decrease in vital capacity in the supine position of >19% indicates a weakness of the diaphragm (Benditt 2019). The most valuable of the parameters is the vital capacity, which is related to respiratory muscle strength and pulmonary compliance. Vital capacity (VC), the tidal volume (TV), and the forced one-second vital capacity (FVC1) decrease because of the weakness of inspiratory muscles in patients with high cervical spinal cord injury. While patients try to maintain a sufficient minute volume, the respiratory rate increases. The reduced strength of expiratory muscles results in a decrease in the end-respiratory reserve volume and, consequently, an increase in the residual capacity. This eventually reduces the vital capacity (Linn et al. 2000, 2001).

Reduction in expiratory muscle strength also reduces FVC, but more importantly, it reduces the intra-airway gas compression that is responsible for the explosive exhalation of gas during the exhalatory phase of cough. Another consequence of the weakness of expiratory muscles is that the ability to cough is limited when the peak cough flow rate decreases. Cough function is best assessed by measuring the cough peak flow, which can be performed easily with a spirometer or a peak flow meter. A value of 160 L/min or less is associated with inadequate clearance of secretion by an efficient coughing (Bach and Saporito 1996). Measuring peak cough flow using a peak flow meter is a simple and inexpensive method to objectively assess the ability of patients for sufficient coughing and indirect strength of the expiratory muscles.

A 30-min resistive inspiratory training each day can improve respiratory muscle strength and endurance and may be useful for successful ventilator weaning. Strengthening programs of the clavicular head of the pectoralis major improve expiratory function (Mueller et al. 2013). Theophylline improves diaphragmatic contractility and reduces fatigue. Anabolic steroids (oxandrolone, 20 mg/day for 1 month in tetraplegics) have been reported to reduce pulmonary complications and improve respiratory parameters (Spungen et al. 1999).

23.2.2 Altered Compliance of the Thorax

The compliance of the lung and thoracic cavity worsens immediately after injury in tetraplegic patients, due to a decrease in vital capacity and changes in the surfactants due to breathing with low tidal volume (Brown et al. 2006; Tow et al. 2001). It also leads to a paradoxical inspiration when the stability of the thorax is reduced due to partially or completely paralyzed intercostal muscles. This means that the chest becomes flat during the inspiration. Stiffness of the chest and potential spasticity of the intercostal muscles contribute to the decrease of compliance of the thoracic wall (Goldmann et al. 1988). When compliance of the abdomen is very increased, the lower abdominal pressure transmitted to the zone of apposition is low and the lower rib cage cannot be inflated efficiently.

23.2.3 Altered Coordination of the Thoracic Cage and Abdomen

The interaction between the abdominal and thoracic muscles is also impaired after high cervical spinal cord injury. Due to the loss of voluntary innervation of abdominal muscles, an increase in compliance of the abdomen results in a caudal shift of the diaphragm. The weight of the intra-abdominal organs also contributes to a ventral and caudal displacement. The vertical diaphragmatic movement decreases, and patient transfers, such as wheelchair mobilization, cause a decrease in the tidal volume and, therefore, a faster onset of dyspnea (Estenne and De Troyer 1987).

23.2.4 Effect of Altered Airway

Bronchial hyperactivity often occurs after cervical spinal cord injury and is significantly associated with decreased airway diameter and patency (Grimm et al. 2000). The proposed mechanisms for reducing the initial airway caliber relative to

lung size in subjects with tetraplegia include unopposed parasympathetic activity following the loss of sympathetic innervation to the lung and/or the inability to stretch airway smooth muscle with deep inhalation (Grimm et al. 2000).

23.2.5 Effect of Position

In case of paralysis of the abdominal muscles, changes in the position of the patient affect the distribution of the visceral contents and the resting length of the diaphragm. In the supine position, the abdominal contents force the diaphragm to a higher resting level than the upright or sitting position. As a result, there will be a greater diaphragmatic excursion in the supine position than in the upright position. Pulling down the abdominal contents by gravity causes the diaphragm to be in a lower resting position, so an upright position creates a larger demand on the diaphragm. Because of the lack of abdominal tone to support visceral contents, which in turn supports the diaphragm, the diaphragm does not return to its normal resting position. The diaphragmatic excursion is decreased and the patient's inspiratory capacity is reduced.

Maximal breathing capacity, vital capacity, tidal volume, lung compliance, and PaO_2 in supine increase in tetraplegic patients with an intact diaphragm. The movement of the diaphragm improves in the supine position because of the more advantageous position that the diaphragm is pushed up by abdominal contents into a domed configuration in the chest (with improved length-tension relation). In the sitting position, gravitational pull on the abdominal contents decreases diaphragmatic excursion and thus increases the work of breathing. The use of abdominal binders or corset in tetraplegic patients will help to minimize postural worsening and decrease in vital capacity resulted from biomechanical disadvantage when the patient is first start seated. Abdominal binders or corset can be used to minimize the effects of gravity and provide support for weak or absent abdominal muscles in the upright position, unless the patient's respiratory capacity is not strengthened. In contrast, normal subjects have a better respiratory function in the sitting or upright position because rib cage muscles and abdominal muscles allow the diaphragm to better expand the rib cage. In high cervical (C1–C2) injuries with diaphragm paralysis, the erect position is advantageous because gravity prevents ascending of abdominal contents into the chest. In addition, sternocleidomastoid muscle function improves in supine or sitting with a corset or abdominal binders.

23.3 Assessment of Respiratory Function

An accurate assessment of respiratory function is essential. Baseline assessments should be established for monitoring improvement or deterioration in function. The comprehensive assessment of respiratory status includes X-rays to evaluate for rib fractures that may occur during trauma; assessment of preexisting lung disease, such as chronic obstructive pulmonary disease or asthma; arterial gas studies to determine the balance of oxygen and carbon dioxide in the blood; and the vital capacity and other parameters including tidal volume, respiratory rate, strength of the respiratory muscles and the accessory muscles, breathing pattern in both supine and sitting positions, ability to cough and clear secretions, chest mobility, and the patient's posture. Here are the various testing modalities that may be applicable without advanced equipment or specialized laboratory setting (Table 23.1).

Table 23.1 Commonly available respiratory function tests in spinal cord injuries

Commonly available respiratory function evaluation
Spirometer
Flow–volume loops
Lung volumes
Static mouth pressures (MIP and MEP)
Coughing evaluation (PCF)
Maximum voluntary ventilation
Positional dependency of respiratory function in the supine or sitting position
Arterial blood gas analysis
Physical measurement of the chest circumference

23.3.1 Spirometric Pulmonary Function Test

The value of spirometry as the sole test for impairment has long been debated, as it has been shown that significant muscle weakness can be present even with normal vital capacity (Smeltzer et al. 1992). The most consistent role of spirometry is in the longitudinal assessment of patients and in determining the prognosis. That is, improvements in spirometric respiratory function parameter were been used as evidence of effective treatment response to neuromuscular diseases (Chiu et al. 2003; Gartman 2018). Spirometric pulmonary function tests in patients with cervical cord lesions show a restrictive spirometry pattern in which the FEV1/FVC ratio is preserved and the lung volume (vital capacity, total lung capacity, and expiratory reserve volume) is decreased. The spirogram is a graphic representation of the volume/time curve and the basic values used to interpret spirometry are the FVC, FEV1, and FEV1/FVC ratio (Fig. 23.6). Tetraplegic patients have paralysis of expiratory muscles and therefore have little or no expiratory reserve volume (ERV), and the vital capacity is equal to the inspiratory capacity. The ERV in paraplegic patients does not change (Fromm et al. 1999). The higher the level of injury, the more severe the reduction in vital capacity.

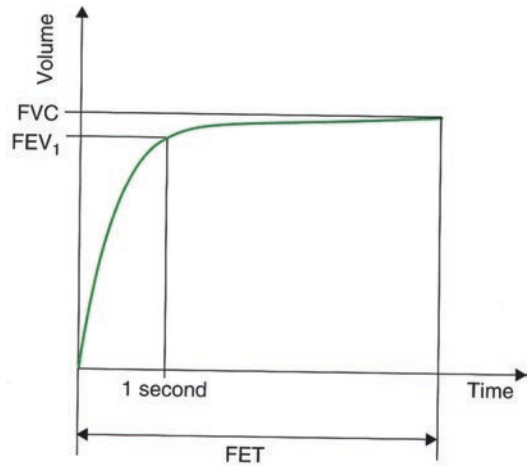


Fig. 23.6 Normal spirogram. FVC forced vital capacity, FEV_1 forced expiratory volume in 1 s, FET forced expiratory time

Measurement of vital capacity is useful, as a reduction to 25–30% of predicted vital capacity or less than twice the tidal volume may be indicated for mechanical ventilation. In normal adults, the vital capacity is an average of 50 mL/kg. Secretion clearance is impaired when vital capacity decreases below 30 mL/kg, and ventilatory failure occurs at a vital capacity of 10 mL/kg (Smith et al. 1987).

Vital capacity is the maximum amount of air that can be exhaled after a maximum inspiratory effort. The measurement of vital capacity is often used clinically as an index of respiratory function. This value is important in determining whether a patient can effectively move secretions from the alveoli to the airways. The larger the vital capacity, the more the patient is able to move secretions to the larger airways. Secretions can then be removed from the airways through the patient's coughing ability or assisted coughing techniques. Normal vital capacity measures 4–5 L, although this varies depending on the difference in height and weight. Vital capacity can be easily measured with a device such as a spirometer. The patient is instructed to take a deep breath and expel as much air as possible (Kelley 2003). The most commonly used measure of respiratory muscle strength is vital capacity, which is an overall assessment of respiratory muscle capacity that includes both inspiratory and expiratory muscle function (Benditt 2019). Supine vital capacity can be very helpful in assessing diaphragm weakness. A decrease in supine vital capacity of >19% suggests diaphragm weakness, and patients with bilateral diaphragm paralysis may drop by up to 50% (Mier-Jedrzelowicz et al. 1988).

The tidal volume is the amount of air that enters the lungs by easy respiration. The tidal volume increases with the improvement of vital capacity and can also be measured using a spirometer. The flow–volume loops represent a full inspiratory and expiratory effort in a single maneuver and are generated by the patient performing a rapid full inhalation to total lung capacity and a maximal expiratory maneuver without hesitation to residual volume, followed by a rapid maximal inspiration (Fig. 23.7). Functional residua capacity (FRC) measurement

serves as the basis for calculating the other volumes and represents the lung volume at which the forces of elastic recoil of the lungs and expansion of the expansion are balanced, and then other values obtained during spirometry are added or subtracted to calculate the entire spectrum of lung volumes (Fig. 23.8).

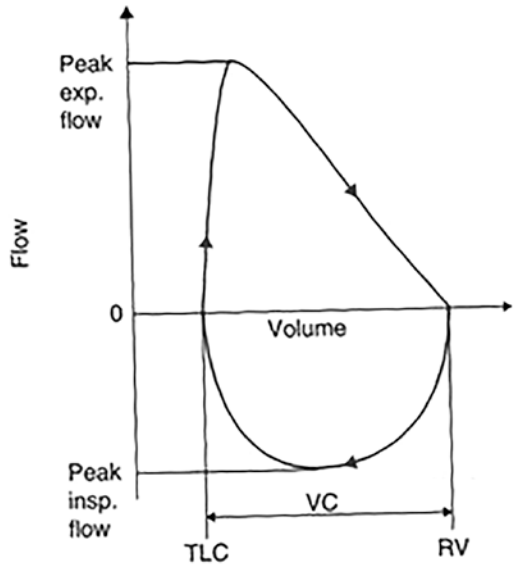


Fig. 23.7 Normal flow-volume loop. TLC total lung capacity, VC vital capacity, RV residual volume

23.3.2 Position Dependency

There may be changes in the vital capacities between seated and supine positions. If there is a significant diaphragm weakness or paralysis, a decrease in vital capacity is observed in the supine position, and the extent of the decrease depends on both the severity of weakness and whether one or both diaphragms are affected. In unilateral paralysis of the diaphragm, the vital capacity can decrease by 15–25%. Paralysis of the right diaphragm is a more severe decrease in vital capacity due to the weight of the liver. Bilateral paralysis can decrease by 40% or more (Celli 2002; Fromageot et al. 2001; Gartman 2018).

Certain conditions lead to an increase in the vital capacity in the supine position, which often leads to clinical confusion. Conditions, such as low cervical spinal cord injuries, leave the diaphragm neurologically intact, but the altered chest wall and abdominal muscles can be such a condition. The decrease in vital capacity in the upright position results from increased abdominal compliance, which leads to diaphragmatic dysfunction caused by the effects on the length-tension properties of the

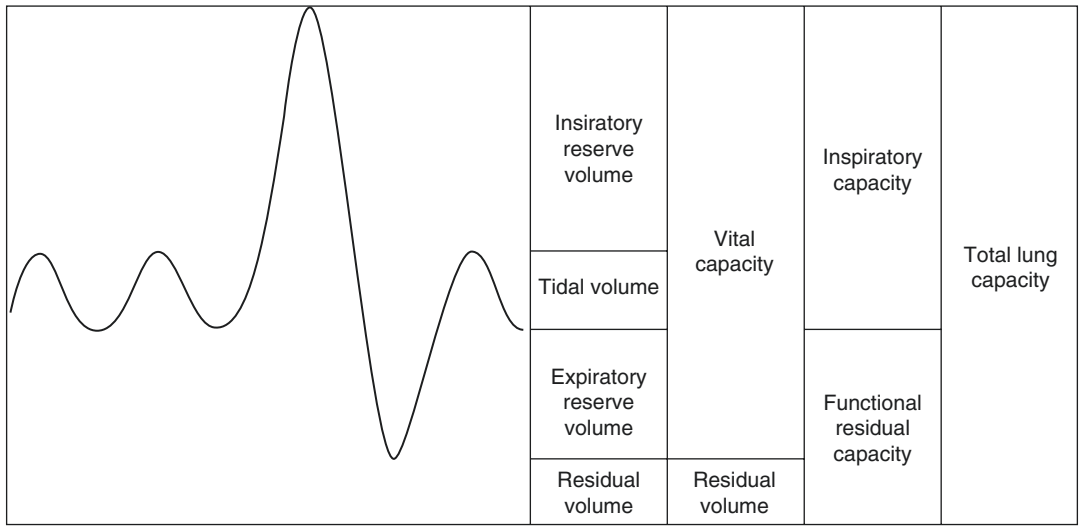


Fig. 23.8 Typical spirogram and components of lung volume

diaphragm and the normal chest wall configuration by the actions of the abdominal muscles on the rib cage. This has led to the suggestion that reducing abdominal compliance by binding the abdominal wall may improve upright inspiratory function in people with low cervical spinal cord injuries (Baydur et al. 2001; Estenne and De Troyer 1986).

23.3.3 Maximum Inspiratory Pressure and Maximum Expiratory Pressure

Maximum inspiratory pressure (MIP) is the maximum pressure that can be generated by the patient attempting to inhale through a blocked mouthpiece beginning at functional residual capacity (FRC). It is a marker of the function and strength of the respiratory muscles, as well as an important and noninvasive index of diaphragm strength. Maximum expiratory pressure (MEP) is the maximum pressure measured during forced expiration with cheeks bulging through a blocked mouthpiece after a full inhalation. MIP and MEP reflect respiratory muscle strength and coughing. Intercostal muscle strength is assessed indirectly by observation and measurement of chest expansion. MIP and MEP can be measured simply and reproducibly at the bedside. An MIP of −70 cmH_2O and an MEP of 100 cmH_2O are considered normal. A normal $PaCO_2$ cannot generally be maintained at a MIP of less than −20 cm H_2O, and ineffective cough typically occurs when MEP decreases to less than 40 cmH_2O (Kelly and Luce 1991). MIP and MEP are decreased in tetraplegic patients. There is some temporal improvement in the MIP but not in the MEP which reflects the impaired coughing and clearing the airway secretion. In patients with cervical and upper thoracic cord injuries, MIP is higher than MEP because a larger amount of muscle of expiration is involved. In patients with tetraplegia, the mean sitting MEP is 48 cmH_2O and the MIP is −64 cmH_2O.

23.3.4 Peak Cough Flow (PCF)

The dynamics of breathing depend on the compliance of the lungs and thorax, airway resistance, and elasticity. Compliance refers to the ease with which the lungs or thorax is inflated during inspiration. If the compliance of the rib cage decreases or the laryngeal muscle is abnormal, it directly affects the MIC, thereby decreasing the vital capacity, leading to impaired coughing. For an effective coughing, the vital capacity must be at least 60% of the predicted value (Andrews et al. 2013). Cough function is best assessed by measuring the peak cough flow (PCF), which is the maximum expiratory flow generated by a patient after a forceful cough (Sahni and Wolfe 2018) and can be performed easily with a spirometer or a peak flow meter. The PCF rate of a normal person is about 6–20 L/s (360–1200 L/min), and PCF of more than 160 L/min is required for an effective cough. Values less than 270 L/min are considered low and put patients at higher risk of respiratory complications. Effective airway clearance with PCF of more than 160 L/min is also associated with successful extubation (Bach and Saporito 1996). The critical flow rate should be at least 4.5 L/s for maximum expiratory flow rate and 1.5 L for vital capacity. Cough augmentation can assist in increasing the cough peak flow. This is achieved with the help of breath stacking (air stacking), mechanical cough augmentation, or manual chest and abdominal compression (manually assisted cough). Sequential breath stacking (lung volume recruitment) utilizes a hand-held resuscitator with a 1-way valve that increases lung volume (Sahni and Wolfe 2018). Air stacking or assisted coughing can make the expiratory flow rate seven times faster.

23.3.5 Arterial Blood Gas Analysis

Arterial blood gas analysis should be performed in patients with a vital capacity, MIP, or MEP less than or equal to 50% of predicted because these

values correlate with the onset of hypercapnia (Bach 1993; Braun et al. 1983). In individuals with less severe abnormalities, noninvasive pulse oximetry may be used to assess oxygenation. If the SaO_2 decreases below 90%, an arterial blood gas analysis should be obtained. Pulse oximetry-measured SpO_2 is accurate if SaO_2 is greater than 75%, but a minor difference may be approximately ±11% compared to actual oxygen saturation. In particular, the accuracy of oxygen saturation measured by pulse oximetry is less accurate at low blood pressure, low body temperature, or congestive heart failure. PaO_2 and SaO_2 by ABGA represent the degree of oxygenation of arterial blood, and $PaCO_2$ and pH represent the degree of ventilation. End-tidal measurement or percutaneous capnometry can be used to monitor long-term CO_2 concentration for ventilation monitoring. Since the CO_2 partial pressure is measured by end-tidal capnometry in air mixed with air in the dead space, it differs from $PaCO_2$ by 3–5 mmHg (Walsh et al. 2011).

23.3.6 Chest Measurement

Chest measurements are taken to assess the excursion of the upper and lower rib cage. A tape measure can be used to record the measurements at the axilla and xiphoid process levels. Measurements of the excursion after maximal exhalation should be compared to the measurements after maximal inhalation. Normal chest expansion is 6.0–7.5 cm.

23.4 Management of Respiratory Dysfunction

Strategies to prevent aspiration and eliminate secretion should be initiated in patients with respiratory muscle weakness. Chest physical therapy, frequent suctioning, incentive spirometry, cough assist maneuvers, and other forms of respiratory therapy may help reverse secretion-related complications such as mucus plugging and atelectasis. Bronchoscopy may be indicated if other method fails.

23.4.1 Secretion Management

Secretion management is essential for the treatment of respiratory complications and for the prevention of further respiratory complications in patients with spinal cord injury. The management of aggressive secretion should be performed in patients with acute cervical spinal cord injuries and in chronic patients. Secretion management or airway clearance therapy is a cornerstone of therapy to minimize the devastating effects of airway obstruction, infection, and inflammation due to mucus stasis on the conducting airways and the lung parenchyma (Volsko 2013). Airway clearance therapy utilizes physical or mechanical means to manipulate air flow, aid in the mobilization of tracheal and bronchial mucus cephalad, and facilitate coughing (Lester and Flume 2009). Breathing maneuvers, gravity-assisted drainage, manual techniques, and/or mechanical devices can be used to modify air flow and/or produce a coughing or coughing-like effect. The lack of absence of an adequate cough contributes to the development of recurrent respiratory tract infections and atelectasis and remains a major cause of death in patients with high cervical spinal cord injuries.

Suctioning can be performed through a tracheostomy, endotracheal tube, or oral mask. Angulation of the left main bronchus makes tubal suctioning of the left lung more difficult, and directional catheters may be useful in such instances. Because the angle of the main bronchus of the left lung is bent more than 50° from the right side at 25°, it is not easy to remove secretion of the left lung (Chatwin et al. 2018). Therefore, it is effective to use the mechanical insufflation-exsufflation (MI-E) device because of the high frequency of pneumonia in the left lung. Hypoxia, cardiac arrhythmia, lung shrinkage, and infection should be taken into account during airway suction. To avoid such complications, the air should be sufficiently inhaled and oxygenated before airway suction and finished within 10 seconds with an appropriately sized catheter (Chatwin et al. 2018). For adults, the outer diameter of the suction catheter should be less than half the inner diameter of the T-tube.

The suction pressure should not exceed 7–15 mmHg for portable devices and 100–120 mmHg for wall-mounted hospital devices. Push the suction catheter slowly until touching the tracheal carina. When you feel the resistance, remove the catheter about 1 cm, and slowly pull out the catheter while intermittently rotating the catheter with your fingers. The time required for the suctioning should be within 10 seconds and should not exceed 20 seconds until the oxygen is reinstalled. Sometimes saline is required for airway suctioning, but it is not recommended to use it normally.

Effective management of mucus and secretion can be achieved by (1) changing the patient's position in bed every 2 h and changing the posture from supine to prone position; (2) hyperinflation of the lungs to the maximum capacity prior to mucus evacuation; (3) specific positioning of the upper body according to target region to be cleared; (4) assisted coughing; (5) deep inspiration by air stacking or glossopharyngeal respiration; (6) insufflation with artificial respiration bag and an intermittent positive pressure volume device (IPPV) or with in-exsufflators followed by manual cough assistance by dorsocranial compression on the upper abdomen; and (7) extra- or intracorporeal chest vibration (Reid et al. 2010; Weidner et al. 2017).

High-frequency airway clearance assist devices, including high-frequency chest wall compression (high-frequency chest oscillation, high-frequency chest compression, vest vibrators) and intrapneumatic positive vibration (intrapulmonary percussion vibrator, IPPV), generate either positive or negative transrespiratory pressure excursions to produce high-frequency, small-volume oscillations in the airways (Chatburn 2007). There is no standardized terminology for high-frequency chest wall compression and intrapneumatic positive vibration. High-frequency chest wall compression (vest chest vibrator) generates negative changes in transrespiratory pressure difference by compressing the chest wall externally to cause short, rapid expiratory flow pulses, and relies on the elastic recoil of the chest wall to return the lungs to functional residual capacity. IPPV creates positive changes in transrespiratory pressure difference by injecting short, rapid inspiratory flow pulses into the airway opening and relies on the recoil of the chest wall for passive exhalation (Chatburn 2007). Chest clapping performed vigorously with a cupped hand or chest vibrators or IPPV can be performed to mobilize secretions in conjunction with positioning for effective postural drainage. Certain positions, such as head-down position to facilitate lower lobe drainage, may not be well tolerated in the presence of respiratory failure or gastroesophageal reflux, but a combination of positions allowing drainage of all the lobes should be attempted.

The liquefaction and loosening of bronchial secretions improve the efficiency of ventilation and prevent atelectasis and pneumonia during temporary and long-term ventilation (Hess 2001; Zakrasek et al. 2017). Nebulized drugs, such as acetylcysteine or sodium bicarbonate, combined with adequate hydration, help loosen secretions. Nebulized acetylcysteine, 1–2 mL of a 10–20% solution diluted with 5–10 mL of saline, may be useful for removing mucus. Since acetylcysteine can cause bronchospasm, it should be given after an inhaled bronchodilator. Anticholinergic agents, such as ipratropium bromide two puffs four times a day, relieve bronchospasm. Nebulized β-agonists, such as metaproterenol 0.3 mL or terbutaline 0.25 mg, every 4–6 h, help eliminate airway secretions by enhancing ciliary action and affect reversal of bronchospasm. Aminophylline not only improves diaphragmatic function and decreases fatigue, but it can also help because it has a synergistic effect with beta-agonists on ciliary action.

Assisted cough is useful for postural drainage and removal of secretions and may be used in combination with an insufflator or with the use of IPPB. Manual-assisted coughing provides an upwardly directed thrust, delivered with an open palm, hands placed just below the lower end of the sternum in coordination with expiratory efforts, and preceded by a deep breathing of the

patient or air stacking via an AMBU bag (Ries et al. 2007). The insufflation-exsufflation treatment is administered through a machine providing a deep breathing followed by exhalation through alternately exerting positive and negative pressure through the respiratory tract. The positive and negative pressures can be adjusted on the machine. Pressure is usually set at around 10 cmH_2O to begin with and increased to 36–60 cmH_2O and − 35 to −60 cmH_2O of positive and negative pressures as tolerance improves. Insufflation with positive pressure is provided for around 3 seconds, followed by exsufflation with negative pressure for around 3–4 s, and repeated if necessary (Ries et al. 2007; Strickland et al. 2013). Repeat four to five times or six to eight times. ±30 cmH_2O is considered to be ineffective. The presence of pneumothorax or emphysema is contraindicated. This treatment is contraindicated in the presence of pneumothorax, pneumomediastinum, or bullous emphysema.

If the vital capacity remains above 12.5 mL/kg and the atelectasis persists, removal of the mucus plug must be removed by bronchoscopy. It is recommended to remove the mucus plug by bronchoscopy daily.

23.4.2 Management of Respiratory Muscle Weakness and Breathing Fatigue

Most studies have focused on the formation of inspiratory muscles. Little is known about the effects of expiratory muscle training, which can be particularly beneficial for patients with weak coughs. Traditional measures designed to increase vital capacity in patients with spinal cord injuries include incentive spirometry, intermittent positive pressure breathing, and deep breathing exercises (Restrepo et al. 2011). Inspiratory muscle training has been shown to reduce symptoms, increase inspiratory muscle strength and endurance, and prevent fatigue in tetraplegia. Such training is achieved by breathing through resistance (Mueller et al. 2013). Training the clavicular portion of the pectoralis major muscle with repetitive isometric contraction can improve expiratory muscle function in tetraplegics, which can increase cough effectiveness and reduce the prevalence of bronchopulmonary infection in these patients.

Tetraplegic patients have an increased work of breathing and a decrease in respiratory muscle strength which are inducing fatigue of the respiratory muscles. These patients are prone to respiratory failure with a further increase in breathing work resulting in increased airway resistance, secretions, bronchospasm, and pneumonia (Rezania et al. 2012). Pharmacological management should be considered along with muscle training to improve the strength of the respiratory muscles. Aminophylline, which is converted to theophylline, improves diaphragmatic function and delays the onset of respiratory fatigue. For adults younger than 40 years with no heart or liver problems, intravenous loading dose of 6 mg/kg with a maintenance of 0.4–0.7 mg/kg is recommended to keep aminophylline levels between 10 and 20 mg/dL. Lower maintenance doses are needed in older patients or in patients with hepatic or cardiac problems. Blood levels should be measured and side effects of nausea, vomiting, or arrhythmias monitored. Higher doses are required in smokers because smoking increases the hepatic metabolism of aminophylline. Beta-agonists such as isoproterenol and terbutaline can be added.

23.4.3 Oxygen Therapy

Oxygen therapy aims to increase PaO_2, O_2 content, and O_2 delivery and is indicated when $PaO_2 \leq 50$ mmHg or $SaO_2 \leq 88\%$ in acute respiratory distress with hypoxemia. Therapeutic goals with oxygen therapy are $SaO_2 \geq 88\%$ measured with pulse oximetry and $PaO_2 \geq 55$–60 mmHg measure with ABGA (Nugent and Nourbakhsh 2011). Oxygen concentrations are determined by oxygen delivery methods. Table 23.2 shows FiO_2 (%) according to the

oxygen delivery method and oxygen flow rate (L/min). The estimated PaO_2 from a given SaO_2 is listed in Table 23.3.

23.4.4 Mechanical Ventilation in the Acute Phase

Patients with injuries at or above C3 and some with lesions at C4 and below with associated pulmonary or traumatic brain injuries require assisted ventilation. Many people with spinal cord injury can be weaned from a ventilator as diaphragm function improves; others need lifelong mechanical ventilation. Late-onset ventilatory failure may occur in people with tetraplegia who were previously ventilator-free. The aims of artificially assisted ventilation in persons with spinal cord injury are sufficient oxygenation with subjective well-being, prevention of atelectasis, and enabling of phonation during ventilation. Clues to impaired ventilation may include shortness of breath, impaired or fluctuating mental alertness, daytime drowsiness, sleep dysfunction, morning headaches, irritability or anxiety, tachypnea, increased respiratory effort, increased postural influences on breathing, or unexplained erythrocytosis (Haitsma 2007).

Table 23.2 Oxygen delivery device, oxygen flow rate, and FiO_2

Delivery device	Oxygen flow rate (L/min)	FiO_2[a] (%)
Nasal cannula	1	24
	2	28
	3	32
	4	36
	5	40
Face mask	5	40
	6–7	50
	7–8	60
Partial rebreather (without side flap)	12–15	70
Non-rebreather	12–15	>90
Venturi mask[b]	3–15	24–50
Endotracheal tube		21–100

From Nugent and Nourbakhsh (2011)
[a]FiO_2 values are approximations
[b]The color of the adapter reflects the delivered oxygen concentration; 4%, blue; 28%, yellow; 31%, white; 35%, green; 40%, pink; 50%, orange

23.4.4.1 Intubation

Intubation may be performed when the patient appears to be tiring or when the patient's condition is unstable. There are guidelines for intubation, but not necessarily followed (Table 23.4).

23.4.4.2 Indications of Mechanical Ventilation

Noninvasive or invasive mechanical ventilatory support is intended to improve oxygenation, increase CO_2 excretion, and reduce the work of breathing. Clinical evidences of mechanical ventilation include apnea, signs of respiratory distress (accessory muscle use, tachypnea, tachycardia, cyanosis, altered mental status), respiratory failure (defined as PaO_2 less than 50 mmHg, or $PaCO_2$ over 50 by arterial blood gas testing while on room air), severe hypoxemia that is unresponsive to oxygen administration, forced vital capacity less than 10 mL/kg or 25% predicted, or intractable and worsening atelectasis (Table 23.5). If PaO_2 is less than 50 mmHg, $PaCO_2$ is greater than 50 mmHg, and FVC is less than 25% of predicted or less than 10 mL/kg, and when atelectasis is not relieved, mechanical ventilation should be performed. However, there are no clear criteria for mechanical ventilation (Akhtar 2003). Not all patients with the above indications require ventilatory support. There is no threshold of $PaCO_2$ or PaO_2 for which mechanical ventilation is required. The indications are flexible. The clinical judgment of the physician is imperative.

Table 23.3 Estimating PaO_2 from a given SaO_2

SaO_2 (%)	80	82	84	86	88	90	92	93	94	95	96	97	98	99
PaO_2 (mmHg)	44	46	49	52	55	60	65	69	73	79	86	96	112	145

From Nugent and Nourbakhsh (2011)

Table 23.4 General indication for intubation. Only guideline, not necessary

• PO_2 <60 mmHg with oxygen therapy
• PCO_2 >45 mmHg with a pH <7.35
• RR >35/min
• Maximum expiratory pressure <20 cmH_2O
• Maximum inspiratory pressure <25 cmH_2O
• Vital capacity <15 mL/kg or < 2 X predicted tidal volume

Table 23.5 Clinical and laboratory evidences of indication for mechanical ventilation

Clinical manifestations of respiratory distress
• Tachypnea
• Tachycardia
• Cyanosis
• Accessory muscle recruitment
• Intercostal recession
• Nasal flaring
• Hypertension or hypotension
• Changes in mental status
Laboratory evidence of impaired gas exchange
$PaCO_2$ >50 mmHg with pH ≤7.25
PaO_2 <50–55 mmHg on a FiO_2 = 60%

23.4.4.3 Ventilator Set-Up and Management

The proposed protocols for ventilator set-up and management have been published by the Consortium for Spinal Cord Medicine (Consortium of Spinal Cord Medicine 2005). Vital capacity, negative inspiratory pressure, and arterial blood gases are monitored to ensure that ventilation is adequate. There are no clear criteria for mechanical ventilation, and this usually tends to depend on individual and institutional experience. Ventilator settings in patients with spinal cord injury remain controversial due to a lack of agreement on optimal tidal volumes (Akhtar 2003). Some centers advocate higher tidal volumes because they have experiences of reduced atelectasis and higher rate of success in weaning. Several spinal cord injury centers follow a protocol that gradually increases the tidal volume from 50–100 mL/day to achieve 15–20 mL/kg.

Usual parameters of ventilators are: tidal volume (for volume control), pressure (for pressure control), respiration rate (RR), FiO_2, PEEP, inspiratory time, I: E ratio, and flow. Definitions of terms used in ventilator setting are given in Table 23.6. Figure 23.9 illustrates typical ventilator waveforms of pressure, flow, and volume.

The patient can titrate tidal volume starting from 12 to 15 mL/kg of ideal body weight. Oxygen is titrated to maintain saturation greater

Table 23.6 Definitions of terms used in ventilator setting

Term	Definition
Tidal volume (TV)	• Volume of gas delivered to the patient with each breath
Respiratory rate (RR)	• Number of breaths delivered by the ventilator per minute
Peak inspiratory pressure (PIP)	• Maximum pressure in the airways at the end of the inspiratory phase • All pressures in mechanical ventilation are indicated in "cmH_2O." It is usually set to target a PIP <40 cm H_2O
Positive end-expiratory pressure (PEEP)	• Positive pressure that remains at the end of exhalation • This additional applied positive pressure helps prevent atelectasis by preventing the end-expiratory alveolar collapse. PEEP is usually set at 5 cmH_2O or greater, as part of the initial ventilator settings. PEEP set by the clinician is also known as extrinsic PEEP, or ePEEP
Intrinsic PEEP (iPEEP), or auto-PEEP	• Pressure that remains in the lungs with incomplete exhalation, as is the case with patients with obstructive lung diseases • This value can be measured by holding the "Expiratory pause" or "Expiratory hold" button on the mechanical ventilator
Inspiratory time (iTime)	• Time allotted for delivery of the set tidal volume (in volume control settings) or the set pressure (in pressure control settings)
Expiratory time (eTime)	• Time it takes to fully exhale the delivered mechanical breath
Inspiratory to expiratory ratio (I: E ratio)	• Usually expressed as 1:2, 1:3, etc. • By convention, decreasing the ratio means increasing the expiratory time
Peak inspiratory flow	• Rate at which the breath is delivered, expressed in L/min

(continued)

Table 23.6 (continued)

Term	Definition
Minute ventilation (MV)	• Ventilation that the patient receives in 1 min • Calculated from the tidal volume multiplied by the respiratory rate (TV x RR) and expressed in L/min • Most healthy adults have a baseline minute ventilation of 4–6 L/min
Fraction of inspired oxygen (FiO_2)	• A measure of the oxygen delivered by the ventilator during inspiration, expressed at a percentage • Room air contains 21% oxygen

From Wilcox et al. (2019)

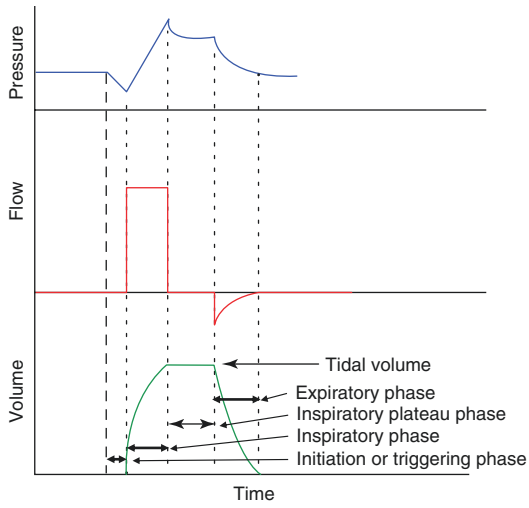


Fig. 23.9 Typical ventilator waveforms showing pressure, flow, and volume

than 92% saturation. If the peak pressure is less than 40 cmH_2O, the tidal volume can be increased by 100 mL/day. The end-tidal pCO_2 is maintained at 28–35 mmHg with or without appropriate dead space. The peak pressure should not exceed 40 cmH_2O. The tidal volume should be increased to a maximum of 25 mL/kg ideal body weight until the patient is afebrile, the secretions are low, and the chest X-ray is clear. Positive end-expiratory pressure (PEEP) is often used during ventilation but may not be optimal in patients with spinal cord injuries. PEEP increases the mean airway pressure and does not allow for surfactant release (Wong et al. 2012). A common protocol for initial ventilation setting is shown in Table 23.7.

Table 23.7 Initial ventilator setting

• Mode CMV (controlled mandatory ventilation)
• TV 12–15 mL/kg or as per setting before
• RR 12, if increased TV, decrease RR
• O_2 saturation 92%
• PEEP zero or same before
• Peak pressure <40 cmH_2O
• Maximum TV 25 mL/kg
• Peak flow <120 L/min

Table 23.8 FiO_2 and PEEP control procedures based on arterial blood gas analysis after initial ventilator setting

1. Adjust FiO_2 and PEEP to alter SaO_2
2. SaO_2 varies directly with FiO_2 and PEEP
3. For hypoxemia (SaO_2 < 94%) requiring FiO_2 > 0.6, first increase PEEP from 5 cmH_2O in steps of 2.5 to a PEEP maximum
4. If hypoxemia persists, then increase FiO_2 in steps of 0.1 until 1.0 is reached or SaO_2 > 93%
5. For SaO_2 > 95% at PEEP maximum, FiO_2 first reduced in steps of 0.1 until <0.6, then PEEP is reduced in steps of 2.5 to a minimum of 5 before further reduction of FiO_2

An initial ventilator is installed, and several measurements of the respiratory system are adjusted according to the results of arterial blood gas analysis. SaO_2 can be adjusted by adjusting FiO_2 and PEEP. If the SaO_2 is kept below 94% even if the FiO_2 is 0.6 or more (0.21 for the indoor air FiO_2), increase it by 2.5 up from the PEEP 5 cmH_2O up to the maximum. If hypoxemia persists afterward, increase FiO_2 by 0.1 to reach 1.0 or SaO_2 93% or more. If the SaO_2 is maintained at 95% or more at the maximum PEEP, the FiO_2 should be lowered by 0.1–0.6 or less, and then the PEEP should be lowered by 2.5–5 (Table 23.8).

In patients with tetraplegia, mechanical ventilation begins in the supine position as vital capacity increases in this position. A 45° head-up position may reduce aspiration risk during mechanical ventilation (Ryken et al. 2013). If there is no intention to wean the ventilator quickly, the patient is often switched to a portable ventilator depending on patient expected to rapidly wean off the ventilator, the patient is often switched to a portable ventilator depending on medical status and ability to tolerate an upright

position. This allows more participation in rehabilitation and early mobilization. Abdominal binders help maintain vital capacity when the patient is sitting (Mahler 1998).

The following recommendations can be provided regarding long-term invasive ventilation of healthy lung persons with tetraplegia (Weidner et al. 2017):

1. The use of pressure-controlled ventilation modes with relatively high tidal volumes and a reduced ventilation frequency, starting from 10 to 12 mL/kg depending on the clinical course may be applied. A maximal inspiratory ventilation pressure of 30 cmH_2O should not be exceeded. If necessary, a tidal volume of 15–20 mL/kg may be used.
2. Although there are general recommendations for ventilation parameters such as inspiratory pressure or ventilation frequency, it is still necessary to apply these settings individually to every patient. This adaptation may be due to thermal and circulatory dysregulations or changes in muscular or bronchial spasticity. They should be based on the results of a volumetric and capnometric assessment.
3. Use a non-blocked or non-cuffed tracheal cannula on an individual basis for as long as possible to improve phonation and prevent tracheal ulcers.

23.4.4.4 Ventilation Modes

The main differences between ventilator modes are determined by the trigger that initiates the inspiratory phase, the cycle length that terminates the inspiratory phase, and the primary output, whether it is a preset tidal volume or a preset pressure (Nugent and Nourbakhsh 2011). Modern ventilators provide at least two basic modes of operation, which are the mandatory and spontaneous ventilation mode. In mandatory ventilation mode, the ventilator controls and performs the breathing work completely or in complemented mode (or supplement mode) if there is a minimal residual respiratory function. The important parameters, including inspiration pressure, tidal volume, and ventilation frequency, are monitored and adjusted by ventilator whenever necessary while working in complemented mode.

The spontaneous ventilation mode allows the patient to breathe completely by himself or to be assisted by the ventilator. Two of the most important parameters in artificial ventilation are volume and pressure. Volume-controlled ventilation (VCV) provides a preset tidal volume and minute ventilation, but the clinician must set the inspiratory flow, flow waveform, and inspiratory time appropriately (Gali and Goyal 2003). During volume-controlled ventilation, decreased compliance or increased resistance may increase airway pressure and may increase the risk of ventilator-induced lung injuries. Volume-controlled ventilation is advantageous because it allows even ventilation and can be used in control, assist, or IMV modes. Pressure-controlled ventilation (PCV) limits the maximum airway pressure delivered to the lung but can vary in tidal and minute volume (Gali and Goyal 2003; Weidner et al. 2017). Figure 23.10 shows the relationship between the commonly used mechanical ventilation modes, separating them into full support or partial support (Wilcox et al. 2019).

The effects of VCV and PCV were not well controlled. When choosing a ventilation mode, the clinician should keep in mind that patients with spinal cord injuries suffer from respiratory pump deficiency without a primary pulmonary disease. Their lungs were basically normal before the injury. In patients with spinal cord injury, PCV appears to be more beneficial in preventing atelectasis and compensating for volume loss, for example, phonation during ventilation with an uncuffed cannula (Gali and Goyal 2003). The positive end-expiratory pressure (PEEP) can help prevent microatelectasis. If the tidal volume used is sufficient, sighs may not need. Sighs are large volume breaths hourly to prevent atelectasis.

23.4.4.5 Tidal Volumes

There have been a few reports about tidal volumes between 900 and 1000 mL, even higher, applied in patients with tetraplegia requiring invasive ventilation (Peterson et al. 1999). In the case of a normal BMI, 10–15 mL/kg ideal body

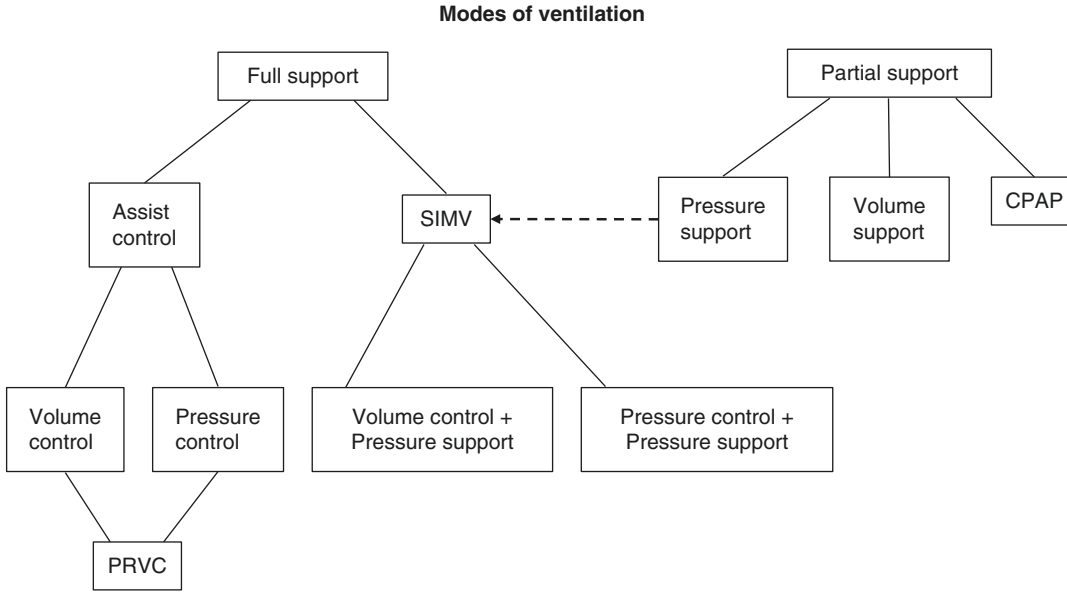


Fig. 23.10 Relationship between the commonly used modes of mechanical ventilation. SIMV usually includes aspects of both assist control ventilation and pressure support ventilation. Pressure regulated volume control (PRVC) is a volume-targeted mode that allows a maximum pressure to reach that volume. From Wilcox et al. (2019), with permission

weight is recommended during the acute phase (Arora et al. 2012). In the presence of atelectasis, a slow increase of 20 mL/kg with a maximal pressure of 30 cmH_2O is described in order to minimize the risk of barotrauma (Brower et al. 2000). In order to avoid chronic hypoventilation, it is advisable to apply larger tidal volumes for successful treatment of atelectasis while reducing the ventilation frequency (Peterson et al. 1999).

Based on the clinical experience with long-term ventilated tetraplegic patients with inserted unblocked tracheal cannula, six main advantages of using higher tidal volumes were stated: improvement of the ability to speak, prevention of atelectasis, alternation of ventilation volumes without developing hypoxemia, maintenance of pulmonary compliance, suppression of residual respiratory muscles activity due to low $PaCO_2$ values, and prevention of subjective dyspnea during ventilation by achieving normal blood gas values (Watt and Fraser 1994). A patient with a cuffless tracheostomy tube requires a higher set tidal volume on the ventilator to compensate for the air leak.

General observation of long-term ventilation with high tidal volumes shows that the respiratory alkalosis associated with the hypocapnia can be completely renally compensated, without pathological pH values. High tidal volumes associated with hyperventilation also provide a risk of potassium loss and increased osteoporosis due to chronic hypocapnia (Bach et al. 1993).

23.5 Rehabilitation of Ventilated Patients During the Acute Phase

23.5.1 Tracheostomy and Tracheostomy Tube

If the patient is tired or when the patient's condition is unstable, intubation can be performed. There are guidelines for intubation, but you do not have to follow them. A tracheostomy is often needed to allow adequate respiration and secretion management in acute care of patients with tetraplegia. Or the patient can be cared for with

noninvasive methods to avoid tracheostomies (Bach 2012). A tracheostomy can be performed either by dilatation percutaneously or surgically as an open tracheostomy.

An early tracheostomy, within 10 days after injury, shortens both the duration of stay in an intensive care unit and the overall ventilation period (Choi et al. 2013). The cuff pressure should be kept below 25 cmH_2O in both tracheostomy and endotracheal intubation. Sustained pressure over 25 cmH_2O may cause tracheal mucosal ischemia and tracheomalacia. Other complications of tracheostomy are tracheal stenosis, tracheoesophageal fistula, swallowing difficulty, and stomal infection (Tow et al. 2001). If possible, a No. 8 or larger tube with a large volume, low-pressure cuff should be used.

A cuffed, nonfenestrated tracheostomy tube is the ideal solution for patients who are extremely dependent on the ventilation system or for acute respiratory failure with pneumonia and other respiratory complications. In stable, chronically ventilated patients, it is recommended that the cuff remains deflated or uncuffed tube is used (Ross and White 2003). Tracheostomy tubes can be used with modifications for speech. Most patients using a home ventilator use a cuffless tracheostomy tube to be able to talk freely. If the patient is in respiratory distress, it is advisable to immediately replace the cuffless tracheostomy tube with a cuffed tracheostomy tube (Wright and Van Dahm 2003).

Routine care of the tracheostomy tube involves daily cleansing of the inner cannula with hydrogen peroxide in saline daily. The outer skin of the stoma should be cleaned with water daily. Tracheostomy tube is changed every other week, weekly, or more often as needed by the patient (Ross and White 2003).

23.5.2 Communication and Mobilization

Spinal cord injured patients with invasive ventilation should be given the opportunity to speak during the acute phase of the injury or during their stay in the intensive care unit. The opportunity to speak creates a higher level of laryngeal awareness. It may help to improve oral intake and prevent episodes of aspiration (Shem et al. 2012). Without the ability to speak, there is a significant limit to the daily life of patients with permanent or partial ventilation (Hess 2005). If only minor or moderate swallowing disorders are present, loud and clear phonation during invasive ventilation is feasible and can be learned. Phonation is always an airflow through the glottis that vibrates the vocal cords to vocalize. Phonation in a ventilated patient occurs mainly during inspiration, because the required airflow from the ventilator is generated during the inspiration, while expiration occurs mainly passively (Prigent et al. 2010). The inspired tidal volume can be increased as needed to compensate for the loss of tidal volume resulting from cuff deflation or use of a fenestrated tube (talking trach). Ventilator adjustments such as decreasing inspiratory flow rate (or prolonged inspiratory time) and adding PEEP can dramatically improve the quality and volume of speech (Hoit et al. 2003; McGrath et al. 2016). Prolonged inspiratory time (or decreased inspiratory flow) increases the time that speech can be produced during inspiration, and PEEP increases the time that speech can be produced during expiration (Brown et al. 2006). Speech produced with invasive positive pressure ventilation delivered via tracheostomy is different from normal speech, primarily because the ventilator-delivered air enters below the larynx. If the tracheostomy tube cuff is inflated (and the tube is unfenestrated), the patient will not be able to speak at all. Therefore, the first and most critical step in allowing a patient to speak is to deflate the cuff. This can be done safely by increasing the ventilator-delivered tidal volume to compensate for air loss through the larynx. Commonly, it uses a tidal volume as high as 1.2 L (Brown et al. 2006).

Patients with acute and long-term ventilation are at high risk for pneumonia, pressure injuries, and deep vein thrombosis. It is therefore recommended to mobilize patients as early as possible, even in an intensive care unit (Grant et al. 2015). To achieve this early mobilization, appropriate equipment and appropriate personal resources must be provided: physicians and therapists

experienced in spinal cord injury and ventilation, intensive care unit/intermediate care unit monitoring, including capnometry and spirometry, and installation of patient-adapted technical assistive devices, e.g., respirators, wheelchairs, and lifter systems.

23.5.3 Glossopharyngeal Breathing

Glossopharyngeal breathing (frog breathing) is a useful independent air stacking method in individuals with no vital capacity or no ventilator-free breathing ability with normal alveolar ventilation and good bulbar function during ventilator-free time or when the ventilator fails (Bach 2012). Glossopharyngeal breathing is a method of inspiration used to push air into the airways by gulping air boluses using the tongue and pharyngeal muscles and in which small amounts of air can be inhaled into the trachea using the upper airway muscles including the tongue, cheek, and pharyngeal and laryngeal muscles. One breath usually consists of six to nine gulps of 40–200 mL each (Bach 2012). When the patients are well trained, they can force air to be injected into the lungs with 10–14 gulping maneuvers per breath. Glossopharyngeal breathing improves lung and thoracic compliance.

23.5.4 Weaning of Mechanical Ventilator

Successful weaning from a ventilator depends on many factors, including prevention of pneumonia and urinary tract infection, depression and anxiety, communication between staff and patients, and patient motivation by family members (Eskandar and Apostolakos 2007). Ventilator weaning is a very distressing situation for the patients, and it is important to explain the procedure to the patients. The goal of the weaning process is to routinely train the diaphragm muscle while avoiding excessive muscle fatigue (Burns 2012). The diaphragm muscles are subject to rapid conversion of slow-fatiguing type I into fast-fatiguing type IIb fibers after paralysis. The strength of the diaphragm muscle determines the vital capacity of the lung. The higher the vital capacity, the better the weaning prognosis. Therefore, if the vital capacity of a patient who is healthy for the lungs is less than 1000 mL, weaning should not be started. Weaning training requires training of the diaphragm and respiratory accessory muscles, good pulmonary toileting, and adequate nutrition (Walker et al. 2011). There are guidelines for weaning from ventilators, but not necessarily followed (Table 23.9).

Weaning should be started when lying down or reclined position (bed or wheelchair) during daytime. Both progressive ventilator-free breathing (PVFB) using a T-piece and synchronized intermittent mandatory ventilation have been used as weaning techniques. T-piece is used to provide humidification and oxygen to the patient but does not provide any ventilatory support (Huang and Yu 2013). If the patient has no problem tolerating the weaning process, the time off the ventilator, using only the T-piece, should be increased gradually. Initially, the T-piece should be used four times a day for 5 minutes. The time must be increased as the patient's endurance improves. Many centers prefer the PVFB method. The PVFB starts 2 minutes off the ventilator

Table 23.9 Proposed criteria for weaning from ventilator

• Afebrile, vital signs stable
• Medically stable for at least 24 h
• Chest X-ray clear
• Psychologically willing to participate in weaning
• Vital capacity >15 mL/kg
• Inspiration pressure >−24 cmH_2O
• Respiratory stable for at least
• PaO_2 >75 mmHg
• $PaCO_2$ <35-45 mmHg
• pH 7.35–7.45
• No PEEP
• FiO_2 <25%

three times a day, with a progressive increase of weaning time at 1 to 3 day intervals depending on the tolerance and cooperation of the patient (Burns 2012). There should be a spontaneous breathing part and a ventilator part every hour during the daytime. The training sessions are gradually increased day by day until the patient is breathing voluntarily for 12 h without ventilator support. If the patient is stable during daytime, the nighttime weaning can be started with increasing periods of spontaneous breathing, e.g., 1 h per night (Raurich et al. 2011).

The patient must be transferred to a reclining wheelchair when the patient is able to tolerate the upright position in bed. The T-piece with a portable oxygen tank should be used for activities outside the patient's room. At the beginning of the weaning process, a manual ventilator (AMBU bag) and suction machine should always accompany the patient.

23.5.5 Weaning of Tracheostomy

Extubation can be considered when the patient meets several requirements after 48 h without ventilator support. The most important prerequisite for successful extubation of PCF >160 L/min (2.7 L/s) or negative inspiratory pressure ≤ 20 cmH2O (Bach and Saporito 1996). Some points to check before extubation are as follows (Galeiras Vázquez et al. 2013): (1) no required surgical or X-ray diagnostic procedures close to extubation that require sedation; (2) no sedative drugs, cooperative; (3) afebrile and with stable vital signs; (4) O_2 saturation > 95% and pCO2 < 40–45 mmHg, after >12 h breathing ambient air; (5) FiO_2 no more than 25% and PEEP <5 cm H2O; (6) X-rays with no abnormalities or an obvious improvement; (7) few bronchial secretions; (8) negative inspiratory pressure < −20 cm H_2O; (9) vital capacity >10–15 mL/kg of ideal weight; (10) a normal fluid balance; (11) no contraindications for performing physical therapy (fractured ribs, etc.) or for the use of noninvasive mechanical ventilation (facial fractures, etc.).

23.5.6 Long-Term Mechanical Ventilation

For permanently ventilated patients, pressure-controlled modes are usually used, while volume-controlled modes are rarely applied. The longer a patient breathes spontaneously, the more often pressure-supported modes are used, especially during the daytime. This could be the best ability to speak when using pressure-supported modes. Although patients have sufficient strength, pressure-controlled modes are often applied during the nighttime to reduce the respiratory effort of the patients (Gounden 1997; Haitsma 2007).

The factors to be assessed in determining the feasibility of home ventilation are (1) the underlying disease-causing respiratory failure, (2) medical stability, (3) patient and family desires about continued care, and (4) availability of home care resources (O'Donohue Jr et al. 1986). For patients who are discharged home with a ventilator for long-term use, it is important to ensure that caregivers receive the necessary education, skills, and support. Issues related to long-term mechanical ventilation include airway management (tracheal stoma care, suctioning, trach tube change), assisted cough and inhalation therapy, safe swallowing, infection control and early recognition, equipment maintenance, emergency measures for power failure and malfunction and care for dislodged trach tube, backup ventilator use, and cardiopulmonary resuscitation (Muir 1993).

23.5.7 Noninvasive Ventilation

The role of noninvasive ventilation (NIV) has been studied for decades in the management of respiratory dysfunction in acute and chronic spinal cord injuries and the evidence supporting the role of NIV in the management of respiratory failure in spinal cord injuries (Daoud et al. 2020). NIV can be used as an alternative to invasive ventilation or as a long-term therapy to compensate for the consequences of respiratory insufficiency, including hypoventilation as well as obstructive

and central apnea. However, due to the resulting complications, the burden on patients with spinal cord injuries, the limited evidence for the effect on overall survival, length of hospital stay, and quality of life, it is viewed as a double-edged sword (No author 1999). The proposed criteria for assessing extubation readiness for mechanical ventilation using NIV in patients with spinal cord injuries are as follows (Bach 2012): (1) fully alert and cooperative, receiving no sedative medications; (2) afebrile and normal white blood cell count; (3) $PaCO_2 \leq 40$ mm Hg at peak inspiratory pressures <30 cm H_2O on full ventilatory support and normal breathing rate, as needed; (4) $SpO_2 \geq 95\%$ for 12 h or more in room air; (5) all oxyhemoglobin desaturations <95% reversed by suctioning via translaryngeal tube; (6) chest radiograph abnormalities cleared or clearing; and (7) air leakage via upper airway sufficient for vocalization on cuff deflation. If indicated, after removal of any naso- or orogastric tube, patients are extubated directly to NIV on assist/control 800–1500 mL, rate 10–14/min in ambient air. Volume cycling is used to promote air stacking to maintain pulmonary compliance and facilitate coughing as well as to maintain normal lung ventilation (Bach 2012).

The following contraindications must be ruled out before starting NIV (Bach 2012; Weidner et al. 2017): lack of cooperation, risk of aspiration, upper airway obstructions, persistent mucus, and pressure injuries in the contact area of the mask. Combined other injuries including facial trauma and brain injury, and opioid therapy for pain control, are also contraindications for NIV use in people with spinal cord injuries. The intact bulbar function is a prerequisite for effective NIV. Patients should also be motivated, cooperative, and medically stable. Nasal, oral-nasal, and nasal interfaces have been suggested for patients requiring chronic NIV. Custom-made molded mouthpieces may be required by some patients for more comfort. If the function of the finger and/or hand is not sufficient and the patient uses an oronasal or full-face mask, any complication during ventilation, e.g., ventilator dysfunction, tube disconnection, could lead to a life-threatening situation because of the patient's inability to actively intervene. With respect to NIV, the compliance of tetraplegic patients compared to non-spinal cord injury patients is rather low. The main reason is the disturbed communication by the use of a mask and facial dysesthesia due to the pressure of the mask (Bach 2012). NIV is not suitable for the management of respiratory failure in all patients who require mechanical ventilation. Many patients with high cervical spinal cord injury (above C4) may require more advanced invasive ventilation using tracheostomy.

Indications for NIV in people with chronic spinal cord injury are similar to the indications in the general population with suspected awake or nocturnal hypoventilation. Polysomnography, capnography, or nocturnal oximetry are usually the diagnostic tests of choice where the results of SpO_2 less than 88% for greater than 5 min, or SpO_2 less than 88% for more than 10% of total sleep time, or end-tidal CO_2 more than 50 mmHg for more than 50% of total sleep time suggest hypoventilation (Robert et al. 1993).

23.5.8 Alternatives for Long-Term Mechanical Ventilation

23.5.8.1 Phrenic Nerve Stimulators

The treatment of chronic respiratory insufficiency in spinal cord injuries of C3 or higher was performed with mechanical positive pressure ventilation through a ventilator. Mechanical ventilation has the psychosocial stigma of ventilator tubing for patients and also pneumonia while preserving life. Electrical activation of the diaphragm muscle, by phrenic nerve stimulation or through diaphragm pacing at the motor point, provides an alternative to mechanical ventilation, which improves speech and mobility and offers the potential to reduce many of the problems associated with mechanical ventilation. To effectively recruit the diaphragm muscle and provide ventilatory support, the phrenic nerve must be

able to provide conduction pathways through the muscle. Therefore, the lower motor neurons in the spinal cord and the phrenic nerve must be intact to prevent muscle denervation and stimulate the muscle at an acceptable level. The advantage is that the inhaled air is forced into the lungs by the diaphragm under negative pressure rather than pushed into the chest as in positive pressure ventilation. This is more physiological and comfortable for the patient.

Phrenic nerve stimulation improves the quality of life by offering several other benefits, such as more physiological patterns of breathing and speech, ease of eating and drinking, and a better sense of smell (Romero et al. 2012). Phrenic nerve stimulation 24 h per day is recommended only for adults. For children and adolescents, a maximum of 12 h per day is recommended, as adequate bone development of the thorax must first be ensured.

Two phrenic nerve stimulation systems are commercially available, the Atrostim Jukka™ (Atrotech, Tampere, Finland) and the Avery System™ (Avery Biomedical Devices Inc., New York, USA). The electrodes are implanted surgically on the two phrenic nerves of the mediastinum at the third to fourth intercostal space. The electrode leads are subcutaneously connected to a radio frequency receiver. Intact lower motor neurons of both phrenic nerves and an intact diaphragm muscle are common prerequisites.

23.5.8.2 Diaphragm Pacemaker

An alternative and more cost-efficient system for diaphragm pacing is the semi-invasive NeuRx® (Synapse Biomedical, Oberlin, OH, USA) system, in which the hook electrodes are laparoscopically inserted into the diaphragm muscle and electrode cables are percutaneously connected to an external stimulator (Tedde et al. 2012). The indications of the diaphragm pacing system and the phrenic nerve stimulation are basically the same. Reconditioning of the diaphragm for several weeks in the postoperative period is necessary before the ventilator is discontinued.

23.6 Respiratory Complications

The most common causes of death after spinal cord injuries are pneumonia and respiratory diseases. Respiratory dysfunction in people with spinal cord injuries occurs due to inspiratory muscle weakness, impaired cough due to expiratory muscle weakness, and decreased production of surfactant. A higher level of spinal cord injury leads to greater respiratory complications, with tetraplegics at the greatest risk of pneumonia morbidity, mucous plugging, respiratory failure, and sleep-disordered breathing (Ong et al. 2020). Aggressive and routine pulmonary toileting is important, especially when people develop respiratory infections. Strategies for the prevention and treatment of atelectasis and pneumonia are summarized in Table 23.10.

23.6.1 Atelectasis

Various methods have been attempted to re-expand atelectasis lung areas. When atelectasis persists despite all the measures, the patient may have to live with a permanently collapsed lobe or lobes if gas exchange remains relatively acceptable. Due to the acute angle of the left main bronchus from the trachea, a directional tip-curved suction catheter for the left lung can be attempted on the left lung. If suctioning is not successful, flexible fiber-optic bronchoscopy is required to remove secretions from the lung segments out of reach of the suction catheter. Direct instillation of mucolytic agents into the atelectatic area through the bronchoscopy can promote re-expansion of the lung. For patients with mechanical ventilation, positive-end expiratory pressure (PEEP) may be the best method for the opening of the atelectatic lobe.

23.6.2 Pneumonia

Pulmonary complications including atelectasis, pneumonia, chest injury, and pulmonary infarc-

Table 23.10 Strategies for prevention and treatment of atelectasis and pneumonia

Problem	Assistive devices	Medications
Atelectasis	• Mechanical Insufflation/exsufflation • Incentive spirometer • Positive end-expiratory pressure devices • Noninvasive or invasive ventilation	• Bronchodilators
Mucous secretions	• Mechanical insufflation/exsufflation • Chest physiotherapy • Chest wall oscillation vest • Flutter valve	• Nebulized normal saline • Nebulized hypertonic (3%) saline • Nebulized acetylcysteine • Bronchodilators
Insufficient ventilation	• Noninvasive ventilation (CPAP/BiPAP/AVAPS) • Invasive home ventilation • Diaphragmatic pacing systems	• Theophylline
Decreased surfactant	• Mechanical insufflation for hyperinflation	• Long-acting beta-agonists • Short-acting beta-agonists • Theophylline

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tion are the most frequent causes of morbidity and mortality among patients with spinal cord injury. Pneumonia is the most common cause of hospitalization in people with tetraplegia, and the leading cause of death in patients with spinal cord injury (Burns 2007). Inappropriate coughing and retention of secretions cause pneumonia in this population. The incidence is higher in the first few weeks of the immediate post-injury period, which can vary from 5% to 20% in acute spinal cord injury to 1%–6% at annual follow-up evaluations (Montgomerie 1997). The risk of developing pneumonia is greatest in the early post-injury period and is influenced by factors such as the inability to cough effectively, prior anesthesia, and the effectiveness of treatments to clear secretions. Pneumonia in patients with spinal cord injury is associated with atelectasis due to changes in breathing patterns and decreased coughing.

Aspiration pneumonia may occur, especially in the presence of impaired consciousness due to associated brain injury or sedation or with impaired swallowing. Patients with mechanical ventilation are at risk for ventilator-associated pneumonia. The presence of a tracheostomy or endotracheal tube may increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*. The preponderance of pneumonia in patients with spinal cord injury occurs in the left lower lobe. The anatomy of the main bronchus probably explains the increased incidence of atelectasis and pneumonia on the left side. The left bronchus has a more acute angle than the right bronchus. Community-acquired pneumonia is most commonly caused by *Streptococcus pneumonia* in patients with spinal cord injury, as in the general population. Other pathogens include *Haemophilus influenzae* and a significant proportion with pseudomonas infections, which are rare pathogens for community-acquired pneumonia in the general population.

The laboratory tests include complete blood count with differential, serum chemistry, and blood cultures. Sputum gram stain and culture, and blood cultures, if necessary, should be performed prior to initiation of antibiotics. Pulse oximetry is monitored. Serial measurement of vital capacity, peak expiratory flow, and negative inspiratory force, especially in patients with high tetraplegia in the acute phase, can be used to monitor the worsening of the patient. Forced vital capacity has been used as a predictor of respiratory problems. Radiographic diagnosis is difficult because atelectasis is frequently present and predisposes patients to pneumonia.

Initial empirical antibiotic treatment covering both Gram-positive and Gram-negative organisms, including anaerobes, is selected based on knowledge of potential organisms and then adjusted based on results of culture and antibiotic sensitivity. A quinolone or combination of a cephalosporin and a macrolide may be initiated

for community-acquired pneumonia (Evans et al. 2012). Hospital-acquired aspiration pneumonia is required antibiotic coverage for anaerobes and Gram-negative organisms. Patients with respirators should be covered empirically for MRSA and pseudomonas pending the results of the culture. Antibiotic treatment for pneumonia is typically continued for 10–14 days. In addition to the appropriate antibiotics, usual treatments with fluids and vasopressors should be performed.

Smoking cessation must be emphasized. Annual influenza vaccination is recommended and has been shown to produce an immunological response similar to the general population. Pneumococcal vaccination is recommended because *Streptococcus pneumoniae* is the most common pathogen of community-acquired pneumonia. Immunizations are performed every year against influenza and streptococcus pneumonia every 5 years. People who received the pneumococcal polysaccharide vaccine before age 65 should be given another dose at 65 years or older if at least 5 years have passed since the previous dose.

23.6.3 Ventilator-Associated Pneumonia

Diagnosis of ventilator-assisted pneumonia may be difficult because of nonspecific signs and symptoms, especially in the acute setting. The frequency of ventilator-associated pneumonia (VAP) due to Gram-negative bacilli such as *Pseudomonas aeruginosa, Staphylococcus aureus*, and methicillin-resistant *Staphylococcus aureus* (MRSA) is high for 4 days. To prevent VAP, the upper body should be raised by about 30 degrees and H_2-blocker, and PPI should be administered. The clinical criteria often applied for the diagnosis of ventilator-assisted pneumonia are the presence of a new infiltrate on chest radiography plus at least two of the following symptoms: fever over 38 °C, leukocytosis or leukopenia, and purulent secretions. Cultures of respiratory secretions may be useful. Blood cultures should also be done before starting antibiotics, if possible, but they are often negative. Prompt initiation of antibiotics is the cornerstone of treatment. Initial treatments should be broad, including coverage for methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*, and should be appropriately modified when culture results are available. The mortality rate by VAP is 27% and *Pseudomonas aeruginosa* infection accounts for 43%. If VAP is suspected, suspect *Pseudomonas aeruginosa* infection and use antipseudomonal β-lactamase and aminoglycoside.

23.6.4 Sleep Apnea

Respiratory sleep disorder results in an abnormal frequency of periods of sleep with sleep cessation (apnea) or reduction (hypopnea) of the airflow that lasts more than 10 seconds (Fuller et al. 2013). Sleep apnea may be obstructive in upper respiratory collapse, central because of reduced respiratory effort, for example, with syringobulbia or associated injury to the brainstem, or mixed. Obstructive sleep apnea is more common in people with tetraplegia than in those with lower levels of injury or the general population (Biering-Sørensen et al. 2009).

A high prevalence of sleep apnea, more than 50% in some studies, has been reported in chronic tetraplegia. Patients with spinal cord injuries tend to spend more time sleeping in the supine position than in the general population, which may contribute to obstructive sleep apnea (Biering-Sørensen et al. 2009; LaVela et al. 2012). Risk factors for obstructive sleep apnea in people with spinal cord injury include a high neurological level of injury, obesity, increased neck circumference, and use of baclofen and/or diazepam (Bauman et al. 2016). In addition to sleep disorders and daytime drowsiness due to sleep apnea, sleep apnea has been associated with an increase in cardiovascular mortality and morbidity, including stroke, hypertension, and heart disease (Fuller et al. 2013).

Pulse oximetry monitoring can detect nocturnal arterial oxygen desaturations and clinical signs of sleep apnea (Bauman et al. 2016). Clinical presentations include intense snoring,

daytime somnolence, morning headaches, cognitive dysfunction such as attention/concentration deficit, etc. In patients with tetraplegia who have an elevated $PaCO_2$ and a decreased ventilatory response to CO_2, alveolar hypoventilation during sleep may aggravate increases in $PaCO_2$ and oxygen desaturation (Bauman et al. 2016). The apnea-hypopnea index (AHI), calculated by dividing the number of events by the hours of sleep, is an index of the severity of sleep apnea. The values of AHI are 5–15/h in mild forms and over 30/h in severe cases.

23.6.4.1 Assessment of Sleep Apnea

Nocturnal pulse oximetry or capnometry may be of limited value. It may detect nocturnal arterial desaturation (Sankari and Badr 2016). Polysomnography can help to detect sleep apnea in patients with respiratory muscle weakness and should be done in patients with excessive fatigue, daytime somnolence, morning headache, and daytime hypercapnia. Sleep studies are also useful for evaluating and treating patients who may be eligible for nocturnal ventilatory support (Berlowitz et al. 2016; Chiodo et al. 2016). This is because appropriate levels of continuous positive airway pressure and noninvasive ventilation can be titrated in this monitored setting. Polysomnography can also help to establish its severity.

23.6.4.2 Management of Sleep Apnea

The patient should be placed in a lateral decubitus position during sleep if this is permitted. Positive airway pressure therapy is indicated for significant sleep-disordered breathing. Continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) is applied through nasal or oropharyngeal mask (Bauman et al. 2016). Weight reduction for obese or overweight individuals can be helpful. Avoidance of alcohol and sedating medications should be considered. Smoking cessation is recommended (Biering-Sørensen et al. 2009). Pharmacological treatments using tricyclic antidepressants are also an option.

Surgical procedures may be considered in patients who do not respond to conservative management, although experience or literature in those with spinal cord injury is rare. These include uvulopalatopharyngoplasty, palatal implants, tracheostomy, and removal of enlarged tonsils and adenoids, especially in children or adolescents.

References

Akhtar SR. Practice variation in respiratory therapy documentation during mechanical ventilation. Chest. 2003;124:2275–82.

Andrews J, Sathe NA, Krishnaswami S, et al. Nonpharmacologic airway clearance techniques in hospitalized patients: a systematic review. Respir Care. 2013;58:2160–86.

Arora S, Flower O, Murray NP, et al. Respiratory care of patients with cervical spinal cord injury: a review. Crit Care Resusc. 2012;14:64–73.

Bach JR. Pulmonary rehabilitation in neuromuscular disorders. Semin Respir Med. 1993;14:515.

Bach JR. Noninvasive respiratory management of high level spinal cord injury. J Spinal Cord Med. 2012;35:72–80.

Bach JR, Saporito LR. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure: a different approach to weaning. Chest. 1996;110:1566–157.

Bach JR, Tilton MC. Life satisfaction and well-being measures in ventilator assisted individuals with traumatic tetraplegia. Arch Phys Med Rehabil. 1994;75:626–32.

Bach JR, Alba AS, Saporito LA. Intermittent positive pressure ventilation via the mouth as an alternative to tracheostomy for 257 ventilator users. Chest. 1993;103:174–82.

Ball PA. Critical care of spinal cord injury. Spine (Phila Pa 1976). 2001;26(234 Suppl):S27–30.

Bauman KA, Kurili A, Schotland HM, et al. Simplified approach to diagnosing sleep-disordered breathing and nocturnal hypercapnia in individuals with spinal cord injury. Arch Phys Med Rehabil. 2016;97:363–71.

Baydur A, Adkins RH, Milic-Emili J. Lung mechanics in individuals with spinal cord injury: effects of injury level and posture. J Appl Physiol (1985). 2001;90:405–11.

Benditt JO. Respiratory care of patients with neuromuscular disease. Respir Care. 2019;64:679–88.

Berlly M, Shem K. Respiratory management during the first five days after spinal cord injury. J Spinal Cord Med. 2007;30:309–18.

Berlowitz DJ, Wadsworth B, Ross J. Respiratory problems and management in people with spinal cord injury. Breathe (Sheff). 2016;12:328–40.

Berney S, Bragge P, Granger C, et al. The acute respiratory management of cervical spinal cord injury in the first 6 weeks after injury: a systematic review. Spinal Cord. 2011;49:17–29.

Biering-Sørensen F, Jennum P, Laub M. Sleep disordered breathing following spinal cord injury. Respir Physiol Neurobiol. 2009;169:165–70.

Braun NM, Arora NS, Rochester DF. Respiratory muscle and pulmonary function in polymyositis and other proximal myopathies. Thorax. 1983;38:616–23.

Brower RG, Matthay MA, Morris A, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342:1301–8.

Brown R, DiMarco AF, Hoit JD, Garshick E. Respiratory dysfunction and management in spinal cord injury. Respir Care. 2006;51:853–68. discussion 869–70

Burns SM. Weaning from mechanical ventilation: where were we then, and where are we now? Crit Care Nurs Clin North Am. 2012;24:457–68.

Burns SP. Acute respiratory infections in persons with spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:203–16.

Celli BR. Respiratory management of diaphragm paralysis. Semin Respir Crit Care Med. 2002;23:275–81.

Chatburn RL. High-frequency assisted airway clearance. Respir Care. 2007;52:1224–35. discussion 1235-7

Chatwin M, Toussaint M, Gonçalves MR, et al. Airway clearance techniques in neuromuscular disorders: a state of the art review. Respir Med. 2018;136:98–110.

Chiodo AE, Sitrin RG, Bauman KA. Sleep disordered breathing in spinal cord injury: a systematic review. J Spinal Cord Med. 2016;39:374–82.

Chiu HC, Yeh JH, Chen WH. Pulmonary function study of myasthenia-gravis patients treated with double-filtration plasmapheresis. J Clin Apher. 2003;18:125–8.

Choi HJ, Paeng SH, Kim ST, et al. The effectiveness of early tracheostomy (within at least 10 days) in cervical spinal cord injury patients. J Korean Neurosurg Soc. 2013;54:220–4.

Consortium of Spinal Cord Medicine. Respiratory management following spinal cord injury. Clinical practice guidelines for health-care professionals. Washington, DC, Paralyzed Veterans of America; 2005.

Daoud A, Haider S, Sankari A. Noninvasive ventilation and spinal cord injury. Sleep Med Clin. 2020;15:461–70.

De Troyer A, Kirkwood PA, Wilson TA. Respiratory action of the intercostal muscles. Physiol Rev. 2005;85:717–56.

Eskandar N, Apostolakos MJ. Weaning from mechanical ventilation. Crit Care Clin. 2007;23:263–74.

Estenne M, De Troyer A. The effects of tetraplegia on chest wall statics. Am Rev Respir Dis. 1986;134:121–4.

Estenne M, De Troyer A. Mechanism of the postural dependence of vital capacity in tetraplegic subjects. Am Rev Respir Dis. 1987;135:367–71.

Evans CT, Weaver FM, Rogers TJ, et al. Guideline-recommended management of community-acquired pneumonia in veterans with spinal cord injury. Top Spinal Cord Inj Rehabil. 2012;18:300–5.

Fromageot C, Lofaso F, Annane D, et al. Supine fall in lung volumes in the assessment of diaphragmatic weakness in neuromuscular disorders. Arch Phys Med Rehabil. 2001;82:123–8.

Fromm B, Hundt G, Gemer HJ, et al. Management of respiratory problems unique to high tetraplegia. Spinal Cord. 1999;37:239–44.

Fuller DD, Lee KZ, Tester NJ. The impact of spinal cord injury on breathing during sleep. Respir Physiol Neurobiol. 2013;188:344–54.

Galeiras Vázquez R, Rascado Sedes P, Mourelo Fariña M, et al. Respiratory management in the patient with spinal cord injury. Biomed Res Int. 2013;2013:168757.

Gali B, Goyal DG. Positive pressure mechanical ventilation. Emerg Med Clin N Am. 2003;21:453–73.

Gartman EJ. Pulmonary function testing in neuromuscular and chest wall disorders. Clin Chest Med. 2018;39:325–34.

Goldmann JM, Willians SJ, Denison DM. The rib cage and abdominal components of respiratory system compliance in tetraplegic patients. Eur Respir J. 1988;1:242–7.

Gounden P. Static respiratory pressures in patients with post-traumatic tetraplegia. Spinal Cord. 1997;35:43–7.

Grant RA, Quon JL, Abbed KM. Management of acute traumatic spinal cord injury. Curr Treat Options Neurol. 2015;17:334.

Grimm DR, Chandy D, Almenoff PL, et al. Airway hyperreactivity in subjects with tetraplegia is associated with reduced baseline airway caliber. Chest. 2000;118:1397–404.

Haitsma JJ. Physiology of mechanical ventilation. Crit Care Clin. 2007;23:117–34.

Hess DR. The evidence for secretion clearance technique. Respir Care. 2001;46:1276–93.

Hess DR. Facilitating speech in a patient with tracheostomy. Respir Care. 2005;50:519–25.

Hoit JD, Banzett RB, Lohmeier HL, et al. Clinical ventilator adjustments that improve speech. Chest. 2003;124:1512–21.

Huang CT, Yu CJ. Conventional weaning parameters do not predict extubation outcome in intubated subjects requiring prolonged mechanical ventilation. Respir Care. 2013;58:1307–14.

Jia X, Kowalski RG, Sciubba DM, et al. Critical care of traumatic spinal cord injury. J Intensive Care Med. 2013;28:12–23.

Kapandji AI. The physiology of the joints: the spinal column, pelvic girdle and head. 6th ed. New York: Churchill Livingstone; 2008.

Kelley A. Spirometry testing standards in spinal cord injury. Chest. 2003;123:725–30.

Kelly BJ, Luce JM. The diagnosis and management of neuromuscular diseases causing respiratory failure. Chest. 1991;99:1485–94.

LaVela SL, Burns SP, Goldstein B, et al. Dysfunctional sleep in persons with spinal cord injuries and disorders. Spinal Cord. 2012;50:682–5.

Lester MK, Flume PA. Airway-clearance therapy guidelines and implementation. Respir Care. 2009;54:733–50. discussion 751-3

Linn WS, Adkins RH, Gong H Jr, et al. Pulmonary function in chronic spinal cord injury: a cross-sectional

survey of 222 southern California adult outpatients. Arch Phys Med Rehabil. 2000;81:757–63.

Linn WS, Spungen AM, Gong H Jr, et al. Forced vital capacity in two large outpatient populations with chronic spinal cord injury. Spinal Cord. 2001;39:263–8.

Mahler DA. Pulmonary rehabilitation. Chest. 1998;113:263S–8S.

McGrath B, Lynch J, Wilson M, et al. A novel technique for communication in the ventilator-dependent tracheostomy patient. J Intensive Care Soc. 2016;17:19–26.

Mier-Jedrzelowicz A, Brophy C, Moxham J, Green M. Assessment of diaphragm weakness. Am Rev Resp Dis. 1988;137:877–83.

Montgomerie JZ. Infections in patients with spinal cord injuries. Clin Infect Dis. 1997;25:1285–90.

Mueller G, Hopman MT, Perret C. Comparison of respiratory muscle training methods in individuals with motor and sensory complete tetraplegia: a randomized controlled trial. J Rehabil Med. 2013;45:248–53.

Muir JF. Pulmonary rehabilitation in chronic respiratory insufficiency. 5. Home mechanical ventilation. Thorax. 1993;48:1264–73.

No author. Clinical indications for noninvasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation—a consensus conference report. Chest. 1999;116:521–34.

Nugent K, Nourbakhsh E. A bedside guide to mechanical ventilation. Lubbock: Texas Tech University Health Science Center; 2011.

O'Donohue WJ Jr, Giovannoni RM, Goldberg AI, et al. Long-term mechanical ventilation. Guidelines for management in the home and at alternate community sites. Report of the Ad Hoc Committee, Respiratory Care Section, American College of Chest Physicians. Chest. 1986;90(1 Suppl):1S–37S.

Ong B, Wilson JR, Henzel MK. Management of the patient with chronic spinal cord injury. Med Clin North Am. 2020;104:263–78.

Peterson WP, Barbalata L, Brooks CA, et al. The effect of tidal volumes on the time to wean persons with high tetraplegia from ventilators. Spinal Cord. 1999;37:284–8.

Prigent H, Garguilo M, Pascal S, et al. Speech effects of a speaking valve versus external PEEP in tracheostomized ventilator-dependent neuromuscular patients. Intensive Care Med. 2010;36:1681–7.

Raurich JM, Rialp G, Ibanez J, et al. CO2 response and duration of weaning from mechanical ventilation. Respir Care. 2011;56:1130–6.

Reid WD, Brown JA, Konnyu KJ, et al. Physiotherapy secretion removal techniques in people with spinal cord injury: a systematic review. J Spinal Cord Med. 2010;33:353–70.

Restrepo RD, Wettstein R, Wittnebel L, et al. Incentive spirometry: 2011. Respir Care. 2011;56:1600–4.

Rezania K, Goldenberg FD, White S. Neuromuscular disorders and acute respiratory failure: diagnosis and management. Neurol Clin. 2012;30:161–85.

Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. Chest. 2007;131:4S–42S.

Robert D, Willig TN, Leger P, et al. Long-term nasal ventilation in neuromuscular disorders: report of a consensus conference. Eur Respir J. 1993;6:599–606.

Romero FJ, Gambarrutta C, Garcia-Forcada A, et al. Long-term evaluation of phrenic nerve pacing for respiratory failure due to high cervical spinal cord injury. Spinal Cord. 2012;50:895–8.

Ross J, White M. Removal of the tracheostomy tube in the aspirating spinal cord-injured patient. Spinal Cord. 2003;41:636–42.

Ryken TC, Hurlbert RJ, Hadley MN, et al. The acute cardiopulmonary management of patients with cervical spinal cord injuries. Neurosurgery. 2013;72:84–92.

Sahni AS, Wolfe L. Respiratory care in neuromuscular diseases. Respir Care. 2018;63:601–8.

Sankari A, Badr MS. Diagnosis of sleep disordered breathing in patients with chronic spinal cord injury. Arch Phys Med Rehabil. 2016;97:176–7.

Schilero GJ, Bauman WA, Radulovic M. Traumatic spinal cord injury: pulmonary physiologic principles and management. Clin Chest Med. 2018;39:411–25.

Schilero GJ, Spungen AM, Bauman WA, et al. Pulmonary function and spinal cord injury. Respir Physiol Neurobiol. 2009;166:129–41.

Shavelle RM, DeVivo MJ, Strauss DJ, et al. Long-term survival of persons ventilator dependent after spinal cord injury. J Spinal Cord Med. 2006;29:511–9.

Shem K, Castillo K, Wong SL, et al. Dysphagia and respiratory care in individuals with tetraplegia: incidence, associated factors, and preventable complications. Top Spinal Cord Inj Rehabil. 2012;18:15–22.

Smeltzer SC, Skurnick JH, Troiano R, et al. Respiratory function in multiple sclerosis. Utility of clinical assessment of respiratory muscle function. Chest. 1992;101:479–84.

Smith PE, Calverley RM, Edwards RH, et al. Practical problems in the respiratory care of patients with muscular dystrophy. N Engl J Med. 1987;316:1197–205.

Spungen AM, Grimm DR, Strakhan M, et al. Treatment with an anabolic agent is associated with improvement in respiratory function in persons with tetraplegia: a pilot study. Mt Sinai J Med. 1999;66:201–5.

Strickland SL, Rubin BK, Drescher GS, et al. AARC clinical practice guideline: effectiveness of nonpharmacologic airway clearance therapies in hospitalized patients. Respir Care. 2013;58:2187–93.

Tedde ML, Onders RP, Teixeira MJ, et al. Electric ventilation: indications for and technical aspects of diaphragmatic pacing stimulation surgical implantation. J Bras Pneumol. 2012;38:566–72.

Tow AM, Graves DE, Carter RE. Vital capacity in tetraplegics twenty years and beyond. Spinal Cord. 2001;39:139–44.
Volsko TA. Airway clearance therapy: finding the evidence. Respir Care. 2013;58:1669–78.
Walker DJ, Walterspacher S, Schlager D, et al. Characteristics of diaphragmatic fatigue during exhaustive exercise until task failure. Respir Physiol Neurobiol. 2011;176:14–20.
Walsh BK, Crotwell DN, Restrepo RD. Capnography/capnometry during mechanical ventilation. Respir Care. 2011;56:503–9.
Watt JW, Fraser MJ. The effect of insufflation leaks in long-term ventilation: waking and sleeping transcutaneous gas tensions in ventilator-dependent patients with an uncuffed tracheostomy tube. Anaesthesia. 1994;49:328–30.
Weidner N, Rupp R, Taney KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.
Welch JF, Kipp S, Sheel AW, Respiratory muscles during exercise: mechanics, energetics, and fatigue. Curr Opin Physiol. 2019:10;102–9.
Wilcox SR, Aydin A, Marcolini EG. Mechanical ventilation in emergency medicine. Cham: Springer; 2019.
Wong SL, Shem K, Crew J. Specialized respiratory management for acute cervical spinal cord injury: a retrospective analysis. Top Spinal Cord Inj Rehabil. 2012;18:283–90.
Wright SE, Van Dahm K. Long-term care of the tracheostomy patient. Clin Chest Med. 2003;24:473–87.
Zakrasek EC, Nielson JL, Kosarchuk JJ, et al. Pulmonary outcomes following specialized respiratory management for acute cervical spinal cord injury: a retrospective analysis. Spinal Cord. 2017;55:559–65.

Recommended Additional Reading

Cairo JM. editor. Pilbeam's mechanical ventilation. Physiological and clinical applications. 5th ed. Elesevier: St. Louis, MO; 2016.
Cardenas DD, Hooton TM. editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Donner CF, Ambrosino N, Goldstein R, editors. Pulmonary rehabilitation. London: Hodder Arnold; 2005.
Esquinas AM, editor. Noninvasive mechanical ventilation: theory, equipment, and clinical applications. 2nd ed. Cham: Springer; 2016.
Hancox RJ, Whyte KF. Pocket guide to lung function tests. New York: The McGraw-Hill Companies, Inc.; 2001.
Lei Y. Medical ventilator system basic: a clinical guide. Oxford: Oxford University Press; 2017.
Russel C, Matta B. Tracheostomy a multiprofessional handbook. Cambridge: Cambridge University Press; 2004.
Simonds AK, editor. Non-invasive respiratory support. A practical handbook. 3rd ed. London: CRC Press; 2007.
Sykes K, Yong JD. Respiratory support in intensive care. London: BMJ Books; 1999.
Wilcox SR, Aydin A, Marcolini EG. Mechanical ventilation in emergency medicine. Cham: Springer; 2019.

Autonomic Dysreflexia

24

Head and Riddock (1917) and Guttmann and Whitteridge (1947) described symptoms associated with autonomic dysreflexia in World War I and World War II, respectively. They described clinical features of autonomic dysreflexia, such as sweating in the skin around and above the level of the lesion, urinary and rectal contraction, penile erection, seminal fluid emission, and skeletal muscle spasm, as well as hypertension, and described "mass reflex" (Head and Riddock 1917). Autonomic dysreflexia is a life-threatening condition for people with cervical or high-thoracic spinal cord injury. Autonomic dysreflexia is a unique manifestation in people with spinal cord injury at T6 or above the neurological level of injury, which is above the level of sympathetic outflow to the splanchnic vascular bed. This means that this large volume of blood vessels (25–30% of cardiac output) is no longer under the influence of supraspinal control and is therefore susceptible to spinal mediated reflex vasoconstriction (Brown et al. 2018; Mathias and Frankel 1988; Teasell et al. 2000).

Autonomic dysreflexia is a dangerous elevation in blood pressure in people with spinal cord injuries, produced by spinally mediated reflex activation of sympathetic vasoconstrictor neurons supplying skeletal muscle and the gut (Brown et al. 2018). It is triggered by noxious or non-noxious stimuli below the level of injury and involves episodes of uncontrolled elevation of systolic blood pressure of more than 20 mmHg and may or may not be accompanied by a decrease in heart rate depending on the level of injury of rostral or caudal lesion to the sympathetic spinal segments to the heart (ASIA 2012; Consortium for Spinal Cord Medicine 2001; Wecht et al. 2021). The guidelines of the Consortium for Spinal Cord Medicine recommend that autonomic dysreflexia in adults considered abrupt elevation in systolic blood pressure of 20 mmHg above baseline, while an increase of 15 mmHg systolic pressure in pediatric spinal cord injury (Consortium for Spinal Cord Medicine 2020; Krassioukov et al. 2021). If the elevation of arterial blood pressure is so severe that it is not treated properly, it can be life-threatening complications including cerebral hemorrhage, seizures, pulmonary edema, and myocardial infarction (Karlsson 1999; Rabchevsky and Kitzman 2011). Autonomic dysreflexia is well recognized during the chronic phase of spinal cord injuries, and it was always evident that it did not occur in the early stages during the period of spinal shock. However, cases have been reported in the first few days of injury. Autonomic dysreflexia can occur at any time from months to years after the spinal shock phase (Furlan and Fehlings 2008; Partida et al. 2016).

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24.1 Epidemiology and Etiology

Spinal cord injury at the neurological level of injury T6 or above, which is above segment of the major splanchnic outflow, may cause autonomic dysreflexia. Rarely lesions as low as T8 can cause autonomic dysreflexia. Autonomic dysreflexia is more common in people with complete injuries compared to incomplete spinal cord injuries (Helkowski et al. 2003). Incidence of autonomic dysreflexia after complete injuries is up to 70% (Snow et al. 1978). Not all individuals with spinal cord injuries at or above T6 develop autonomic dysreflexia, it develops in 50–90% (Vaidyanathan et al. 2012). This discrepancy is likely attributed to differences in the completeness of spinal cord injury and the time since injury. Up to 90% of patients with spinal cord injuries above T6 are susceptible to autonomic dysreflexia (Allen and Leslie 2021). It can occur more than 30 times a day after spinal cord injury (Hubli et al. 2015). Autonomic dysreflexia is often present in the chronic phase of spinal cord injury, with a majority of cases first occurring 3–6 months after injury (Lindan et al. 1980).

Symptoms of autonomic dysreflexia can be caused by a wide variety of stimuli below the neurological level of spinal cord injury. Noxious stimuli of the bladder, including overdistention, overactivity, urinary tract infection, or calculi, are the most common precipitating causes accounting for more than 75% of the episodes, followed by bowel distention or fecal impaction. Most instrumentations or procedures of the bladder or rectum can cause autonomic dysreflexia. However, all noxious stimuli below the level of injury may be the cause of autonomic dysreflexia (Weaver 2002) (Table 24.1). All imaginable stimuli below the level of injury include occult intra-abdominal processes; testicular torsion; pressure on the testicles and glans penis; sexual intercourse; passive stretching; bed position change; hip dislocation; many cutaneous and proprioceptive stimuli including cold exposure, sunburn, and tight clothing; functional electrical stimulation; and so on (Consortium for Spinal Cord Medicine 2020; Sheel et al. 2005). Recent use of a vasopressor such as midodrine, fludrocortisone, pseudoephedrine, or droxidopa, may help explain the rise in blood pressure or additive effect of another causative cause, as these medications can exacerbate another trigger for autonomic dysreflexia (Consortium for Spinal Cord Medicine 2020).

For susceptible women, autonomic dysreflexia may occur during labor in up to two-thirds of women. Abdominal spasms are difficult to perceive or distinguish, but symptoms of autonomic

Table 24.1 Triggers and conditions associated with autonomic dysreflexia

System	Condition
Genitourinary	Bladder distention, severe detrusor overactivity, detrusor-sphincter dyssynergia, UTI, bladder or renal stone, vaginal dilatation, epididymitis, testicular torsion, scrotal compression, urological procedures including inserting a catheter
Gastrointestinal	Constipation, fecal impaction, rectal irritation (enema or manual evacuation), bowel distension, esophageal reflux, gastric ulcer, cholecystitis, cholelithiasis, anal fissure, hemorrhoid, appendicitis, GI instrumentation
Skin	Pressure injuries, cutaneous stimulation, sunburn, burn, frostbite, insect bites
Extremities	DVT, ingrowing toenail, cellulitis, spasticity, tight clothing, bone fracture, heterotopic ossification, FES, ROM exercise, stretching exercise, position change, IM injection, lumbar disc herniation, spondylolisthesis, acupuncture
Reproductive	Sexual activity, sexual intercourse, high sexual arousal
Male	Ejaculation, priapism, penile stimulation, scrotal compression, electroejaculation, vibratory stimulation, masturbation
Female	Menstruation, lactation, breastfeeding, pregnancy, labor, delivery, ectopic pregnancy, sexual intercourse, masturbation
Procedures	Urodynamic study, cystoscopy, surgical procedure, radiological procedure, electroejaculation
Others	Pulmonary embolism, medications

dysreflexia appear with labor at the same time. Hypertension due to autonomic dysreflexia must be distinguished from preeclampsia.

24.2 Pathophysiology

The sympathetic division of the autonomic nervous system has its cells in the preganglionic cell bodies which are located in the intermediolateral gray matter of the spinal cord from T1 to L2. The preganglionic fibers reach the paravertebral ganglia. The postganglionic sympathetic fibers that innervate the heart, arteries, and vein come from the paravertebral ganglia. In normal subjects, stimuli, such as visceral or cutaneous stimuli, tend to increase the arterial blood pressure by activation of the splanchnic bed by the sympathetic nervous system. Clinically, autonomic dysreflexia is characterized by episodes of acute hypertension resulting from sympathetic hyperactivity and the disruption of descending input to sympathetic preganglionic neurons below the level of lesion that regulates sympathetic output to the splanchnic circulation (Cívicos Sánchez et al. 2021). The baroreceptors thus stimulated in the carotid sinus and the aorta activate the efferent impulses from the vasomotor center via the cranial nerve X in order to inhibit the sympathetic outflow and to reduce blood pressure by vasodilation and slowing of the heart rate (Krassioukov and Claydon 2006; Teasell et al. 2000).

In autonomic dysreflexia, the spinal reflexes below the neurological level of injury remained intact despite the spinal cord damage.

However, noxious stimuli below the level of the spinal cord injury cause a generalized sympathetic response and the release of noradrenaline and dopamine (Bauman et al. 2012). This results in systemic vasoconstriction below the level of the spinal cord injury. That is, the preganglionic neurons within the spinal cord below the lesion can be excited by segmental sensory inputs because spinal circuitry is intact. Visceral or somatic stimuli can activate sympathetic neurons reflexively and elicit viscerosympathetic or somatosympathetic reflex responses which, because many of these neurons are vasoconstrictor in function, lead to sustained and dangerous increase in blood pressure in autonomic dysreflexia (Karlsson 1999; Mathias and Frankel 2002).

In patients with spinal cord injury, noxious stimuli below the neurological level of injury are ascending in the spinothalamic tract and posterior columns. These, in turn, trigger sympathetic hyperactivity by stimulating neurons in the intermediolateral gray matter of the spinal cord. Inhibitory impulses of the sympathetic reflex through the vagus nerve that rise above the level of injury are blocked so that there is an unopposed sympathetic outflow (T6-L2) with excessive catecholamine release, including norepinephrine, 5-hydroxytryptamine (serotonin), dopamine beta-hydroxylase, and dopamine. Increased sensitivity of the vasculature to neurally released norepinephrine is another explanation for the increased reflex responses that contribute to the development of autonomic dysreflexia (Gao et al. 2002; McLachlan 2007; Michael et al. 2019) (Fig. 24.1). Denervation hypersensitivity of peripheral adrenergic receptors below the level of injury can also contribute to the pathophysiology (Krassioukov et al. 2009; McLachlan 2007). The sympathetic neural outflow below the T6 segment, which incorporates neural control of the large splanchnic vascular bed, is clearly of major importance in generating the blood pressure response during dysreflexia and also in maintaining blood pressure homeostasis (Eldahan and Rabchevsky 2018; Krassioukov et al. 2009; West et al. 2012). The level of the spinal cord injury is important. Increased hypersensitive responses to stimuli generally do not occur in patients with lesions below T6, indicating that sympathetic efferent flow above this level is essential for controlling blood pressure. Lesions below T6 may allow sufficient supraspinal neural control of the large and crucial splanchnic vascular bed (Krassioukov et al. 2009; Teasell et al. 2000).

The afferent nerve impulse from a potential source of nociception below the level of spinal cord injury enters the spinal cord via the dorsal

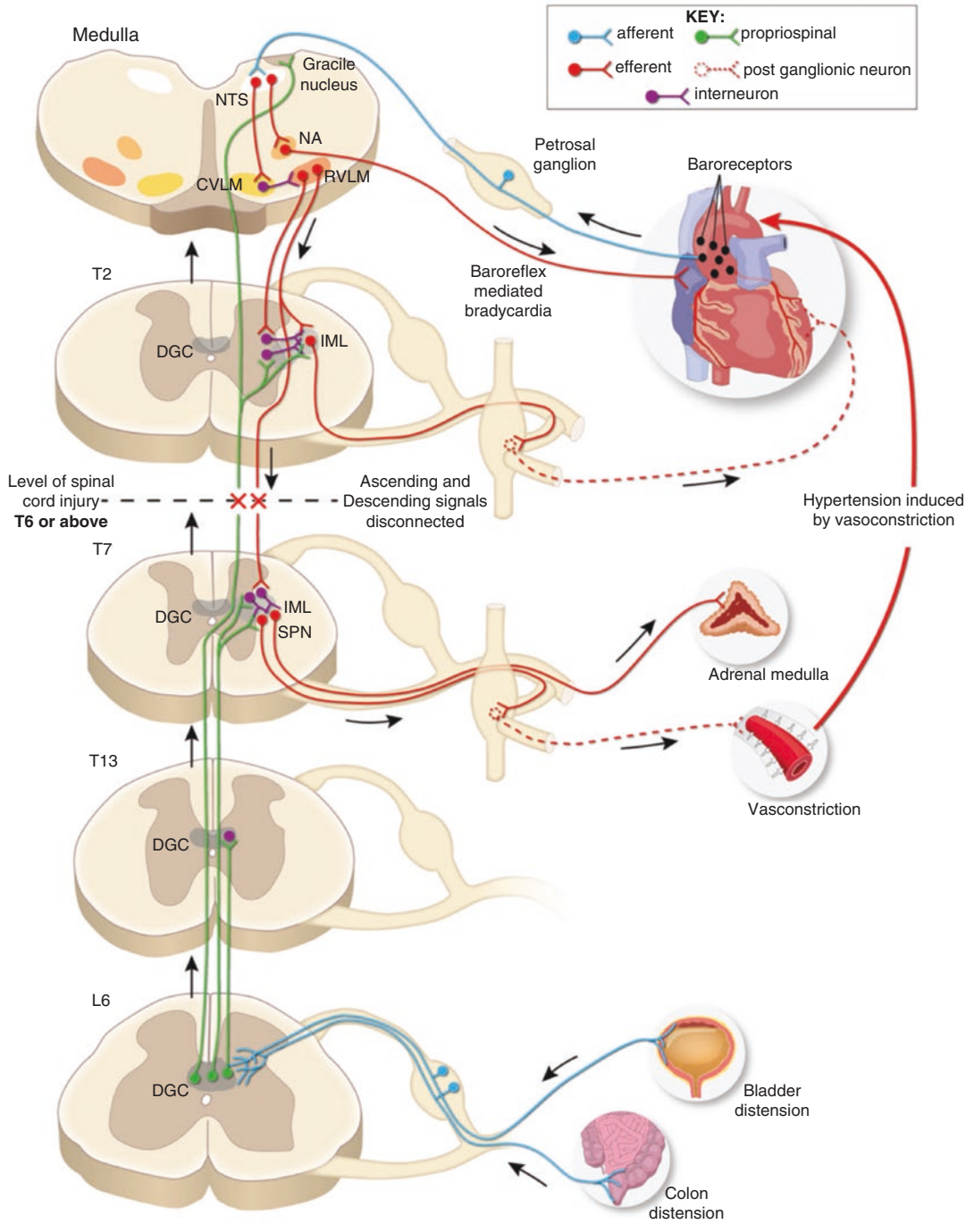

Fig. 24.1 Schematic representation of neuronal pathways disrupted by a complete spinal cord injury above the T6 spinal cord level associated with the development of autonomic dysreflexia, caused by noxious stimuli below the neurological level of injury. NTS nucleus tractus solitarius, NA nucleus ambiguous, CVLM caudal ventrolateral medulla, RVLM rostral ventrolateral medulla, DGC dorsal gray commissure, IML intermediolateral cell column, SPN sympathetic preganglionic neurons. From Michael et al. (2019), open access

horn and ascends in the dorsal columns and spinothalamic tract. As the signal ascends, collateral connections are thought to activate the intermediolateral column of the spinal cord to the level of spinal cord injury and lead to sympathetic efferent activity. In patients with high spinal cord injury with a complete lesion, this sympathetic efferent activity is no longer under supraspinal control. The major splanchnic outflow of the sympathetic nervous system occurs from T5 to L2 and can be regulated through inhibition by supraspinal centers (Eldahan and Rabchevsky 2018; Sharif and Hou 2017). Constriction of the critical mass of blood vessels, including the splanchnic vascular bed, causes hypertension. Raised blood pressure is sensed by baroreceptors in the aortic arch and carotid bodies. This stimulates the parasympathetic nervous system via the cranial nerves IX and X and results in bradycardia. Descending sympathetic inhibitory outflow from the vasomotor centers in the brainstem causes vasodilation, which also creates a headache and nasal congestion. The resulting flushing and sweating occur only above the spinal cord injury level because the injury stops the inhibitory signals from being transmitted further down the spinal cord. These passive vasodilation effects above the level of the lesion are not sufficient to lower the blood pressure (Bauman et al. 2012). The only active way to counteract the increase in blood pressure is to slow the heart rate via the vague nerve. Although this vagal-mediated bradycardia can be pronounced, it is usually insufficient to control hypertension, so it is very important to identify and quickly remove the stimulus is very important (Brown et al. 2018). Bradycardia is often considered to be a feature of autonomic dysreflexia, but increases in heart rate have also been reported in some studies (Karlsson 1999). Presumably, this depends on the level of lesion: if the sympathetic outflow to the heart is reflexively activated, tachycardia may be apparent, although its magnitude will depend on the competing inhibition via the vagus nerve (Brown et al. 2018; Karlsson 1999).

24.3 Clinical Presentation

Twenty to forty mmHg of arterial blood pressure (15 mmHg for adolescents and children) above the baseline may indicate autonomic dysreflexia. To measure the blood pressure of children, it is important to use a cuff of the appropriate size (about 40% of arm circumference). If the cuff is too large, it tends to underestimate, and if the cuff is too small, the blood pressure tends to be overestimated. The systolic blood pressure of tetraplegia or high paraplegia is low. A systolic blood pressure of 120 mmHg may indicate an autonomic dysreflexia with a baseline blood pressure of 90–100 mmHg in patients with tetraplegia. During autonomic dysreflexia, blood pressure can exceed 200 mmHg in both systolic and diastolic pressures. Activation of carotid and aortic baroreceptor occurs in response to hypertension and can reduce heart rate through the vagus nerve. However, this reduction is not enough to significantly lower blood pressure (Mathias and Frankel 1983). Bradycardia (<60/min) is considered a characteristic of autonomic dysreflexia, but it does not appear frequently. A reflex bradycardia often accompanied hypertension episodes, particularly if the level of injury is caudal to the spinal segments providing sympathetic control of the heart (T1-T4) (Rabchevsky 2006). Tachycardia is less common than bradycardia, but it also occurs with cardiac arrhythmia and atrial fibrillation or flutter. Patients with the lesions above T1 may have predominant cardiac sympathetic tone, leading to tachycardia (Kewalramani 1980).

All signs and symptoms of autonomic dysreflexia are attributed to hyperactivity of the sympathetic impulses below the level of injury and parasympathetic impulses above the level of injury (Table 24.2). The afferent impulses of the sympathetic chain by stimuli below the lesion that goes up the spinal cord are blocked at the level of the lesion. As a result, hypertension and other adrenergic manifestations including piloerection and pallor skin may appear below the level of injury, and clinical presentations of

Table 24.2 Clinical presentation of autonomic dysreflexia

• Paresthesiae in neck, shoulders, and upper extremities
• Fullness in head
• Throbbing headache especially in the occiput and frontal regions
• Tightness in chest and dyspnea
• Hypertension and bradycardia or tachycardia
• Pupillary dilatation
• Above the spinal cord injury level: pallor initially, followed by flushing of face and neck, and sweating in areas above and around the lesion
• Below the spinal cord injury level: cold peripheries, piloerection
• Contraction of urinary bladder and large bowel
• Penile erection and seminal fluid emission

compensatory parasympathetic activation including slowing of the heart rate, sweating, and flushing about the level of injury, and Horner's sign may occur (Lee et al. 1995).

As blood pressure increases, patients suffer from a throbbing headache, bitemporal, bifrontal, or occipital headaches in location. This headache is thought to be due to dilatation of cerebral blood vessels or elevation of prostaglandin E2. Excessive sweating above and around the level of injury is triggered by sympathetic cholinergic activity. Ocular findings include mydriasis and ptosis due to compensatory sympathetic discharge above the lesion. The predominance of papillae of the skin and piloerection can be observed as a result of stimulation of sympathetic postganglionic fibers of the skin (Kewalramani 1980).

The severity of autonomic dysreflexia varies considerably. Untreated autonomic dysreflexia with a rapid increase in blood pressure can lead to serious and potentially life-threatening complications. This includes cardiac arrhythmias, myocardial infarction, seizures, or intracranial hemorrhage (Dolinak and Balraj 2007; Elliott and Krassioukov 2006; Valles et al. 2005). Retinal hemorrhage and detachment may occur. The most common symptom of autonomic dysreflexia is a headache that usually occurs in the frontal or occipital areas. Autonomic dysreflexia should always be considered when patients with spinal cord injuries present with a new headache due to elevated blood pressure. Headache, sweating, and cutaneous vasodilatation (facial flushing) are a triad of diagnostic symptoms of autonomic dysreflexia.

It is important to note that many people with spinal cord injuries cannot detect when they are having an episode of autonomic dysreflexia, a term known as "silent" autonomic dysreflexia (Kirshblum et al. 2002; Wecht et al. 2021). Approximately 64% during autonomic dysreflexia episode are silent dysreflexia (Cívicos Sánchez et al. 2021). Silent dysreflexia with a systolic blood pressure of at least 20 mmHg increase in the absence of subjective symptoms may occur during the ejaculation procedures (Ekland et al. 2008). Silent dysreflexia is also recognized in bladder voiding and bowel procedures (Kirshblum et al. 2002; Linsenmeyer et al. 1996).

24.4 Assessment

Autonomic dysreflexia is a clinical diagnosis mainly because of the characteristics of classic clinical features of autonomic dysreflexia. Laboratory or imaging studies are generally not required. Immediate identification of the triggering factor and treatment of the condition are usually the main focus. However, you may need to find potential precipitating factors that require laboratory and/or imaging studies, such as a urinary tract infection or bladder calculi, limb edema to exclude deep vein thrombosis or fracture, or abdominal pathology.

Toxemia of pregnancy, pheochromocytoma, posterior fossa neoplasms, migraine, cluster headaches, and primary hypertension are conditions with clinical features similar to autonomic dysreflexia (Armenti-Kapros et al. 2003). Pheochromocytoma shows symptoms similar to autonomic dysreflexia (Schmitt and Adler 1987) (Table 24.3). Since pheochromocytoma causes paroxysmal hypertension, diagnosis of pheochromocytoma can be considered when patients with spinal cord injury exhibit such symptoms.

Table 24.3 Clinical differentiation between autonomic dysreflexia and pheochromocytoma

Clinical presentation	Autonomic dysreflexia	Pheochromocytoma
Hypertension	Present intermittently	Present (may be intermittent)
Bradycardia during proxysma	Often	Absent
Headache	Often present	Sometimes
Provoked by visceral stimulation, e.g., bladder	Usually	Rarely
Vasodilation above spinal cord lesion	Present	Absent
Sweating	Localized to upper body, above spinal cord lesion level	Diffuse
Horner's sign	Occasionally present	Absent

However, pheochromocytoma can be distinguished from autonomic dysreflexia, as pallor and vasoconstriction below the level of spinal cord injury association with facial flushing are not characteristic. Pheochromocytoma is a very rare disease in patients with hypertension less than 1/1000. Serum and 24-h urine epinephrine and norepinephrine concentration and urinary excretion of catecholamine metabolites (vanillymandelic acid, VMA) in pheochromocytoma are usually significantly elevated during hypertensive period (Schmitt and Adler 1987).

24.5 Management

The Clinical Practice Guidelines on Acute Management of Autonomic Dysreflexia by the Consortium for Spinal Cord Medicine has described the treatment of autonomic dysreflexia in patients with spinal cord injury (Consortium for Spinal Cord Medicine 2001). Acute episode management of autonomic dysreflexia generally focuses on the reduction of elevated blood pressure and the identification and elimination of episodic stimuli. The first step is to lift the patient's head, sit the patient upright, and monitor blood pressure every 5 min. Upright posture can lower blood pressure by venous pooling in the lower extremities. All tight clothing, shoes, compression stockings, straps of a drainage leg bag, or constrictive devices must be loosened or removed to allow for more blood pooling below the level of injury and eliminate possible triggering causes of noxious sensory stimuli (Bycroft et al. 2005). Check the urine bag and, if patients are on indwelling urethral catheter, make sure there is no catheter kinking. You should ask when patients had their last bowel movement. Check what their normal resting blood pressure is, and if it rises 20 mmHg above the resting blood pressure, it is defined as autonomic dysreflexia. Blood pressure quickly returns to baseline once the noxious stimulus is removed or alleviated; however, short-acting antihypertensives are sometimes required (Ong et al. 2020). The treatment algorithm of autonomic dysreflexia was well developed by the Consortium for Spinal Cord Medicine (Consortium for Spinal Cord Medicine 2020) (Fig. 24.2). Figure 24.3 is a simplified procedure for the management of autonomic dysreflexia.

After taking these general measures, you should focus on identifying the noxious stimulus. Because of the rapid elimination of the cause, the autonomic dysreflexia can be reversed more quickly than the drug, so you have to quickly find an individual for the provocating causes that start with a bladder distention or obstruction. In most cases, finding and removing or alleviating stimuli can often resolve the episodes quickly and eliminate the need for pharmacologic agents. If there is an indwelling catheter, kinks, folds, constrictions, or obstruction of the catheter should be removed. If this cannot restore urine flow, the catheter must be gently irrigated with normal saline at body temperature. When the catheter is not draining and the blood pressure remained elevated, the catheter should be changed. Compression or tapping on the bladder to confirm urine flow should be avoided. If an indwelling

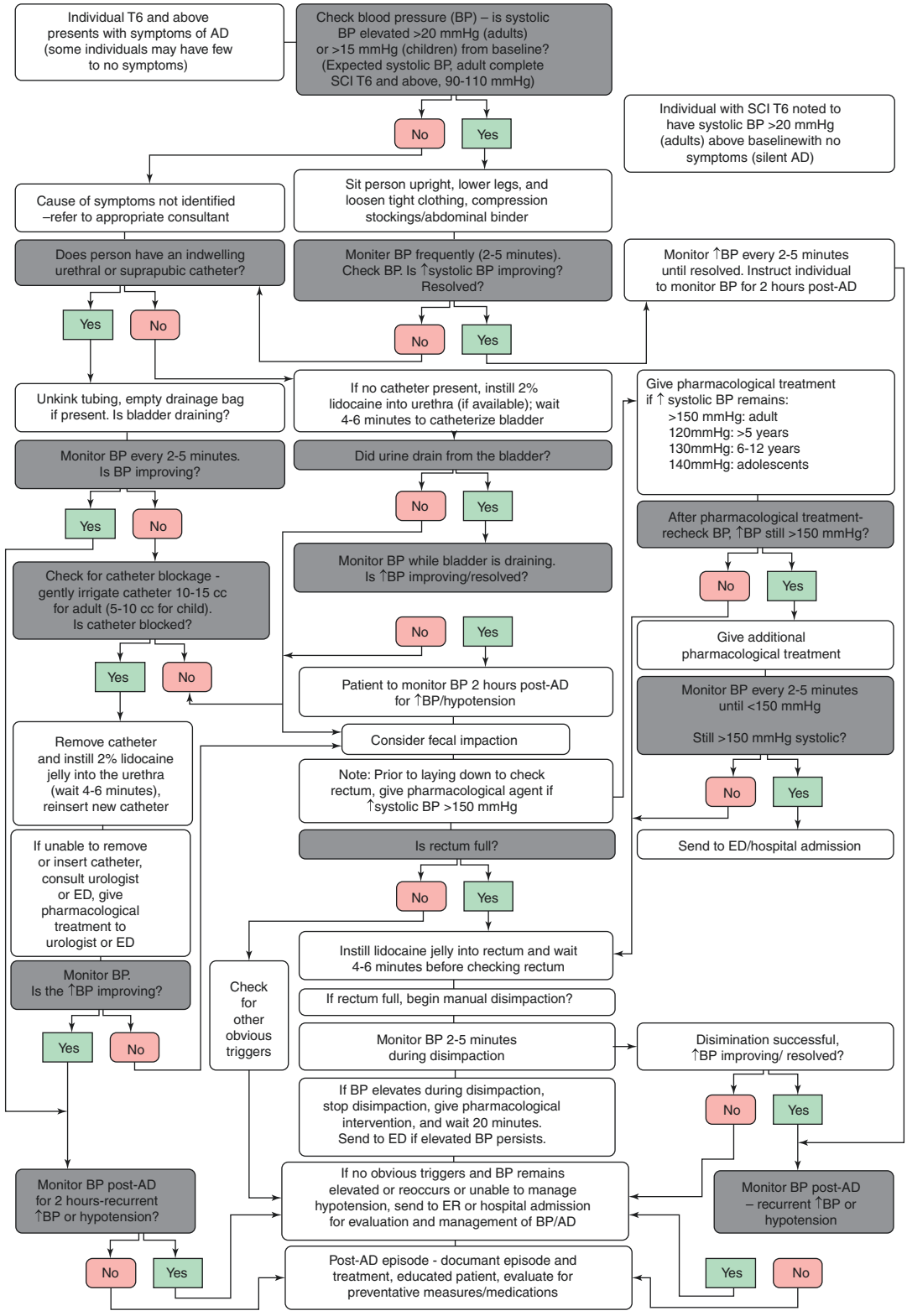

Fig. 24.2 Treatment algorithm of autonomic dysreflexia. From Consortium for Spinal Cord Medicine (2020)

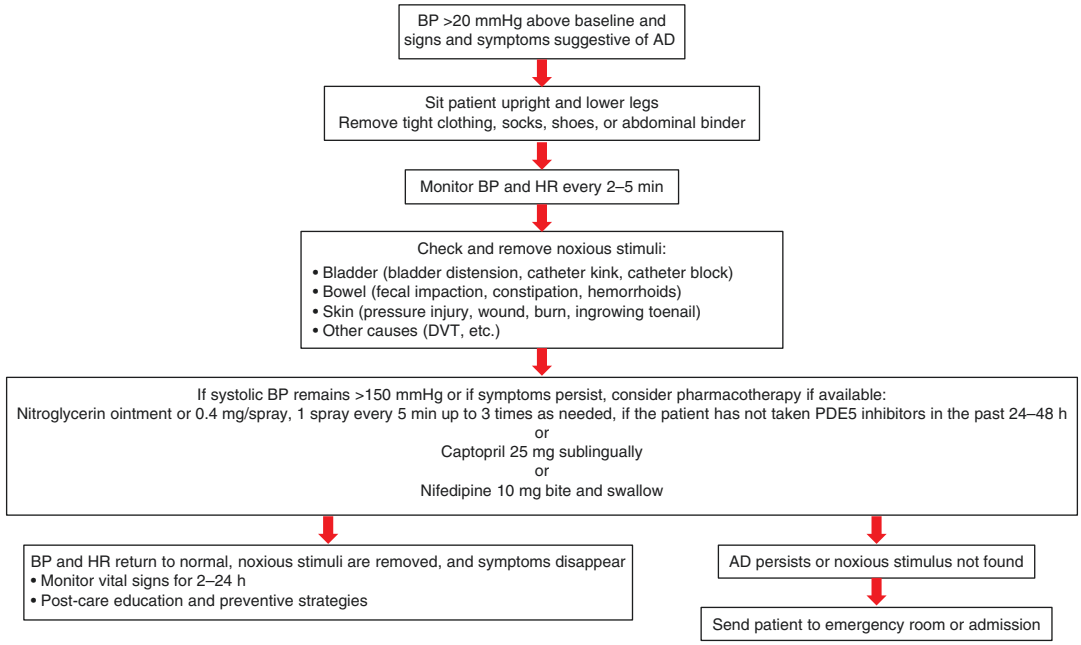

Fig. 24.3 Simplified procedure for management of autonomic dysreflexia. BP blood pressure, AD autonomic dysreflexia, HR heart rate, DVT deep vein thrombosis

urinary catheter is not in place, insert a catheter to check for urinary retention. Prior to inserting the catheter, instill 2% lidocaine jelly into the urethra and wait a few minutes. The blood pressure during bladder drainage is monitored.

If acute symptoms of autonomic dysreflexia persist, including persistent hypertension, fecal impaction may be suspected. Care must be taken before performing a rectal examination or manually removing it. The procedure itself can aggravate the episode. A topical anesthetic agent, 2% lidocaine jelly, should be injected gently into the rectum. It should be waited approximately 5 min prior to disimpaction with a gloved hand. If symptoms of autonomic dysreflexia worsen, stop the manual evacuation, and inject additional lidocaine jelly. Checking and evaluation are performed after 20 min. If the precipitating cause of autonomic dysreflexia has not yet been determined, you should find other less frequent causes.

If blood pressure cannot be lowered and systolic blood pressure is greater than 150 mmHg or diastolic blood pressure is greater than 100 mmHg, pharmacologic management should be considered immediately. It is advisable to use fast-acting and short-duration antihypertensive agents while investigating the cause of autonomic dysreflexia. Current medications for autonomic dysreflexia are mainly used empirically, and further studies are needed to establish a standard of treatment for autonomic dysreflexia (Table 24.4). The use of medication for the treatment of acute episodes of autonomic dysreflexia is aimed primarily at decreasing severe hypertension responsible for the acute symptoms and can lead to more serious sequelae. Medications should be carefully controlled for the safety of the pregnancy and breastfeeding (Table 24.5). Commonly used antihypertensive drugs to treat autonomic dysreflexia in spinal cord injuries are not safe for the fetus.

Commonly used drugs include nifedipine, 2% nitroglycerin ointment, and captopril. Nifedipine, an immediate-acting calcium channel blocker, is the most commonly used agent for the treatment of autonomic dysreflexia. It is a potent peripheral arterial vasodilator (McMahon et al. 2009). Nifedipine, 10 mg, immediate-release form, instructs the patient to bite and swallow. Sublingual administration or swallow without

Table 24.4 Pharmacological agents for treatment of autonomic dysreflexia

Drug	Dose and administration route	Onset of action	Duration of action	Precautions
2% Nitroglycerin ointment (first-line treatment)	• Spread thin layer of 1 inches (1.25–5 cm) topically on clean, dry, hair-free site on chest or back • Additional inch may be given after 15 min if needed	15–30 min	7 h	• Do not administer within 24 h of sildenafil or vardenafil or within 48 h of tadalafil • Avoid in individuals with severe anemia. • Avoid in individuals with increased intracranial pressure
Nitroglycerin	• 0.3 mg sublingual • 0.4 mg pump spray onto or under tongue • 0.1–0.8 mg/h transdermal patch	• 1–3 min (sublingual) • 2–4 min (translingual spray) • In 30 min (transdermal patch)	• 30–60 min (sublingual) • 30–60 min (translingual spray) • 8–234 h (transdermal patch)	Same precautions with the ointment
Nitroprusside	0.5–1.5 mg/min IV	• 1–2 min • Peaks immediately	1–10 min	Same precautions with nitroglycerine
Nifedipine	• 10 mg orally or sublingually • It may repeat after 30 min if necessary	• 20 min (oral) and 10 min (sublingual) • Peaks at 0.5–2 h	7–8 h	• Avoid in individuals with symptoms of acute angina or coronary artery disease • Avoid in elderly individuals • Avoid in individuals with hepatic disease
Captopril	25 mg sublingually once	• Within 15 min. • Peaks at 1–2 h	2–6 h (prolonged in renal impairment)	Avoid in individuals with rental failure, inability to predict effect
Clonidine	0.1–0.2 mg orally	• 30–60 min • Peaks at 1–3 h	8 h	Avoid in individuals with severe renal impairment and with a history of cerebral vascular disease, recent myocardial infarction, or severe heart failure
Hydralazine	• 10–20 mg orally • 20–40 mg IV or IM	• 20–30 min (oral) • Peaks at 1–2 h (oral) • Affected by food	2–4 h, although some sources state up to 12 h (hypotension may last longer)	• Avoid in individuals with rental failure • Avoid in individuals with coronary artery disease or rheumatic heart disease. • Avoid in individuals with acute stroke • Avoid in individuals with congestive heart failure
Prazosin	1–2 mg orally, BID	• 0.5–1.5 h • Peaks at 2–4 h	7–10 h	Use prazosin cautiously in patients with renal impairment
Terazosin	1–2 mg once	• 15 min • Peaks at 2–3 h	24 h	

Note: Nitroglycerin ointments or patches are not available in some countries. Before using nitroglycerin ointment or any other nitrate product, find out if the person has recently taken a phosphodiesterase inhibitor (PDEi). The use of nitroglycerin agent if a person has recently taken a PDEi is contraindicated because a combination of the two drugs can cause a sudden severe drop in BP. Sublingual nifedipine has variable and unpredictable absorption and is not recommended as there is little difference in bioavailability compared to swallowing nifedipine whole. During post-treatment with pharmacological agents, it is important to monitor BP for possible hypotension or recurrence of hypertension as the pharmacological agent wears off

Table 24.5 Pregnancy and breastfeeding precautions with medications for autonomic dysreflexia

Medication	Pregnancy risk	Breastfeeding risk	Other risks
Nitroglycerin	Crosses placenta, but data show that concentrations at birth in umbilical cord are low	Limited data; no adverse events noted in breastfeeding infants of mothers using topical nitroglycerin for anal fissures	Unknown
Nifedipine	Crosses the placenta	Present in breast milk; RID of 0.27–3.2% is less than the 10% considered acceptable; use has been recommended for Raynaud phenomenon of nipple in breastfeeding women	Increase in perinatal asphyxia, cesarean delivery, prematurity, and intrauterine growth retardation
Hydralazine	Crosses placenta; IV hydralazine is the recommended agent for use in acute hypertension of systolic BP >160 mmHg in women with preeclampsia or during the postpartum period	Present in breast milk; however, the RID is 0.3–3%, which is under the acceptable concentration of <10%	Unknown; adverse events have been reported in animal studies
Clonidine	Crosses placenta and umbilical concentrations are similar to maternal serum; amniotic fluid up to 4× maternal serum concentration	Do not use in breastfeeding women; concentration in milk is up to 2× that of maternal serum	Apathy syndrome, hypoglycemia, hypotonia, drowsiness, feeding difficulties, and hyperexcitability
Captopril	Crosses placenta; contraindicated in pregnancy	Present in breast milk; RID of 0.01–0.02% is under acceptable concentration of <10%	Decreased fetal renal function, fetal lung hypoplasia and skeletal hypoplasia, hypotension, and death of neonate/fetus

RIC relative infant dose (infant dose exposure via breast milk)
From Consortium for Spinal Cord Medicine (2020)

bite is not recommended because absorption is delayed. If hypertension recurs, nifedipine can be given repeatedly at the same dose after 10–15 min. Nifedipine requires a great deal of attention for elderly people or patients with coronary artery disease (McMahon et al. 2009). If the patient has a high risk of autonomic dysreflexia, nifedipine 10 mg p.o. is given 30 min before procedures.

Nitrates are direct-acting vasodilators, and their main action is dilation of the venous system. Any form of nitrate, ointment, intravenous nitroglycerin and nitroprusside, sublingual nitroglycerin, and inhaled amyl nitrate is effective in the treatment of hypertension due to autonomic dysreflexia but is usually reserved for the most severe cases that do not respond to other intervention. One inch of 2% nitroglycerine ointment may be applied to the chest or back above the level of injury. This has the advantage of being able to remove it easily and quickly by simply wiping if the blood pressure drops excessively. Other forms of nitrates (e.g., sodium nitroprusside drip) can also be used (McMahon et al. 2009). Any form of nitrate, including nitroglycerin ointment, is contraindicated in patients treated with phosphodiesterase type 5 inhibitors (PDE5I) such as sildenafil within the last 24–48 h. Many male patients with spinal cord injuries are prescribed drugs for erectile dysfunction, such as sildenafil, and the use of nitrates is contraindicated. Therefore, patients who have been prescribed drugs for erectile dysfunction should be asked.

Sublingual administration of captopril 25 mg has beneficial effects. Other drugs include alpha-adrenergic blockers or direct-acting vasodilators such as hydralazine. Hydralazine, a direct-acting arterial vasodilator, can be administered at a dose of 10 mg by slow intravenous injection. The

blood pressure and pulse should be measured every 2–5 min until the patients are stabilized (McMahon et al. 2009). To prevent a recurrence, the individual's symptoms and blood pressure should be monitored for a least 2 h after symptoms of autonomic dysreflexia resolve. If the hypertension is unresponsive to management and the cause of autonomic dysreflexia is not identified, the patient should be hospitalized to maintain pharmacologic management of the blood pressure and to investigate other causes of the autonomic dysreflexia. If the patient has hypotensive in medication, the patient should return to the supine position. Pharmacological treatment can be used to prevent frequent recurrent autonomic dysreflexia. Prazosin, a selective alpha-1 adrenergic blocker starting at 0.5–1.0 mg twice daily, is an appropriate option.

Various invasive diagnostic and therapeutic procedures have been reported to cause symptoms of autonomic dysreflexia in patients with spinal cord injuries, including cystoscopy, urodynamic study, and extracorporeal shock wave lithotripsy (Yoon et al. 2018). In particular, autonomic dysreflexia during the urodynamic study is independently predicted by the level of lesion, i.e., T6 or above, and the presence of the detrusor overactivity (Walter et al. 2018). Autonomic dysreflexia during surgery has been reported in patients receiving regional or general anesthesia rather than local anesthesia. Despite the use of local, regional, or general anesthesia, episodes can occur during surgical procedures. The use of halothane may be more effective in preventing autonomic dysreflexia when general anesthesia is used. Nifedipine is effective when administered preoperatively and when autonomic dysreflexia occurs during urologic procedures such as urodynamic study, cystoscopy, and extracorporeal shock wave lithotripsy. The dose used is usually 10 mg orally preoperatively and 10–20 mg orally when an episode occurs during a procedure. Women with spinal cord injury who become pregnant are at risk of developing a dysreflexia episode during labor and delivery (Soh et al. 2019). In women with spinal cord injury, symptoms of labor may include just some abdominal discomfort, increased spasticity, and autonomic dysreflexia. Epidural anesthesia has been reported to be the superior choice for control of autonomic dysreflexia during labor.

Once the autonomic dysreflexia episode is resolved, it should be discussed in the patient's medical record describing symptoms, blood pressure, pulse, and response to treatment. If the person with spinal cord injury is stable, review the precipitating causes with the patient, members of the patient's family, relatives, and caregivers and provide the necessary education. Patients with spinal cord injuries and their caregivers should be able to recognize and treat autonomic dysreflexia and should receive emergency treatment if the problem is not resolved quickly. It is a good idea to provide a written explanation for the treatment of autonomic dysreflexia at discharge to the patient with spinal cord injury that can be referred to in an emergency.

24.6 Prevention and Education

The key in the management of recurrent episodes and in the prevention of autonomic dysreflexia is to identify and avoid factors or stimuli that can cause episodes. Patient and family education is an important part of managing current episodes and preventing future occurrences. It is important that patients with spinal cord injury and their caregivers are well informed in order to recognize and treat autonomic dysreflexia properly and to seek emergency treatment if the problem is not resolved promptly. They must prevent common potential causes and recognize the importance of preventive measures. Autonomic dysreflexia is often unrecognized by non-spinal cord injury providers because of the unique occurrence in patients with spinal cord injuries. Measures should be taken to educate medical providers, including primary care physicians, and emergency department and emergency medical service personnel. It can direct your care in such an environment, as it emphasizes the importance of educating and empowering people with spinal cord injury and their families. Appropriate knowledge of the condition of autonomic dysreflexia and a handy card containing this informa-

tion can help other healthcare providers or persons who are not accustomed to the treatment of acute or recurrent episodes of autonomic dysreflexia.

The prophylactic use of a pharmacologic agent may be indicated in patients who continue to experience recurrent episodes of autonomic dysreflexia despite general measures. More selective alpha-1 blocking agents such as prazosin and terazosin can be selected as effective prophylactic agents without the side effects commonly associated with other alpha-adrenergic blockers. Treatment with prazosin is usually started at 1 mg daily, given at night, and can be increased by 1 mg twice a day.

References

Allen KJ, Leslie SW. Autonomic dysreflexia. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2021.

American Spinal Injury Association (ASIA). International standards to document remaining autonomic function after spinal cord injury (ISAFSCI). Atlanta, GA: American Spinal Injury Association; 2012.

Armenti-Kapros B, Nambiar PK, Lippman HR, et al. An unusual cause of autonomic dysreflexia: pheochromocytoma in an individual with tetraplegia. J Spinal Cord Med. 2003;26:172–5.

Bauman CA, Milligan JD, Lee FJ. Autonomic dysreflexia in spinal cord injury patients: an overview. J Can Chiropr Assoc. 2012;56:247–50.

Brown R, Burton AR, Macefield VG. Autonomic dysreflexia: somatosympathetic and viscerosympathetic vasoconstrictor responses to innocuous and noxious sensory stimulation below lesion in human spinal cord injury. Auton Neurosci. 2018;209:71–8.

Bycroft J, Shergill IS, Chung EA, et al. Autonomic dysreflexia: a medical emergency. Postgrad Med J. 2005;81:232–5.

Cívicos Sánchez N, Acera M, Murueta-Goyena A, et al. Quantitative analysis of dysautonomia in patients with autonomic dysreflexia. J Neurol. 2021;268:2985–94.

Consortium for Spinal Cord Medicine. Acute management of autonomic dysreflexia: individuals with spinal cord injury presenting to health care facilities. 2nd ed. Washington, DC: Paralyzed Veterans of America; 2001. https://pva.org/research-resources/publication/

Consortium for Spinal Cord Medicine. Evaluation and management of autonomic dysreflexia and other autonomic dysfunctions: preventing the highs and lows. Management of blood pressure, sweating, and temperature dysfunction. Washington, DC: Paralyzed Veterans of America; 2020. https://pva.org/research-resources/publication/

Dolinak D, Balraj E. Autonomic dysreflexia and sudden death in people with traumatic spinal cord injury. Am J Forensic Med Pathol. 2007;28:95–8.

Ekland MB, Krassioukov AV, McBride KE, et al. Incidence of autonomic dysreflexia and silent autonomic dysreflexia in men with spinal cord injury undergoing sperm retrieval: implications for clinical practice. J Spinal Cord Med. 2008;31:33–9.

Eldahan KC, Rabchevsky AG. Autonomic dysreflexia after spinal cord injury: systemic pathophysiology and methods of management. Auton Neurosci. 2018;209:59–70.

Elliott S, Krassioukov A. Malignant autonomic dysreflexia in spinal cord injured men. Spinal Cord. 2006;44:386–92.

Furlan JC, Fehlings MG. Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis, and management. Neurosurg Focus. 2008;25:E13.

Gao SA, Ambring A, Lambert G, et al. Autonomic control of the heart and renal vascular bed during autonomic dysreflexia in high spinal cord injury. Clin Auton Res. 2002;12:457–64.

Guttmann L, Whitteridge D. Effects of bladder distention on automatic mechanisms after spinal cord injuries. Brain. 1947;70:361.

Head H, Riddock G. The automatic bladder, excessive sweating and some other reflex conditions in gross injuries of the spinal cord injuries of the spinal cord. Brain. 1917;40:188.

Helkowski WM, Ditunno JF Jr, Boninger M. Autonomic dysreflexia: incidence in persons with neurologically complete and incomplete tetraplegia. J Spinal Cord Med. 2003;26:244–7.

Hubli M, Gee CM, Krassioukov AV. Refined assessment of blood pressure instability after spinal cord injury. Am J Hypertens. 2015;28:173–81.

Karlsson AK. Autonomic dysreflexia. Spinal Cord. 1999;37:383–91.

Kewalramani LS. Autonomic dysreflexia in traumatic myelopathy. Am J Phys Med. 1980;59:1–21.

Kirshblum SC, House JG, O'Connor KC. Silent autonomic dysreflexia during a routine bowel program in persons with traumatic spinal cord injury: a preliminary study. Arch Phys Med Rehabil. 2002;83:1774–6.

Krassioukov A, Claydon VE. The clinical problems in cardiovascular control following spinal cord injury: an overview. Prog Brain Res. 2006;152:223–9.

Krassioukov A, Linsenmeyer TA, Beck LA, et al. Evaluation and management of autonomic dysreflexia and other autonomic dysfunctions: preventing the highs and lows: management of blood pressure, sweating, and temperature dysfunction. Top Spinal Cord Inj Rehabil. 2021;27:225–90.

Krassioukov A, Warburton DE, Teasell R, et al. A systematic review of the management of autonomic dysreflexia after spinal cord injury. Arch Phys Med Rehabil. 2009;90:682–95.

Lee BY, Karmakar MG, Herz BL, et al. Autonomic dysreflexia revisited. J Spinal Cord Med. 1995;18:75–87.
Lindan R, Joiner E, Freehafer A, et al. Incidence and clinical features of autonomic dysreflexia in patients with spinal cord injury. Spinal Cord. 1980;18:285–92.
Linsenmeyer T, Campagnolo D, Chou I. Silent autonomic dysreflexia during voiding in men with spinal cord injuries. J Urol. 1996;55:519–22.
Mathias CJ, Frankel HL. Clinical manifestations of malfunctioning sympathetic mechanisms in tetraplegia. J Auton Nerv Syst. 1983;7:303–12.
Mathias CJ, Frankel HL. Cardiovascular control in spinal man. Annu Rev Physiol. 1988;50:577–92.
McLachlan EM. Diversity of sympathetic vasoconstrictor pathways and their plasticity after spinal cord injury. Clin Auton Res. 2007;17:6–12.
McMahon D, Tutt M, Cook AM. Pharmacological management of hemodynamic complications following spinal cord injury. Orthopedics. 2009;32:331.
Michael FM, Patel SP, Rabchevsky AG. Intraspinal plasticity associated with the development of autonomic dysreflexia after complete spinal cord injury. Front Cell Neurosci. 2019;13:505.
Ong B, Wilson JR, Henzel MK. Management of the patient with chronic spinal cord injury. Med Clin North Am. 2020;104:263–78.
Partida E, Mironets E, Hou S, et al. Cardiovascular dysfunction following spinal cord injury. Neural Regen Res. 2016;11:189–94.
Rabchevsky AG. Segmental organization of spinal reflexes mediating autonomic dysreflexia after spinal cord injury. Prog Brain Res. 2006;152:265–74.
Rabchevsky AG, Kitzman PH. Latest approaches for the treatment of spasticity and autonomic dysreflexia in chronic spinal cord injury. Neurotherapeutics. 2011;8:274–82.
Schmitt J, Adler R. Endocrine metabolic consequences of spinal cord injury. Phys Med Rehabil State Art Rev. 1987;1:425–41.
Sharif H, Hou S. Autonomic dysreflexia: a cardiovascular disorder following spinal cord injury. Neural Regen Res. 2017;12:1390–400.
Sheel AW, Krassioukov AV, Inglis JT. Autonomic dysreflexia during sperm retrieval in spinal cord injury: influence of lesion level and sildenafil citrate. J Appl Physiol (1985). 2005;99:53–8.
Snow JC, Sideropoulos HP, Kripke BJ, et al. Autonomic hyperreflexia during cystoscopy in patients with high spinal cord injuries. Paraplegia. 1978;15:327–32.
Soh SH, Lee G, Joo MC. Autonomic dysreflexia during pregnancy in a woman with spinal cord injury: a case report. J Int Med Res. 2019;47:3394–9.
Teasell RW, Arnold MO, Krassioukov A, et al. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil. 2000;81:506–16.
Vaidyanathan S, Soni B, Oo T, et al. Autonomic dysreflexia in a tetraplegic patient due to a blocked urethral catheter: spinal cord injury patients with lesions above T-6 require prompt treatment of an obstructed urinary catheter to prevent life-threatening complications of autonomic dysreflexia. Int J Emerg Med. 2012;5:1–5.
Valles M, Benito J, Portell E, et al. Cerebral hemorrhage due to autonomic dysreflexia in a spinal cord injury patient. Spinal Cord. 2005;43:738–40.
Walter M, Knüpfer SC, Cragg JJ, et al. Prediction of autonomic dysreflexia during urodynamics: a prospective cohort study. BMC Med. 2018;16:53.
Weaver LC. What causes autonomic dysreflexia after spinal cord injury? Clin Auton Res. 2002;12:424–6.
Wecht JM, Krassioukov AV, Alexander M, et al. International Standards to document Autonomic Function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.
West CR, Mills P, Krassioukov AV. Influence of the neurological level of spinal cord injury on cardiovascular outcomes in humans: a meta-analysis. Spinal Cord. 2012;50:484–92.
Yoon JA, Shin YB, Shin MJ, et al. Cardiovascular monitoring during video urodynamic studies in persons with spinal cord injury. Am J Phys Med Rehabil. 2018;97:1–6.

Recommended Additional Reading

Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.
Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. New Delhi: Wolters Kluwer; 2015.
Eltorai IM, Schmit JK, editors. Emergencies in chronic spinal cord injury patients. New York: Eastern Paralyzed Veterans Association; 2001.
Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.
Jallo J, Vaccaro AR, editors. Neurotrauma and critical care of the spine. 2nd ed. New York: Thieme; 2018.
Kirshblum S, Lin VW, editors. Spinal cord medicine. 3rd ed. New York: Demos Medical Publishing; 2019.
Low PA, Benarroh EE, editors. Clinical autonomic disorders. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
Robertson D, Bigaaioni I, Burnstock G, et al. Primer on the autonomic nervous system. 3rd ed. London: Elsevier; 2011.
Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

Orthostatic Hypotension and Supine Hypertension

25

In addition to low resting arterial blood pressure, many people with high spinal cord injuries also experience a further drop in blood pressure when they assume an upright position (Consortium for Spinal Cord Medicine 2020). Orthostatic hypotension is a common problem among people with spinal cord injuries and a major problem that should be managed earlier to improve active participation in rehabilitation after spinal cord injuries. People with high spinal cord injury are subject to orthostatic hypotension when moving from the horizontal to the upright position. According to the American Autonomic Society and the American Academy of Neurology (The Consensus Committee of AAS/AAN 1996), orthostatic hypotension is defined as a decrease in systolic blood pressure of at least 20 mmHg or a decrease in diastolic blood pressure of at least 10 mmHg for the first 3 min of the upright position or a head-up tilt (HUT) to at least 60° on a tilt table (Gibbons et al. 2017). It does not matter whether symptoms develop. In general, patients who cannot stand or sit are defined as orthostatic hypotensive when the systolic blood pressure falls below 20 mmHg, or the diastolic blood pressure falls below 10 mmHg within 3 min with a tilt angle of 60° on the tilt table (Bradley and Davis 2003; Claydon and Krassioukov 2006). Orthostatic hypotension can be diagnosed within 1 min after tilting or standing at 60°. Two minutes are required to determine the severity of orthostatic hypotension by observing the additional decrease in blood pressure. Orthostatic hypotension is rarely seen after 3 min (Deegan et al. 2007).

The prevalence of orthostatic hypotension and the degree of fall in blood pressure are higher in patients with cervical spinal cord injuries than those with thoracic spinal cord injuries. The correlation between resting blood pressure and spinal cord injuries is very high (Bilello et al. 2003). Generally, the mean arterial pressure of patients with tetraplegia is as low as 57 mmHg. Patients with high-level spinal cord injuries in both the acute phase and the chronic phase have low blood pressure. Orthostatic hypotension has been reported to be more common in traumatic spinal cord injuries than in nontraumatic spinal cord injuries. Low plasma volume, hyponatremia, and cardiovascular deconditioning may be additional factors (Lehmann et al. 1987). Symptoms of orthostatic hypotension vary with orthostatic stress, and it is important to recognize subtle symptoms such as tiredness and cognitive impairment. It is necessary to couple non-pharmacologic and pharmacologic methods in order to improve orthostatic change in arterial blood pressure. Standard drug treatment is efficacious in improving orthostatic hypotension and its symptoms, but will worsen supine hypertension (Low and Singer 2008).

In patients with autonomic failure causing neurogenic orthostatic hypotension, supine hypertension is common and part of the underlying disease

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process because these patients lack the normal blood pressure buffering mechanisms that compensate for hypertension. In addition, frequent periods of orthostatic hypotension can lead to chronic activation of the renin–angiotensin system (Gibbons et al. 2017). Supine hypertension further confuses therapy, as pharmacologic treatments to normalize standing blood pressure may exacerbate supine hypertension (Goldstein et al. 2003). According to the eighth Joint National Committee hypertension guidelines, essential hypertension is a blood pressure consistently ≥140/90 mmHg (James et al. 2014). Supine hypertension in patients with orthostatic hypotension is arbitrarily defined as a systolic blood pressure ≥150 mmHg or diastolic blood pressure ≥90 mmHg in the supine position. General treatment guidelines recommend intervention for hypertension, but supine hypertension associated with orthostatic hypotension requires additional considerations.

25.1 Orthostatic Hypotension

25.1.1 Pathophysiology

Sympathetic control of the upper extremity vasculature and heart originates from the thoracic cord between T1 and T5, and the splanchnic bed and lower extremity vasculature receive sympathetic neural input from the lower cord between segments T5 and L2. The vasculature is not directly innervated by the parasympathetic nervous system, but the SA node is innervated via the cranial nerve X by postganglionic vagal nerve fibers. Segmental differences in sympathetic cardiovascular innervation highlight the effect of neurological level of lesion on orthostatic cardiovascular control after spinal cord injury. Due to impaired cardiovascular control of the sympathetic nerves, many people with spinal cord injuries, especially those with lesions above T6, are prone to orthostatic hypotension and orthostatic intolerance (Wecht and Bauman 2018; Wecht et al. 2021).

A major abnormality of orthostatic hypotension associated with spinal cord injury is the lack of reflex vasoconstriction by the sympathetic activities, particularly in large vascular beds such as those supplied to the splanchnic vasculature and skeletal muscles. Decreased skeletal muscle mass and smooth muscle vascular tone can contribute to orthostatic hypotension in people with spinal cord injuries. The distention of the lower extremity vasculature causes activation of muscle sympathetic nerve activity and increased mean arterial pressure, independent of the baroreceptor reflex (Wecht and Bauman 2018). However, this local reflex may be absent or diminished in people with spinal cord injuries, and there is evidence to suggest that reduction in reflex vasoconstriction to the splanchnic bed and the lower extremity vasculature results in venous pooling (Claydon et al. 2006; Claydon and Krassioukov 2008; Wecht and Bauman 2018). The gravitational effect of venous pooling in the lower extremities decreases blood pressure because there are not enough compensatory changes in other vascular beds. Venous pooling leads to a reduction in cardiac filling pressure, a decrease in the end-diastolic filling volume, and a reduction in stroke volume. In the standing position, the blood is retained in the lower extremities with a volume of 500 mL (300–800 mL), and the parasympathetic activity of the heart is reduced, resulting in tachycardia (Dumont et al. 2001; Myers et al. 2007) (Fig. 25.1). However, it is not sufficient to compensate for the decrease in cardiac output, leading to continued hypotension. This phenomenon is different from the case in which normal function of the sympathetic nervous system such as poliomyelitis does not occur or the orthostatic hypotension does not appear significantly despite motor paralysis in the legs. Changing head-up posture usually causes an immediate drop in blood pressure often it falls to a very low levels. After initial drop in blood pressure, the subsequent responses vary. Tachycardia may be due to reflex vagal inhibition, but is not sufficient to compensate for the reduced sympathetic response (Claydon and Krassioukov 2006).

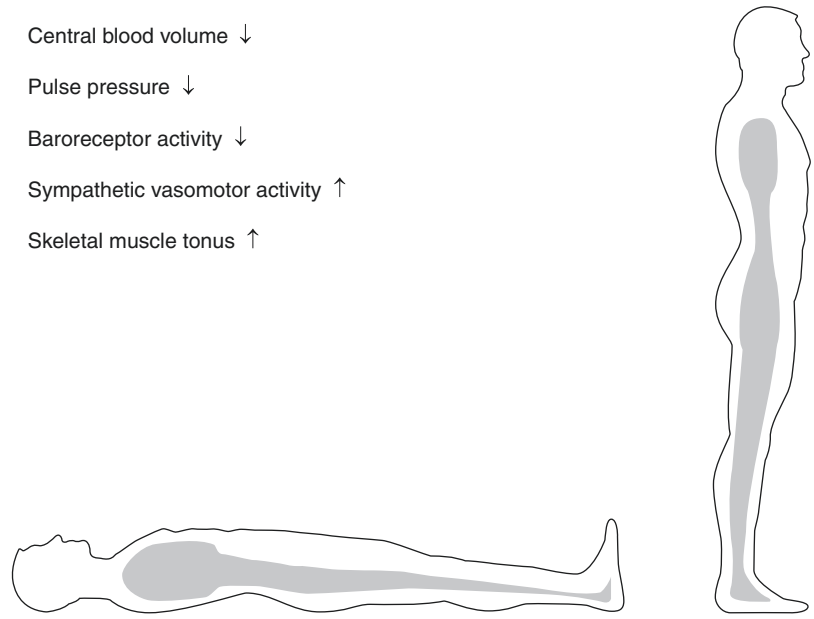

Fig. 25.1 Gravity effects on intravascular fluid shift

However, despite marked orthostatic hypotension, the heart rate usually does not exceed 100 per minute. Despite an increase in heart rate, this response is not usually sufficient to compensate for the decreased stroke volume, and blood pressure remains low.

Several mechanisms have been proposed for the development of orthostatic hypotension after spinal cord injury. The interruption of sympathoexcitatory efferent pathways from the brainstem to the spinal preganglionic neurons involved in vasoconstriction results in a failure of the regulation of reflex arterial pressure in the short term (Claydon et al. 2006). This results in a pooling of blood in the viscera and dependent vasculature below the level of injury. The splanchnic-mesenteric capacitance bed is a large-volume, low-resistance system that constitutes 25–30% of total blood volume (Rowell et al. 1972). There is much clinical and research evidence to support the importance of this bed and splanchnic outflow in the maintenance of postural normotension. Unlike muscle veins, the splanchnic veins have an abundance of smooth muscle and a rich sympathetic innervation, largely from the greater splanchnic nerve (Low and Singer 2008). The excessive venous pooling in the lower extremities and reduction in blood volume in the intrathoracic veins cause a reduction of pressure in the large veins draining into the atria of the heart (Faghri et al. 2001).

If HUT is prolonged, orthostatic hypotension after spinal cord injury often improves with time. Compensatory changes in other vascular beds can contribute to blood pressure homeostasis. This is partially related to activation of the renin-angiotensin-aldosterone system. Decreased blood flow to the kidneys may activate afferent glomerular dilatation and cause stimulation of the renin-angiotensin-aldosterone system. Renin release is not mediated by reflex sympathetic activation and may be secondary to renal baroreceptor stimulation by the reduced renal perfusion pressure (Mathias 2006; Mathias et al. 1976). Renin induces the formation of angiotensin II, a potent vasoconstrictor that facilitates peripheral norepinephrine release and promotes the release of aldosterone from the adrenal cortex. The salt and water-retaining effects of aldosterone increase intravascular volume. These various effects of the renin-angiotensin-aldosterone system help increase blood pressure (Teasell et al. 2000). Hypersensitivity to the receptor of the vessel wall, recovery of postural reflexes at the spinal level, and an increase in skeletal muscle tone are other mechanisms for improvement over time

(Furlan et al. 2003). Tolerance to symptoms of orthostatic hypotension often occurs over time, when postural reduction in blood pressure is maintained in the upright position. Autoregulation of blood flow has been suggested to play an important role in adaptation to orthostatic hypotension rather than systematic blood pressure (Gonzalez et al. 1991).

25.1.2 Epidemiology

Orthostatic maneuvers performed during physical therapy and mobilization would induce orthostatic hypotension in 74% of people with spinal cord injuries, suggesting that this condition is common in people with spinal cord injuries. Signs and symptoms associated with orthostatic hypotension were observed in 59% of cases and seen as limiting treatment on 43% of cases (Illman et al. 2000). Orthostatic hypotension is less common in spinal cord injuries below the origin of the major splanchnic outflow at T6 and incomplete lesions (Claydon and Krassioukov 2006; Nobunaga 1998).

Drugs such as diuretics or alpha-blockers, calcium channel blockers, other antihypertensive drugs, insulin, and tricyclic antidepressants are drugs that can cause vasodilation and promote or exacerbate orthostatic hypotension (Gibbons et al. 2017; Iwanczyk et al. 2006) (Table 25.1).

25.1.3 Precipitating Factors

Orthostatic hypotension can be affected by many factors, many of which are reversible. These include rapid change of position and prolonged recumbency. Hypotension can be worse in the morning when getting up. Heavy meals may reduce blood pressure after meals by postprandial shunting of blood to the splanchnic circulation (Freeman 2008). Physical activity, alcohol consumption, or high-temperature environment can promote vasodilatation and cause hypotension. Sepsis and dehydration can worsen symptoms. Deconditioning after prolonged bed rest will worsen orthostatic hypotension. Anemia is common precipitating factor of orthostatic hypo-

Table 25.1 Medications causing orthostatic hypotension and exacerbating the symptoms of orthostatic hypotension

Class of medications	Examples
1. Antihypertensive agents	
Preload reducers	
Diuretics	Furosemide, torsemide, acetazolamide, hydrochlorothiazide, spironolactone
Nitrates	Nitroprusside, isosorbide dinitrate, nitroglycerin
Phosphodiesterase E5 inhibitors	Sildenafil, vardenafil, tadalafil
Vasodilators	
Alpha-1 adrenergic antagonists	Alfuzosin, doxazosin, prazosin, terazosin, tamsulosin (used primarily for benign prostatic hyperplasia)
Dihydropyridine calcium channel blockers	Amlodipine, nifedipine, nicardipine
Other direct vasodilators	Hydralazine, minoxidil
Negative inotropic/chronotropic agents	
Beta-adrenergic blockers	Propranolol, metoprolol, atenolol, bisoprolol, nebivolol (also vasodilator), carvedilol (also alpha-1 antagonist), labetalol (also alpha-1 antagonist)
Non-dihydropyridine calcium channel blockers	Verapamil, diltiazem
Central sympatholytic agents	
Centrally acting alpha-2 agonists	Clonidine
False neurotransmitters	Alpha-methyldopa
Renin–angiotensin system (RAS) antagonists	
Angiotensin-converting enzyme (ACE) inhibitors	Captopril, enalapril, perindopril
Angiotensin receptor type II blockers (ARB)	Losartan, telmisartan, candesartan
2. Antidepressants (particularly tricyclic agents	Amitriptyline, nortriptyline, imipramine, desipramine
3. Anticholinergics	Atropine, glycopyrrolate, hyoscyamine
4. Dopaminergic agents	Levodopa, dopamine agonists

From Gibbons et al. (2017), with permission
Diuretics, nitrates, alpha1-antagonists, and TCA may cause more significant worsening of orthostatic hypotension

tension (Biaggioni et al. 1994). Some medications can cause or aggravate postural hypotension. These drugs include tricyclic antidepressants, antihypertensives, diuretics, narcotic analgesics, α-blockers, β-blocker, PDE5 inhibitors, and centrally acting α2-agonists (clonidine or tizanidine) (Palma and Kaufmann 2020). If orthostatic hypotension several months or years after spinal cord injury develops or worsens late, it can be a sign of posttraumatic syringomyelia.

25.1.4 Clinical Presentations

Symptomatic orthostatic hypotension, which can lead to orthostatic intolerance, is the result of a temporary decrease in cerebral perfusion pressure, and symptoms can include dizziness, lightheadedness, nausea, blurred vision, ringing in the ears, headache, and syncope. However, many, if not most, people with spinal cord injuries who suffer from persistent and episodic hypotension and orthostatic hypotension do not report symptoms of cerebral hypoperfusion (Wecht and Bauman 2018). Chronic hypotension in people with spinal cord injuries may be associated with a lack of memory, attention, and processing speed (Jegede et al. 2010). As a reference, the World Health Organization (WHO) defines hypotension as systolic blood pressure of less than 100 mmHg for women and less than 110 mmHg for men, without regard to diastolic blood pressure (WHO 1978). In addition to low resting arterial blood pressure, many people with high spinal cord injuries also experience a further drop in blood pressure when they are in an upright position (Consortium for Spinal Cord Medicine 2020). Orthostatic hypotension is known to affect the ability of people with spinal cord injuries to participate in activities that can cause a decrease in blood pressure. It has a significant impact on the activities of daily living, particularly participation in rehabilitation programs, as symptoms occur during sitting or standing, and has a serious impact on the quality of life (Claydon et al. 2006; Illman et al. 2000). Seventy-four percent of patients with spinal cord injuries show orthostatic hypotension due to changes in posture during physical therapy or mobilization, and 59% have symptoms associated with orthostatic hypotension (Illman et al. 2000). About 40% of patients develop asymptomatic orthostatic hypotension. Orthostatic hypotension due to postural changes is more likely to occur during physical therapy than with passive standing on the tilt table. This reason why passive tilting is less likely to produce orthostatic hypotension is unclear (Claydon et al. 2006). In general, the higher the spinal cord injury level, the more likely it is to develop orthostatic hypotension due to the wider retention areas of blood flow to the postural changes (Illman et al. 2000). The association that orthostatic hypotension in the traumatic spinal cord injury is more common than the nontraumatic spinal cord injury is unclear.

Symptoms associated with orthostatic hypotension in patients with spinal cord injuries, such as light-headedness or dizziness beginning within a few seconds after sitting or standing, fatigue, weakness, blurred vision, and shortness of breath are the same as in the general population. Orthostatic hypotension in the acute phase often occurs in the chronic phase. The main symptoms of orthostatic hypotension are caused by cerebral hypoperfusion. These include dizziness, drowsiness, loss of consciousness, impaired concentration, and visual disturbances such as blurred vision, scotoma, tunnel vision, graying out, and color defects (Weimer and Zadeh 2009). Pallor or auditory deficits can also occur. Excessive sweating can occur above the level of injury.

25.1.5 Symptom Grading of Orthostatic Intolerance

It is important to obtain an estimate of the severity and its effect on the patient's activities of daily living. An orthostatic intolerance grade has been defined, which grades patients on the basis of the frequency and severity of symptoms, standing time before the onset of symptoms, influence on activities of daily living, and blood pressure (Low et al. 2008; Low and Singer 2008) (Table 25.2). A patient with grade I orthostatic hypotension might not need drugs, whereas those with grades III or IV will need aggressive therapy (Low and Singer 2008).

Table 25.2 Symptom grade of orthostatic intolerance

Grade I	
1	Orthostatic symptoms are infrequent, inconstant, or only under conditions of increased orthostatic stress
2	Standing time typically ≥15 min
3	Unrestricted activities of daily living
4	Blood pressure indices may or may not be abnormal
Grade II	
1	Orthostatic symptoms are frequent, developing at least once a week. Orthostatic symptoms commonly develop with orthostatic stress
2	Standing time ≥5 min on most occasions.
3	Some limitation in activities of daily living.
4	Some change in cardiovascular indices. These might be OH, reduction in pulse pressure ≥ 50%, excessive oscillations in BP.
Grade III	
1	Orthostatic symptoms develop on most occasions and are regularly unmasked by orthostatic stressors.
2	Standing time ≥1 min on most occasions.
3	Marked limitation in activities of daily living.
4	Orthostatic hypotension in present on ≥50% of the time, recorded on different days.
Grade IV	
1	Orthostatic symptoms consistently present.
2	Standing time < 1min on most occasions.
3	Patient is seriously incapacitated, being bed- or wheel-chair bound because of orthostatic intolerance. Syncope/presyncope is common if the patient attempts to stand.
4	Orthostatic hypotension is consistently present.

From Low and Singer (2008), with permission
OH orthostatic hypotension, BP blood pressure

25.1.6 Diagnosis

It has been recognized that spinal cord injuries are the cause of orthostatic hypotension in patients with spinal cord injuries, but it is necessary to determine the underlying diseases and conditions associated with the symptoms. An accurate assessment of the underlying causes is essential to determine the appropriate treatment recommendation. Laboratory studies (Table 25.3) may be needed to assess related conditions such as sepsis or dehydration with electrolyte imbalance and to rule out conditions such as hypoglycemia, which may have similar symptoms. A stepwise approach is recommended for the diagnosis of orthostatic hypotension, specifically starting with the measurement of orthostatic blood pressure and heart rate, followed by more detailed autonomic testing in some cases (Gibbons et al. 2017). Autonomic testing for

Table 25.3 Initial laboratory testing to evaluate individuals presenting with orthostatic hypotension

Laboratory test	Function in differential diagnosis of neurogenic and non-neurogenic OH
EKG	To evaluate cardiac electrical activity
CBC	To evaluate for anemia, or infection that could contribute to non-neurogenic orthostatic hypotension
Basic metabolic panel (sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine and fasting glucose)	To look for hypo/hypernatremia, hypo/hyperkalemia, acid–base disorders, blood volume depletion (BUN:Cr ratio [20 mg/dL:1 mg/dL]), renal dysfunction or diabetes
TSH	To evaluate for thyroid dysfunction
Vitamin B12 level, Methylmalonic acid	To look for evidence of vitamin B12 deficiency
Secondary laboratory tests (considered for use in select patients)	**Function in differential diagnosis of neurogenic and non-neurogenic OH**
Albumin	To identify poor nutrition or chronic illness
Liver enzyme testing, albumin	To evaluate for hepatic dysfunction in patients with weight loss and constitutional symptoms
Neurological antibody studies (paraneoplastic panel)	To identify autoantibodies; rarely indicated; only in patients with subacute onset of orthostatic hypotension in the presence of other neurological or constitutional symptoms suggesting an autoimmune or paraneoplastic syndrome. A pure autonomic failure syndrome should be tested for anti-ganglionic acetylcholine receptor antibodies
Serum and urine protein electrophoresis	To identify a monoclonal gammopathy; only in patients with features of peripheral neuropathy

From Gibbons et al. (2017), with permission

heart rate variability with deep breathing and during Valsalva maneuver as well as a HUT table test to assess orthostatic stress can be performed (Alexander et al. 2009; ASIA 2012; Claydon and Krassioukov 2008). If the onset or worsening of orthostatic hypotension is delayed after months or years after spinal cord injury, posttraumatic syringomyelia may be suspected, and appropriate diagnostic imaging such as spinal magnetic resonance imaging may be indicated.

The characteristic test for orthostatic hypotension is the measurement of change in blood pressure from supine, after at least 5 min of rest, to standing or HUT. Orthostatic hypotension is defined as a sustained fall of systolic blood pressure of at least 20 mmHg or a diastolic blood pressure of 10 mmHg within 3 min of standing or HUT to at least 60° on a tilt table (Freeman et al. 2011; The Consensus Committee of the American Autonomic Society and the American Academy of Neurology 1996). In particular, orthostatic hypotension in patients with supine hypertension (supine blood pressure ≥ 150/90 mmHg) applies different criteria: a decrease of 30 mmHg in systolic blood pressure or 15 mmHg in diastolic blood pressure (Freeman et al. 2011). The standard measurement of orthostatic hypotension is asking patients to rest in the supine position for at least 5 min, and then stand for 3 min, with blood pressure measurements taken just before standing and at 1 and 3 min of standing (Shibao et al. 2013). In the alternative method, patients sit for at least 5 min and then stand for 3 min, with blood pressure measured just before standing and at 1 and 3 min of standing. The use of a tilt table in the head-up position, at an angle of at least 60°, was accepted as an alternative (Low and Singer 2008). If the test is negative but symptoms are strongly suggesting orthostatic hypotension, a supine-to-standing blood pressure test or HUT should be considered. Healthy people typically experience a slight decrease in systolic blood pressure (<10 mmHg), a very slight increase in diastolic blood pressure (approximately 2.5 mmHg), and a slight increase in heart rate (10–20 bpm) (Freeman 2008; Gibbons et al. 2017). The most sensitive and consistent measurements are the ones obtained early in the morning, when patients are usually more symptomatic (Shibao et al. 2013).

Measuring the change in heart rate from the supine and/or sitting to standing can help distinguish between neurogenic orthostatic hypotension and non-neurogenic orthostatic hypotension (cariogenic, vascular, or iatrogenic). If a person develops orthostatic hypotension upon standing, an increase in heart rate of <15 bpm suggests a diagnosis of neurogenic orthostatic hypotension. In contrast, individuals with non-neurogenic orthostatic hypotension typically show an increase in heart rate of >15 bpm within 3 min of standing (Gibbons et al. 2017).

25.1.7 Management

For spinal cord injuries, a single treatment for orthostatic hypotension is not always effective. Success can be increased by combination and individualization of management (Figueroa et al. 2010). Once a patient has been diagnosed with orthostatic hypotension, the goal of treatment should not be to normalize blood pressure while standing. The main goals of treatment, however, should be to reduce symptom-related disability: to improve orthostatic blood pressure without excessive supine hypertension; to relieve orthostatic symptoms including reducing the fall risk; to improve standing time; and to improve physical capabilities in orthostatic activities of daily living and participation in rehabilitation. Symptoms of orthostatic hypotension can always be relieved, but doing so without inducing unacceptable supine hypertension is difficult because impaired baroreflexes and loss of postural regulation of blood pressure are common. Patients with asymptomatic orthostatic hypotension do not require treatment (Low and Singer 2008).

The first thing to do after diagnosing orthostatic hypotension is pharmacologic simplification by reducing or discontinuing medications that exacerbate orthostatic hypotension. Many medications, such as drugs for spasticity, bladder, hypertension, and pain, can cause orthostatic hypotension or worsen symptoms of orthostatic hypotension (Table 25.1). The next measure is a number of

non-pharmacological managements. If non-pharmacological measures do not sufficiently improve the symptom of orthostatic hypotension, pharmacotherapy should be initiated. Since orthostatic stress varies from moment to moment and drug treatment is suboptimal, it is necessary to combine pharmacological treatment of orthostatic hypotension with non-pharmacological approaches (Low and Singer 2008). Figure 25.2 is a flow diagram of the procedure for evaluating and treating orthostatic hypotension.

25.1.7.1 Non-Pharmacological Measures

Orthostatic hypotension is an important medical problem to be solved first in the rehabilitation process of patients with spinal cord injuries. This is because orthostatic hypotension interferes with the patient's normal postural changes and mobilities and participation in activities of daily living, thereby delaying rehabilitation and reducing quality of life (Figueroa et al. 2010). Some patients have limited evidence of effectiveness in

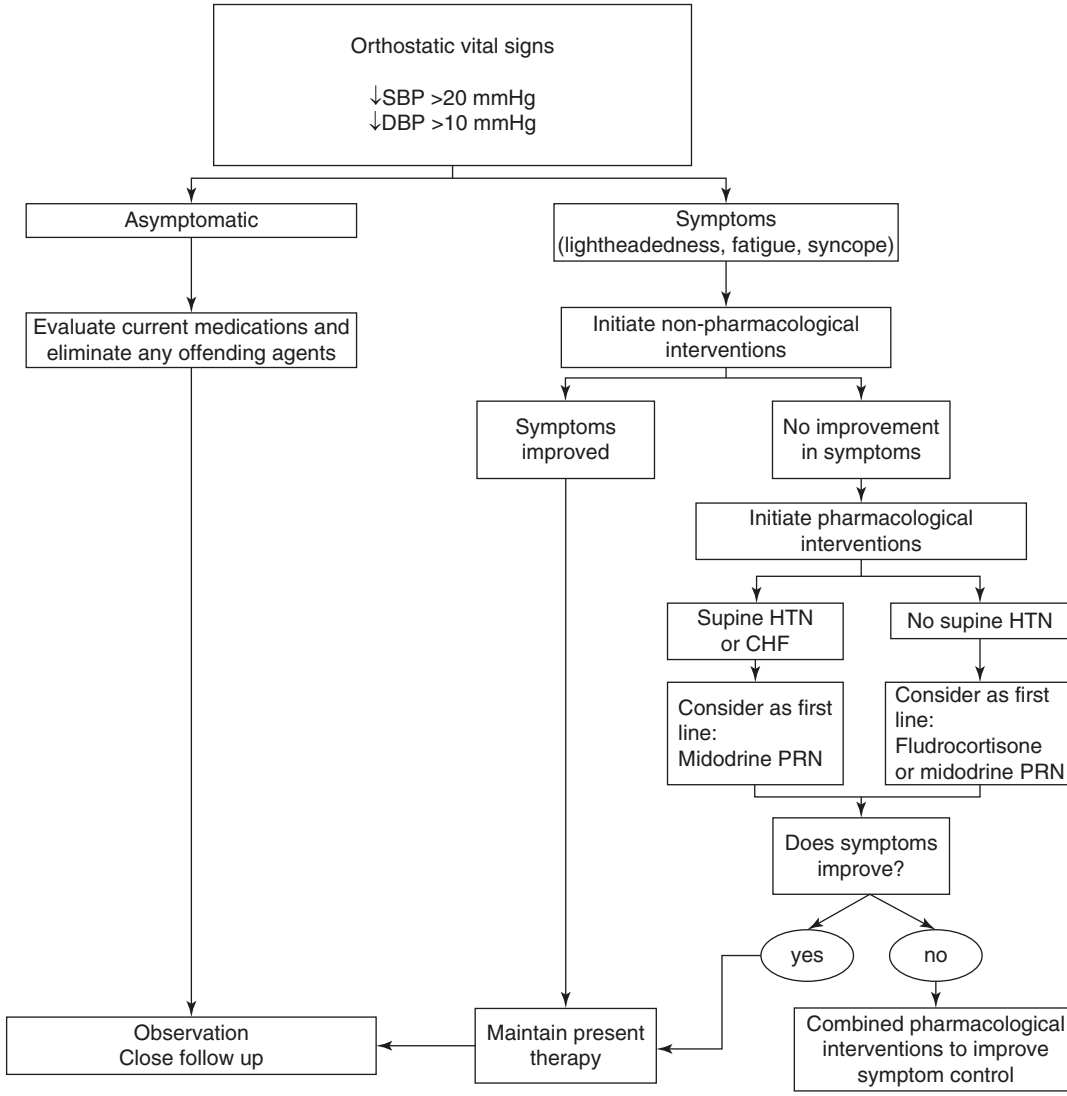

Fig. 25.2 Approach flow diagram for the evaluation and treatment of orthostatic hypotension. SBP systolic blood pressure, DBP diastolic blood pressure, HTN hypertension, CHF congestive heart failure, PRN as needed. From Shibao et al. (2013), with permission

spinal cord injury, but actual non-pharmacological measures can be used to minimize hypotensive effects (Figueroa et al. 2010; Freeman 2008). Patient medication review is essential, and modification may be necessary to minimize the hypotensive side effects. If the resting systolic blood pressure is less than 110 mmHg and the moderate resting hypotensive state persists, it will affect cognitive function and cause fatigue. In a patient with spinal cord injury, a drop in blood pressure due to postural changes in the presence of resting hypotension may lead to more severe symptoms than in normal blood pressure. In addition, if the usual low blood pressure is persisting, a slight increase in blood pressure may result in symptoms of autonomic dysreflexia more severe than expected (Gillis et al. 2008).

The management goal of orthostatic hypotension is not to normalize blood pressure. Therapeutic goals should be to prevent deterioration of function and quality of life due to orthostatic hypotension and serious consequences caused by hypotension. Therefore, the important thing in treatment is to increase the blood volume and reduce the retention of venous blood in the lower extremities. Patients and caregivers should avoid sudden head movements or abrupt changes in posture and early morning activity or postural change to promote orthostatic hypotension. Excessive exertion in high-temperature environments and rapid changes of position should be avoided. Repeated and gradual increase in postural changes, such as tilting table, can be helpful in the acute stages. A tilt-in-space or reclining wheelchairs are beneficial to accommodate the gradual increase in sitting angle and can be tilted in response to symptoms. Patients should gradually move from supine to upright, especially in the morning, and avoid exercise in hot weather. Hot showers and saunas should be avoided. It is important for patients not to stop exercising but rather to exercise in a recumbent or seated position, as these positions are better tolerated than the standing position. Exercise in the swimming pool is recommended as the hydrostatic pressure of the water counteracts the decrease in blood pressure caused by gravity and improves orthostatic tolerance. Note that patients should be very careful when getting out of the swimming pool, as the sudden decrease in hydrostatic pressure at the exiting the pool can trigger venous pooling and worsen symptoms of orthostatic hypotension (Palma and Kaufmann 2020). Low glycemic index carbohydrates are preferred, and frequent smaller meals is recommended.

When symptoms of orthostatic hypotension such as dizziness are seen, it is most important to prevent the cerebral ischemia by lying down the patient and elevating the legs. The goal of non-pharmacological treatment is to increase blood circulation and eliminate venous retention in the lower extremities. In particular, it may be beneficial to drink enough water just before eating and to increase salt intake in the morning to reduce the occurrence of postprandial orthostatic hypotension. When 500 mL of tap water is rapidly swallowed in 3–4 min, the effect of norepinephrine on blood vessel contraction is activated, and the systolic blood pressure of the upright posture is increased by 20 mmHg for 2 h. The blood pressure effect is observed in the first 5–10 min and peaks around 30 min after ingestion (Jordan et al. 2000). It is recommended to consume 2 L of water per day to maintain adequate plasma capacity.

Postprandial hypotension is prone to occur, and exposure to a hot environment may worsen symptoms of orthostatic hypotension. It is recommended to avoid intense exercise and to encourage mild or moderate aerobic exercise. Restricting water intake at night for nocturnal polyuria and voiding management, including an effective voiding schedule using intermittent catheterization, is prone to orthostatic hypotension in the morning. Patients should allow enough water intake before and during the morning and at 30 min before the activity begins. When a patient experiences an episode of orthostatic hypotension while sitting in a wheelchair, the legs are folded, and the flexion of the trunk is directed toward the thigh. In addition, patients with orthostatic hypotension or alpha-agonists may experience hypertension when they are lying down (Figueroa et al. 2010; Goldstein and Sharabi 2009; Wecht et al. 2016).

Alcohol and caffeine intake promotes diuretic and should be avoided. In addition, drugs and foods that dilate the blood vessels such as alcohol should be avoided and habit of eating regularly small amounts of food as possible to minimize postprandial hypotension. Patients may have more functional abilities before meals than in the hour following a meal and may adjust their activities accordingly. Although the benefits of salt loading in patients with spinal cord injuries have not been well demonstrated, liberalizing salt and water intake can lead to an increase in blood volume. In the morning, whatever the meal salt, 10 g of salt per day (5–6 g twice) are taken. Usually, a full teaspoon contains about 5–6 g of salt and put it in water or soup. Fludrocortisone and high-salt diet are prone to potassium deficiency, so it is recommended to consume bananas and vegetables rich in potassium. If the amount of sodium in the urine is less than 170 nmol for 24 h, additional 1–2 g of salt is required three times (El-Sayed and Hainsworth 1996). When blood pressure is elevated later in the day, physical exertion, such as exercise programs or physical therapy, may be better tolerated in the afternoon rather than early in the morning. Nocturnal diuresis, which sometimes occurs in spinal cord injury, may lead to insufficient blood volume (Gillis et al. 2008).

Abdominal binders and compressive stockings can be used to increase venous pressure and reduce venous pooling by reducing the capacity of the legs and abdominal vascular bed. In the standing posture, approximately 500 mL of blood flow stagnates in the lower limb, causing a relative hypovolemia to the whole body. Therefore, thigh-high compression stockings to the proximal femur and abdominal binder to physically compress the visceral vascular bed, such as splanchnic vascular bed, containing 20–30% of the total blood volume, results in an increase in systolic blood pressure of 11 mmHg and diastolic blood pressure of 6 mmHg in the upright posture. However, donning them can cause practical problems for people with spinal cord injury, and there is conflicting evidence of efficacy (Gillis et al. 2008; Goldstein and Sharabi 2009). Compression of 30–40 mmHg (at least 15–20 mmHg) is required to improve venous return and achieve a significant impact on blood pressure. Knee-high compression stockings are not effective. For abdominal binders, 40 mmHg compression is as just effective as midodrine in treating orthostatic hypotension (Okamoto et al. 2016).

Elevating the head of the bed by 5–10 inches (reverse Trendelenburg position) can reduce nocturnal diuresis, morning postural hypotension, morning supine hypertension, and hypovolemia. The posture activates the renin-angiotensin-aldosterone system during sleep, increases blood volume, and reduces sodium excretion during the night. Renin produces angiotensin II to contract peripheral blood vessels and angiotensin II promotes the release of norepinephrine and aldosterone, which reduces the loss of sodium and water. During sleep, the abdominal binder, compression stockings, and compression bandages help reduce blood accumulation below the level of injury. There is a risk of a significant drop in blood pressure when intrathoracic pressure increases by 20–30 mmHg. It is advisable to avoid excessive Valsalva maneuver or severe coughing and should observe blood pressure. Caution should be taken if the abdominal binder is worn incorrectly or pushed up during sleep, the chest is compressed, intrathoracic pressure rises, and blood pressure drops.

There is evidence for the role of functional electrical stimulation in the treatment of orthostatic hypotension in spinal cord injury. Functional electrical stimulation-induced contraction of the leg muscles can increase venous return, increasing cardiac output and stroke volume, which can increase blood pressure and reduce symptoms associated with hypotension. The response appears to be dose-dependent and appears to be independent of the stimulation site. Further research in this area is needed. Biofeedback has also been used to manage orthostatic hypotension in spinal cord injury. Evidence for use of body weight-supported treadmill training to improve orthostatic tolerance is not currently sufficient. The non-pharmacological managements described above are summarized in Table 25.4.

25.1.7.2 Pharmacological Management

Medication, like non-pharmacological management, also aims to increase blood volume and reduces venous blood retention. Drugs with sympathetic effects, either directly or indirectly, are used. Several drugs have been used to treat orthostatic hypotension, but their effects vary. The most experienced drugs for orthostatic hypotension associated with spinal cord injury include midodrine, fludrocortisone, droxidopa, ephedrine, midodrine, and pseudoephedrine (Lamarre-Cliché 2002) (Table 25.5). Among them, midodrine and droxidopa have been approved by the Food and Drug Administration (FDA) for the treatment of neurogenic orthostatic hypotension (Gibbons et al. 2017; Mitka 2012). A summary of the commonly used sympathomimetic medications for orthostatic hypotension and their side effects is shown in Table 25.6.

Table 25.4 Non-pharmacological managements used in the management of orthostatic hypotension

To be avoided
Sudden head-up postural change
Prolonged recumbency
Straining during micturition and defecation
High environmental temperature including hot baths
Drugs with vasodepressor properties
To be introduced
Head-up tilt during sleep
High-salt intake
Adopting different body positions
Physical activity with recumbent exercises
To be considered
Elastic stocking
Waist-high compressing stocking (15–20 mmHg pressure)
Abdominal binders
Water ingestion

Midodrine

Midodrine is a direct α1-agonist. Midodrine binds to and activates adrenergic receptors in the arterial and venous vessels, which leads to an increase in vascular tone and blood pressure. The minimum effective dose is 5 mg, but most patients respond best to 10 mg (Low and Singer 2008). Usually, 5 mg are taken two to three times and 10 mg can be taken three times. The duration of action is as short as 2–4 h and shows a very fast effect, reaching the peak serum concentration at 0.5–1.0 h after oral administration. If administrated three times a day, administration is desirable before the morning, before lunch, and in the early evening (Figueroa et al. 2010). If the blood pressure is 180/100 mmHg or higher when lying or sitting, midodrine should not be given. If the plasma volume is not sufficient, the effect of vasoconstriction is reduced. Sufficient water consumption is recommended. Midodrine increases bladder neck pressure due to its alpha-agonist effect, which aggravates urinary voiding. It has common adverse effects such as pruritus of the

Table 25.5 Commonly used drugs for orthostatic hypotension in spinal cord injuries

Medication	Mechanism	Dose	Side effects	Considerations
FDA approved for orthostatic hypotension				
Midodrine	Alpha1-adrenergic receptor agonist	2.5–10 mg BID or TID	• Supine hypertension • Piloerection, pruritus	• Until mid-afternoon • Supine hypertension
Droxidopa	Synthetic norepinephrine precursor	100–600 mg TID	• Supine hypertension • Headache, nausea, fatigue	• Dosed morning, midday, and 3–4 h before bedtime
FDA not approved for orthostatic hypotension				
Fludrocortisone	• Renal sodium and water retention • Synthetic mineralocorticoid	0.1–0.4 mg daily	• Hypokalemia • Supine hypertension • Edema • Weight gain • Interaction with warfarin (decrease warfarin effect)	• Dose increase not faster than biweekly
Ephedrine	Nonselective sympathomimetic	25–50 mg TID	• Anxiety • Supine hypertension	• p.r.n 15–30 min before arising

Table 25.6 Sympathomimetic agents for management of orthostatic hypotension

Pharmacologic agent	Mechanism of action	Dose	Side effects
Direct actions			
Midodrine HCL	Alpha1-adrenergic agonist with activation of arteriolar and venous vasculature, and decreases venous pooling	2.5–10 mg every 3–4 h, to maximal dose of 50–60 mg	Piloerection, urinary retention, supine hypertension, anxiety
Mixed direct and indirect actions			
Ephedrine, Pseudoephedrine	Stimulation alpha/beta receptors Action depends on receptors and baroreceptor defects	12.5–25 mg TID, 30–60 mg TID	Nervousness, tremors, anxiety, insomnia, agitation, arrhythmias, supine hypertension
Phenylpropanolamine	Action depends on norepinephrine release from postganglionic neurons	12–25 mg TID	Nervousness, tremors, anxiety, insomnia
Methylphenidate		5–10 mg TID dose before 6 PM	Agitation, arrhythmias, supine hypertension
Antagonists			
Clonidine	Antagonizes alpha2-adrenoreceptors	0.1–0.8 mg in divided doses	Dry mouth, tiredness, sedation, altered mental status, hypertension
Yohimbine		5.4 mg doses	Unpredictable response, hypertension, anxiety, mood stimulation

scalp and piloerection. Because of the characteristic side effects of midodrine, it can be misdiagnosed as a symptom of autonomic dysreflexia. In particular, sensitivity to midodrine is very high because of its high sensitivity to catecholamines in patients with autonomic dysreflexia and with combination therapy with midodrine and fludrocortisone. It is recommended to increase the dose of midodrine very gradually. All sympathomimetic medications should be taken in the morning before getting up and in the early evening, because of the risk of supine hypertension (≥150/90 mmHg) at night (Wecht et al. 2016). Patients are advised to take the drug before getting out of bed, before lunch, and the mid-afternoon (Low and Singer 2008). Midodrine should not be taken after 6 PM, at least 5 h before sleep to avoid nocturnal supine hypertension. Patients are also advised to skip a dose if supine or sitting blood pressure is 180/110 mmHg or higher.

Fludrocortisone

The mineralocorticoid, fludrocortisone, reduces the excretion of sodium and water, increases blood volume, and increases the sensitivity of α-adrenergic receptors. It is used when the plasma volume does not increase while salt intake is sufficient, or when orthostatic hypotension is not treated even with midodrine administration (Groomes and Huang 1991). If 0.1–0.2 mg/day is used and orthostatic hypotension is not controlled, increase to 0.4–0.6 mg/day. It is usually given 0.1–0.2 mg before bed, and it is recommended to raise the head by 30 cm. When body weight increases by 2 kg with fludrocortisone, plasma volume is thought to increase appropriately. Fludrocortisone may cause hypokalemia and supine hypertension and should not be used for the elderly or patients with congestive heart failure or chronic renal failure due to water retention. For the person with fludrocortisone, it is often necessary to measure serum potassium and supine blood pressure. In addition, the interaction of drugs with warfarin inhibits the prolongation of INR with warfarin. The onset of action occurs over 3–7 days. The main side effects of fludrocortisone are supine hypertension, hypokalemia, and edema. Supine hypertension and hypokalemia are very common, especially at higher doses (Maule et al. 2007).

Droxidopa

Droxidopa (L-Threo-3,4-dihydroxyphenylserine) is a synthetic amino acid approved by the FDA in 2014 for use in the treatment of symptomatic neurogenic orthostatic hypotension. However, the use of droxidopa for the treatment of orthostatic hypotension in patients with spinal cord injuries is not well established. Droxidopa is an orally administered norepinephrine prodrug that is converted to norepinephrine both in the central nervous system and in peripheral tissues, including sympathetic peripheral nerve endings. The increase in circulating plasma level of norepinephrine peaks 6 h after administration of droxidopa, and norepinephrine levels remain elevated for at least 46 h. It is believed that neural norepinephrine replenishment is the primary mechanism of action for improving standing blood pressure with droxidopa (Gibbons et al. 2017; Kaufmann 2008). Droxidopa improves orthostatic hypotension with less supine hypertension than standard drugs such as midodrine (Low and Singer 2008). The starting dose of droxidopa is 100 mg three times a day and can be titrated up to 1800 mg per day during waking hours. A recommended dosing schedule would be at 8 AM, noon, and 4 PM (Gibbons et al. 2017). As with other drugs used to treat orthostatic hypotension, it is not recommended to take droxidopa within 5 h of bedtime to avoid the risk of supine hypertension (Chisholm and Anpalahan 2017). Side effects with droxidopa included headache, dizziness, nausea, fatigue, and supine hypertension.

Pyridostigmine

Pyridostigmine, an acetylcholinesterase inhibitor, improves ganglionic transmission mainly when the patient is standing. It increases orthostatic blood pressure without worsening supine hypertension. The dose is started with 30 mg two or three times a day and gradually increased to 60 mg three times a day (Low and Singer 2008). The main side effects are cholinergic hyperactivity, which can worsen detrusor overactivity and decrease vesical capacity and abdominal colic in spinal cord injuries.

Other Drugs

Amezinium methylsulfate (Risumic®) inhibits MAO activity and interferes with norepinephrine uptake, increasing norepinephrine leading to high blood pressure by vasoconstriction (Jones et al. 2015; Kaufmann 2008). Desmopressin is used when nocturnal polyuria causes orthostatic hypotension in the morning, nocturnal frequency, and bladder overdistention. Desmopressin is given orally or nasally, but there is a risk of supine hypertension, hyponatremia, and water poisoning. Desmopressin is administered 0.1–0.2 mg orally or by nasal spray (0.5 mg/5 mL) at the rate of 10 μg per puff. The dose can be controlled while watching urine formation as needed.

Although various supplementary agents have been used to treat orthostatic hypotension, there is little or no published experience in treating orthostatic hypotension associated with spinal cord injury. These include physostigmine, recombinant human erythropoietin, the vasopressin analog desmopressin (DDAVP), and the somatostatin analog octreotide. Nonsteroidal anti-inflammatory drugs such as indomethacin or ibuprofen work by inhibiting prostaglandin-induced vasoconstriction. Clonidine has been reported to cause a paradoxically beneficial increase in blood pressure in some patients with orthostatic hypotension (Krassioukov et al. 2009).

25.2 Postprandial Hypotension

Abnormally low systolic blood pressure following a meal is termed postprandial hypotension. Postprandial hypotension is usually defined as a decrease of ≥20 mmHg in systolic blood pressure or a systolic blood pressure of <90 mmHg after having been >100 mmHg before the meal, either occurring within 2 h after completion of the meal (Jansen and Lipsitz 1995; Pavelić et al. 2017; Trahair et al. 2014). Spinal cord injury has a profound effect on gastrointestinal function, causing delayed gastric emptying and colonic transit time. Although splanchnic blood flow is under autonomic control, it is unclear how spinal

cord injury affects postprandial intestinal blood flow (Fynne et al. 2012; Kao et al. 1999). The prevalence of postprandial hypotension that meets the criteria for postprandial hypotension is about 50% of people with spinal cord injuries, and the risks increases with increasing age, higher levels of spinal cord injuries, and lesion completeness (Hansen et al. 2021). Postprandial hypotension is associated with an increased risk of falls, syncope, coronary events, stroke, asymptomatic lacunar infarction, asymptomatic cerebrovascular damage, and death (Hansen et al. 2021; Luciano et al. 2010). Management begins with eating smaller and more frequent meals with low carbohydrates and avoiding alcohol. Midodrine taken just before or with meals can also help (Palma and Kaufmann 2020).

25.3 Supine Hypertension

Supine hypertension is a common finding in autonomic failure and complicates the treatment of the orthostatic hypotension. Supine hypertension can worsen orthostatic hypotension. Supine hypertension in patients with neurogenic orthostatic hypotension is defined as a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg while in the supine position (Fanciulli et al. 2018). General treatment guidelines recommend intervention for hypertension, but supine hypertension associated with orthostatic hypotension requires additional considerations. In patients with autonomic dysfunction causing orthostatic hypotension, supine hypertension is common and part of the underlying disease process because these patients lack the normal blood pressure buffering mechanisms that offset hypertension. In addition, frequent periods of orthostatic hypotension can lead to chronic activation of the renin–angiotensin system. Supine systolic blood pressure of up to 160 mmHg should be monitored but usually does not warrant treatment, especially if symptoms of orthostatic hypotension have improved. The management of supine hypertension is recommended intervention if systolic blood pressure exceeds 160–180 mmHg (Arnold and Biaggioni 2012; Gibbons et al. 2017).

The supine assessment should be performed in the morning before arising and at bedtime, with the patient in their normal sleeping position with the head of the bed raised. If supine hypertension of systolic blood pressure of 160–180 mmHg or diastolic blood pressure of 90–100 mmHg occurs in patients with orthostatic hypotension, the treatment decision should be individualized. The best approach to management of supine hypertension is prevention. Management of supine hypertension includes avoiding recumbency during the day, especially when using compression devices or pressor agents; sleeping with the head of the bed raised; taking carbohydrate-rich snacks at bedtime; and avoiding liquid within an hour of bedtime. Alcohol may be used in appropriate clinical circumstances. The judicious use of pressor agents for orthostatic hypotension is an important aspect of managing supine hypertension (Chisholm and Anpalahan 2017). Midodrine and other pressor drugs should not be taken after 4–6 PM. Managements to control supine hypertensions are listed in Table 25.7.

If non-pharmacological measures are not successful or if patients with orthostatic hypotension develop severe supine hypertension of systolic blood pressure of >180 mmHg or diastolic blood pressure of >110 mmHg, they can be treated in the evening or at bedtime using short-acting antihypertensive agents (captopril 25 mg, losartan 50 mg, or nitroglycerin patch 0.1 mg/h) (Table 25.8). At night, tilting the head of the bed to a 30° or 45° angle lowers blood pressure. In

Table 25.7 Managements to control supine hypertension

1.	Avoid supine position during daytime.
2.	Patients can sit in a reclining chair with their feet on the floor when they need rest.
3.	Avoid pressure medications after 4 pm.
4.	Elevated the bed head by 20–30 cm.
5.	Have a snack just before going to bed to reduce postprandial hypotension.
6.	Fludrocortisone can exacerbate supine hypertension. Switching to short-acting pressor agents such as midodrine or droxidopa may be beneficial.

Adapted from Arnold and Biaggioni (2012)

Table 25.8 Proposed treatment for supine hypertension

Treatment options	Mechanism of action	Typical dose
Captopril	ACE inhibitor	25 mg qhs
Clonidine	Central α2-agonist	0.2 mg with evening meal
Hydralazine	Peripheral smooth muscle relaxant	10–25 mg ahs
Losartan	Angiotensin II receptor antagonist	50 mg qhs
Nitroglycerine patch	Vasodilator	0.1 mg/h patch qhs (remove patch in the early morning)

From Gibbons et al. (2017), with permission
Short-acting antihypertensive drugs used to treat supine hypertension should only be administered at bedtime, not during daytime hours. Many drugs have BID or TID as the recommended dosing regimen, and patients may accidentally start taking these medications during daytime hours and worsen symptoms of orthostatic hypotension. Use of clonidine carries a risk of a morning" hangover" effect

particular, nocturnal bathroom visits can be dangerous if supine hypertension is treated too aggressively. It is also important for these patients to avoid the use of diuretics and long-acting antihypertensive agents. Patients with orthostatic hypotension should avoid the supine posture during the day. A head-up reclining posture is recommended for rest (Gibbons et al. 2017).

References

Alexander MS, Biering-Sorensen F, Bodner D, et al. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord. 2009;47:36–43.

American Spinal Injury Association (ASIA). International standards to document remaining autonomic function after spinal cord injury. Atlanta, GA: American Spinal Injury Association; 2012.

Arnold AC, Biaggioni I. Management approaches to hypertension in autonomic failure. Curr Opin Nephrol Hypertens. 2012;21:481–5.

Biaggioni I, Robertson D, Krantz S, et al. The anemia of primary autonomic failure and its reversal with recombinant erythropoietin. Ann Intern Med. 1994;121:181–6.

Bilello JF, Davis JW, Cunningham MA, et al. Cervical spinal cord injury and the need for cardiovascular intervention. Arch Surg. 2003;138:1127–9.

Bradley JG, Davis KA. Orthostatic hypotension. Am Fam Physician. 2003;68:2393–8.

Chisholm P, Anpalahan M. Orthostatic hypotension: pathophysiology, assessment, treatment and the paradox of supine hypertension. Intern Med J. 2017;47:370–9.

Claydon VE, Krassioukov AV. Orthostatic hypotension and autonomic pathways after spinal cord injury. J Neurotrauma. 2006;23:1713–25.

Claydon VE, Krassioukov AV. Clinical correlated of frequency analyses of cardiovascular control after spinal cord injury. Am J Physiol Heart Circ Physiol. 2008;294:H668–78.

Claydon VE, Steeves JD, Krassioukov A. Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord. 2006;44:341–51.

Consortium for Spinal Cord Medicine. Evaluation and management of autonomic dysreflexia and other autonomic dysfunctions: preventing the highs and lows. Management of blood pressure, sweating, and temperature dysfunction. Washington, DC: Paralyzed Veterans of America; 2020. https://pva.org/research-resources/publication/

Deegan BMT, O'Connor M, Donnelly T, et al. Orthostatic hypotension: a new classification system. Europace. 2007;9:937–41.

Dumont RJ, Okonkwo DO, Verma S, et al. Acute spinal cord injury, part I: pathophysiologic mechanisms. Clin Neurophamacol. 2001;24:254–64.

El-Sayed H, Hainsworth R. Salt supplementation increases plasma volume and orthostatic tolerance in patients with unexplained syncope. Heart. 1996;75:134–40.

Faghri PD, Yount JP, Pesce WJ, et al. Circulatory hypokinesis and functional electric stimulation during standing in persons with spinal cord injury. Arch Phys Med Rehabil. 2001;82:1587–95.

Fanciulli A, Jordan J, Biaggioni I, et al. Consensus statement on the definition of neurogenic supine hypertension in cardiovascular autonomic failure by the American Autonomic Society (AAS) and the European Federation of Autonomic Societies (EFAS) : Endorsed by the European Academy of Neurology (EAN) and the European Society of Hypertension (ESH). Clin Auton Res. 2018;28:355–62.

Figueroa JJ, Basford JR, Low PA. Preventing and treating orthostatic hypotension: as easy as A, B, C. Cleve Clin J Med. 2010;77:298–306.

Freeman R. Clinical practice. Neurogenic orthostatic hypotension. N Engl J Med. 2008;358:615–24.

Freeman R, Wieling W, Axelrod FB, et al. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. Auton Neurosci. 2011;161:46–8.

Furlan JC, Fehlings MG, Shannon P, et al. Descending vasomotor pathways in humans: correlation between axonal preservation and cardiovascular dysfunction after spinal cord injury. J Neurotrauma. 2003;20:1351–63.

Fynne L, Worsøe J, Gregersen T, et al. Gastric and small intestinal dysfunction in spinal cord injury patients. Acta Neurol Scand. 2012;125:123–8.

Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. J Neurol. 2017;264:1567–82.

Gillis DJ, Wouda M, Hjeltnes N. Non-pharmacological management of orthostatic hypotension after spinal cord injury: a critical review of the literature. Spinal Cord. 2008;46:652–9.

Goldstein DS, Pechnik S, Holmes C, et al. Association between supine hypertension and orthostatic hypotension in autonomic failure. Hypertension. 2003;42:136–42.

Goldstein DS, Sharabi Y. Neurogenic orthostatic hypotension: a pathophysiological approach. Circulation. 2009;119:139–46.

Gonzalez F, Chang JY, Banovac K, et al. Autoregulation of cerebral blood flow in patients with orthostatic hypotension after spinal cord injury. Paraplegia. 1991;29:1–7.

Groomes TE, Huang CT. Orthostatic hypotension after spinal cord injury: treatment with fludrocortisone and ergotamine. Arch Phys Med Rehabil. 1991;72:56–8.

Hansen RM, Krogh K, Sundby J, et al. Postprandial hypotension and spinal cord injury. J Clin Med. 2021;10:1417.

Illman A, Stiller K, Williams M. The prevalence of orthostatic hypotension during physiotherapy treatment in patients with an acute spinal cord injury. Spinal Cord. 2000;38:741–7.

Iwanczyk L, Weintraub NT, Rubenstein LZ. Orthostatic hypotension in the nursing home setting. J Am Med Dir Assoc. 2006;7:163–7.

James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311:507–20.

Jansen RW, Lipsitz LA. Postprandial hypotension: epidemiology, pathophysiology, and clinical management. Ann Intern Med. 1995;122:286–95.

Jegede AB, Rosado-Rivera D, Bauman WA, et al. Cognitive performance in hypotensive persons with spinal cord injury. Clin Auton Res. 2010;20:3–9.

Jones PK, Shaw BH, Raj SR. Orthostatic hypotension: managing a difficult problem. Expert Rev Cardiovasc Ther. 2015;13:1263–76.

Jordan J, Shannon JR, Black BK, et al. The pressor response to water drinking in humans: a sympathetic reflex? Circulation. 2000;101:504–9.

Kao CH, Ho YJ, Changlai SP, et al. Gastric emptying in spinal cord injury patients. Dig Dis Sci. 1999;44:1512–5.

Kaufmann H. L-dihydroxyphenylserine (Droxidopa): a new therapy for neurogenic orthostatic hypotension: the U.S. experience. Clin Auton Res. 2008;18(Suppl 1):19–24.

Krassioukov A, Eng JJ, Warburton DE, Teasell R. Spinal cord injury rehabilitation evidence research team. A systematic review of the management of orthostatic hypotension after spinal cord injury. Arch Phys Med Rehabil. 2009;90:876–85.

Lamarre-Cliché M. Drug treatment of orthostatic hypotension because of autonomic failure or neurocardiogenic syncope. Am J Vardiovasc Drugs. 2002;2:23–35.

Lehmann KG, Lane JG, Piepmeier JM, et al. Cardiovascular abnormalities accompanying acute spinal cord injury in humans: incidence, time course and severity. JACC. 1987;10:46–52.

Low PA, Sandroni P, Benarroh EE. Chapter 1. Clinical autonomic disorders: classification and clinical evaluation. In: Low PA, Benarroh EE, editors. Clinical autonomic disorders. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 8–9.

Low PA, Singer W. Management of neurogenic orthostatic hypotension: an update. Lancet Neurol. 2008;7:451–8.

Luciano GL, Brennan MJ, Rothberg MB. Postprandial hypotension. Am J Med. 2010;123:281.e1–6.

Mathias CJ. Orthostatic hypotension and paroxysmal hypertension in humans with high spinal cord injury. Prog Brain Res. 2006;152:231–43.

Mathias CJ, Christensen NJ, Corbett JL, et al. Plasma catecholamines, plasma renin activity and plasma aldosterone in tetraplegic man, horizontal and tilted. Clin Sci Mol Med. 1976;49:291–9.

Maule S, Papotti G, Naso D, et al. Orthostatic hypotension: evaluation and treatment. Cardiovasc Hematol Disord Drug Targets. 2007;7:63–70.

Mitka M. Trials to address efficacy of midodrine 18 years after it gains FDA approval. JAMA. 2012;307:1124–7.

Myers J, Lee M, Kiratli J. Cardiovascular disease in spinal cord injury. Am J Phys Med Rehabil. 2007;86:1–11.

Nobunaga AI. Orthostatic hypotension in spinal cord injury. Top Spinal Cord Inj Rehabil. 1998;4:73–80.

Okamoto LE, Diedrich A, Baudenbacher FJ, et al. Efficacy of servo-controlled splanchnic venous compression in the treatment of orthostatic hypotension: a randomized comparison with midodrine. Hypertension. 2016;68:418–26.

Palma JA, Kaufmann H. Management of orthostatic hypotension. Continuum (Minneap Minn). 2020;26:154–77.

Pavelić A, Krbot Skorić M, Crnošija L, et al. Postprandial hypotension in neurological disorders: systematic review and meta-analysis. Clin Auton Res. 2017;27:263–71.

Rowell LB, Detry JM, Blackmon JR, et al. Importance of the splanchnic vascular bed in human blood pressure regulation. J Appl Physiol. 1972;32:213–20.

Shibao C, Lipsitz LA, Biaggioni I, et al. Evaluation and treatment of orthostatic hypotension. J Am Soc Hypertens. 2013;7:317–24.

Teasell RW, Arnold MO, Kraussioukov A, et al. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. Arch Phys Med Rehabil. 2000;81:506–156.

The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. Neurology. 1996;46:1470.

Trahair LG, Horowitz M, Jones KL. Postprandial hypotension: a systematic review. J Am Med Dir Assoc. 2014;15:394–409.

Wecht JM, Krassioukov AV, Alexander M, et al. International Standards to document Autonomic Function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.

Wecht JM, Bauman WA. Implication of altered autonomic control for orthostatic tolerance in SCI. Auton Neurosci. 2018;209:51–8.

Wecht JM, Weir JP, Martinez S, et al. Orthostatic hypotension and orthostatic hypertension in American veterans. Clin Auton Res. 2016;26:49–58.

Weimer LH, Zadeh P. Neurological aspects of syncope and orthostatic intolerance. Med Clin N Am. 2009;93:427–49.

WHO. Arterial hypertension. Report of a WHO expert committee. World Health Organ Tech Rep Ser. 1978;628:7–56.

Recommended Additional Reading

Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.

Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation, Phys Med Rehabil Clin N Am. Philadelphia, PA: Elsevier; 2014.

Cardenas DD, Hooton TM. editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Engler GL, Cole J, Merton WL, editors. Spinal cord diseases: diagnosis and treatment. New York: Marcel Dekker Inc.; 1998.

Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston: Butterworth-Heinemann; 1996.

Lee BY, Ostrander LE, editors. The spinal cord injured patient. 2nd ed. New York: Demos; 2002.

Low PA, Benarroh EE, editors. Clinical autonomic disorders. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008.

Preston RA. Acid-base, fluids and electrolytes: made ridiculously simple. 2nd ed. Miami: MedMaster, Inc.; 2011.

Stuhal W, Lehrmann H, Franciulli A, et al., editors. Bedside approach to autonomic disorders. Cham: Springer; 2017.

Vodusek DB, Boller F. Neurology of sexual and bladder disorders. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, third series, vol. 130. London: Elsevier; 2015.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

26 Deep Vein Thrombosis and Pulmonary Embolism in Spinal Cord Injuries

Deep vein thrombosis is emphasized as a major clinical problem in patients with spinal cord injuries due to their high prevalence, high morbidity and mortality rates, changes in clinical symptoms due to the neurological deficit in the lower extremities, and availability of effective prophylactic and therapeutic strategies (Ryken et al. 2013; Watson 1968). Despite growing awareness of this potentially life-threatening condition and improved preventive measures, thromboembolism continues to occur with a significant frequency, especially in the acute period following injury (Chen 2003). Venous thromboembolism, which includes deep vein thrombosis and pulmonary embolism, is a common and serious health problem in people with spinal cord injuries.

Deep vein thrombosis is the most common peripheral vascular disorder in people with spinal cord injuries. The prevalence of deep vein thrombosis in patients with spinal cord injuries is between 5.3% and 64% when prophylaxis is used and between 47% and 100% when no prophylactic measures are used (Furlan and Fehlings 2007; Mackiewicz-Milewska et al. 2016; Teasell et al. 2009). The known incidence of deep vein thrombosis among patients with spinal cord injuries is roughly 12–100%. Variability of these wide ranges of prevalence rates is influenced by time after spinal cord injury, the associated risk factors, the diagnostic modalities, and the presence of prevention and prevention modalities. The incidence of deep vein thrombosis and pulmonary embolism is high in the first 3 months after a spinal cord injury, thus emphasizing the prophylaxis of this period reasonably. The development of deep vein thrombosis is relatively rare in children with spinal cord injuries (Vogel and Anderson 2003). In a series, no deep vein thrombosis was identified in children under 5 years of age, and only 1.9% of those 6–12 years of age from 7.9 to 9.1% in adolescents (Vogel and Anderson 2003). Venous thromboembolism is known to be a higher percentage of deaths during the first year after spinal cord injuries, approximately 9.7% (Furlan and Fehlings 2007).

Patients with spinal cord injuries have a particularly high risk of developing deep vein thrombosis (Watson 1968). In patients with spinal cord injuries, the loss of active calf muscle pump in the paralyzed limbs significantly reduces blood flow. As a result, sluggishness of venous return is further exacerbated by the hypercoagulability associated with spinal cord injury. In combination with the pressure that the bed exerts on the calf muscles, this sluggishness causes the bedridden spinal cord injured patient to be at high risk of developing deep vein thrombosis. The deep veins involved may be distal, the soleal and peroneal vessels, or proximal, the popliteal, femoral, and iliac veins. Clots in the proximal veins usually become embolized to the lung (Messier 2005; Moser and LeMoine 1981; Muriel et al. 2003). Asymptomatic venous thromboembolism

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is particularly common in spinal cord injuries due to absent or decreased pain sensitivity and impaired autonomic function.

26.1 Pathophysiology

Deep vein thrombosis is common in patients with spinal cord injury and can cause a fatal pulmonary embolism. Most pulmonary embolisms occur in the proximal vein of the legs (Moser and LeMoine 1981). Small emboli can be clinically silent and physiologically well tolerated. Larger emboli can cause lung infarction. Important factors in preventing venous thromboembolism are increasing venous flow, decreasing blood viscosity, preserving endothelium, and maintaining an adequate concentration of circulating anticoagulants.

The exact role of immobilization to induce thrombus formation processes is unknown, but several possible mechanisms have been proposed (Table 26.1). Three factors that affect the occurrence of deep vein thrombosis are venous stasis, hypercoagulability, and vessel injury, and in bedridden spinal cord injury patients, one can add pressure on the calf muscles. Virchow's triad of risk factors for deep vein thrombosis includes hypercoagulability, decreased blood flow (venous stasis), and vessel wall damage. There are at least the first two factors in patients with spinal cord injury. Without muscle pumping action to empty the leg veins, dehydration and edema increase blood viscosity. Edema refers to the loss of fluid to the extravascular space. Continuous external pressure on more superficial veins due to immobility and edema can cause vascular damage.

Table 26.1 Factors associated with the hypercoagulability of immobilization

Factor	Description
Rheologic	• Decreased venous emptying because of impaired muscular pumping • Increased viscosity because of dehydration, transudation of fluid into soft tissues, and raised fibrinogen levels
Vascular	• Trauma to vessel wall caused by extrinsic pressure on immobile limbs
Clotting constituents	• Increased levels of procoagulants (factor VIII, von Willebrand factor, fibrinogen) associated with stress and trauma • Decrease in antithrombin III accompanying protein wasting • Reduction in fibrinolytic activity due to lack of muscular contraction and increase in plasminogen activator inhibitor-1

In venous stasis, both volume and flow rate are reduced. The exact mechanism of the thrombus formation due to venous stasis is uncertain, but after the onset of thrombus formation, the thrombus develops rapidly, grows, and extends into the lumen of the blood vessels, causing more stasis. Immobility is the most common precipitating factor in the development of venous thrombosis. The contraction of the calf muscles compresses the veins and expels them into the proximal portion of the larger veins. Repetitive contractions thus lead to the emptying of the deep veins. Without the calf muscle pump activity in patients with spinal cord injuries, the development of venous stasis, platelet aggregation, and activation of the coagulation system are promoted.

The stress associated with spinal cord injury can increase the levels of important procoagulants such as factor VIII, von Willebrand factor, and fibrinogen, and platelet aggregation is enhanced (Rossi et al. 1980). Factor VIII antigen (meaning endothelial damage) and factor VIII procoagulant activity increase during the 10–12 days of immobilization in acute spinal cord injury. Fibrinolytic activity decreases during the first 24 h after spinal cord injury. Factor VII and VIII activities are higher in patients with spinal cord injury. Factor VIII antigens and procoagulant activity ratio greater than 2:1 are predictive of the occurrence of deep vein thrombosis.

The endothelium of the blood vessels is important for preventing thrombus formation because it contains several antithrombotic substances such as tissue plasminogen activator, prostacyclin, and many glycosaminoglycans (Peterson 1986). Endothelial damage resulting in subendothelial exposure provides a stimulus for thrombus formation as the platelets adhere, aggregate, and release the contents of their secretory granules (Baumgartner et al. 1976).

26.2 Diagnosis

26.2.1 Deep Vein Thrombosis

Clinical diagnosis of deep vein thrombosis may not be accurate. The symptoms and signs are usually related to clinical presentations commonly found in a variety of other disorders such as heterotopic ossification or cellulitis. Diagnostic studies are becoming more important because of the lack of awareness of physical signs of deep vein thrombosis, such as calf pain in patients with spinal cord injury. For the diagnosis of deep vein thrombosis, unilateral venous stasis edema and unexplained fever in patients with spinal cord injury should be considered (Hadley et al. 2013; Koopman and Bossuyt 2003). Problems such as cellulitis, heterotopic ossification, hematoma, or fractures should be excluded. A summary of the various diagnostic tests for deep vein thrombosis described above is provided in Table 26.2. Diagnostic algorithm of deep vein thrombosis is

Table 26.2 Objective diagnostic tests of deep vein thrombosis

Test	Feature of DVT leading to positive test	Advantages	Disadvantages
Plethysmography (electrical, mechanical)	• Obstruction	• Noninvasive • Sensitive to proximal DVT • Objective • Equipment portable–can be taken to bedside	• Indirect • Less sensitive to calf DVT and incompletely obstructing DVT • Equipment expensive, requires technician • Extrinsic impression may give possible result
Doppler ultrasound	• Obstruction • Evidence of collateral circulation (less reliable)	• Noninvasive • Sensitive to proximal DVT • Equipment relatively inexpensive • Equipment portable–can be taken to bedside • Some assessment of venous incompetence is possible	• Indirect • Less sensitive to calf DVT and incompletely obstructing DVT • Subjective–requires some experience
^{125}I-labeled fibrinogen	Active thrombus formation	• Most sensitive method available for diagnosing calf DVT • Detects early, actively forming thrombus–can be used for prospective monitoring of high-risk patients (e.g., spinal cord injury) • Minimally invasive–can be done at patient's bedside	• Not valid in upper thigh DVT • Usually takes at least 24–48 h for diagnosis • Will not detect if thrombus not actively forming • Anticoagulants may lead to false-positive results • Other causes of inflammation or hematoma may lead to false-positive results
Radionuclide (imaging) venography	• Obstruction, collateral circulation • Uptake by thrombus and/or endothelium	• Can obtain pulmonary perfusion scan at same time • Minimally invasive–easily repeatable	• Less sensitive to calf or incompletely obstructing DVT
Radiocontrast venography	• Presence of thrombus	• Gold standard • Direct visualization of veins	• Invasive • Relatively expensive • Finite (1–5%) incidence of phlebitis • Not all veins consistently visualized

shown in Fig. 26.1. Table 26.3 is Wells' clinical decision rule for evaluating patients with suspected deep vein thrombosis to assess clinical probability.

26.2.1.1 D-Dimer

In general, D-dimer is a sensitive test but it lacks specificity for the diagnosis of deep vein thrombosis. D-dimer is increased in deep vein thrombosis and pulmonary embolism as well as a variety of inflammatory and prothrombotic conditions associated with activation of coagulation, such as infection, surgery, trauma, pre-eclampsia, and pregnancy. D-dimer for the assessment of patients with suspected acute deep vein thrombosis provides the greatest accuracy when combined with an assessment of clinical probability. A positive D-dimer is 0.5 μg/mL or greater. Since this is a screening test, a positive D-dimer is a positive screen (Rinde et al. 2020). Many researchers have shown that the D-dimer test is more than 95% sensitive to detect deep vein thrombosis, pulmonary embolism, or both. The absence of D-dimer is a strong indicator that there is no thromboem-

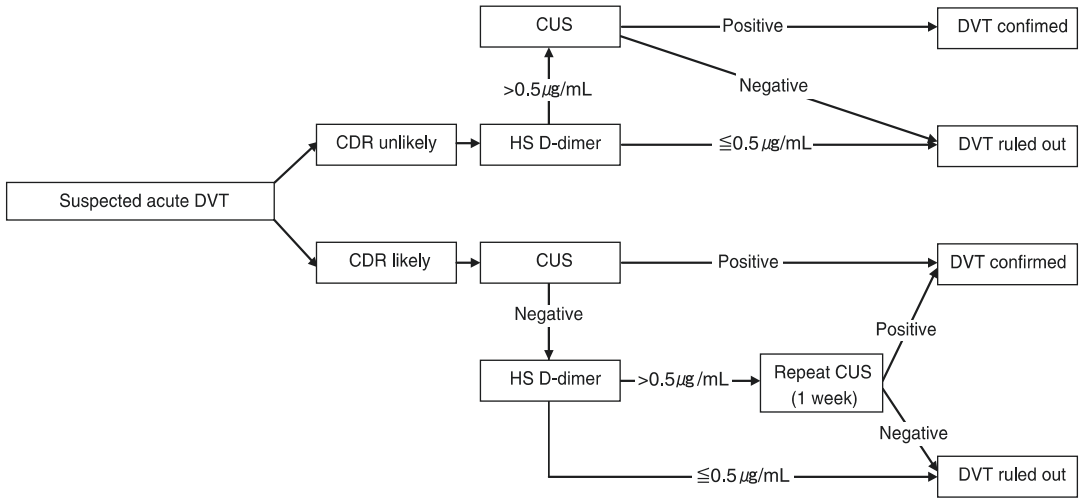

Fig. 26.1 Diagnostic algorithm for clinically suspected deep vein thrombosis. DVT deep vein thrombosis, CDR clinical decision rule, HS high sensitivity, CUS compression ultrasonography From Huisman and Klok (2013), with permission

Table 26.3 Wells score of clinical decision rule for the evaluation of patients with suspected deep vein thrombosis

Clinical characteristics	Score
Swelling of entire leg	1 point
Pitting edema confined to the symptomatic leg	1 point
Calf swelling >3 cm greater than the other side	1 point
Localized tenderness over the affected deep vein	1 point
Nonvaricose collateral superficial veins	1 point
History of previous DVT	1 point
Recent history of bedridden for ≥3 days or major surgery within 12 weeks	1 point
Recent paralysis or plaster immobilization of legs	1 point
Active cancer within 6 months	1 point
Alternate diagnosis at least as likely as DVT	–2 points
Clinical probability	
Score < 2 points	Unlikely
Score ≥ 2 points	Likely

DVT deep vein thrombosis

bolism (Stein et al. 2004). However, this test is nonspecific (Bounameaux et al. 1991; Masuda et al. 2015). An ELISA D-dimer test should be performed when a thrombosis is suspected. If the test result is positive, venous ultrasonography and ventilation-perfusion scanning should be performed to confirm the presence and location of the thrombi. Combined D-dimer and ultrasound screening in patients with acute spinal cord injuries improve the detection of venous thromboembolism, including pulmonary embolism, compared to D-dimer screening alone (Kumagai et al. 2020). The D-dimer test is recommended as a routine screening test or to assess suspected deep vein thrombosis in the rehabilitation setting, as it is a reliable method to rule out venous thromboembolism (Akman et al. 2004).

26.2.1.2 Ultrasonography

Doppler ultrasound detects thrombi in the common femoral or popliteal veins above the knee in symptomatic patients, with a positive predictive value of 97% (Scarvelis and Wells 2006). Usually, ultrasound testing is limited to the proximal veins, from the common femoral vein caudally to the region of the calf veins where they join the popliteal vein. Figure 26.2 shows the anatomy of the deep veins of the leg. Doppler ultrasound study is less reliable in diagnosing calf vein thrombosis (Furlan and Fehlings 2007). In symptomatic persons, the sensitivity and specificity of ultrasound is high; however, in asymptomatic individuals without spinal cord injury, the sensitivity of this modality has been found to be quite low, which calls into question its role as a screening tool for deep vein thrombosis (Chen 2003; Davidson et al. 1992).

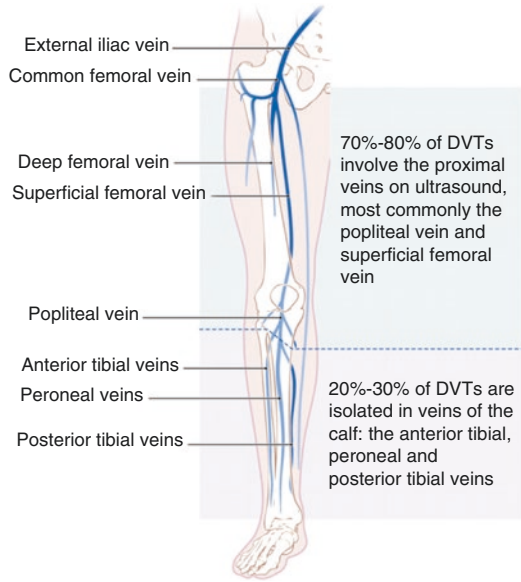

Fig. 26.2 Diagram of the deep veins in the leg. From Scarvelis and Wells (2006)

Compression ultrasonography refers to a sonographic assessment of fluid-filled structures with compression to assess distension, flow, and intraluminal masses. Duplex and triplex refer to the use of two or more sonographic modalities, including standard B mode (assessment of architecture), Doppler (assessment of flow/velocity), and color flow Doppler (direction of flow) (Thachil and Bagot 2018). Duplex ultrasonography is the most frequently used noninvasive diagnostic modality for deep vein thrombosis: the Doppler and the scan. Compression ultrasonography and Doppler ultrasonography are noninvasive tests that are sensitive to the diagnosis of deep vein thrombosis. Compression ultrasonography has been shown to be accurate for the diagnosis of proximal deep vein thrombosis. If a vein is not fully compressed (noncompressibility), which is characteristic of an obstructed vessel, it is a diagnosis of deep vein thrombosis (Piazza et al. 2015).

26.2.1.3 Impedance Plethysmography

Impedance plethysmography (IPG) measures changes in the electrical conductivity or venous flow changes of the leg caused by obstruction of venous outflow. Mechanical impedance plethysmogram can measure the increase in venous volume after inflation of a pneumatic cuff that is placed around the lower thigh. The maximum venous outflow is measured as the decrease in volume for the first 3 s after the release of the occluding cuff. This test does not detect the presence of hemodynamically insignificant thrombi or small isolated calf thrombi. The specificity of IPG in people with spinal cord injuries is lower due to decreased venous outflow and capacity

found in most people with spinal cord injuries (Frieden et al. 1987). In addition, IPG has a very low sensitivity for deep vein thrombosis below the popliteal vein.

26.2.1.4 Radioactive Fibrinogen Uptake Test

Radioactive fibrinogen deposited at the coagulation site is highly sensitive to the diagnosis of deep vein thrombosis for detecting a developing thrombus or thrombus that is extending or lysing. This method can detect very small thrombi since radiolabeled fibrinogen is absorbed by the developing thrombus. This test is not specific for the presence of deep vein thrombosis (Green 1996). Increased radioactive levels are also observed in patients with superficial thrombophlebitis, hematoma, ulceration, arthritis, fractures, wounds, and cellulitis. The presence of a thrombus in the groin or pelvis areas is not detected because of the high background radioactivity of the bladder.

26.2.1.5 Venography

Contrast venography is considered the gold standard test for assessing deep vein thrombosis, primarily based on its long history and purported accuracy. However, this technique has many problems and makes it a less than ideal choice. Cannulation of a pedal vein may be difficult in patients with gross swelling and edema. Some veins, such as the muscular branches of the calf veins or the profunda femoris, are routinely not fully filled with contrast medium, which can cause extravasation or reaction of contrast medium. Contrast venography has little role in the standard contemporary assessment of suspected deep vein thrombosis. However, it remains an available and supposedly definitive test for abnormal but nonspecific ultrasound findings or when a potentially false-positive diagnosis carries significant risk (Thachil and Bagot 2018). The presence of a thrombus may be identified in several ways: constant intraluminal filling defect, cutoff of the contrast medium at a constant site below a non-filled segment with reappearance above the site, or persistent non-filling of the deep venous system above the knee despite adequate dye infusion (Chen 2003). The procedure can produce phlebitis and hypersensitivity reaction can occur with the contrast media.

26.2.2 Pulmonary Embolism

Pulmonary embolism is one of the leading causes of death in patients with acute spinal cord injury. Most pulmonary emboli originate from the deep vein thrombosis of the proximal veins in the lower limb. Thrombi embolize from the deep veins of the lower extremities and travel through inferior vena cava, right atrium, and right ventricle to lodge in the pulmonary arterial tree, where they cause a variety of hemodynamic and gas exchange disorders. Acute pulmonary embolism causes a sudden increase in pulmonary vascular resistance and right ventricular afterload through direct physical obstruction, hypoxemia, and release of pulmonary artery vasoconstrictors. The sudden increase in right ventricular afterload can lead to right ventricle dilation and hypokinesis, tricuspid regurgitation, and ultimately acute right ventricular failure. Right ventricular pressure overload can also result in interventricular septal flattening and deviation toward the left ventricle in diastole, thereby impairing left ventricular filling. Patients with right ventricular failure may rapidly decompensate and develop systemic arterial hypotension, cardiogenic shock, and cardiac arrest (Piazza and Goldhaber 2006).

Massive embolization with occlusion of more than 60% of the pulmonary vasculature is associated with acute right-sided heart failure, circulatory collapse, and death (Teasell et al. 2009). Patients with acute pulmonary embolism may hyperventilate, leading to hypocapnia and respiratory alkalosis. Tachypnea is the most common sign of pulmonary embolism. Hypercapnia indicates a massive pulmonary embolism, which leads to an increased anatomical and physiological dead space and impaired minute ventilation (Piazza et al. 2015). Unexplained symptoms of dyspnea, chest pain, cough, and hemoptysis are the suspected symptoms of pulmonary embolism. Table 26.4 shows the differential diagnosis of the clinical symptoms associated with pulmonary embolism. Signs of pulmonary embolism include cyanosis, hypotension, fever, hypoxemia,

Table 26.4 Differential diagnosis of the presenting symptoms of pulmonary embolism

Presenting symptom	Differential diagnosis
Dyspnea	Asthma, COPD, pneumonia, pleural fluid, bronchitis, pneumothorax, neuromuscular disease, foreign body, cardiac asthma, hyperventilation syndrome, direct pulmonary injury, pulmonary hemorrhage
Cough	Bronchitis, asthma, COPD, smoking, infectious disease
Chest pain	Coronary artery disease, aortic dissection, pericarditis pleuritis, pneumonia, bronchitis, pneumothorax, tumor, musculoskeletal chest pain syndromes (costochondritis, Tietze syndrome), rheumatic diseases, gastrointestinal (GE reflux, esophageal spasm), pancreatobiliary diseases (pancreatitis, cholecystitis), herpes zoster
Hemoptysis	Nasopharyngeal bleeding, neoplasm, bronchitis, bronchiectasis, foreign body, lung abscess, pneumonia, tuberculosis, Granulomatosis with polyangiitis and other vasculitis, lung contusion, pulmonary arteriovenous malformation, heart failure
Symptoms or signs suggestive of DVT	Cellulitis, trauma, ruptured Baker's cyst, hematoma, lymphangitis, post-thrombotic syndrome
Syncope	Myocardial infarction, cardiac arrhythmia, bleeding, ruptured aortic aneurysm, pericardial tamponade, tension pneumothorax, aortic dissection, sepsis, anaphylaxis, intoxication, vasovagal collapse

Adapted from Thachil and Bagot (2018)

hemoptysis, pleural friction rub, and loud S2, S3, or S4 gallop. The physician should be vigilant in patients with spinal cord injuries as patients with spinal cord injuries especially tetraplegics do not experience chest pain and are suspected of having other causes. Pulmonary embolisms sometimes manifest as syncope, hypotension, and arrhythmia, which are also signs of sepsis. Unfortunately, in some people, the initial presentation of pulmonary embolism is sudden death. It is important that clinicians strongly suspect pulmonary embolism as there are no specific symptoms and frequent and silent clinical symptoms can have catastrophic consequences (Chen 2003). Arterial blood gas measurements, chest radiographs, and electrocardiograms may be helpful in differential diagnosis, but there are no abnormal patterns specific for pulmonary embolism.

The most important problem in diagnosing pulmonary embolism in individuals with spinal cord injury is that it is often misdiagnosed as pneumonia or atelectasis. As mentioned above, there are many nonspecific symptoms and clinical presentations that may be suspicious of pulmonary embolism. A sensitive test for thrombosis is the measurement of circulating D-dimers, fragments of fibrin formed during thrombolysis (Bounameaux et al. 1991). A normal or near-normal chest X-ray in a patient with dyspnea or hypoxemia may indicate pulmonary embolism. However, the majority of patients with pulmonary embolism will have some abnormalities such as cardiomegaly or pleural effusion on chest X-rays (Piazza and Goldhaber 2015). If pulmonary embolism is suspected, a perfusion lung scan with or without a ventilation scan or spiral contrast-enhanced CT scan should be performed immediately. Areas that are ventilated but not perfused are the sites of pulmonary embolism. Multiple defects with wedge-shaped or segmental or concave defects on the lateral edges of the lung or on a pleural surface, which are unmatched on the ventilation scans, on perfusion scans of the ventilation-perfusion lung scan are diagnostic of pulmonary embolism. Sometimes, mucus plugs in patients with spinal cord injuries may present a pulmonary embolism like clinical symptoms such as dyspnea and hypoxemia and show abnormalities in perfusion scans. Normal perfusion scans in abnormal ventilation scans by mucus plugs can rule out pulmonary embolism. Spiral CT scan angiography is sensitive for the detection of a thrombus in the proximal pulmonary arteries but is not sensitive in the segmental and subsegmental arteries. The most common electrocardiographic abnormalities are sinus tachycardia, nonspecific ST, and T-wave changes. Algorithm for the diagnostic approach in suspected pulmonary embolism is shown in Fig. 26.3. Table 26.5 contains clinical decision rules for suspected pulmonary embolism to estimate clinical probability.

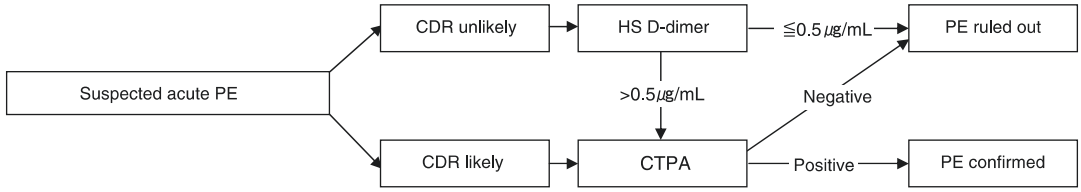

Fig. 26.3 Diagnostic algorithm for clinically suspected pulmonary embolism. PE pulmonary embolism, CDR clinical decision rule, HS high sensitivity, CTPA computed tomography pulmonary angiography. From Huisman and Klok (2013), with permission

Table 26.5 Clinical decision rules for suspected pulmonary embolism

Wells score			Revised Geneva score		
Variables	Original	Simplified	Variables	Original	Simplified
Previous PE or DVT	1.5	1	Previous DVT or PE	3	1
Heart rate > 100/min	1.5	1	Heart rate 75–94/min	3	1
			Heart rate ≥ 95/min	5	2
Surgery or immobilization <4 weeks	1.5	1	Surgery or fracture within 1 mon	2	1
Hemoptysis	1	1	Hemoptysis	2	1
Active malignancy	1	1	Active malignancy	2	1
Clinical signs of DVT	3	1	Unilateral lower limb pain	3	1
Alternative diagnosis less likely than PE	3	1	Pain on lower limb deep vein palpation and unilateral edema	4	1
			Age > 65 years	1	1
Clinical probability			**Clinical probability**		
Low	<2		Low	0–3	
intermediate	2–6		Intermediate	4–10	
High	>6		High	≥11	
PE unlikely	≤4	≤1	PE unlikely	≤5	≤2
PE likely	>4	>1	PE likely	>5	>2

From Huisman and Klok (2013), with permission

26.3 Prevention of Deep Vein Thrombosis

A number of methods are available for the prevention of deep vein thrombosis, including early mobilization, external pneumatic compression, pressure gradient elastic stockings, adjusted-dose heparin, low dose heparin, low molecular weight heparin, warfarin, and dextran.

Patients with acute spinal cord injuries should be screened twice daily for signs of deep vein thrombosis, including an increase in circumference of the calf and thigh, pain or tenderness in the extremities, or low-grade fever. For reference, the thigh and lower leg circumferences of the lower extremities are measured at the proximal 10 cm and distal 15 cm from the medial knee joint space, respectively, and the upper extremity is measured at the proximal and distal 10 cm points of the medial epicondyle of the elbow, respectively. Smoking cessation, avoidance of constricting devices on the lower extremities, exercise, and weight loss reduce the risk of deep vein thrombosis. It is desirable to minimize immobility and start out-of-bed activities as soon as possible, which may be beneficial in preventing thromboembolism in the hospitalized patient. Early ambulation of patients following acute myocardial infarction has been shown to significantly reduce the incidence of deep vein throm-

bosis (Miller et al. 1976). Intermittent pneumatic calf compression and thigh-high compression stocking, preferably waist-high stockings, should be used. Intermittent pneumatic compression is recommended over compression stockings. An inflation pressure of 40–45 mmHg is found to produce sufficient emptying of the calf veins (Christie et al. 2011).

The Consortium for Spinal Cord Medicine has established guidelines for the prevention of deep vein thrombosis in patients with spinal cord injury (Consortium for Spinal Cord Medicine 2016). In the first 2 weeks after spinal cord injury, compression hoses or pneumatic devices should be applied to the legs to prevent venous stasis. Anticoagulation with either low molecular weight heparin or adjusted-dose unfractionated heparin should begin within 72 h of spinal cord injury in the absence of active bleeding or coagulopathy (Morris 2003). Low molecular weight heparin administered subcutaneously every 12 h is superior to unfractionated heparin in the prevention of deep vein thrombosis in patients with spinal cord injuries with less hemorrhagic complications. Anticoagulants should be continued until discharge in patients with incomplete injuries, for 8 weeks in patients with uncomplicated complete motor injury, and for 12 weeks or until discharge from rehabilitation in those with complete motor injury and other risk factors, such as lower limb fractures or a history of thrombosis, cancer, obesity, or age over 70.

The prophylaxis of deep vein thrombosis includes anticoagulation and graded elastic stocking for older children and adolescents. Elastic wraps should not be used because the unevenness of wrapping can cause venous obstruction, increasing the risk of deep vein thrombosis (Rozzelle et al. 2013). Because of its ease of administration, low molecular weight heparin is ideal for prophylactic anticoagulation and laboratory monitoring is generally unnecessary. The dose of low molecular heparin is 0.5 mg/kg administered subcutaneously every 12 h or 1 mg/kg every 24 h. The dose of low molecular weight heparin should be monitored with antifactor Xa levels.

26.4 Treatment of Deep Vein Thrombosis and Pulmonary Embolism

The treatment of deep vein thrombosis and pulmonary embolism is similar, as most pulmonary emboli originate from deep vein thrombi or blood clots in the lower extremities. The goal of anticoagulant therapy is to prevent further clot formation. Within 1–3 weeks, thrombosis is endothelialized and attached to the vessel wall, reducing the risk of dislodgment. Initial treatment with oral anticoagulant therapy alone is unacceptable. The ease of administration and efficacy of low molecular weight heparin (LMWH) make it the preferred anticoagulant, whether administered on an outpatient or an inpatient basis. LMWH administer once daily for 5–7 days as initial treatment. It is still not clear whether it is better to administer LMWH once or twice a day (Scarvelis and Wells 2006). The current anticoagulant or antithrombotic drugs mainly include three types of agents: heparins; vitamin K antagonists; and the more recently developed direct oral anticoagulants (DOACs) (Table 26.6).

26.4.1 Unfractionated Heparin

A loading dose of 80 units/kg of unfractionated heparin (UFH) (5000–7000 units) is administered as an IV bolus, followed by continued infusion of heparin at an average rate of 18 units/kg/h (average 1000 units/h). UFH is delivered at a rate sufficient to maintain the activated partial thromboplastin time (aPTT) at 1.5–2.5 times that of the control or approximately 60–80 s. If an aPTT of at least 1.5 times the control is not achieved within 24–72 h, thromboembolism and recurrence of thrombosis are significantly increased (Hull et al. 1986; Hull and Raskob 1991). UFH neither prevents the embolization from existing thrombus nor induces the dissolution of blood clots. Heparin activates antithrombin III, which inhibits the clotting cascade (Deitelzweig and Jaff 2004).

Table 26.6 Characteristics of current anticoagulants and their laboratory monitoring

	LMWH	VKAs	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Action	Inhibition of FXa	Inactivation of vitamin K-dependent factors	Thrombin inhibition	Inhibition of FXa	Inhibition of FXa	Inhibition of FXa
Administration	Parenteral (i.e., subcutaneous)	Oral	Oral	Oral	Oral	Oral
Half-life	3–6 h	10–60 h	12–17 h	5–9 h	6–12 h	6–8 h
Laboratory test (reference)	Anti-FXa chromogenic assay	PT-INR	dTT (or ECT)	Anti-FXa chromogenic assay	Anti-FXa chromogenic assay	Anti-FXa chromogenic assay
Urgent screening	APTT	PT-INR	APTT (ratio) or dRVVT	PT (ratio) or dRVVT	PT (ratio) or dRVVT	Not established

Adapted from Thachil and Bagot (2018)
APTT activated partial thromboplastin time, dRVVT dilute Russell viper venom time, dTT dilute thrombin time, ECT ecarin clotting time, Fxa activated factor X, LMWH low molecular weight heparin, PT prothrombin time, VKAs vitamin K antagonists

High-Dose Unfractionated Heparin in Massive Pulmonary Embolism

As soon as massive pulmonary embolism is suspected, high-dose UFH should be administered (Piazza and Goldhaber 2006, 2015). The majority of patients will require at least a 10,000 units bolus of UFH followed by a continuous infusion of at least 1250 units/h with a target aPTT of at least 80 s (Piazza and Goldhaber 2015). Right ventricular function should be augmented to manage hemodynamic instability. Excessive volume resuscitation should be avoided as it may exacerbate right ventricular failure. An initial trial of 500 mL of normal saline is most likely to be successful in patients without signs of increased right-sided preload, such as those with central venous pressures below 12–15 mmHg. Volume loading should be avoided in patients with central venous pressures higher than 12–15 mmHg, and the administration of vasopressors and inotropes should be the first step in hemodynamic support. Preferred agents to support the hemodynamic instability due to massive pulmonary embolism are norepinephrine, epinephrine, and dopamine, which have dual mechanisms of action as both vasopressors and inotropes (Piazza and Goldhaber 2015). ECMO can be considered for pulmonary embolism in refractory right ventricular failure and cardiogenic shock.

26.4.2 Low Molecular Weight Heparin

Low molecular weight heparin (LMWH), including enoxaparin, dalteparin, and tinzaparin, offers several advantages over unfractionated heparin, including longer half-life, more consistent bioavailability, and more predictable dose response. LMWH provides equivalent or superior antithrombotic activity to UFH with fewer hemorrhagic complications. LMWH is administered subcutaneously twice a day at a dose determined by body weight and does not need dose adjustments or laboratory monitoring of the coagulation parameters under routine circumstances (Piazza and Goldhaber 2015; Koopman and Bossuyt 2003; Sprague et al. 2003). In contrast to UFH, which is largely eliminated by the liver, LWMH is excreted renally. When laboratory monitoring of LMWH is required in patients with impaired renal clearance or unexpected bleeding, anti-Xa levels are used to determine the level of anticoagulation with LMWH. The therapeutic target range of anti-Xa levels is 0.5–1.0 anti-Xa

IU/mL. Anti-Xa levels should be measured 4–6 h after the second or third dose of LMWH (Bounameaux and de Moerloose 2004; Harenberg 2004; Piazza and Goldhaber 2015). Treatment for deep vein thrombosis in children and adolescents with spinal cord injury is similar to that in adults. Patients with deep vein thrombosis are anticoagulated with LMWH (1 mg/kg every 12 h subcutaneously). Oral anticoagulation with warfarin sodium is initiated simultaneously to maintain a prothrombin time of 2–3 INR (Rozzelle et al. 2013).

26.4.3 Warfarin

Oral anticoagulation is started concurrently with UFH or LMWH. Typically, overlap therapy of heparin with warfarin is required for at least 5 days to prevent thrombus extension or embolization until full therapeutic efficacy is achieved, target INR between 2.0 and 3.0. Warfarin therapy usually begins on the first day if aPTT is prolonged to the therapeutic range after the initial doses of heparin. Loading doses of warfarin is not needed. The starting dose is usually 5–10 mg. This dose is continued for 2–4 days. The dosage is then adjusted to maintain a therapeutic international normalized ratio (INR). That is, heparin administration continues until the prothrombin time (PT) is 2 to 3 times that of the control, and then heparin is stopped. Warfarin inhibits the synthesis of the vitamin K-dependent factors II, VII, IX, and X. Warfarin also lowers the level of protein C, a naturally occurring antithrombic protein, and has a short half-life. Thus, warfarin may temporarily induce a hypercoagulable state before inhibiting the synthesis of cofactors with a longer half-life. For this reason, heparin continues for 4–5 days after warfarin is started. It is recommended to keep the INR value between 2 and 3. Warfarin should be continued for at least 3 months. If a second episode of pulmonary embolism or deep vein thrombosis occurs, anticoagulation over a longer period is recommended. A third episode may be an indication of lifelong anticoagulation. Management of warfarin anticoagulation can often be difficult due to many drug–drug, drug–food, drug–alcohol interactions. Complications of anticoagulation therapy are summarized in Table 26.7.

Table 26.7 Complications of anticoagulant therapy

Anticoagulant	Complications
Heparin	1. Bleeding: dose-related; rare in first 48 h of therapy; more common in elderly women. Unusual sites of bleeding include gut wall with bowel obstruction, adrenal (may be massive), retroperitoneal, intrapulmonary, compartment syndrome with nerve entrapment 2. Osteoporosis (with long-term therapy) 3. Thrombocytopenia (1–2% incidence; may be associated with thrombosis including stroke, myocardial infarction, or gangrene of an extremity) 4. Alopecia (rare) 5. Transaminase increase
LMWH	1. Bleeding: Appears to be less frequent than with standard heparin. Most often in patients also receiving NSAIDs 2. Osteoporosis (may be less common than with standard heparin) 3. Thrombocytopenia (significantly less than with standard heparin, but 90% of patients with heparin-associated thrombocytopenia will also have syndrome with LMWH)
Warfarin	1. Bleeding: Dose related; potentiated by various medications, alcohol, starvation, liver disease 2. Teratogenicity in first and possibly second trimester; neonatal bleeding in third trimester 3. Skin and muscle necrosis related to effects on proteins C and S 4. Cholesterol embolization (purple toes syndrome)

From Green (1996)

26.4.4 Direct Oral Anticoagulants (Non-Vitamin K Oral Anticoagulants)

Treatment of the vast majority of patients with deep vein thrombosis has been based on the use of heparins, either UFH or LMWH, followed by oral vitamin K antagonists (warfarin) (Kearon

et al. 2012). However, all of these compounds have some limitations, including parenteral administration of heparins and the need for routine coagulation monitoring and dose adjustments for warfarin (Ageno et al. 2012). The precedents of oral anticoagulant therapy with vitamin K antagonists are clinically effective but have always suffered from several disadvantages. Patients should regularly monitor the INR to ensure that drug levels remain within a therapeutic window. This causes regular inconvenience and requires significant resources in the form of anticoagulation clinics or widely available point of care testing. Warfarin is notorious for its interacting with many drugs and other substances (Thachil and Bagot 2018). Direct oral anticoagulants (DOACs) have been developed to overcome some of these limitations (Barnes et al. 2015). The DOACs have a favorable pharmacologic profile (e.g., rapid onset and short half-life) and a predictable anticoagulant response, which makes their use particularly attractive for both the acute phase treatment and for the long-term secondary prevention of venous thromboembolism. In the acute treatment of venous thromboembolism, their effectiveness was not inferior to that of standard treatment and was associated with less major bleeding complications (Riva and Ageno 2016). The use of DOACs has steadily increased since their approval and are now recommended over warfarin for stroke prevention in nonvalvular atrial fibrillation and for treatment of venous thromboembolism (Rawal et al. 2019). However, studies on the use of DOAC to prevent and treat deep venous thrombosis in patients with spinal cord injuries have not been well conducted (Hamidi et al. 2019).

DOACs or non-vitamin K oral anticoagulants such as rivaroxaban, edoxaban, apixaban, and dabigatran have been shown to be safe and effective for oral anticoagulation for venous thromboembolism and are all approved by the FDA in the United States. These drugs principally consist of direct factor Xa inhibitors (rivaroxaban, edoxaban, apixaban) or direct thrombin inhibitors (dabigatran etexilate). Rivaroxaban is the most commonly prescribed DOAC (Barnes et al. 2015). DOACs offer several advantages over warfarin for oral anticoagulation in patients with venous thrombosis. The major differences or advantages of DOACs compared to warfarin are summarized in Table 26.8. Under routine conditions, DOACs do not require laboratory monitoring or dose adjustment, unlikely warfarin which requires careful INR monitoring and dose adjustment. They have a rapid onset over 1–2 h and are rapidly and efficiently excreted through the renal and biliary system, resulting in a half-life of 7–12 h. DOACs also avoid the many drug–drug and drug–food interactions that complicate warfarin management. Unlikely treatment with warfarin in which INR can remain therapeutic despite one or two missed dose, therapeutic anticoagulation with DOACs is lost soon after an omitted dose (Piazza and Goldhaber 2015). However, problems of the DOACs in clinical practice are accumulation in renal failure unlike warfarin, the absence of a rapid available antidote, and a lack of real-world clinical experience (Thachil and Bagot 2018). For more information of the DOACs, see Chap. 10.

Table 26.8 Major differences and advantages of direct anticoagulants over warfarin

Feature	DOAC	Warfarin
Onset of action	Rapid	Slow
Half-life	Short	Long
Routine laboratory monitoring	No	Yes
Dosing	Fixed	Variable
Drug–drug interactions	Few	Many
Drug–food interactions	No	Yes
Antidote	Not all yet	Yes

DOAC direct oral anticoagulant

26.4.5 Inferior Vena Cava Filter

If the anticoagulation is contraindicated or if there is recurrent pulmonary embolism despite adequate therapeutic anticoagulation, the inferior vena cava (IVC) filter, Greenfield filter, through the right internal jugular vein or the common femoral vein, is indicated to prevent clots delivery from the venous system to the lung. Retrievable IVC filters are inserted to provide temporary protection from pulmonary embolism in cases of

increased vulnerability of anticoagulation. IVC filters should be retrieved as soon as they are no longer needed. In patients with spinal cord injuries, there is a high risk of complications due to Greenfield filter placement (Stavropoulos 2004). Regardless of the chronicity and complexity, retrieval should be attempted for all IVC filters. Tine penetration through the caval wall is almost ubiquitous (Morrow et al. 2020). Because of the high risk of displacement or movement of the filter or bowel perforation, the use of assisted coughing or vigorous pulmonary toileting after placement of the filter should be avoided. Other reported device-related complications include strut fracture, strut embolization, filter migration, device tilt, IVC penetration, and perforation of surrounding structures including the aorta and small intestine (Quencer et al. 2020).

26.4.6 Others

Thrombolytic treatment may be indicated in patients with high risk of death from pulmonary embolism as a direct consequence of pulmonary circulation obstruction (Murphy 2004).

References

Ageno W, Gallus AS, Wittkowsky A, et al. American College of Chest Physicians. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e44S–88S.

Akman MN, Cetin N, Bayramoglu M, et al. Value of the D-dimer test in diagnosing deep vein thrombosis in rehabilitation inpatients. Arch Phys Med Rehabil. 2004;85:1091–4.

Barnes GD, Lucas E, Alexander GC, et al. National trends in ambulatory oral anticoagulant use. Am J Med. 2015;128:1300–5.e2.

Baumgartner HR, Muggli R, Tschopp TB, et al. Platelet adhesion, release and aggregation in flowing blood: effects of surface properties and platelet function. Thromb Haemost. 1976;35:124–38.

Bounameaux H, Cirafici P, de Moerloose P, et al. Measurement of D-dimer in plasma as diagnostic aid in suspected pulmonary embolism. Lancet. 1991;337:196–200.

Bounameaux H, de Moerloose P. Is laboratory monitoring of low-molecular-weight heparin therapy necessary? No J Thromb Haemost. 2004;2:551–4.

Chen D. Treatment and prevention of thromboembolism after spinal cord injury. Top Spinal Cord Inj Rehabil. 2003;9:14–25.

Christie S, Thibault-Halman G, Casha S. Acute pharmacological DVT prophylaxis after spinal cord injury. J Neurotrauma. 2011;28:1509–14.

Consortium for Spinal Cord Medicine. Prevention of venous thromboembolism in individuals with spinal cord injury. 3rd ed. Washington, DC: Paralyzed Veterans of America; 2016.

Davidson BL, Elliott CG, Lensing AW. Low accuracy of color Doppler ultrasound in the detection of proximal leg vein thrombosis in asymptomatic high-risk patients. The RD Heparin Arthroplasty Group. Ann Intern Med. 1992;117:735–8.

Deitelzweig S, Jaff MR. Medical management of venous thromboembolic disease. Tech Vasc Interv Radiol. 2004;7:63–7.

Frieden RA, Ahn JH, Pineda HD, et al. Venous plethysmography values in patients with spinal cord injury. Arch Phys Med Rehabil. 1987;68:427–9.

Furlan JC, Fehlings MG. Role of screening tests for deep venous thrombosis in asymptomatic adults with acute spinal cord injury: an evidence-based analysis. Spine (Phila Pa 1976). 2007;32:1908–16.

Green D. Venous thromboembolism. In: Green D, Olson DA, editors. Medical management of long-term disability. Boston, MA: Butterworth-Heinemann; 1996. p. 199–216.

Hadley MN, Walters BC, Aarabi B, et al. Clinical assessment following acute cervical spinal cord injury. Neurosurgery. 2013;72(Suppl 2):40–53.

Hamidi M, Zeeshan M, Kulvatunyou N, et al. Operative spinal trauma: thromboprophylaxis with low molecular weight heparin or a direct oral anticoagulant. J Thromb Haemost. 2019;17:925–33.

Harenberg J. Is laboratory monitoring of low-molecular-weight heparin therapy necessary? Yes J Thromb Haemost. 2004;2:547–50.

Huisman MV, Klok FA. Diagnostic management of acute deep vein thrombosis and pulmonary embolism. J Thromb Haemost. 2013;11:412–22.

Hull RD, Raskob GE. Venous thromboembolic disease. Curr Opin Cardiol. 1991;6:750–6.

Hull RD, Raskob GE, Hirsh J, et al. Continuous intravenous heparin compared with intermittent subcutaneous heparin in the initial treatment of proximal-vein thrombosis. N Engl J Med. 1986;315:1109–14.

Kearon C, Akl EA, Comerota AJ, et al. American College of Chest Physicians. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e419S–94S.

Koopman MM, Bossuyt PM. Low molecular weight heparin for outpatient treatment of venous thromboembo-

lism: safe, effective, and cost reducing? Am J Med. 2003;115:324–5.
Kumagai G, Wada K, Kudo H, et al. D-dimer monitoring combined with ultrasonography improves screening for asymptomatic venous thromboembolism in acute spinal cord injury. J Spinal Cord Med. 2020;43:353–7.
Mackiewicz-Milewska M, Jung S, Kroszczyński AC, et al. Deep venous thrombosis in patients with chronic spinal cord injury. J Spinal Cord Med. 2016;39:400–4.
Masuda M, Ueta T, Shiba K, et al. D-dimer screening for deep venous thrombosis in traumatic cervical spinal injuries. Spine J. 2015;15:2338–44.
Messier MH. Lower extremity venous anatomy. Semin Intervent Radiol. 2005;22:147–56.
Miller RR, Lies JE, Carretta RF, et al. Prevention of lower extremity venous thrombosis by early mobilization. Confirmation in patients with acute myocardial infarction by 125I-fibrinogen uptake and venography. Ann Intern Med. 1976;84:700–3.
Morris TA. Heparin and low molecular weight heparin: background and pharmacology. Clin Chest Med. 2003;24:39–47.
Morrow KL, Bena J, Lyden SP, et al. Factors predicting failure of retrieval of inferior vena cava filters. J Vasc Surg Venous Lymphat Disord. 2020;8:44–52.
Moser KM, LeMoine JR. Is embolic risk conditioned by location of deep venous thrombosis? Ann Intern Med. 1981;94(4 Pt 1):439–44.
Muriel K, Green RM, Greenberg RK, et al. The anatomy of deep venous thrombosis of the lower extremity. J Vasc Surg. 2003;31:895–900.
Murphy KD. Mechanical thrombectomy for DVT. Tech Vasc Interv Radiol. 2004;7:79–85.
Peterson CW. Venous thrombosis: an overview. Pharmacotherapy. 1986;6(4 Pt 2):12S–7S.
Piazza G, Goldhaber SZ. Acute pulmonary embolism, Part I: epidemiology and diagnosis. Circulation. 2006;114:e28–32.
Piazza G, Goldhaber SZ, Hohlfelder B. Handbook for venous thrombosis. Cham: Springer; 2015.
Quencer KB, Smith TA, Deipolyi A, et al. Procedural complications of inferior vena cava filter retrieval, an illustrated review. CVIR Endovasc. 2020;3:23.
Rawal A, Ardeshna D, Minhas S, et al. Current status of oral anticoagulant reversal strategies: a review. Ann Transl Med. 2019;7:411.
Rinde FB, Fronas SG, Ghanima W, et al. D-dimer as a stand-alone test to rule out deep vein thrombosis. Thromb Res. 2020;191:134–9.
Riva N, Ageno W. Use of the direct oral anticoagulants for the treatment of venous thromboembolism. Hematol Oncol Clin North Am. 2016;30:1035–51.
Rossi EC, Green D, Rosen JS, et al. Sequential changes in factor VIII and platelets preceding deep vein thrombosis in patients with spinal cord injury. Br J Haematol. 1980;45:143–51.
Rozzelle CJ, Aarabi B, Dhall SS, et al. Management of pediatric cervical spine and spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):205–26.
Ryken TC, Hurlbert RJ, Hadley MN, et al. The acute cardiopulmonary management of patients with cervical spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):84–92.
Scarvelis D, Wells PS. Diagnosis and treatment of deep-vein thrombosis. CMAJ. 2006;175:1087–92.
Sprague S, Cook DJ, Anderson D, et al. A systematic review of economic analyses of low-molecular-weight heparin for the treatment of venous thromboembolism. Thromb Res. 2003;112:193–201.
Stavropoulos SW. Inferior vena cava filters. Tech Vasc Interv Radiol. 2004;7:91–5.
Stein PD, Hull RD, Patel KC, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. Ann Intern Med. 2004;140:589–602.
Thachil J, Bagot C, editors. Handbook of venous thromboembolism. 1st ed. Oxford: Wiley Blackwell; 2018.
Teasell RW, Hsieh JT, Aubut JA, et al. Venous thromboembolism after spinal cord injury. Arch Phys Med Rehabil. 2009;90:232–45.
Vogel LC, Anderson CJ. Spinal cord injuries in children and adolescents: a review. J Spinal Cord Med. 2003;26:193–203.
Watson N. Venous thrombosis and pulmonary embolism in spinal cord injury. Paraplegia. 1968;6:13–21.

Recommended Additional Reading

Bhattacharya V, Stansby G, Kesteven P, editors. Prevention and management of venous thromboembolism. London: Imperial College Press; 2015.
Blank A. Deep vein thrombosis and pulmonary embolism. A guide for practitioners. Cumbria, CA: M&K Publishing; 2009.
Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Crossman A, Neary D. Neuroanatomy: an illustrated colour test. 5th ed. Philadelphia, PA: Elsevier; 2015.
Eltorai IM, Schmit JK, editors. Emergencies in chronic spinal cord injury patients. New York: Eastern Paralyzed Veterans Association; 2001.
Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.
Kirshblum S, Lin VW, editors. Spinal cord medicine. third ed. New York: Demos Medical Publishing; 2019.
Konstantinides SV, editor. Management of acute pulmonary embolism. Totowa, NJ: Humana Press; 2007.
Piazza G, Goldhaber SZ, Hohlfelder B. Handbook for venous thrombosis. Cham: Springer; 2015.
Thachil J, Bagot C, editors. Handbook of venous thromboembolism. 1st ed. Oxford: Wiley Blackwell; 2018.
Young RR, Woolsey RM, editors. Diagnosis and management of disorders of the spinal cord. Philadelphia, PA: W. B. Saunders; 1995.

27 Electrolyte Disorders in Spinal Cord Injuries

In patients with spinal cord injuries, various fluid and electrolyte disorders occur. Mechanical effects, fluid responses, and autonomic changes due to various conditions including prolonged recumbency, muscle paralysis, cardiovascular disorder, urinary tract infection, renal insufficiency, endocrinological disorder, and neurogenic dysfunction can cause fluid migration and electrolyte imbalance in people with chronic diseases or disorders including patients with spinal cord injuries (Green and Olson 1996; Soni et al. 1994). Some patients may be asymptomatic but have symptoms such as chronic dependent edema, dehydration, orthostatic hypotension, and chronic renal failure. Hyponatremia, hypernatremia, metabolic acidosis, and metabolic alkalosis are clinically frequent.

Serum sodium levels in early spinal cord injury are low. Early muscle tissue damage is probably associated with a significant increase in exchangeable sodium as a result of hyperaldosteronism. This sodium is likely to be stored in the relatively increased extracellular space. Serum excretion is similar to the control level in patients with chronic injuries (>8 months), with more sodium excretion in later stages. Changes in potassium regulation are similar to sodium. Immediately after spinal cord injury, cellular injury results in the loss of intracellular fluid and solute, causing relatively large urinary potassium excretion (Claus-Walker et al. 1977). Urinary potassium excretion is greater in the early post-injury stages (<8 weeks) than in the chronic stages (>8 months), but the mean urinary potassium level is consistently within the normal range (Claus-Walker et al. 1977).

Total body water (TBW) accounts for about 60% of total body weight in men and about 50% in women. This rate decreases with aging and increased body fat. Therefore, the water content is 55% of the total body weight in obese individuals. TBW is distributed between two major compartments: the extracellular fluid (ECF) and intracellular fluid (ICF). Approximately one-third of the TBW is in the extracellular fluid volume (ECFV). About two-thirds of the TBW is in the intracellular fluid volume (ICFV). The plasma volume is about one-fourth of the ECFV; other ECFV constitutes the interstitial fluid and lymph volume, bone and dense connective tissue water, and transcellular fluid (cerebrospinal, pleural, peritoneal, synovial, and digestive secretions) (Preston 2011; Reddi 2018) (Table 27.1; Fig. 27.1).

27.1 Sodium

Since sodium is mainly confined to the ECF compartment, the amount of sodium in the compartment of extracellular fluid is sometimes referred to as total body sodium. Sodium is a major extracellular cation with associated anions (chloride and bicarbonate) and is responsible for most of

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the osmotic driving force that maintains the size of the ECFV. More than 95% of sodium is extracellular. As the total amount of sodium in the ECF increases, this ultimately leads to an overload of the ECFV. Due to the increase in ECF sodium, the expansion of ECFV is clinically presented as edema. Other clinical presentations of ECF overload include pleural effusions, pulmonary edema, and acute spinal cord injury. It is important that the body maintains a narrow range of extracellular sodium concentrations (135–145 mEq/L) and the size of the ECFV (Table 27.2). As the total amount of sodium in the extracellular compartment decreases, ECFV size decreases. ECFV depletion (volume depletion) causes poor skin turgor, tachycardia, and orthostatic hypotension (Buffington and Abreo 2016).

The balance between sodium intake and sodium excretion by the kidney determines the amount of sodium in the ECF compartment and the size of the ECFV. As the ECFV increases, the mechanisms of increasing sodium excretion are activated to prevent ECF overload, and a reduction in ECFV activates a mechanism to promote renal sodium retention to prevent ECFV depletion.

Table 27.1 The body fluid compartments

ECFV (1/3 TBW)	ICFV (2/3 TBW)
Sodium 135–145 mEq/L	Sodium 10–20 mEq/L
Potassium 3.5–5.0 mEq/L	Potassium 130–140 mEq/L
Chloride 95–105 mEq/L	Magnesium 20–30 mEq/L
Bicarbonate 22–26 mEq/L	Urea nitrogen 10–20 mg/dl
Glucose 90–120 mEq/dl	
Calcium 8.5–10.0 mg/dl	
Magnesium 1.4–2.1 mEq/L	
Urea nitrogen 10–20 mg/dl	

From Preston (2011)
Women: Total body water (TBW) = 0.5 × Body weight (kg)
Men: Total body water (TBW) = 0.6 × Body weight (kg)

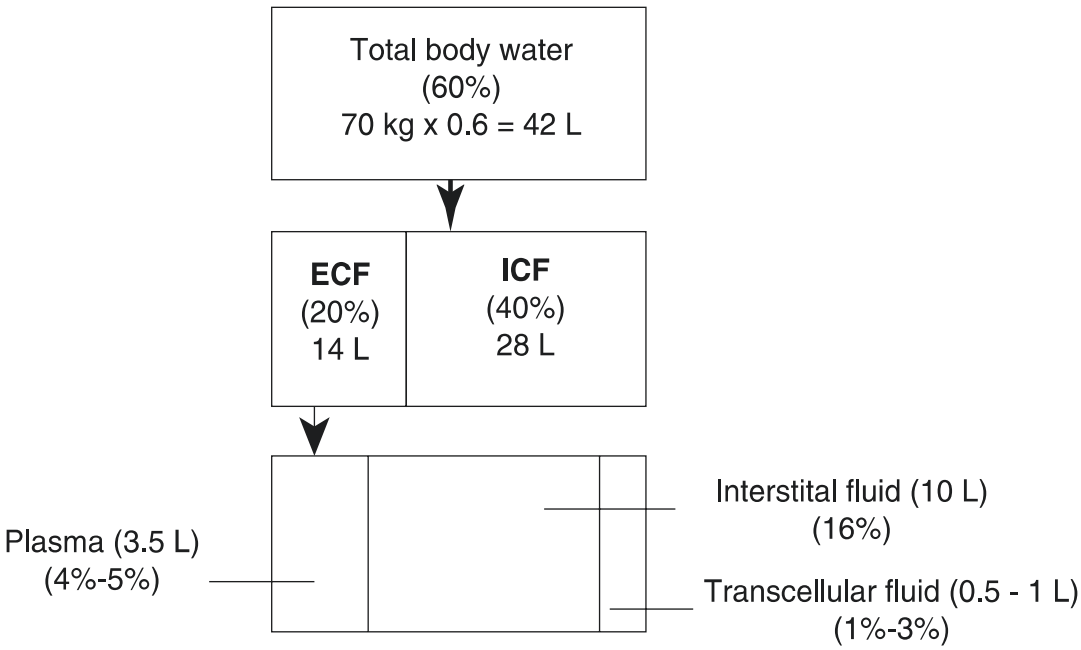

Fig. 27.1 Approximate distribution of water in various body fluid compartments: ECF extracellular fluid, ICF intracellular fluid. A 70 kg lean man has 42 L of water, assuming the total body water content is 60% of the bodyweight (70 × 0.6 = 42 L). From Reddi (2018)

Table 27.2 States of abnormal ECF volume and abnormal ECF sodium concentration

Disorders	Implication	Primary problem	Examples of common clinical causes
Hyponatremia with ECFV normal	Water excess relative to sodium	Abnormal water control (too much water relative to sodium)	SIADH
Hypernatremia with ECFV normal	Water deficit relative to sodium	Abnormal water control (too little water relative to sodium)	Diabetes insipidus Insensible losses
Sodium concentration normal with ECFV increased	Increased total body sodium	Abnormal sodium control (too much sodium)	CHF Cirrhosis Nephrotic syndrome Renal failure
Sodium concentration normal with ECFV decreased	Decreased total body sodium	Abnormal sodium control (too little sodium)	Vomiting, Diarrhea Loop diuretics
Hyponatremia with increased ECFV	Water excess relative to sodium and increased total body sodium	Abnormal water control (too much water relative to sodium) and abnormal sodium control (too much sodium)	CHF Cirrhosis Nephrotic syndrome Renal failure
Hyponatremia with decreased ECFV	Water excess relative to sodium and decreased total sodium	Abnormal water control (too much water relative to sodium) and abnormal sodium control (too little sodium)	Vomiting Thiazide diuretics
Hypernatremia with increased ECFV	Water deficit relative to sodium and increased total body sodium	Abnormal water control (too little water relative to sodium) and abnormal sodium control (too much sodium)	Administration of hypertonic sodium solutions or $NaHCO_3$ (iatrogenic)
Hypernatremia with decreased ECFV	Water deficit relative to sodium and decreased total body sodium	Abnormal water control (too little water relative to sodium) and abnormal sodium control (too little sodium)	Osmotic diuresis Diarrhea

From Preston (2011)

There are three main systems that regulate total body sodium and ECFV size (Buffington and Abreo 2016):

1. Renin–angiotensin–aldosterone system by the renal receptor. Receptors are present in the juxtaglomerular cells of the kidney, activating the renin–angiotensin–aldosterone system by altering renal perfusion and release of renin. Renin is released in response to decreased renal perfusion and is used to convert the angiotensinogen to angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin-converting enzyme. Angiotensin II directly promotes renal sodium retention and causes a release of aldosterone by the zona glomerulosa of the adrenal cortex.
2. Large venous and atrial volume receptors are activated by increased atrial filling and promote renal sodium excretion.
3. Pressure receptors in the aorta and carotid sinus are activated by a decrease in ECFV, leading to renal sodium retention.

The amount of water relative to sodium in the ECF determines the ECF sodium concentration. The osmolality is determined by the total solute concentration in the fluid compartment. The sodium concentration contributes significantly to the total serum osmolality compared to other solutes of the ECF (glucose and urea). The serum osmolality is maintained within a narrow range. The tonicity is the ability of all the solutes to produce an osmotic driving force to cause water movement between compartments, that is, between the ECF and the ICF. The extracellular sodium concentration is a major determinant of plasma tonicity. Increased tonicity increases the extracellular sodium concentration. Hypertonicity is an important stimulus for thirst and antidiuretic

hormone (ADH) release and an important factor in total body water regulation. With increasing the sodium concentration, thirst (leading to water ingestion) and ADH release (water retention by the kidney) are stimulated. ADH is released as a slight increase in ECFV tonicity. Absence of ADH is the most important determinant of final urine concentration or dilution of urine. Release of ADH leads to water retention and a decrease in the tonicity of the ECFV. Nonosmotic release of ADH can lead to water retention and can cause hyponatremia. The nonosmotic release of ADH leads to pathologic water retention and hyponatremia, which is referred to as a syndrome of inappropriate ADH (SIADH). A high sodium concentration tells us that the water is too low for sodium. Other solutes of ECF, glucose, and urea do not contribute significantly to serum osmolality or tonicity (Adrogue and Madias 2000).

27.1.1 Hyponatremia

Hyponatremia is not a rare problem for patients with spinal cord injuries. Hyponatremia is defined as a low serum or plasma sodium (Na+) concentration, less than 135 mEq/L. This means that there is an excess water to sodium, regardless of whether the total ECF sodium is increased, decreased, or normal (Adrogue and Madias 2000). Hyponatremia does not develop in a normal individual unless water intake is greater than renal excretion. A defect in renal water excretion with normal water intake is a prerequisite for the development of hyponatremia (Kriz et al. 2015). This defect in water excretion is due to high circulating levels of ADH. The etiology of hyponatremia in tetraplegic patients is multifactorial, with common factors such as the use of diuretics and the intravenous infusion of hypotonic fluids, as well as specific mechanisms that function in people with spinal cord injuries: decreased renal water excretion by both intrarenal and arginine vasopressin dependent mechanism (resetting of the osmostat) with habitually increased fluid intake and low salt diet intake (Soni et al. 1994).

Clinical findings of hyponatremia include lethargy, malaise, and muscle cramps. If hyponatremia is not treated quickly, serious symptoms may be caused by brain edema, such as lethargy, coma, psychosis, and seizures (Furlan and Fehlings 2009). Lack of sympathetic tone leads to venous pooling and orthostatic hypotension. Effective reduction in blood volume thus increases the activity of the renin–angiotensin system and the release of ADH. Hyponatremia is classified as dilutional hyponatremia, depletional hyponatremia, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and factitious hyponatremia (Buffington and Abreo 2016; Kugler and Hustead 2000; Rondon-Berrios et al. 2014; Zenenberg et al. 2010). Hyperosmolarity rules out factitious (pseudo) hyponatremia and hypertonic hyponatremia. Hypotonic hyponatremia is called true hyponatremia (Reddi 2018) (Figs. 27.2 and 27.3).

27.1.1.1 Types of Hyponatremia

Dilutional Hyponatremia (Hyponatremia with Hypotonicity, Hypotonic Hyponatremia, True Hyponatremia)

Hyponatremia with hypotonicity is the most common form of hyponatremia. This is due to renal water excretion with continued water intake. Normally, the kidneys produce a large amount of dilute urine to excrete excess water. Normal kidney function forms about 150 liters of glomerular filtrate every 24 h. Approximately 60% of this filtrate is reabsorbed in the proximal convoluted tubule. Normal plasma osmolality is maintained at a narrow range from 280 to 290 mOsm/kg. Secretion of ADH is inhibited at plasma osmolality below 280 mOsm/kg, leading to maximal urine dilution. The reasons why the kidney cannot appropriately excrete excess water resulting in hyponatremia are GFR impairment, decreased ECFV due to vomiting with continued water ingestion, edema, SIADH, adrenal insufficiency or hypothyroidism, and thiazide diuretics. Based on volume status, hypotonic hyponatremia is classified into hypovolemic hyponatremia (rel-

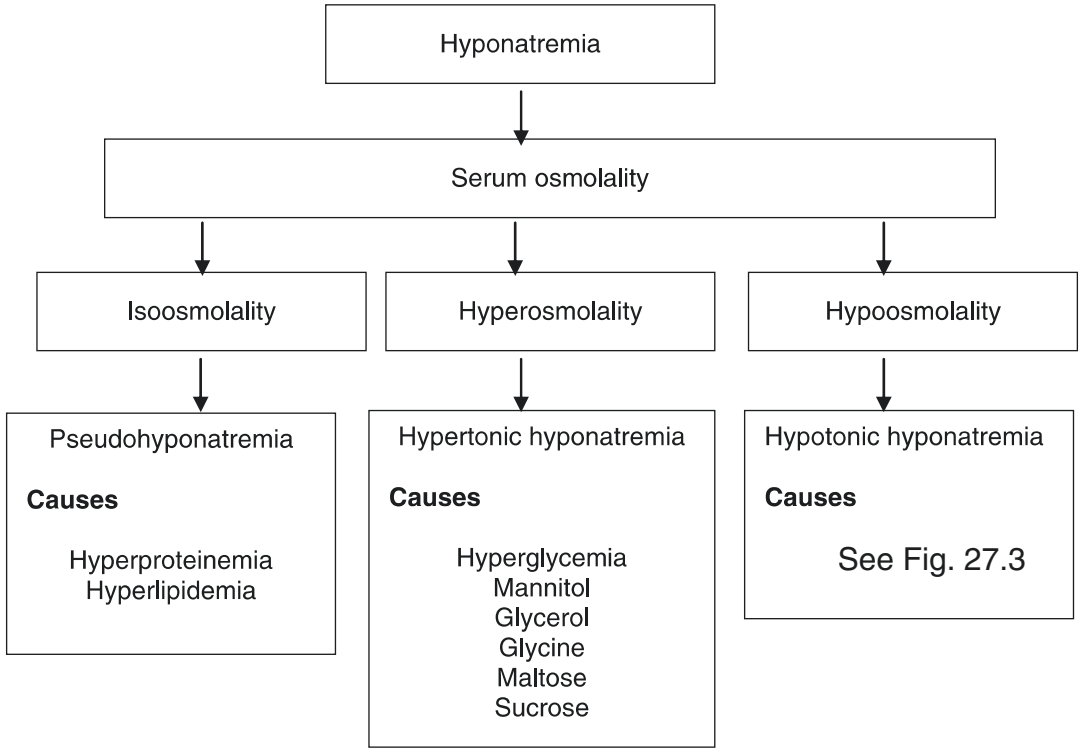

Fig. 27.2 Differentiation of hypotonia according to osmolarity. From Reddi (2018), with permission

atively more sodium than water loss), hypervolemic hyponatremia (relatively more water than sodium gain), and normovolemic hyponatremia (relatively more water relative to sodium).

Depletional Hyponatremia (Hyponatremia with Hypertonicity, Hypertonic Hyponatremia, Translocational Hyponatremia)

Patients with depletional hyponatremia require more water than the total body salt due to gastrointestinal (vomiting, diarrhea, nasogastric suction, or ileostomy losses) or renal (hyperglycemia, mannitol, diuretics) losses of both salt and water. Hyponatremia with hypertonicity is most commonly caused by severe hyperglycemia in uncontrolled diabetes mellitus. Since glucose is an effective osmole, high glucose concentrations in ECF can cause water to migrate from the intracellular compartments to the extracellular compartments, reducing the extracellular sodium concentration. Serum sodium falls about 2.4 mEq/L for every 100 mg/dL increase in serum glucose >100 mg/dL. Sodium is low because of transcellular migration of water (translocation), but both tonicity and measured serum osmolality are very high. Correction of hyperglycemia corrects hyponatremia. Hypertonic mannitol, glycerol, glycol, and maltose can also cause hyponatremia with increased tonicity.

Factitious Hyponatremia (Pseudohyponatremia, Isotonic Hyponatremia)

Factitious hyponatremia is defined as hyponatremia associated with a low serum sodium concentration and normal serum osmolality. Pseudohyponatremia occurs in severe hyperlipidemia, severe hyperproteinemia, and hyperglycemia. Reduction in sodium is due to displacement of serum water by excess lipid or protein, but the serum osmolality is normal. These patients are

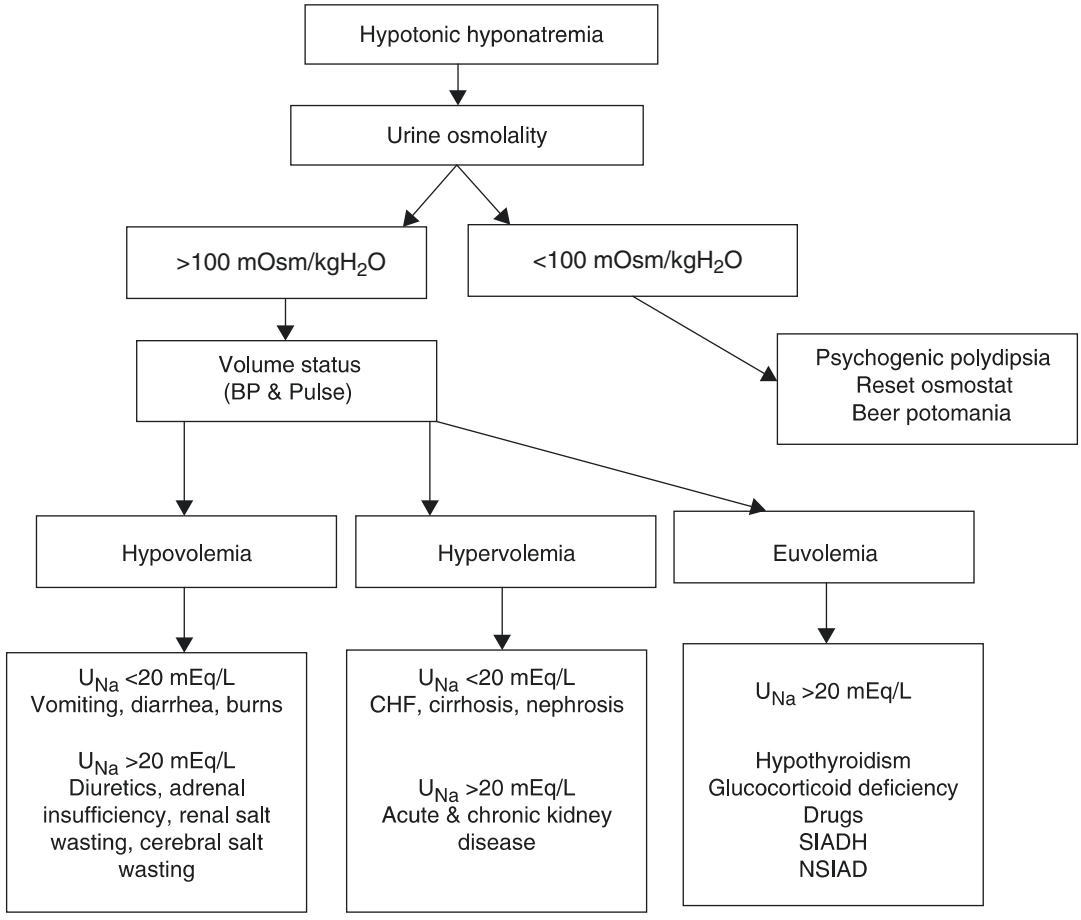

Fig. 27.3 Classification, causes, and diagnosis of hypotonic hyponatremia. From Reddi (2018), with permission

asymptomatic from hyponatremia because serum osmolality is normal. Low serum sodium concentration does not require treatment.

Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

In SIADH, ADH release is inappropriate for both the volume and osmolar state of the patient. Adequate secretion of ADH is released in response to an appropriate baroreceptor stimulus. SIADH can be seen in a variety of clinical conditions including brain pathology, malignancies, and medications (Table 27.3). The diagnostic criteria of SIADH are as follows: (1) hypotonic hyponatremia (plasma osmolality < 270 mOsm/kg H2O); (2) inappropriate urinary concentration (>100 mOsm/kg H2O) or inability to dilute urine

Table 27.3 Causes of syndrome of inappropriate ADH (SIADH)

Categories	Causes
CNS disorders	Head injury, brain tumors, meningitis, encephalitis, CVA, pain, schizophrenia or other psychoses, anxiety, brain abscess, Guillain–Barré syndrome
Pulmonary diseases	Carcinoma, pneumonia, emphysema, tuberculosis, respiratory failure, abscess, asthma
Malignancies	Lymphoma, lung cancer, others
Drugs	Cyclophosphamide, vincristine, NSAID, chlorpropamide, tolbutamide, carbamazepine, oxytocin, clofibrate, colchicine, amitriptyline, thioridazine, nicotine, morphine, barbiturates, isoproterenol, sulfonylureas

From Green and Olson (1996)

osmolality below 100 mOsm/kg H2O; (3) urinary Na+ >30 mEq/L on regular diet; (4) euvolemia; (5) absence of thyroid, adrenal, liver, cardiac, and renal disease (Reddi 2018).

27.1.1.2 Differential Diagnosis of Hyponatremia

History is important in finding conditions associated with dilutional hyponatremia, depletional hyponatremia, and SIADH (Kriz et al. 2015). Diagnostic tests can be performed by physical examination. In dilutional hyponatremia, patients may have edema, ascites, pleural effusion, or pulmonary edema. The patient appears to be "wet." In depletional hyponatremia, however, the patient appears to be "dry" without edema but is more likely to have dry mucous membranes, orthostatic hypotension or orthostatic tachycardia, and increased blood urea nitrogen (BUN) to creatinine ratio, suggesting volume depletion. In SIADH, patients appear euvolemic without signs of volume overload or depletion. Patients with factitious hyponatremia also appear euvolemic on physical examination. Whatever the etiology, hyponatremia itself may be associated with characteristic symptoms and signs. These symptoms are moderate to severe hyponatremia, serum sodium <130 mEq/L. An increase in BUN-creatinine ratio means dehydration and thus depletional hyponatremia. Hyperlipidemia or severe hyperglycemia is consistent with factitious hyponatremia. Urine osmolality is greater than serum osmolality in SIADH.

27.1.1.3 Treatment of Hyponatremia

The cause of hyponatremia should be evaluated and corrected. The goal of the treatment of hyponatremia is to carefully correct the serum sodium concentration to normal and to correct for coexisting changes in the ECFV. Asymptomatic hyponatremia generally does not require aggressive treatment (Soni et al. 1994). Management of situational hyponatremia is limiting free water intake. Fluid restriction to less than 1 L/day will result in a negative water balance but achieve only a slow increase in the serum sodium concentration. Sodium administration is almost always a contraindication to these patients because the total body sodium is already increased, and additional sodium intake further increases the volume of the already increased amount of extracellular fluid. If there is a serious neurologic sign of hyponatremia and if the patient has no pulmonary edema, careful administration with furosemide diuretics and hypertonic sodium chloride (3% saline) should be attempted if the serum sodium concentration is less than 115 mEq/L. Hypertonic saline should be administered in sufficient amounts to raise the serum sodium level to 118–120 mEq/L. The use of angiotensin-converting enzyme (ACE) inhibitors such as captopril may be particularly beneficial. The combination of ACE inhibitor and a loop diuretic appears to be effective in the management of dilutional hyponatremia. ACE inhibitors may cause not only the onset of hypercalcemia but also a decrease in kidney function. Depletional hyponatremia is effectively treated by administration of isotonic saline solution (Zenenberg et al. 2010).

If SIADH has a serum sodium level of more than 115 mEq/L, no symptoms will occur. SIADH is being administered at a fluid limit of 800 mL/24 h. A serum sodium concentration <115 mEq/L or symptomatic hyponatremia indicates an emergency situation where immediate treatment is required.

Acute, severe symptoms of hyponatremia usually require immediate treatment in an intensive care setting. Failure to treat this condition immediately may result in permanent neurological sequelae or death. Patients with chronic hyponatremia are generally less likely to be symptomatic, and treatment should be less aggressive than acute hyponatremia. Correction of chronic, asymptomatic hyponatremia should be gradual and careful. Rapid correction of ECF osmolality causes water to migrate quickly out of the cells. Rapid correction or overcorrection of chronic hyponatremia can cause fatal neurologic symptoms, such as osmotic demyelination syndrome (central pontine myelinolysis). Symptoms of the osmotic demyelination syndrome may progress gradually from first day after correction of the serum sodium concentration. Symptoms include mental status changes, seizures, dysphagia, visual disturbance, and tetraplegia (Goh 2004).

Treatment of Acute, Symptomatic Hyponatremia

Hyponatremia with acute, severe symptoms requires emergency treatment. Signs of emergency treatment with hypertonic saline are signs of significant central nervous system symptoms such as mental changes, seizures, or other signs of increased intracranial pressure. Water restriction prevents the deterioration of hyponatremia. This condition is caused by an overloaded hypotonic solution such as D5W or 0.45% saline in ECFV depletion, SIADH, polydipsia, ECFV depletion secondary to protracted vomiting with continued water intake, and IV administration of cyclophosphamide (Zenenberg et al. 2010).

Fluid restriction must be initiated. Patients with asymptomatic or mild symptoms should generally be treated with 3% saline. The main risk of 3% saline is overcorrection of hyponatremia leading to osmotic demyelination syndrome. Patients with chronic disease and female patients are at increased risk for osmotic demyelination syndrome. In severe acute symptomatic hyponatremia, the purpose of using 3% saline is not to correct the sodium concentration itself but to temporarily relieve cerebral edema and to prevent neurologic sequelae. The problem with osmotic demyelination syndrome appears to occur after correction of cerebral edema (Goh 2004; Preston 2011). Three percent saline should be given carefully in a controlled environment to correct the serum sodium to a level of approximately 118–120 mEq/L. In general, it is optimal to infuse at a rate of 50–100 mL/h or 200–400 mL or more of 3% saline to correct the serum sodium to 118–120 mEq/L or to control neurologic symptoms. Correction of the sodium concentration should not initially be faster than 0.5–1.0 mEq/L/h until 6–8 mEq/L increase, and then it should be less than 0.5 mEq/L per hour. An increase in sodium concentration of 6–8 mEq/L should be sufficient to significantly decrease symptoms. Sodium concentrations in excess of 10–12 mEq/L for the first 24 h or in excess of 20 mEq/L during for the first 48 h are not permitted due to concerns about osmotic demyelination syndrome which can lead to severe neurological sequelae (Yee and Rabinstein 2010). The endpoint is an increase of 20–25 mEq/L in plasma sodium concentration, or reaches 130 mEq/L, or asymptomatic. The serum sodium concentration should not be corrected to normal values and hypernatremia should not develop. Initial infusion of 3% saline in 50–100 mL/h is generally safe for a short period of time for an average-sized person with severe symptoms. In general, the infusion of 3% saline does not exceed a total of 6–8 h. When sodium is corrected to 6–8 mEq/L, 3% saline is discontinued. Using 3% saline does not require sodium correction close to the normal range.

An oral vasopressin receptor antagonist (tolvaptan, convivaptan, lixivaptan), which blocks the action of ADH, can increase serum sodium concentration by increasing electrolyte-free water excretion. When using vasopressin antagonist, monitoring serum sodium concentration and cautions is the same as using 3% saline.

Osmotic Demyelination Syndrome

Care should be taken not to correct hyponatremia too quickly. Clinicians treating patients with hyponatremia are therefore faced with the dilemma of correcting hyponatremia quickly enough to avoid morbidity due to cerebral edema without precipitating osmotic demyelination syndrome (Thurman and Beri 2013). Longer lasting (>48 h) correction of correction of hyponatremia is associated with an increased risk of osmotic demyelination syndrome. Osmotic demyelination syndrome is neurologic abnormality caused by demyelination, typically within the central basis pontis, but also occurring in extrapontine sites. Osmotic demyelination syndrome, formerly known as central pontine myelinolysis, which is a destruction of the myelin in the central nervous system, can lead to death (Goh 2004). Osmotic demyelination syndrome is a complication of treatment of acute and chronic hyponatremia (Reddi 2018). The rapid correction of hyponatremia is hypertonic stress to astrocytes, which have depleted osmolytes and trigger apoptosis, disruption of the blood–brain barrier and finally brain demyelination (Sterns 2015).

When serum sodium is increased rapidly, plasma osmolality for the brain becomes hypertonic, causing water movement from the brain.

This appears to be the case when serum sodium is corrected to normal levels at a rate greater than 0.5–1.0 mEq/L/h or too quickly. Just as the rapid development of hypotonicity causes passage of water into the cells of the brain, too rapid correction of hypotonicity induces an osmotic passage of water out of these same cells. It takes several days for cells to decrease intracellular osmolytes in response to a decrease in extracellular tonicity (Thurman and Beri 2013). This cerebral dehydration likely leads to myelinolysis and osmotic demyelination syndrome (Reddi 2018). The development of osmotic demyelination syndrome can occur several days after the correction of the hyponatremia (Berl and Rastegar 2010). The clinical spectrum of the osmotic demyelination syndrome is broad and can include seizures, behavioral abnormalities, pseudobulbar palsy, lethargy, altered mental status, coma, and movement disorders and it is often but not always fatal (Sterns et al. 1994). The most severely affected, patients become "locked in," unable to move, speak, or swallow due to demyelination of the central pons. Although osmotic demyelination can result in permanent disability or death, many patients, even those who require ventilator support, have complete functional recovery (Sterns 2015). On the other hand, excessive delay of serum sodium concentration correction may increase the risk of seizures and irreversible damage to the central nervous system. It is recommended to use a 3% saline solution to correct the serum sodium concentration with or without furosemide at a rate of 0.5–1.0 mEq/L/h or less to approximately 120 mEq/L. Correcting the serum sodium to this level will reduce the risk of serious central nervous system symptoms and improve central nervous system symptoms. Then, stop 3% saline and reevaluate patients. The serum sodium concentration can then be adjusted more gradually to 130–135 mEq/L over the next 48–72 h by limiting the intake of free water (both oral and intravenous) (Green and Olson 1996).

The diagnosis of osmotic demyelination syndrome is confirmed by the presence of foci of demyelination on brain MRI, but initially, the MRI findings are normal and may be found 3–4 weeks later.

Treatment of Chronic Hyponatremia

Asymptomatic chronic hyponatremia (>48 h) to 120 mEq/L does not require urgent correction. Treatment depends on the cause of hyponatremia. Until more information is available, the water limit for water (fluid and dietary foods) is 800 mL/24 h and will work temporarily for several hours. If it is because of volume depletion, if the serum sodium is above 120 mEq/L, and if the patient is asymptomatic and hemodynamically stable, the patient can rehydrate by consuming water. The treatment of ECFV depletion is replaced with 2.0 L of 0.9% normal saline as long as tolerated by cardiovascular status (Zenenberg et al. 2010).

The first treatment of hyponatremia associated with edema formation is also water restriction. Thiazide diuretics are contraindicated. For SIADH, water restriction is always important until the underlying cause is determined. Medications that are known to affect water excretion should be discontinued. Drugs that inhibit water excretion include amitriptyline, haloperidol, carbamazepine, SSRI, NSAID, nicotine, and narcotics. Long-term management of SIADH can be problematic if the underlying disorder cannot be effectively treated (Zenenberg et al. 2010; Goh 2004).

27.1.2 Hypernatremia

Hypernatremia is defined as serum sodium >145 mEq/L and hyperosmolality (serum osmolality >295 mOsm/kg H2O) due to water deficit. Hypernatremia is usually the result of sweating, loss from gastrointestinal tract or insensible losses. Drugs that interfere with ADH release, such as phenytoin or ethanol, or with the renal response to ADH, such as demeclocycline, lithium, and amphotericin, can be causes of excessive water losses. Patients with spinal cord injuries who have inappropriate thermoregulation or cannot drink without assistance are prone to hyponatremia. Hypernatremia is vulnerable to person with a lack or absence of thirst mechanism. Due to the decreased thirst sensitivity due to aging, hypernatremia is common in elderly

patients, especially in pulmonary or urinary tract infections, chronic debilitating diseases, and neurological disorders. The consequence of hypernatremia is that water may move out of cells to achieve osmotic equilibrium and may result in brain cell shrinkage.

Clinical symptoms of hypernatremia include dehydration, poor skin turgor, tremors, irritability, ataxia, spasticity, confusion, seizures, and coma. Neurologic symptoms are mostly due to brain shrinkage and tearing of the cerebral vessels. Acute hypernatremia is more symptomatic than chronic hypernatremia. The mortality rate for patients with serum sodium greater than 160 mEq/L over 48 h is 60%.

27.1.2.1 Types of Hypernatremia

Hypernatremia from Extrarenal Water Loss

The most common causes of hypernatremia due to extrarenal water loss are fever, excessive sweating, mechanical ventilation-related hyperventilation, and severe diarrhea. The greater the deficiency of water than sodium, the higher the serum sodium concentration.

Hypernatremia from Renal Water Loss

The characteristic of pronounced renal water loss is polyuria, which is defined as a urine volume of 3L/24 h or more. The main assessment of renal water loss is the urine osmolality test. Polyuria is an important indication of the presence of osmotic diuresis (urine osmolality >300 mOsm/L). Patients with hypernatremia due to osmotic diuresis show clinical signs of ECFV deficiency. The causes of osmotic diuresis related to hypernatremia are uncontrolled diabetes mellitus, hyperalimentation (increased load of urea), and mannitol and sodium-containing solutions.

Diabetes insipidus may have been caused by a deficiency or lack of ADH, which cannot concentrate urine properly. Urine is improperly diluted (urine osmolality <150 mOsm/L) and has a low sodium concentration and increased serum sodium concentration.

27.1.2.2 Treatment of Hypernatremia

Treatment of hypernatremia should first focus on restoring the intravenous volume of patients who are hypovolemic with the administration of isotonic intravenous fluids such as normal saline. If the patient is severely deficient in ECFV, 0.9% isotonic saline should be administered until evidence of overt circulatory insufficiency is corrected. Thereafter body fluids should be replaced with hypotonic fluid (D5W or 0.45% saline). Rapid correction of hypernatremia is dangerous and can lead to coma and seizure due to cerebral edema (Yee and Rabinstein 2010). A safe hypernatremia correction rate is the reduction of serum sodium concentration initially by about 0.5–1 mEq/L/h and not more than 12 mEq/L in the first 24 h. It should not be completely corrected for 36–72 h.

27.2 Potassium

Potassium is the main cation in the intracellular fluid. Maintaining a stable plasma potassium concentration is essential for normal cell function, cardiac rhythm, and proper neuromuscular transmission. The intracellular potassium concentration of potassium is 130–140 mEq/L compared to the extracellular (blood) concentration of 3.5–5.0 mEq/L. A decrease in serum potassium by 1 mEq/L reduces total body potassium by 300 mEq. A small amount of total body potassium is in the extracellular compartment. A small amount of potassium in the extracellular space into the intracellular space can significantly change the plasma potassium concentration. Metabolic alkalosis and theophylline toxicity can transport potassium to cells. Severe diarrhea causes loss of potassium and $HCO3^-$, resulting in hypokalemia and metabolic acidosis. Chronic use of laxatives can lead to severe potassium loss and metabolic alkalosis. Excessive sweating, fasting, or inadequate intake can cause potassium deficiency.

27.2.1 Hypokalemia

In patients with spinal cord injuries, lean muscle mass decreases. Since 98% of total body potassium is in the lean tissue, the total body potassium decreases in patients with spinal cord injuries. Vomiting, diarrhea, chronic use of laxatives, and the result of side effects from medications such as diuretics or beta-2 agonists in patients with spinal cord injuries can cause hypokalemia (serum potassium less than 3.5 mEq/L).

Mild hypokalemia, serum potassium 3.0–3.4 mEq/L, is mostly asymptomatic. Clinical symptoms of more severe hypokalemia, serum potassium less than 3.0 mEq/L, include neuromuscular manifestations (weakness, fatigue, respiratory muscle dysfunction, and rhabdomyolysis), gastrointestinal manifestations (constipation, ileus), diabetes insidious, cardiac arrhythmia, and electrocardiographic changes (sinus bradycardia, QT prolongation, AV blocks, presence of U waves, T wave flattening, ST segment depression). However, muscle weakness generally does not occur until serum potassium level is less than 2.5 mEq/L.

27.2.1.1 Treatment of Hypokalemia

Oral potassium replacement is preferred to intravenous administration. Potassium chloride or potassium citrate of salts of potassium and gluconate are most commonly used to correct the hypokalemia in metabolic alkalosis with ECFV depletion and most other hypokalemia. Serum potassium levels of 2.5–3.4 mEq/L can usually be treated with 20 mEq of oral potassium chloride two to four times daily based on the severity of hypokalemia. More severe hypokalemia, less than 2.5 mEq/L of serum potassium, can be treated orally unless the patient has arrhythmia, muscle weakness, and rhabdomyolysis or cannot tolerate oral intake. Potassium chloride can be not tolerated because of potential for gastrointestinal irritation and small bowel perforation. Intravenous administration of potassium to patients with profound and life-threatening hypokalemia is appropriate. Intravenous administration is potentially dangerous due to severe, acute hyperkalemia. Concentrations above 30–40 mEq/L and doses above 10 mEq/h are not recommended.

27.2.2 Hyperkalemia

Hyperkalemia, serum potassium above 5.0 mEq/L, may result from acute or chronic kidney disease, strenuous exercise, rhabdomyolysis, and side effects of medications such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), direct renin inhibitors, potassium-sparing diuretics, NSAID, beta-blockers, and digoxin. Severe hyperkalemia is a medical emergency that requires immediate treatment. Clinical manifestations of hyperkalemia (>6.5 mEq/L) include neuromuscular signs and typical electrocardiographic changes (peaked T waves, flattened P waves, shortening of QT interval, prolonged PR interval, widened QRS duration, and deep S waves).

27.2.2.1 Diagnosis and Treatment of Hyperkalemia

Peaked T wave is the earliest electrocardiographic manifestation of hyperkalemia and confirms the elevated potassium concentration. The main purpose of treatment for severe hypokalemia, serum potassium above 6.5 mEq/L, is to shift potassium from extracellular space to intracellular space. Administration of either 1000 mg of calcium gluconate IV or 500–1000 mg of calcium chloride IV to stabilize the cardiac membrane should be performed. This should be followed by therapies to shift extracellular potassium into cells. Intravenous administration of 50 mL of D50 with 10 units of regular insulin over 30 min rapidly reduces serum potassium. Administration of glucose without insulin may temporarily aggravate hyperkalemia. Sodium bicarbonate also shifts potassium into the cells, especially in acidosis. As potassium is transferred into cells, measures to remove it from the body

should be instituted. A treatment that actually removes potassium from the body can be done by using sodium polystyrene sulfonate (Kayexalate®) or dialysis.

27.3 Calcium

27.3.1 Hypercalcemia

Immobilization-related hypercalcemia in children and adolescents with spinal cord injuries is a common metabolic complication during the first several months after injury. Hypercalcemia is defined as serum calcium (Ca^{2+}) > 10.5 mg/dL or ionized serum calcium >5.3 mg/dL. Generally, severe hypercalcemia is considered when serum calcium is above 14 mg/dL. Hypercalcemia affects multiple organs in the body, including the kidney, heart, brain, peripheral nerves, and gut (Reddi 2018). Most cases of immobilization hypercalcemia occur in adolescent boys after a recent spinal cord injury. In addition to gender (male), the risk factors include age <21 years, complete neurological injuries, high cervical cord injuries, dehydration, and a prolonged period of immobilization. A preinjury history of large ingestion of milk and/or extreme exposure to sunshine can also be contributory factors (Maynard 1986). Symptoms most common in the milder clinical syndrome include anorexia, nausea, lightheadedness, headache, malaise, constipation, depression. The persistence of any of these symptoms should alert the physician to check for serum calcium. The predominant symptoms in the more severe clinical syndrome include persistent nausea and vomiting, acute gastric dilatation, fecal impaction, and abdominal pain mimicking an "acute abdomen." Polyuria and polydipsia can result from an inability of the kidneys to concentrate urine, due to microscopic nephrocalcinosis. Polyuria accompanying nausea and anorexia may lead to dehydration. Other serious symptoms include bradycardia, cardiac irregularities, syncope, and seizures. Severe orthostatic hypotension associated with nausea and light headedness can also make wheelchair mobilization of the patients difficult (Maynard 1986).

Laboratory studies include an elevated serum calcium, normal serum phosphorus, normal or only slightly elevated serum alkaline phosphatase, and a normal chloride to phosphorus ratio (Maynard 1986). Since immobilization hypercalcemia is self-limiting until a new equilibrium of bone formation and resorption is reached, treatment is aimed at preventing complications. Asymptomatic or mild hypercalcemia, calcium 10.5–12 mg/dL, does not require urgent treatment. Calcium 12–14 mg/dL, moderate hypercalcemia, does not require urgent treatment if it is chronic and if it is not related to symptoms. Adequate oral fluid intake is recommended, and the underlying disease should be treated. Treatment of severe hypercalcemia, calcium >14 mg/dL, or symptomatic hypercalcemia is performed by infusion of intravenous saline at a rate of at least 200 mL/h as tolerated, with close monitoring for volume overload. In the treatment of hypercalcemia, vigorous hydration is the most important. If volume overload occurs, a loop diuretics such as furosemide 40 mg IV may be administered concurrently to reduce the large sodium load. Furosemide-induced volume depletion may increase the reabsorption of calcium by the proximal tubule, so the use of furosemide in the management of acute hypercalcemia has been questioned by many clinicians. Administration of intravenous bisphosphonates such as pamidronate or zoledronic acid is usually the next step because saline diuresis alone does not usually achieve normal calcium levels with severe hypercalcemia (Table 27.4). To avoid ingestion of vitamin D, milk and multivitamin preparation containing vitamin D should be restricted.

27.3.2 Hypocalcemia

Hypocalcemia, serum calcium <8.5 mg/dL or ionized serum calcium <4.65 mg/dL, rarely occurs in rehabilitation populations. The leading causes of hypocalcemia are parathyroid hormone disorder and vitamin D deficiency. Severe hypomagnesemia can be a contributing cause. Asymptomatic mild hypocalcemia, serum calcium 7.5–8.4 mg/dL, does not require emergency treatment. Mild symptoms, such as paresthesias

Table 27.4 Treatment of acute hypercalcemia

Treatment	Dosage	Route	Duration of effect	Mechanism
Promote Ca^{2+} excretion				
Normal saline	1–2 L every 6 h	IV	4–6 h	Improves GFR and promotes Ca^{2+} excretion
Furosemide	40–120 mg every 2–4 h	IV	2–4 h	Inhibits Ca^{2+} reabsorption in TALH
Decrease bone resorption				
Calcitonin	2–4 MRC units/kg every 4–8 h	IV	4–12 h	Inhibits bone resorption
Pamidronate	30–90 mg in 100–200 mL saline or D5W once	IV over 4–24 h	2–3 weeks	Inhibits bone resorption. Clinical response takes 2–3 days
Zoledronate	4 mg in 50 mL of saline or D5W once	IV over 15–20 min	2–3 weeks	Inhibits bone resorption. Clinical response takes 2–3 days
Gallium citrate	200 mg/m^2/day in 1L of saline for 5 days	IV	1–2 weeks	Inhibits bone resorption
Decrease intestinal absorption				
Prednisone	20–30 mg every 12 h	Oral	2–4 days	Inhibits gut absorption
Decrease plasma [Ca^{2+}]				
Hemodialysis	Use dialysate bath containing low Ca^{2+}		Few hours	Removal from blood

From Reddi (2018)
IV intravenous, MRC Medical Research Council, TALH thick ascending limb of Henle's loop, GFR glomerular filtration rate, D5W 5% dextrose in water

associated with serum calcium levels above 7.5 mg/dL, can be treated with oral calcium supplements such as calcium carbonate.

27.4 Hormonal Changes

Renin release is continuously stimulated by eliminating the descending inhibition of the sympathetic nervous system in the renal apparatus that synthesizes and releases renin. Increased plasma renin activity stimulates angiotensin II formation and promotes the synthesis of aldosterone. The effect of increased aldosterone promotes renal sodium reabsorption and potassium excretion observed in new tetraplegic patients. In addition, enhanced sodium reabsorption leads to water retention (Claus-Walker and Halstead 1981). The levels of supine plasma renin activity were found to be between 3.45 and 4.19 ng/mL/h in tetraplegic patients and significantly higher than the 1.04 ng/mL/h in healthy subjects (Claus-Walker et al. 1977). Supine plasma aldosterone levels are also higher in tetraplegic patients. Tetraplegic patients showed a fourfold increase in ADH during rapid tilting and a similar but less dramatic rise in plasma ADH level after gradual tilt. In contrast, no change in ADH concentration occurred in normal subjects during a rapid or gradual tilt (Sved et al. 1985).

27.5 Chronic Dependent Edema

Dependent edema is a common and clinically significant complication in patients with spinal cord injuries. The edema that usually occurs in the lower extremities is relatively symmetrical and tends to be most severe in the distal portion of the limbs and may occur in the upper extremities or trunks and is most prominent in the dorsal surfaces of the lower and upper extremities. Problems caused by swelling of the lower extremities include pressure injuries, contractures, wheelchair seating, and difficult shoe fitting. Other causes of lower extremity swelling, including deep vein thrombosis, heterotopic ossification, cellulitis, intramuscular bleeding, or other medical complications, should be excluded. In general, the timing, symmetry, appearance,

and clinical situation of these problems differ from those of dependent edema.

One of the causes of the edema is the pooling of fluid and blood in the veins and interstitial spaces of the lower extremities, which are often placed in the dependent position by most paraplegics and tetraplegics. The concomitant reduction in muscle pumping action results in loss of the normal propulsion of fluid and blood in a cephalic direction against gravity. Loss of autonomic regulation of the vascular smooth muscle tone and venous valve activity, which provides a continuous upward flow of blood and fluids, provides additional causes of dependent edema. The best treatment for dependent edema is prevention. It is desirable to avoid the dependent portion. Thigh-high compression stockings are the most effective way to reduce the amount of edema.

References

Adrogue HJ, Madias NE. Hyponatremia. NEJM. 2000;342:1581–9.

Berl T, Rastegar A. A patient with severe hyponatremia and hypokalemia: osmotic demyelination following potassium repletion. Am J Kidney Dis. 2010;55:742–8.

Buffington MA, Abreo K. Hyponatremia: a review. J Intensive Care Med. 2016;31:223–6.

Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: I. The nervous system before and after transection of the spinal cord. Arch Phys Med Rehabil. 1981;62:595–601.

Claus-Walker J, Spencer WA, Carter RE, et al. Electrolytes and the renin-angiotensin-aldosterone axis in traumatic quadriplegia. Arch Phys Med Rehabil. 1977;58:283–6.

Furlan JC, Fehlings MG. Hyponatremia in the acute stage after traumatic cervical spinal cord injury: clinical and neuroanatomic evidence for autonomic dysfunction. Spine (Phila Pa 1976). 2009;34:501–11.

Goh KP. Management of hyponatremia. Am Fam Phys. 2004;69:2387–94.

Green F, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.

Kriz J, Schuck O, Horackova M. Hyponatremia in spinal cord injury patients: new insight into differentiating between the dilution and depletion forms. Spinal Cord. 2015;53:291–6.

Kugler JP, Hustead T. Hyponatremia and hypernatremia in the elderly. Am Fam Physician. 2000;61:3623–30.

Maynard FM. Immobilization hypercalcemia following spinal cord injury. Arch Phys Med Rehabil. 1986;67:41–4.

Preston RA. Acid-base, fluids and electrolytes: made ridiculously simple. 2nd ed. Miami, FL: MedMaster, Inc.; 2011.

Reddi AS. Fluid, electrolyte and acid-base disorders: clinical evaluation and management. 2nd ed. Cham: Springer; 2018.

Rondon-Berrios H, Agaba EI, Tzamaloukas AH. Hyponatremia: pathophysiology, classification, manifestations and management. Int Urol Nephrol. 2014;46:2153–65.

Soni BM, Vaidyanthan S, Watt JW, et al. A retrospective study of hyponatremia in tetraplegic/paraplegic patients with a review of the literature. Paraplegia. 1994;32:597–607.

Sterns RH. Disorders of plasma sodium—causes, consequences, and correction. N Engl J Med. 2015;372:55–65.

Sterns RH, Cappuccio JD, Silver SM, et al. Neurologic sequelae after treatment of severe hyponatremia: a multicenter perspective. J Am Soc Nephrol. 1994;4:1522–30.

Sved AF, McDowell FH, Blessing WW. Release of antidiuretic hormone in quadriplegic subjects in response to head-up tilt. Neurology. 1985;35:78–82.

Thurman JM, Beri T. Disorders of water metabolism. In: Mount DB, Sayegh MH, Singh AK, editors. Core concepts in disorders of fluid, electrolytes and acid-base balance. New York: Springer; 2013.

Yee AH, Rabinstein AA. Neurologic presentations of acid-base imbalance, electrolyte abnormalities, and endocrine emergencies. Neurol Clin. 2010;28:1–16.

Zenenberg RD, Carluccio AL, Merlin MA. Hyponatremia: evaluation and management. Hosp Pract (1995). 2010;38:89–96.

Recommended Additional Reading

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.

Reddi AS. Fluid, electrolyte and acid-base disorders: clinical evaluation and management. 2nd ed. Cham: Springer; 2018.

Mount DB, Sayegh MH, Singh AK, editors. Core concepts in disorders of fluid, electrolytes and acid-base balance. New York: Springer; 2013.

Preston RA. Acid-base, fluids and electrolytes: made ridiculously simple. 2nd ed. Miami, FL: MedMaster, Inc.; 2011.

Reddi AS. Fluid, electrolyte and acid-base disorders: clinical evaluation and management. 2nd ed. New York: Springer; 2018.

Weaver LC. In: Polosa C, editor. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

Metabolic Disorders in Spinal Cord Injuries

28

As the life expectancy of people with spinal cord injuries increases, health concerns related to aging become an important role in their overall health (Lavis et al. 2007). People with spinal cord injuries live longer and experience the same health problems as able-bodied people, but they also have secondary health problems that are unique to spinal cord injuries (Mishori et al. 2016), because spinal cord injuries profoundly affect almost all aspects of a person's life, including anatomy, physiology, psychosocial interactions, spirituality, and self-esteem, all of which contribute to a person's body composition (Garter and Farkas 2016). Although life expectancy has increased through improved emergency care and long-term management techniques, the life expectancy of people with spinal cord injuries remains below that of the general population (NSCISC 2021). Changes in basal metabolism and body composition after spinal cord injury often increase the risk of metabolic syndrome and cardiovascular disease. The prevalence of metabolic syndrome in people with spinal cord injuries is higher than that of the general population (Gater et al. 2019). Since people with chronic spinal cord injuries are predisposed to accelerated atherogenesis, dyslipidemia, and glycemic dysregulation, it is not surprising that cardiovascular disease has become a leading cause of mortality among people with spinal cord injury (Milligan et al. 2020; Yarar-Fisher et al. 2017). Neurogenic obesity is common in people with chronic spinal cord injuries, resulting in the cardiometabolic syndrome of insulin resistance, dyslipidemia, hypertension, and ultimately accelerated arteriosclerosis (Yarar-Fisher et al. 2017).

Metabolic syndrome is a group of a cardiovascular risk factors that predispose an individual to cardiovascular disease and type 2 diabetes (Holt 2005). Unique considerations related to spinal cord injury that impact both assessment and management of cardiometabolic risks including obesity, impaired glucose tolerance/insulin resistance, dyslipidemia, and hypertension should be evaluated and managed to optimize the cardiometabolic health of this population (Sabharwal 2019). Cardiovascular disease is also seen as a major cause of mortality and morbidity in people with spinal cord injuries, particularly with aging and longer life span of this population. Asymptomatic heart diseases have also been found in people with spinal cord injuries, making early detection of risk factors, diagnosis, and primary prevention of coronary heart disease even more important (Bauman et al. 1993, 1994). Rapid bone loss due to lack of axial loading on the bones and immobility also increases the risk of fracture after spinal cord injury.

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28.1 Metabolic Syndrome

The average survival rate of patients with spinal cord injuries has increased, and this population is prone to the same chronic condition as the general population (Bauman and Spungen 2000). Cardiovascular disease is the most common cause of death in the general population and is also one of the leading causes of death in chronic spinal cord injury. Persons with spinal cord injuries had higher incidence and earlier occurrence of cardiovascular disease than the general population (NSCISC 2021). It is believed that the accumulation of adipose tissue is a significant contribution to the development of the metabolic syndrome in people with spinal cord injuries. Similarly, altered body composition after spinal cord injury has been proposed as a major cause of increased glucose intolerance, insulin resistance, dyslipidemia, and cardiovascular disease (Bauman et al. 2001). Spinal cord injury itself causes an additional risk of cardiovascular disease due to significant changes in metabolic function and physical activity (Claus-Walker and Halstead 1982d). One study showed that more than 75% of veterans with chronic spinal cord injuries are observed and more than 50% have metabolic syndrome (Gater et al. 2019).

Metabolic syndrome is defined as a cluster of cardiovascular risk factors that predispose to cardiovascular disease and type 2 diabetes. One of the most commonly used criteria for diagnosis of metabolic syndrome is central obesity established by the International Diabetes Federation, which is more than 94 cm for men and 80 cm for women and includes two of the following four factors: hypertriglyceridemia, low HDL cholesterol, hypertension, and raised fasting glucose (Nash and Mendez 2007). People with spinal cord injuries with the same body mass index (BMI) as able-bodied individuals are about 13% fatter due to loss of skeletal muscle and characteristic increase in adipose tissue after injury (Spungen et al. 2003). Therefore, the application of these criteria to individuals with spinal cord injuries, including BMI or waist circumference, may not be appropriate.

28.1.1 Changes in Body Composition after Spinal Cord Injury

Energy expenditure is even more complex and difficult to quantify. Total daily energy expenditure is composed of the basal metabolic rate, thermic effect of activity, and thermic effect of food (Gater et al. 2019). Basal metabolic rate, often used interchangeably with resting energy expenditure, is the minimal energy expenditure required to sustain life; it represents approximately 70% of the total daily energy expenditure, and it is highly correlated with an individual's fat-free mass (Gater et al. 2019; Illner et al. 2000). Fat-free lean mass consisting of muscle, bone, and organ tissue contributes significantly to the basal metabolism (Illner et al. 2000). Spinal cord injury interferes with basal metabolism due to the somatic nervous system disorder resulting in significant muscle atrophy below the level of injury. The interruption of the autonomic nervous system in higher level spinal cord injury leads to a dominance of the parasympathetic nervous system, which reduces the metabolic demands (Buchholz and Pencharz 2004). The basal metabolic rates after spinal cord injury were associated with an increased adiposity, abnormal glucose homeostasis, reduced high-density lipoprotein (HDL), elevated low-density lipoprotein (LDL), triglycerides (TG), and total cholesterol and are 14–27% lower than controls (Monroe et al. 1998). Skeletal muscle atrophy, changes in body metabolism, and reduced activity levels following spinal cord injury ultimately lead to significant changes in body composition with reduced lean body mass and increased body fat ratios (Gater 2007b).

HDL accounts for about 20–30% of total serum cholesterol levels. LDL makes up approximately 60–70% of serum cholesterol levels. It is believed to be the primary atherogenic cholesterol compound (Lavis et al. 2007). Low levels of HDL increase the risk of developing coronary heart disease. Conversely, increased levels of serum HDL show a protective effect. HDL levels <40 mg/dL are independent risk factors for the development of coronary heart disease. Major risk factors for coronary heart disease that all

Table 28.1 Major risk factors for coronary heart disease

Modifiable risk factors	Non-modifiable risk factors
Cigarette smoking Hypertension (BP ≥140/90 mmHg or on antihypertensive medication) Low HDL <40 mg/dL[a] Diabetes	Age (men ≥45, women ≥55) Family history

Data from NCEP (2002)
[a]HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor

individuals face are listed in Table 28.1. Approximately 10% of the general population have HDL levels <35 mg/dL, compared with up to 40% in people with spinal cord injuries (Bauman et al. 1992, 1999a). Approximately 25% of the general population is considered high in LDL cholesterol. People with spinal cord injuries have been shown to have LDL levels similar to that of the general population (Bauman et al. 1999b). Changes in lipid metabolism develop early and progress over time after spinal cord injury. The major disruption in spinal cord injury is a profound reduction in HDL cholesterol. Reduced HDL cholesterol levels are associated with higher neurologic level of injury, motor complete injuries, and increased abdominal circumference. It has been reported that serum LDL, total cholesterol, and TG in male and female spinal cord injuries are similar to the general population (Bauman et al. 1999a). Elevated triglycerides are very commonly associated with some nonlipid risk factors for coronary artery disease, including diabetes, obesity, high carbohydrate diets, sedentary lifestyles, hypertension, excess alcohol intake, and cigarette smoking (NCEP 2002).

BMI is a measure of body weight in kilograms divided by the square of height in meters (kg/m^2). It is believed that the BMI reflects obesity. In the general population, people with BMI >25 kg/m^2 are considered overweight and those with BMI >30 kg/m^2 are considered obese. In spinal cord injury, BMI or body weight may not accurately reflect obesity, with the threshold specified for able-bodied individuals, given the increased percentage of body fat. Lower BMI cutoff for overweight is recommended for patients with spinal cord injuries (e.g., 22 kg/m^2 instead of 25 kg/m^2 to consider overweight) (Gater 2007a; Laughton et al. 2009). Depending on the neurological level and completeness of injury, lower caloric intake for spinal cord injury may be more appropriate than recommended by standard guidelines based on body weight (Gater 2007b). In addition to cardiovascular risk, overweight and obesity in people with spinal cord injuries can have many adverse effects such as functional impairment, increased susceptibility to overuse injuries, and increased risk of respiratory impairment.

28.1.2 Diagnosis

An international consensus definition of the metabolic syndrome presented by the International Diabetes Federation (IDF), which is one of the most commonly used criteria, has been more strictly defined in relation to central obesity. The IDF definition of metabolic syndrome is central obesity of waist circumference ≥94 cm in men and ≥80 cm in women plus any two of the following four criteria: (1) hypertriglyceridemia (TG ≥150 mg/dL or on specific treatment for this lipid abnormality); (2) low HDL cholesterol (HDL <40 mg/dL for men and <50 mg/dL for women or on specific treatment for low HDL); (3) hypertension (≥130/85 mmHg or on treatment for hypertension); and (4) raised fasting glucose (≥100 mg/dL or previously diagnosed with type 2 diabetes mellitus) (Alberti et al. 2006; Gater et al. 2019; Holt 2005; Nash and Mendez 2007). For reference, the definition of metabolic syndrome in the National Cholesterol Education Project Adult Treatment Panel III (NCEP ATP III) (Eckel and Cornier 2014) is as follows: central obesity (waist circumference >102 cm in males, >88 cm in females), atherogenic dyslipidemia (triglyceride >150 mg/dL, and/or high-density lipoprotein (HDL)-c <40 mg/dL in men, <50 mg/dL in women), hypertension (blood pressure >130/85 mmHg), and insulin resistance and hyperglycemia (fasting glucose >110 mg/dL) (NCEP 2002) (Table 28.2).

Obesity and overweight were defined by the World Health Organization (WHO) as BMI

Table 28.2 Clinical identification of the metabolic syndrome (any 3 of the following)

Risk factor	Defining level
Abdominal obesity	*Waist circumference*
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/85 mmHg
Fasting glucose	≥110 mg/dL

From NCEP (2002)

≥30.0 kg/m^2 and 25 kg/m^2, respectively (WHO 2000). Although the BMI is used as a marker for obesity in most populations, it grossly underestimates obesity in populations with low bone mass and sarcopenia and overestimates obesity in athletic populations with high muscle and bone mass because it does not take into account the relative densities of fat and fat-free mass in these populations. Therefore, traditional measures of obesity, including BMI or waist circumference, have not been properly validated in people with spinal cord injuries, whose obesity appears to be significantly increased compared to able-bodied persons of similar age, weight, and gender. In fact, the standard application of BMI grossly underestimates obesity in people with spinal cord injuries (Garter and Farkas 2016). Paralysis of the abdominal muscles in spinal cord injuries may not be an accurate assessment of central obesity by increasing waist circumference measurement (Gater 2007a). Orthostatic hypotension or neurogenic resting hypotension or autonomic dysreflexia can confuse blood pressure. Laboratory tests for specific aspects of nutritional assessment include lipid profile, prealbumin and albumin levels for protein status assessment, and level of vitamin D levels to confirm deficiency and replacement need (Groah et al. 2009; Ingenbleek et al. 1975).

Ideal body weight for paraplegic patients may need to be adjusted downward by 5% to 10% and 10% to 15% for tetraplegic patients. As mentioned above, BMI may underestimate obesity in patients with spinal cord injuries, so lowering the cutoff level for overweight is recommended. Other anthropometric measurements, such as arm circumference or skinfold thickness, are also considered to be inaccurate in patients with spinal cord injuries. Despite fasting glucose intolerance and/or hyperinsulinemia, it is also important to recognize that fasting glucose levels are usually within the normal range after spinal cord injury. Therefore, it is advisable to screen patients with a 2 h glucose intolerance test.

28.1.3 Treatment

Diet and exercise interventions are considered the cornerstone of treatment because changes in body composition are an underlying etiology of metabolic syndrome after spinal cord injury. Strategies such as diet changes that are low-fat, low-cholesterol dietary changes and increased physical activity are often first-line therapeutic strategies. There is no consensus on optimal type, intensity, or duration of exercise after spinal cord injury, but it seems to have minimal limitations on cardiovascular health. A moderate-intensity exercise that is performed at least 20–60 min/day for at least 3 days per week is recommended. The American College of Sports Medicine and Dietary Guidelines of America recommendation of 150 min of exercise per week are likely not enough for people with spinal cord injuries due to their obligatory sarcopenia and osteopenia, which significantly reduces their energy expenditure (Collins et al. 2010). Upper extremity ergometry may be a good option for many individuals with spinal cord injuries. There is no clear guideline on nutritional recommendations for people with spinal cord injury with glucose intolerance, dyslipidemia, and cardiovascular disease. However, regular nutritional assessment and education should be performed.

The general parameters of caloric intake based on weight or BMI may not be accurate in spinal cord injuries. To determine the ideal caloric intake, the difference in age, sex, body habits, and activities should be considered. The average daily caloric requirement, however, should be less than 5% to 10% of the ideal body weight for paraple-

gics and 10% to 15% less than the standard for tetraplegics. The average estimated energy requirement was reported to be about 23 kcal/kg/d in people with paraplegia and about 28 kcal/kg/d in people with tetraplegia. In addition to proper caloric intake, nutritional counseling should emphasize increased intake of fruits and vegetables and reduced saturated fat and refined carbohydrates intake. Protein requirement is significantly increased during the acute hypercatabolic stage in the initial weeks after spinal cord injury, when a negative nitrogen balance is typical. However, the protein requirement after the acute phase is about 0.8 gm/kg, which is similar to the general population. The presence of pressure injuries increases protein requirement, especially in Stage 3 and 4 wounds (Groah et al. 2009).

In persons with impaired glucose tolerance, metformin is considered the first-line pharmacologic treatment to reduce risks of hypoglycemia and fluid retention and to improve cost-effectiveness. For lipid changes, it is advisable to focus on HDL cholesterol in patients with spinal cord injuries. People with elevated LDL levels and two or more risk factors (Table 28.1) are treated much more aggressively with lipid-lowering medications and have lower target LDH values (Lavis et al. 2007; NCEP 2002) (Table 28.3). The intensity of statin therapy is divided into 3 categories: high-intensity, moderate-intensity, and low-intensity. High-intensity statin therapy typically lowers LDL-C levels by ≥50%, moderate-intensity statin therapy by 30% to 49%, and low-intensity statin therapy by <30% (Grundy et al. 2019) (Table 28.4). People with clinical vascular disease should be treated, as tolerated, with high-intensity statins, and people with LDL levels ≥190 mg/dL should be offered high-intensity statins. In addition, adults aged 40 or older with LDL levels ≥70 mg/dL should be offered treatment with a moderate-intensity statin (Stillman et al. 2020).

Table 28.3 Classification of LDL, total, and HDL cholesterol (mg/dL)

LDL cholesterol—Primary target of therapy	
<100	Optimal
100–129	Near optimal/above optimal
130–159	Borderline high
160–189	High
≥190	Very high
Total cholesterol	
<200	Desirable
200–239	Borderline high
≥240	High
HDL cholesterol	
<40	Low
≥60	High

From NCEP (2002)

28.2 Disorder of Glycemic Regulation

The physical inactivity observed in tetraplegia leads to muscle wasting and fat deposition, which impair the effectiveness of insulin. The average cross-sectional area of atrophied skeletal muscle of the legs in the patients was 45–80% of that of age- and weight-matched able-bodied controls 24 weeks after complete spinal cord injury (Castro et al. 1999). The loss of muscle mass is critical as insulin acts peripherally on the individual's muscle mass for glucose metabolism (Lavis et al. 2007). When people with spinal cord injuries develop diabetes mellitus, the medical burden of an already devastating disorder increases. Conversely, the presence of spinal cord injuries increases the difficulty of managing diabetes mellitus. The incidence of non-insulin-dependent diabetes mellitus (type II) appears to be increased in people with spinal cord injuries. Insulin levels during oral glucose tolerance testing are significantly higher in the diabetic spinal cord injury persons than in the general population, suggesting that diabetes mellitus in spinal cord injuries is the result of insulin resistance, which results in decreased fall in blood glucose following intravenous insulin when compared to controls (Duckworth et al. 1980, 1983). There was no correlation between oral glucose tolerance test and HbA1c results (Stillman et al. 2017). Insulin resistance in spinal cord injuries appears to be the result of central obesity, which increases fatty acid metabolites and proinflammatory cytokines in liver and muscle (Stillman et al. 2020).

Table 28.4 High-, moderate-, and low-intensity statin therapy

	High-intensity statin therapy	Moderate-intensity statin therapy	Low-intensity statin therapy
LDL-C lowering	≥50%	30–49%	<30%
Statins	Atorvastatin (40 mg) 80 mg Rosuvastatin 20 mg (40 mg)	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20–40 mg Pravastatin 40 mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1–4 mg	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

From Grundy et al. (2019), with permission

Caloric reduction and exercise are the most important therapies of type 2 diabetes mellitus patients. Since muscle mass is decreased in spinal cord injuries and activity is reduced, caloric intake must be decreased depending on the level of injury. Caloric requirements for a paraplegic, for example, should be based on a body weight that is 5–10% below standard ideal body weight. Ideal body weight for a tetraplegic is below 10–15% less than the standard.

The American Diabetes Association (ADA) guidelines are used to diagnose diabetes and pre-diabetes based on fasting plasma glucose (FPG), the 2-h plasma glucose value after a 75-g oral glucose tolerance test (OGTT), or HbA1c criteria (Consortium for Spinal Cord Medicine 2018). Standards of Medical Care in Diabetes published by the ADA described methods and criteria for identifying type 2 pre-diabetes and diabetes (American Diabetes Association 2017; Marathe et al. 2017) (Table 28.5). Criteria for the diagnosis of diabetes include either HbA1c ≥6.5% or fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L) after no caloric intake for at least 8 h, or 2-h PG ≥200 mg/dL (11.1 mmol/L) during an OGTT with the test performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L) is also considered diagnostic of diabetes in the general population. However, in spinal cord injuries this could be confusing since such symptoms, including polyuria, polydipsia, weight loss, and fatigue, often have other etiologies. Criteria for identifying pre-diabetes include either A1c 5.7 to 6.4% (39 to 47 mmol/mol), or FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L), or 2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L). In all three tests, the risk is continuous, extends below the lower limit of the range, and becomes disproportionately larger at the higher end of the range (Consortium for Spinal Cord Medicine 2018).

Table 28.5 Criteria for the diagnosis of pre-diabetes and diabetes

Criteria	Pre-diabetes	Diabetes
A1C	5.7–6.4%	≥6.5%
Fasting plasma glucose	100–125 mg/dL (5.6–6.9 mmol/L)	≥126 mg/dL (7.0 mmol/L)
Oral glucose tolerance test	140–199 mg/dL (7.8–11.0 mmol/L)	≥200 mg/dL (11.1 mmol/L)[a]
Random plasma glucose		≥200 mg/dL (11.1 mmol/L)[b]

Oral glucose tolerance test: 2 h, 75 g glucose
[a]In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing
[b]Only diagnostic in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis

The ADA's 2017 Standards of Care include a new classification for hypoglycemia: clinically significant hypoglycemia is defined as blood glucose levels <54 mg/dL, while blood glucose levels <70 mg/dL should be used as an "alert value" to help individuals avoid more severe hypoglycemia (American Diabetes Association 2017; Marathe et al. 2017). Hypoglycemia can also result from exercise with increased glucose utilization, insufficient intake, nausea, and vomiting. If hypoglycemia is recognized, taking glu-

cose quickly in the form of juice or candy or intravenous dextrose to prevent serious neurological complications such as seizure or coma is required. Some people with diabetes may not be aware of hypoglycemic symptoms. The most common causes of hyperglycemia, fasting blood sugar over 140 mg/dL, or postprandial blood glucose over 180 mg/dL are inadequate hypoglycemics, infection, and adverse effects of some medications including glucocorticoids and some psychotropic drugs. Optimal glucose control should avoid blood sugar levels below 90–100 mg/dL to prevent hypoglycemic complications. Drug therapy is generally recommended to achieve blood glucose targets ranging from 90 to 180 mg/dL.

28.3 Bone Loss after Spinal Cord Injury

There is uncoupling of the normal homeostatic mechanisms responsible for bone maintenance (bone formation and bone resorption) due to a significant increase in bone resorption after spinal cord injury. Immediately after spinal cord injury, it affects osteoclastic bone resorption and osteoblastic bone formation, but osteoblast function is slowed over the next few months, resulting in bone resorption and rapid bone loss (Ashe et al. 2007; Maïmoun et al. 2011). It is clinically reflected when the hypercalciuria develops. Bone loss begins within days to weeks after injury, and bone mineral density (BMD) decreases up to 4% a month at accelerated rates from the first 6 months to 12 months (Giangregorio and McCartney 2006). Bone loss lasts for years at a slow rate until it stabilizes. 25–50% of BMD will disappear in the lower extremities in 2–3 years. Lower extremity bone mineral content plateaus at 2/3 normal, while upper limb bone mineral content is preserved or even increased, depending on the neurological level of injury due to wheelchair propulsion and transfers (Clasey et al. 2004; de Bruin et al. 2005; Frey-Rindova et al. 2000). Although both cortical and trabecular bone loss occur, trabecular bone appears to be particularly susceptible (e.g., in proximal and distal femoral and tibial epiphysis and diaphysis). Calcium released by bone is excreted by the kidneys, and hypercalciuria occurs within the first week and lasts for 6 to 18 months. Hypercalcemia may peak at 1 to 6 months (Ashe et al. 2007; Maïmoun et al. 2011).

The degree of bone loss in the acute period after spinal cord injury varies between 2 and 4% per month (Edwards et al. 2014). This is significantly faster in bone loss compared to microgravity (0.25% per week) (Vico et al. 2000) and bed rest (0.1% per week) (Leblanc et al. 1990). Rapid bone loss after spinal cord injury occurs at sites that are predominantly below the level of injury (Dauty et al. 2000). Bone loss in the upper extremities is seen in tetraplegia but not in paraplegia. Lumbar spine BMD is normal or increases in patients with chronic spinal cord injury (Biering-Sörensen et al. 1998).

28.3.1 Assessment

Dual-energy X-ray absorptiometry (DXA) is the gold standard for the diagnosis of osteoporosis and is the most widely used assessment technique for determining treatment effectiveness. Imaging with DXA exaggerates BMD in the presence of osteophytes, vascular calcification, microcompression fractures, and other skeletal abnormalities (Bauman et al. 2009). The test results are presented in the form of two scores, a T score (BMD compared with a young adult of the same sex with peak bone mass) and a Z score (BMD compared to the same age group, size, and gender). T scores are used to predict fracture risk. T score above −1 is considered normal, −1 to −2.5 is defined as osteopenia, and below −2.5 is defined as osteoporosis. The diagnosis of osteoporosis in postmenopausal women using the WHO criteria is made using DXA with a serial BMD T score that is ≥2.5 standard deviation below the young adult mean. Other able-bodied populations, including men under the age of 50 and premenopausal women, use a Z score that compares individual's BMD with age-matched peers. If the Z score is ≤–2 SD, it is considered useful to begin treatment.

Unlike osteoporosis management in the general population, clinicians differ in screening, prevention, and treatment of bone loss after spinal cord injury (Bauman et al. 2010). The standard sites for DXA measurements do not match with the most common sites of fracture after spinal cord injury. Hip BMD has a moderate correlation with distal femur BMD and has a slight correlation with proximal BMD (Shields et al. 2005). The distal femur and proximal tibia were proposed as sites for BMD measurements in patients with spinal cord injuries and were found to be the best predictors of fracture risk (Dionyssiotis 2011; Lala et al. 2013).

Plain films have limitations for early diagnosis. Plain films can be normal until BMD is reduced by 30%. Peripheral quantitative computed tomography (pQCT) has been proposed as an imaging technique to assess bone loss after spinal cord injury. It can distinguish cortical bone from trabecular bone and quantify bone architecture. QCT has limited availability of osteoporosis assessment beyond the research setting. Vitamin D levels should be measured. Bone turnover biomarkers include hydroxyproline, C-telopeptide, and N-telopeptide. Their role in clinical management is unclear.

28.3.2 Management

Treatment of bone loss after spinal cord injury includes treatment of secondary cause of osteoporosis, lifestyle modifications, supplementation, rehabilitation interventions, and pharmacologic intervention. The best way to treat bone loss after spinal cord injury is a combination of these treatments (Charmetant et al. 2010). Standing and walking, electrical stimulation, and functional electrical stimulation have been studied to prevent bone loss after spinal cord injury (Biering-Sörensen et al. 2009; Dolbow et al. 2011). There is evidence that bisphosphonates and human monoclonal IgG antibody to receptor activator of nuclear factor-κB ligand (RANKL) (denosumab) (Cirnigliaro et al. 2020; Gifre et al. 2016) can mitigate bone loss in the lower limbs in individuals with spinal cord injuries when they are administered early or even later after the onset of neurologic injury (Cirnigliaro et al. 2020; Sadowsky et al. 2020). Pharmacological prevention of bone loss in acute spinal cord injury focuses on the use of bisphosphonates to inhibit osteoclast recruitment, reduce osteoclast lifespan, inhibit osteoclast activity, and inhibit bone resorption (Bauman et al. 2010). Bisphosphonates, weekly alendronate or every 6–12 months zoledronic acid infusion, are the most commonly prescribed pharmacological drugs. Treatment also includes early initiation of weight loading and other physical modalities through adequate rehabilitation (Sadowsky et al. 2020). Patients with chronic spinal cord injuries who have decreased BMD are recommended to administer calcium 1000 mg/d with rapid bone resorption and without renal or bladder pathology.

28.4 Fractures

A fracture below the level of injury is a well-known complication of bone loss after spinal cord injury. Fractures are relatively rare in the first year after spinal cord injury and increase linearly over time. Many fractures have been shown to increase the risk of fractures after spinal cord injury, such as female, age, increased time post-injury, paraplegia, motor complete injuries, low body mass index, low knee BMD, and medications including anticonvulsants, heparin, and opioids. The prevalence of fractures in chronic spinal cord injured population is 25–46%. The most common sites of fractures are the knee (distal femur and proximal tibia), followed by the distal tibia, femoral shaft, femoral neck, and humerus (Friesbie 1997). Most fractures are caused by minor injuries when performing normal activities of daily living such as transfers, range of motion, low-impact collisions, falls, or even stretching. It is known that torsional loads are the major impact of fractures.

Symptoms of acute fractures can vary but may include fever, pain, swelling, increased spasticity, or autonomic dysreflexia. As a rule, work-up with a standard X-ray is sufficient. During the physical examination, the shortening or narrowing of the Bryant's triangle (Fig. 28.1) by palpating the

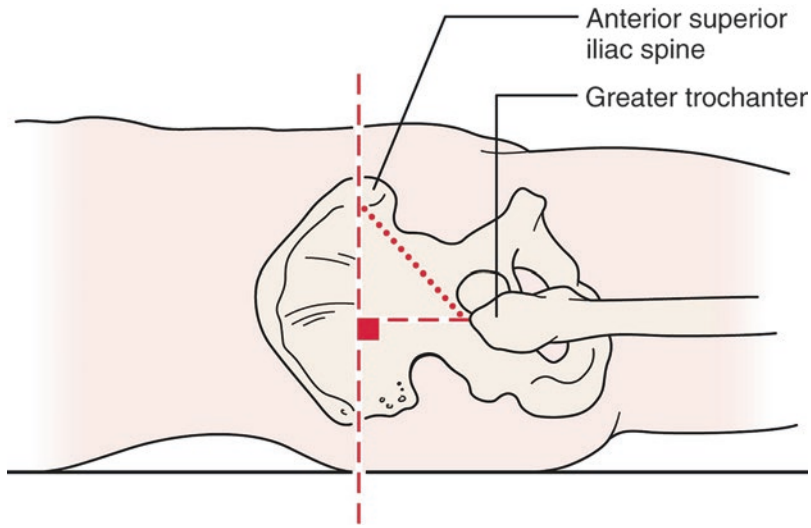

Fig. 28.1 Bryant's triangle. From Magee (2020), with permission

lateral hip area in a wheelchair is important for people with spinal cord injury in order to assess the fracture of the femur neck or hip dislocation. The Bryant's triangle (or iliofemoral triangle) is represented by the right-angled triangle on a line from the anterior superior iliac spine to the top of the greater trochanter (Magee 2020). The two sides should be compared. For those who are ambulatory, fracture management is similar to the non-spinal cord injury population. For individuals who do not use their lower extremities for functional mobility, the main objective of the treatment is to preserve the function before fracture and maintain a satisfactory alignment while minimizing complications. Surgery, circumferential casting, and external fixation are not indicated as decreased bone mass and risk of recurrent bacteremia, skin breakdown, and osteomyelitis.

Nonsurgical treatment with soft padded splints, such as a well-padded knee immobilizer for femoral supracondylar, femoral shaft, and proximal tibia fractures or a well-padded ankle immobilizer for distal tibia fractures, is generally recommended. The patients can sit in a few days, and the ROM starts in 3–4 weeks. Surgical intervention is generally recommended for proximal femur fracture and severely displaced fractures and rotational deformities. Fracture-related complications after spinal cord injury include nonunion, contracture, skin breakdown, and deep vein thrombosis.

28.5 Nutrition

Nutrition, the process by which a body nourishes itself by converting food into energy and body tissues, is the most important factor in maintaining health, responding to injury or illness, short- and long-term rehabilitation, and longevity. Nutrition plays a vital role in the maintenance, growth, reproduction, health maintenance, and response to disease and includes food intake, absorption, assimilation, biosynthesis, catabolism, and excretion (Cifu et al. 2020). In patients with spinal cord injuries, hypercatabolism can cause adverse effects, such as loss of lean body mass, obesity, increased susceptibility to infections, and reduced wound healing. This population is at risk for disease such as diabetes, coronary heart disease, and dyslipidemias (Khalil et al. 2013). Body fat has been identified as an important predictor of mortality. In addition, disorders such as carbohydrate intolerance, insulin resistance, lipid abnormalities, and heart disease occur prematurely and can be associated with immobilization and skeletal muscle denervation with a high prevalence in a population with a disability (Bauman and Spungen 2001; Shetty 2003; Dionyssiotis 2012). The term malnutrition should include obesity as well as undernourishment (Dionyssiotis 2012). Optimal nutritional assessment and management for people with disabilities including spinal cord injury can minimize the

complications associated with acute trauma and long-term rehabilitation (Harris and Haboubi 2005; Peiffer et al. 1981). While there are many formulas that calculate the resting metabolic rate (RMR), Harris–Benedict formula is most commonly used.

$$\text{Men}: \text{Resting Metabolic Rate}\left(RMR\right)\left(\text{kcal}/\text{d}\right) = 67 + \text{Body Weight(kg)} \times 13.75 + \text{Height(cm)} \times 5 - \text{Age(years)} \times 6.8$$

$$\text{Women}: RMR\left(\text{kcal}/\text{d}\right) = 655 + \text{Body Weight} \times 9.6 + \text{Height} \times 1.85 - \text{Age} \times 4.7$$

Ideal body weight (IBW) is calculated according to Hamwi equation, and the metabolically active weight (MAW) is calculated as 25% of excess weight (actual weight − ideal weight) added to the ideal body weight.

IBW (for male) = 106 lb for the first 5 ft + 6 lb for each additional inch or 48 kg for the first 152.4 cm + 1.1 kg for each additional cm.

IBW (for female) = 100 lb for the first 5 ft + 5 lb for each additional inch or 45 kg for the first 152.4 cm + 0.9 kg for each additional cm.

Ireton–Jones equations include equation for obese patients and one for general critical care populations:

$$\text{Obesity}: RMR\left(\text{kcal}/\text{d}\right) = Weight \times 9 + \text{Gender} \times 606 - \text{Age} \times 12 + 1844$$

$$\text{Nonobese}: RMR\left(\text{kcal}/\text{d}\right) = Weight \times 5 - \text{Age} \times 10 + \text{Gender} \times 281 + \text{Trauma} \times 292 + 1925 \quad \left(\text{for gender}: \text{male} = 1, \text{female} = 0\right)$$

BMI is calculated using the equation weight (kg)/height (m^2). In able-bodied subjects overweight is defined as a BMI of 25–29.9 kg/m^2 and obesity as a BMI of ≥30.0 kg/m^2 and extreme obesity ≥40 kg/m^2 (Table 28.6). However, there is a debate about whether BMI is useful for obesity in patients with spinal cord injuries.

Specific proteins (albumin, prealbumin, and transferrin) are biochemical indicators used to assess nutritional status (Charney 1995; Dawodu et al., accessed on Jan 2021). Levels of serum albumin are not a definitive measure for visceral protein status but reflect complex relationship between synthesis, degradation, and distribution. Because of the long half-life of 21 days, serum albumin cannot be used effectively to monitor acute response to nutritional therapy. Thus, albumin levels should be included in the initial profile for food control and monitoring purposes as an indicator of inpatient or chronic nutritional status to measure trends of visceral proteins. In addition to these limitations, many of factors reduce the level of albumin (Dionyssiotis 2012, 2014) (Table 28.7).

Table 28.6 Classifications based on the weight for BMI and obesity category

Classification	BMI (kg/m^2)	Obesity category
Underweight	<18.5	–
Normal	18.5–24.9	–
Overweight	25.0–29.9	–
Obesity	30, 0–34, 9	I
Moderate obesity	35.0–39.9	II
Extreme obesity	>40.0	III

From Dionyssiotis (2012)

The second protein biochemical indicator, prealbumin, has a very short half-life (2 days) and is used as an excellent indicator of nutritional status and is increasingly used as an indicator of response to nutritional therapy. Reference values for prealbumin are 16–35 mg/dL. Values below 11 mg/dL are associated with malnutrition; therefore, the value of dietary intervention is 11 mg/dL. Concentrations should increase by about 1 mg/dL per day or twice a week when nutritional treatment is appropriate. Non-dietary factors to reduce prealbumin include stress and inflammation (Devoto et al. 2006; Robinson et al. 2003). For additional information, see *Chap. 9. Commonly Used Laboratory Tests in the Management of Spinal Cord Injuries.*

Table 28.7 Basic levels of albumin and nutritional status distribution

Albumin (g/dl)	3.5–5	3–3.5	<3.5	<3.0	<2.5
Nutritional status	Normal	Point that dietary intervention should be revised or adjusted	Associated with poor outcome of surgery, rising costs of hospitalization, and prolonged stay in ICU	Severe malnutrition	Increased morbidity and mortality

From Dionyssiotis (2012)

Normal transferrin levels are between 200 and 400 mg/dL, and 150 mg/dL is considered to be the point at which nutritional decision points or nutritional support needs to be corrected or adjusted. Transferrin can be reduced by several causes that interfere with the synthesis of transferrin, including chronic infection and fluid overload. The serum concentration of transferrin is about 0.8 times the total iron-binding capacity (TIBC).

Physical measurements include protein nitrogen balance studies and creatinine/height index (CHI) measurements. Nitrogen balance studies measure the net change in total body protein. Assessment of nitrogen balance can be performed by measuring urinary urea nitrogen (UUN) and simultaneously comparing it to the intake of nitrogen. The nitrogen balance is calculated as follows:

$$\text{Nitrogen balance} = [\text{Nitrogen in}] - [\text{Nitrogen out}]$$

$$\text{Nitrogen balance} = [\text{Protein in}(\text{gm}) / 6.26\,\text{gm protein per gm nitrogen}] - [24\,\text{h urinary urea nitrogen}] - 3\,\text{gm}$$

or

$$\frac{[\text{protein}(\text{gm})] - (24\,\text{h UUN} + 3)}{[6.25\,\text{gm nitrogen}]}$$

Screening is important for the early detection of patients at risk of malnutrition. The Short Nutritional Assessment Questionnaire (SNAQ) is the recommended screening tool in this benchmark (Hertroijs et al. 2012). However, in many medical settings, various screening tools have been developed to determine the nutritional status of patients, but not in the rehabilitation setting (Harris and Haboubi 2005).

28.5.1 Nutritional Problems in the Acute Phase of Spinal Cord Injury

During the acute phase of spinal cord injury, energy expenditure, endogenous protein catabolism, and nitrogen excretion increase dramatically. Trauma of various organs, soft tissue injuries, and fractures can further increase severe catabolism. The nitrogen loss after injury is always present and lasts up to 7 weeks. Acute injuries usually result in a negative nitrogen balance, despite a sufficient supply of calories and protein. Nitrogen requirement after acute trauma is much higher than normal. Another serious metabolic problem is negative nitrogen balance due to excessive nitrogen secretion in the first week as the body uses proteins to meet energy needs, with a peak at 3 weeks and a duration of 7 weeks (Thibault-Halman et al. 2011). Poor appetite and dysphagia can lead to nutritional problems in the acute phase. Patients show nutritional depletion based on several measures: anthropometric, biochemical, and nitrogen balance. Biochemical and anthropometric testing can be useful in the assessment of metabolic demands (Dvorak et al. 2004; Kaufman et al. 1985). Predictive equations, such as the Harris–Benedict equation, have been used to determine a patient's predicted energy expenditure and establish a caloric target.

Glucose intolerance is not readily apparent during the acute phase of spinal cord injury but may be caused by complications and physiological processes of acute treatment such as early

metabolism-catabolism, steroid administration, parenteral/enteral nutrition, and atrophy as a consequence of adiposity leading to gluconeogenesis. Increased hepatic gluconeogenesis and regional reactions to insulin lead to hyperglycemia. Prevention of hyperglycemia is especially important for optimal recovery in the first 2 to 8 h after injury. Elevated blood glucose levels 2 to 8 h after injury may result in intestinal or parenteral feedings within a short time after injury. Glucose is an important energy molecule for the central nervous system, red blood cells, cellular tissue, etc. To perform this function and prevent the consumption of endogenous protein, at least 100–150 gm glucose per day is needed. The normal rate at which the body metabolizes carbohydrates or glucose is approximately 2–4 mg/kg/min. Severe stress can increase glucose metabolism by 3–5 mg/kg/min. In most patients, 400–500 gm of glucose is administered daily to exceed the body's metabolic capacity and is stored as energy. Excess glucose is converted into fat (lipogenesis) leading to an increased ratio of VCO_2/VO_2 (Burr et al. 1993). There is also a possibility that the serum triglyceride levels may elevate due to the acceleration of lipogenesis, the decrease of lipoprotein lipase activity, and the impaired clearance of triglycerides (Heyland et al. 2003; Robertson and Grossman 1987).

Serum hemoglobin and hematocrit can reflect general nutritional state. Anemia, defined as low hemoglobin levels (<14 mg/dL) and hematocrit (<36%), reduces blood oxygenation and impairs wound healing. Low levels of total serum protein (<6.4 mg/dL) and protein (<3.5 mg/dL) accelerate the development of edema. Paralytic ileus is a complication of hypokalemia, abdominal trauma, or sepsis. It usually lasts for 72 h to 1 week and can limit the movement of the diaphragm (Blissitt 1990). Parenteral nutrition is indicated when paralytic ileus lasts for more than 3–5 days.

Deficiency of zinc and vitamin C is associated with poor wound healing. The opposite physiological effects such as copper metabolism, copper deficiency, and anemia can be triggered by long-term supplementation of large amounts of zinc (Eleazer et al. 1995). The role of vitamin C in collagen synthesis is important.

28.5.2 Nutritional Support

The preferred initial route for enteral feeding in critically ill patients is nasogastric route. Patients who do not tolerate nasogastric feeding as evidenced either by vomiting or by high residual volumes, 250 mL more than the amount delivered since the last gastric aspirate, should proceed to the nasojejunal route (Davies et al. 2002). The nasogastric or nasoenteric feeding tubes should not be used for more than 4 weeks as this may cause discomfort and risk of nasal injury and sinusitis. The major advantage of nasogastric feeding is the ability to measure gastric residuals. If the gastric residual is greater than 75 mL just before the next feeding, continuous feeding or bolus feeding should be discontinued. In patients who continue to require enteral nutrition after 4 weeks, the placement of a percutaneous endoscopic gastrostomy (PEG) tube should be considered (Magnuson et al. 1994). PEG also appears to be the first-line intervention in situations where enteral feeding is expected to require more than 2–4 weeks.

With increasing frequency, the nasogastric feeding tube is being replaced with PEG, providing semi- or long-term enteral nutrition due to the various benefits of PEGs in daily use. In general, the gastrostomy tubes are stable and can remain in place for 6 months or even longer. Unlike nasogastric feeding tubes, PEG does not interfere with the swallowing mechanism and reduces the risk of choking, especially when oral feeding begins during neurological recovery. The cosmetic benefits of PEG, which can be worn invisibly under the patients' clothing, can play a psychological role during recovery. The risk of aspiration associated with nasogastric feeding tubes is not eliminated by PEG placement (Fay et al. 1991; Vincent and Preiser 2013). Jejunostomy tubes are much less commonly used than gastrostomy tube. Jejunostomy tubes are

generally used in situations where the patient has repeated gastric aspiration and pneumonia.

28.6 Coronary Heart Disease

Smoking, hypertension, diabetes mellitus, and lipid abnormalities are the major risk factors for coronary heart disease. Specific risk factors for coronary artery disease in patients with spinal cord injuries include low levels of HDL, lack of physical inactivity, increased body fat, and higher incidence of glucose intolerance (Bauman and Spungen 2008; Brenes et al. 1986; Claus-Walker and Halstead 1982c). Low HDL cholesterol level is a major risk factor for coronary artery disease in spinal cord injury. The reduced level of the HDL_2 subtraction is a strong predictor of coronary artery disease. There is evidence that HDL levels are lower in patients with chronic spinal cord injury than in the general population. In 24% to 40% of patients with spinal cord injuries, HDL cholesterol levels are below 35 mg/dL compared to 10% of the general population. LDL cholesterol levels in patients with spinal cord injuries are similar to those of the general population (Aidinoff et al. 2017; Bauman and Spungen 2008). Thus, HDL cholesterol is a strong protective factor, and high HDL levels are inversely related to the risk of coronary artery disease.

Type II diabetes mellitus is more common in patients with spinal cord injuries than in general population due to insulin resistance and can contribute to the development of hypertension and coronary artery disease. The prevalence of impaired glucose tolerance, insulin resistance, and hyperinsulinemia has been reported to increase in patients with chronic spinal cord injuries. Potential factors of inflammation, prothrombotic factors or platelet dysfunction, as well as autonomic dysfunction also contribute to coronary artery disease in patients with spinal cord injuries (Claus-Walker and Halstead 1982a). The risk for coronary artery disease is especially high in people with diabetes. Most of these risks are caused by lipid abnormalities, but factors such as insulin levels and blood glucose also appear to have an independent role. There is a positive correlation between insulin levels and the risk of cardiovascular disease. The risk factors for metabolic syndrome include abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance, and prothrombotic and proinflammatory conditions (Claus-Walker and Halstead 1982a, b).

Hypertension treatments reduce morbidity and mortality from heart disease. In patients with spinal cord injuries, blood pressure is not higher than baseline. Autonomic dysreflexia in patients with spinal cord injuries above T6 differs clinically from essential hypertension in terms of clinical symptoms, context, course, and episodic nature. The association between autonomic dysreflexia and chronic heart disease has not yet been established. There is strong evidence that sedentary lifestyles are an independent risk factor for coronary artery disease. Several possible mechanisms for the positive effects of physical activity have been proposed. There are antiatherogenic effects associated with physical activity such as increased HDL cholesterol, a decrease in LDL cholesterol and triglycerides, beneficial effects on platelet adhesion and blood viscosity, increased insulin sensitivity, increased cardiac efficacy of oxygen through conditioning, and low blood pressure. In addition to the risk factors described, the studies identified a number of additional risk factors for coronary artery disease, but many people do not currently have a clear indication of their importance or interventional strategies. Some of these factors include inflammatory markers such as C-reactive protein (CRP) and other prothrombotic and proinflammatory markers, oxidants, platelet activators, elevated plasma homocysteine, and lipoprotein.

Tetraplegics can cause complications of myocardial infarction without chest pain. Patients with spinal cord injuries above T5 cannot feel cardiac pain due to angina because they enter the spinal cord via afferent sympathetic nerves between T1 and T5.

28.6.1 Diagnosis

Diagnosis of myocardial ischemia is difficult in tetraplegics. Patients with cervical or thoracic injuries above T4 may have disrupted the sympathetic afferent fibers, including cardiac pain fibers; their sensation of ischemic cardiac pain may be changed (referred pain) or absent (Groah and Menter 1998). Resting electrocardiogram is not a sensitive test for cardiac ischemia. Traditional treadmill stress test is not generally available for patients with spinal cord injuries. In people with paraplegia, however, arm ergometry can be performed. Arm exercise usually produces lower heart rates than leg exercise and may not be able to detect heart disease. Since tetraplegics may not be performed at all, an alternate test for the diagnosis of myocardial infarction is required. Pharmacological stress test is often the most practical alternate. This is done by administration of dipyridamole (Persantin), adenosine, or dobutamine, which induces myocardial stress with myocardial imaging (thallium 201 scanning or 2-D echocardiography) upon injecting dipyridamole. Dipyridamole induces vasodilation of the coronary arteries, and dobutamine increases myocardial work and oxygen demand. Angiography is the best standard for diagnosing coronary artery disease. However, there are some special considerations for tetraplegics. Respiratory dysfunction leads to difficulty with the supine position during the procedure, and a large amount of contrast deteriorates kidney function.

28.6.2 Management

The principle of treating coronary artery disease in spinal cord injuries is essentially the same as the general population and is intended for the secondary prevention. Interventions, including lifestyle changes, medications, angioplasty, and cardiac revascularization, should be appropriate for patients with spinal cord injuries (Anson and Shepherd 1996; Carlson et al. 2009).

Traditional antianginal drug doses should be used with caution in tetraplegic patients who are already suffering from low basal arterial pressure or orthostatic hypotension because the drugs cause hypotension. Therefore, it may be necessary to monitor the blood pressure carefully while taking the dose. Sublingual nitroglycerin reduces angina in less than 2 min and lasts for 15–30 min. If a third dose does not relieve the pain, medical attention for the possibility of a myocardial infarction should be considered. Long-acting oral nitrates (5–20 mg isosorbide sublingually every 3–4 h or 40 mg orally three times a day) and topical nitrates (2% nitroglycerin ointment on skin, 1–2 inch every 4–6 h) can be applied. Patients with spinal cord injuries may take sildenafil and other phosphodiesterase-5 (PDE-5) inhibitors for treatment of spinal cord injury-related erectile dysfunction. Therefore, the use of nitrate in angina can cause life-threatening hypotension.

Aspirin and β-blockers are recommended for patients with atherosclerotic cardiovascular disease and postmyocardial infarction unless they have contraindications. Beta-blockers have antianginal effects as they reduce myocardial contractility and slow heart rate. Propranolol acts on β1- and β2-receptors. There are clinically significant side effects of β-blocker in patients with spinal cord injuries such as postural hypotension, bronchospasm, and salt retention. Beta-blockers also reduce awareness of hypoglycemic symptoms and reduce HDL cholesterol levels. Aspirin can reduce platelet aggregation and prevent coronary thrombosis. Otherwise, aspirin (80–325 mg/d) should be given to all patients with known coronary disease. Calcium channel blockers (nifedipine 10–30 mg three or four times a day) act as peripheral vasodilators and coronary vasodilators and have various effects on myocardial contractility and conduction.

If medical care failed, invasive treatment of coronary artery disease, such as percutaneous coronary angioplasty and coronary artery bypass grafts, is indicated. Cardiac rehabilitation programs for patients with spinal cord injuries are performed according to the same principles as the general population. However, the program will be modified accordingly to account for patient mobility and wheelchair activity.

Treatment guidelines to control blood pressure in patients with spinal cord injuries have not been established. It is advisable to keep the upright blood pressure below 140/85–90 mmHg. People with spinal cord injury with high blood pressure should use antihypertensive agents.

References

Aidinoff E, Bluvshtein V, Bierman U, et al. Coronary artery disease and hypertension in a non-selected spinal cord injury patient population. Spinal Cord. 2017;55:321–6.

Alberti KG, Zimmet P, Shaw J. Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med. 2006;23:469–80.

American Diabetes Association. Standards of medical care in diabetes – 2017. Diabetes Care. 2017;40(Suppl. 1):1–142.

Anson CA, Shepherd C. Incidence of secondary complications in spinal cord injury. Int J Rehabil Res. 1996;19:55–66.

Ashe MC, Craven C, Eng JJ, et al. Prevention and treatment of bone loss after a spinal cord injury: a systematic review. Top Spinal Cord Inj Rehabil. 2007;13:123–45.

Bauman WA, Spungen AM. Carbohydrate and lipid metabolism in chronic spinal cord injury. J Spinal Cord Med. 2001;24:266–77.

Bauman WA, Spungen AM. Metabolic changes in persons after spinal cord injury. Phys Med Rehab Clin North Am. 2000;11:102–40.

Bauman WA, Spungen AM. Coronary heart disease in individuals with spinal cord injury: assessment of risk factors. Spinal Cord. 2008;46:466–76.

Bauman WA, Spungen AM, Zhong YG, et al. Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury. Paraplegia. 1992;30:697–703.

Bauman WA, Raza M, Chayes Z, et al. Tomographic thallium-201 myocardial perfusion imaging after intravenous dipyridamole in asymptomatic subjects with quadriplegia. Arch Phys Med Rehabil. 1993;74:740–4.

Bauman WA, Raza M, Spungen AM, et al. Cardiac stress testing with thallium-201 imaging reveals silent ischemia in individuals with paraplegia. Arch Phys Med Rehabil. 1994;75:946–50.

Bauman WA, Adkins RH, Spungen AM, et al. Is immobilization associated with an abnormal lipoprotein profile? Observations from a diverse cohort. Spinal Cord. 1999a;37:485–93.

Bauman WA, Kahn NN, Grimm DR, Spungen AM. Risk factors for atherogenesis and cardiovascular autonomic function in persons with spinal cord injury. Spinal Cord. 1999b;37:601–16.

Bauman WA, Spungen AM, Adkins RH, et al. Metabolic and endocrine changes in persons aging with spinal cord injury. Assist Technol. 2001;11:88–96.

Bauman WA, Schwartz E, Kirshblum S, et al. Dual energy X-ray absorptiometry overestimates bone mineral density of the lumbar spine in persons with spinal cord injury. Spinal Cord. 2009;47:628–33.

Bauman WA, Schnitzer TJ, Chen D. Management of osteoporosis after spinal cord injury: what can be done? Point/counterpoint. PM R. 2010;2:566–72.

Biering-Sörensen F, Bohn HH, Schaadt OP. Bone mineral content of the lumbar spine and lower extremities years after spinal cord lesion. Paraplegia. 1998;26:293–301.

Biering-Sörensen F, Hansen B, Lee BS. Nonpharmacological treatment and prevention of bone loss after spinal cord injury: a systematic review. Spinal Cord. 2009;47:508–18.

Blissitt PA. Nutrition in acute spinal cord injury. Crit Care Nurs Clin North Am. 1990;2:375–84.

Brenes G, Dearwater S, Shapera R, et al. High density lipoprotein cholesterol concentrations in physically active and sedentary spinal cord injured patients. Arch Phys Med Rehabil. 1986;67:445–50.

Buchholz AC, Pencharz PB. Energy expenditure in chronic spinal cord injury. Curr Opin Clin Nutr Metab Care. 2004;7:635–9.

Burr RG, Clift-Peace L, Nuseibeh I. Haemoglobin and albumin as predictors of length of stay of spinal injured patients in a rehabilitation centre. Paraplegia. 1993;31:473–8.

Carlson KF, Wilt TJ, Taylor BC, et al. Effect of exercise on disorders of carbohydrate and lipid metabolism in adults with traumatic spinal cord injury: systematic review of the evidence. J Spinal Cord Med. 2009;32:361–37.

Castro MJ, Apple DF Jr, Hillegass EA, et al. Influence of complete spinal cord injury on skeletal muscle cross-sectional area within the first 6 months of injury. Eur J Appl Physiol Occup Physiol. 1999;80:373–8.

Charmetant C, Phaner V, Condemine A, et al. Diagnosis and treatment of osteoporosis in spinal cord injury patients: a literature review. Ann Phys Rehabil Med. 2010;53:655–68.

Charney P. Nutrition assessment in the 1990s: where are we now? Nutr Clin Pract. 1995;10:131–9.

Cifu DX, Carne W, Pushkin H, et al. The basics of nutrition: a primary rehabilitation intervention. Phys Med Rehabil Clin N Am. 2020;31:665–84.

Cirnigliaro CM, La Fountaine MF, Parrott JS, et al. Administration of denosumab preserves bone mineral density at the knee in persons with subacute spinal cord injury: findings from a randomized clinical trial. JBMR Plus. 2020;4:e10375.

Clasey JL, Janowiak AL, Gater DR. Relationship between regional bone density measurements and the time since injury in adults with spinal cord injuries. Arch Phys Med Rehabil. 2004;85:59–64.

Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: II (section 1). Consequences of partial decentralization of the auto-

nomic nervous system. Arch Phys Med Rehabil. 1982a;63:569–75.
Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: II (section 2). Partial decentralization of the autonomic nervous system. Arch Phys Med Rehabil. 1982b;63:576–80.
Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: III. Less quanta of sensory input plus bedrest and illness. Arch Phys Med Rehabil. 1982c;63:628–31.
Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury: IV. Compounded neurologic dysfunctions. Arch Phys Med Rehabil. 1982d;63:632–8.
Collins EG, Gater D, Kiratli J, Butler J, Hanson K, Langbein WE. Energy cost of physical activities in persons with spinal cord injury. Med Sci Sports Exerc. 2010;42:691–700.
Consortium for spinal cord medicine. Identification and management of cardiometabolic risk after spinal cord injury. Washington, DC: Paralyzed Veterans of America; 2018.
Dauty M, Perrouin Verbe B, Maugars Y, et al. Supralesional and sublesional bone mineral density in spinal-cord injured patients. Bone. 2000;27:305–9.
Davies AR, Froomes PR, French CJ, et al. Randomized comparison of nasojejunal and nasogastric feeding in critically ill patients. Crit Care Med. 2002;30:586–90.
Dawodu TS, Scott DD, Chase M. Nutritional management in the rehabilitation setting, 2013. http://emedicine.medscape.com/article/318180-overview. Accessed Jan 2021.
de Bruin ED, Vanwanseele B, Dambacher MA, et al. Long-term changes in the tibia and radius bone mineral density following spinal cord injury. Spinal Cord. 2005;43:96–101.
Devoto G, Gallo F, Marchello C, et al. Prealbumin serum concentrations as a useful tool in the assessment of malnutrition in hospitalized patients. Clin Chem. 2006;52:2281–5.
Dionyssiotis Y. Spinal cord injury-related bone impairment and fractures: an update on epidemiology and physiopathological mechanisms. J Musculoskelet Neuronal Interact. 2011;11:257–65.
Dionyssiotis Y. Malnutrition in spinal cord injury: more than nutritional deficiency. J Clin Med Res. 2012;4:227–36.
Dionyssiotis Y. Malnutrition in paraplegia. In: Dionyssiotis Y, editor. Topics in paraplegia. London: IntechOpen; 2014. https://doi.org/10.5772/58382. Available from: https://www.intechopen.com/books/topics-in-paraplegia/malnutrition-in-paraplegia.
Dolbow DR, Gorgey AS, Daniels JA, et al. The effects of spinal cord injury and exercise on bone mass: a literature review. NeuroRehabilitation. 2011;29:261–9.
Duckworth WC, Solomon SS, Jallepalli P, et al. Glucose intolerance due to insulin resistance in patients with spinal cord injuries. Diabetes. 1980;29:906–10.
Duckworth WC, Jallepalli P, Solomon SS. Glucose intolerance in spinal cord injury. Arch Phys Med Rehabil. 1983;64:107–10.
Dvorak MF, Noonan VK, Belanger L, et al. Early versus late enteral feeding in patients with acute cervical spinal cord injury: a pilot study. Spine (Phila Pa 1976). 2004;29:E175–80.
Eckel RH, Cornier MA. Update on the NCEP ATP-III emerging cardiometabolic risk factors. BMC Med. 2014;12:115.
Edwards WB, Schnitzer TJ, Troy KL. The mechanical consequence of actual bone loss and stimulated bone recovery in acute spinal cord injury. Bone. 2014;60:141–7.
Eleazer GP, Bird L, Egbert J, et al. Appropriate protocol for zinc therapy in long term care facilities. J Nutr Elder. 1995;14:31–8.
Fay DE, Poplausky M, Gruber M, et al. Long-term enteral feeding: a retrospective comparison of delivery via percutaneous endoscopic gastrostomy and nasoenteric tubes. Am J Gastroenterol. 1991;86:1604–9.
Frey-Rindova P, de Bruin ED, Stüssi E, et al. Bone mineral density in upper and lower extremities during 12 months after spinal cord injury measured by peripheral quantitative computed tomography. Spinal Cord. 2000;38:26–32.
Friesbie JH. Fractures after myelopathy: the risk quantified. J Spinal Cord Med. 1997;20:66–9.
Garter DR, Farkas GJ. Alterations in body composition after SCI and the mitigating role of exercise. In: Taylor JA, editor. The physiology of exercise in spinal cord injury. New York: Springer; 2016.
Gater DR. Obesity after spinal cord injury. Phys Med Rehabil Clin North Am. 2007a;18:333–51.
Gater DR. Pathophysiology of obesity after spinal cord injury. Top Spinal Cord Inj Rehabil. 2007b;12:20–34.
Gater DR Jr, Farkas GJ, Berg AS, et al. Prevalence of metabolic syndrome in veterans with spinal cord injury. J Spinal Cord Med. 2019;42:86–93.
Giangregorio L, McCartney N. Bone loss and muscle atrophy in spinal cord injury: epidemiology, fracture prediction, and rehabilitation strategies. J Spinal Cord Med. 2006;29:489–500.
Gifre L, Vidal J, Carrasco JL, et al. Denosumab increases sublesional bone mass in osteoporotic individuals with recent spinal cord injury. Osteoporos Int. 2016;27:405–10.
Groah SL, Menter RR. Long-term cardiac ischemia leading to coronary artery bypass grafting in a tetraplegic patient. Arch Phys Med Rehabil. 1998;79:1129–32.
Groah SL, Nash MS, Ljungberg IH, et al. Nutrient intake and body habitus after spinal cord injury: an analysis by sex and level of injury. J Spinal Cord Med. 2009;32:25–33.
Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task

Force on Clinical Practice Guidelines. Circulation. 2019;139:e1082–143.
Harris D, Haboubi N. Malnutrition screening in the elderly population. J R Soc Med. 2005;98:411–4.
Hertroijs D, Wijnen C, Leistra E, et al. Rehabilitation patients: undernourished and obese? J Rehabil Med. 2012;44:696–701.
Heyland DK, Dhaliwal R, Drover JW, et al. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. JPEN J Parenter Enteral Nutr. 2003;27:355–73.
Holt RI. International Diabetes Federation re-defines the metabolic syndrome. Diabetes Obes Metab. 2005;7:618–20.
Illner K, Brinkmann G, Heller M, et al. Metabolically active components of fat free mass and resting energy expenditure in nonobese adults. Am J Physiol Endocrinol Metab. 2000;278:E308–15.
Ingenbleek Y, Van Den Schrieck HG, De Nayer P, et al. Albumin, transferrin and the thyroxine binding prealbumin/retinol-binding protein (TBPARBP) complex in assessment of malnutrition. Clin Chim Acta. 1975;63:61–7.
Kaufman HH, Rowlands BJ, Stein DK, et al. General metabolism in patients with acute paraplegia and quadriplegia. Neurosurgery. 1985;16:309–13.
Khalil RE, Gorgey AS, Janisko M, et al. The role of nutrition in health status after spinal cord injury. Aging Dis. 2013;4:14–22.
Lala D, Craven BC, Thabane KL, et al. Exploring the determinants of fracture risk among individuals with spinal cord injury. Osteoporosis Int. 2013;25:177–85.
Laughton GE, Buchholz AC, Martin Ginis KA. Lowering body mass index cutoffs better identifies obese persons with spinal cord injury. Spinal Cord. 2009;47:757–62.
Lavis TD, Scelza WM, Bockenek WL. Cardiovascular health and fitness in persons with spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:317–31, vii
Leblanc AD, Schneider VS, Ecvans HJ, et al. Bone mineral loss and recovery after 17 weeks of bed rest. J Bone Miner Res. 1990;5:843–50.
Magee DJ. Orthopedic physical assessment. 6th ed. St. Louis: Elsevier; 2020.
Magnuson B, Hatton J, Zweng TN, et al. Pentobarbital coma in neurosurgical patients: nutrition considerations. Nutr Clin Pract. 1994;9:146–50.
Maïmoun L, Fattal C, Sultan C. Bone remodeling and calcium homeostasis in patients with spinal cord injury: a review. Metabolism. 2011;60:1655–63.
Marathe PH, Gao HX, Close KL. American Diabetes Association Standards of medical care in diabetes 2017. J Diabetes. 2017;9:320–4.
Milligan J, Burns S, Groah S, et al. A primary care provider's guide to preventive health after spinal cord injury. Top Spinal Cord Inj Rehabil. 2020;26:209–19.
Mishori R, Groah SL, Otubu O, et al. Improving your care of patients with spinal cord injury/disease. J Fam Pract. 2016;65:302–9.
Monroe MB, Tataranni PA, Pratley R, et al. Lower daily energy expenditure as measured by a respiratory chamber in subjects with spinal cord injury compared with control subjects. Am J Clin Nutr. 1998;68:1223–7.
Nash MS, Mendez AJ. A guideline-driven assessment of need for cardiovascular disease risk intervention in persons with chronic paraplegia. Arch Phys Med Rehabil. 2007;88:751–7.
National Cholesterol Education Program (NCEP). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143–421.
National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham: University of Alabama at Birmingham; 2021. https://www.nscisc.uab.edu Last access: November 2021
Peiffer SC, Blust P, Leyson JF. Nutritional assessment of the spinal cord injured patient. J Am Diet Assoc. 1981;78:501–5.
Robertson CS, Grossman RG. Protection against spinal cord ischemia with insulin-induced hypoglycaemia. J Neurosurg. 1987;67:739–44.
Robinson MK, Trujillo EB, Mogensen KM, et al. Improving nutritional screening of hospitalized patients: the role of prealbumin. JPEN J Parenter Enteral Nutr. 2003;27:389–95.
Sabharwal S. Addressing cardiometabolic risk in adults with spinal cord injury: acting now despite knowledge gaps. Spinal Cord Ser Cases. 2019;5:96.
Sadowsky CL, Mingioni N, Zinski J. A primary care provider's guide to bone health in spinal cord-related paralysis. Top Spinal Cord Inj Rehabil. 2020;26:128–33.
Shetty P. Malnutrition and under nutrition. Medicine. 2003;31:18–22.
Shields RK, Schlechte J, Dudley-Javoroski SD, et al. Bone mineral density after spinal cord injury: a reliable method for knee measurement. Arch Phys Med Rehabil. 2005;86:1969–73.
Spungen AM, Adkins RH, Stewart CA, et al. Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Physiol. 2003;95:2398–407.
Stillman M, Graves D, Lenneman C, et al. Neurogenic bowel, disordered glycemic control and chronic spinal cord injury: a preliminary investigation. Phys Med Rehabil Int. 2017;4:1–3.
Stillman M, Babapoor-Farrokhran S, Goldberg R, et al. A provider's guide to vascular disease, dyslipidemia, and glycemic dysregulation in chronic spinal cord injury. Top Spinal Cord Inj Rehabil. 2020;26:203–8.
Thibault-Halman G, Casha S, Singer S, et al. Acute management of nutritional demands after spinal cord injury. J Neurotrauma. 2011;28:1497–507.

Vico L, Collet P, Guignandon A, Lafage-Proust MH, et al. Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts. Lancet. 2000;355:1607–11.

Vincent JL, Preiser JC. When should we add parenteral to enteral nutrition? Lancet. 2013;381:354–5.

WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i–xii, 1–253

Yarar-Fisher C, Heyn P, Zanca JM, et al. Early identification of cardiovascular diseases in people with spinal cord injury: key information for primary care providers. Arch Phys Med Rehabil. 2017;98:1277–9.

Recommended Additional Reading

Ahima RS, editor. Metabolic syndrome. A comprehensive textbook. Switzerland: Springer; 2016.

Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation. Phys Med Rehabil Clinical N Am. Philadelphia, PA: Elsevier; 2014.

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Lee BY, Ostrander LE, editors. The spinal cord injured patient. 2nd ed. New York: Demos; 2002.

Mittal S. The metabolic syndrome in clinical practice. London: Springer; 2008.

Taylor JA, editor. The physiology of exercise in spinal cord injury. New York: Springer; 2016.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

29 Neurogenic Lower Urinary Tract Dysfunction and Genitourinary Complications

Neurogenic lower urinary tract dysfunction following spinal cord injuries has a significant impact on quality of life. Only decades ago, urologic sequelae were primarily responsible for the high mortality rates among patients with neurogenic bladder. In the 1950s, upper urinary tract damage was the leading cause of death in patients with spinal cord injuries. Renal failure and urinary tract infections were the major causes (Capoor and Stein 2005). Since then, advances in the treatment of urinary tract infection, improvement of neurogenic bladder management strategies, and the use of diagnostic tools such as urodynamics have dramatically reduced previously high mortality rates from complications of the neurogenic bladder: 80% of patients with spinal cord injuries in the 1940s to 3% of renal complication-related mortality in this population nearly 4 decades later (Gormley 2010; Nseyo and Santiago-Lastra 2017). Despite these advances, morbidity from voiding dysfunction and genitourinary complications remains common and very important, and lifelong problems in people with spinal cord injuries. Diseases of the genitourinary system are the most common cause of rehospitalizations after spinal cord injuries/disease and the eleventh leading cause of mortality (NSCISC 2021). In this regard, optimal urinary tract management is critical not only for the prevention of complications and illnesses but for the optimal social integration of the persons with spinal cord injuries.

Urinary incontinence contributes to embarrassment and social isolation and inhibits rehabilitation. Failure to empty the bladder can lead to urinary tract infection, calculi, and renal failure. Therefore, the diagnosis and management of neurogenic bladder dysfunction is an important component of total rehabilitation. Advances in the detection and management of urinary dysfunctions and complications in spinal cord injuries have significantly reduced mortality from related complications and renal failure over the past few decades, but genitourinary problems are still a major source of morbidity. Urinary tract infection remains a leading cause of hospitalization for people with spinal cord injuries. Lifelong monitoring and management of ongoing genitourinary function is an important part of the treatment of spinal cord injuries. The goal of neurogenic bladder management is to minimize the lower urinary tract complications, preserve the upper urinary tract, prevent incontinence, and adapt to person's lifestyle (Samson and Cardenas 2007).

Preserving renal function, promoting urinary continence, minimizing risks for associated sequelae such as urinary tract infections and bladder or kidney stones, and enhancing the patient's quality of life are primary concerns from both a clinician and a patient perspective (Nseyo and Santiago-Lastra 2017). Dysfunction of the pelvic organs with bladder, bowel, and sexual functions is a major problem in

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rehabilitation for people with spinal cord injuries. Recovery of sexual function and control of the bladder and bowel were considered high priorities in patients with spinal cord injuries (Anderson 2004). Therefore, examination and treatment of the pelvic organ dysfunction following spinal cord injury is important for the quality of life of these patients. It is also important to achieve urinary continence and maintain integrity of the upper urinary traction function. Regular follow-up examinations of the genitourinary system are recommended to maintain lower urinary tract function and prevent deterioration of renal function. Treatment goals should be individualized by the neurological level of injury, the completeness of the lesion, the patient's age and general constitution, participation in daily activities, social conditions, and hand function and dexterity.

The two main functions of the bladder are the storage and emptying of urine (Miller 1996). This complex activity requires coordinated functions of the peripheral nervous system, the sacral micturition center, the pontine micturition center, and the cerebral cortex. A complex cascade of genitourinary regulation mechanisms plays a role at various levels of the central nervous system. The supraspinal centers, such as the frontal cortex, the pontine micturition center, and the insula, and the lowest sacral segments are responsible for micturition. Complex interactions of sympathetic, parasympathetic, and somatic neural systems should regulate the coordinated storage and evacuation of urine and preserve the connections between cortical and supraspinal centers and spinal neurons. In infants, voiding is not significantly influenced by the cortex, and voiding is initiated reflexively in response to fullness of the bladder. In contrast, in adults, the pontine micturition center is modulated by higher centers and facilitates at socially appropriate time (de Groat et al. 2001).

29.1 Anatomy of the Urinary Tract System

The lower urinary tract comprises the fundus (body), trigone, and neck of the bladder, the pelvic diaphragm, the urethra, and urethral sphincter. The urinary bladder is a four-layered musculomembranous structure composed primarily of smooth muscle cells that can contract when stretched. The four layers consist of (1) a three-layered detrusor muscle; (2) a serous layer; (3) a submucous, areolar layer; and (4) a thin mucous layer continuous with the ureteral and urethral linings. Functional urethral sphincters include the external urethral sphincter with skeletal muscle fibers under the control of the somatic system and the bladder neck (internal sphincter) under the control of the autonomic nervous system (Fig. 29.1).

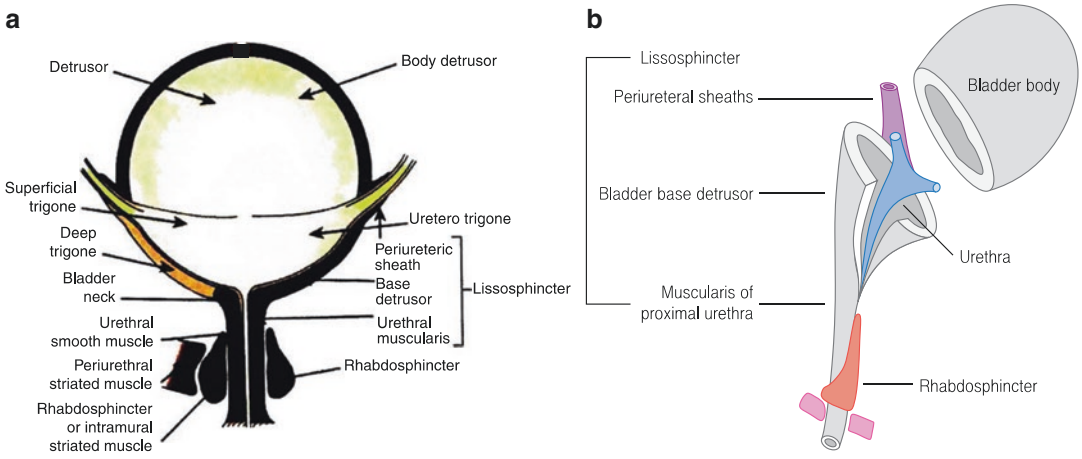


Fig. 29.1 (**a**) Anatomy of the bladder and lower urinary tract. (**b**) Detailed structure of the lower urinary tract

The upper urinary tract includes the kidneys and ureters. The kidney consists of the renal parenchyma that secretes, concentrates, and excretes urine and the collecting system that drains urine into the renal pelvis and ureter. The renal parenchyma includes the external cortex and the internal medulla. The ureters extend from the ureteropelvic junction of the kidney to the base of the bladder where they course submucosally in an oblique direction at the ureterovesical junction and open in the ureteral orifices. The ureterovesical junction is anatomically designed to flow urine into the bladder, but it is designed to prevent reflux. The increase in vesical pressure simultaneously compresses the ureter to form a one-way valve.

29.2 Innervation of the Lower Urinary Tract

The medial frontal lobe, corpus callosum, limbic system, hypothalamus, basal ganglia, and cerebellum are all involved in the control of bladder function. Sensory stimulation from the proprioceptive nerve endings in the mucosal wall of the bladder, abdominal wall, urethra, and periurethral areas travels through the lateral somatic and posterior columns in the spinal cord. These impulses are transmitted to different regions of the brain. Motor control of bladder and sphincter function is regulated by descending bulbospinal, reticulospinal, and corticospinal tracts (Anderson and Bradley 1976). They act by facilitating or inhibiting the bladder by projecting impulses through the pontine micturition center or directly to the sacral segments (Anderson and Bradley 1976). The pontine micturition center coordinates contraction and relaxation of the detrusor and the sphincter. During voiding, the detrusor muscle contracts after relaxation of the sphincter. The opposite should occur during storage. The detrusor muscle must be relaxed during sphincter contraction (genitourinary guarding reflex). This coordination of the contraction and relaxation is called detrusor-sphincter synergia.

The lower urinary tract is innervated by the somatic, parasympathetic, and sympathetic nervous systems (Table 29.1). The preganglionic parasympathetic neurons originate from the intermediolateral horn of the gray matter of the S2 to S4 segments. These fibers pass through the pelvic nerves. The postganglionic parasympathetic fibers supply the detrusor muscle of the bladder. It is excitatory and causes contraction of the detrusor through muscarinic receptors (M2, M3). The neurotransmitter is acetylcholine. If the parasympathetic tone increases, detrusor contraction and voiding occur (Fig. 29.2). The sympathetic fibers originate from the T10 to L2 spinal cord segments and project through the sympathetic chain and inferior mesenteric ganglion. These neurons travel into the bladder via the hypogastric nerve. It acts on the adrenergic receptors and the neurotransmitter is norepinephrine. It facilitates storage with relaxation of detrusor muscle (β-receptors) and excitation of the bladder base/urethra (α1- and α2-receptors). The α-adrenergic sympathetic nerves cause contraction of the bladder neck. This is the main mechanism to prevent urinary incontinence and prevent retrograde ejaculation. Beta-adrenergic stimulation suppresses detrusor contraction and promotes urine storage (Anderson and Bradley

Table 29.1 Neural innervation of the lower urinary tract system

Segments	Innervations	Nerves	Receptors, neurotransmitters	Functions
S2-S4	Parasympathetic	Pelvic nerve	• M2, M3 • Acetylcholine	• Detrusor contraction
T10-L2	Sympathetic	Hypogastric nerve	• Adrenergic • Norepinephrine	• Bladder neck contraction (α1) • Detrusor relaxation (β)
S2-S4 Onuf's nucleus	Somatic	Pudendal nerve	• Nicotinic • Acetylcholine	• EUS contraction

1976; Burnstock 1986; de Groat et al. 2001; Vignoli 2017). The somatic nuclei are located in the anterior horn of the gray matter of the S2 to S4 spinal cord segment (Onuf's nucleus) (Pullen et al. 1997). These fibers project through the pudendal nerve and are innervated to the external urethral sphincter (striated muscle) (Fig. 29.3). It may act on nicotinic receptors. The neurotransmitter is acetylcholine. It is excitatory and causes contractions of the external urethral sphincter. Voluntary voiding is achieved by voluntary relaxation of the external urethral sphincter. Figure 29.4 is a diagram that affects the increase or decrease in bladder contractility and urethral resistance to achieve urine retention and voiding.

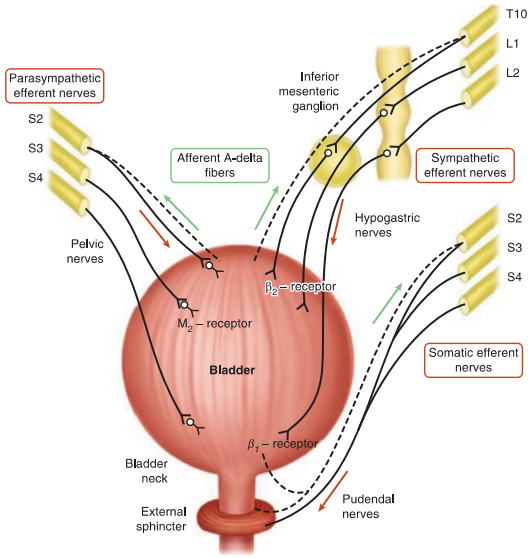
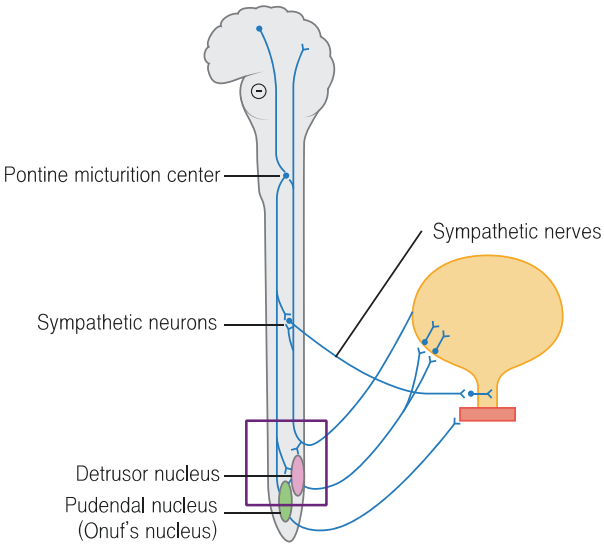


Fig. 29.2 Afferent and efferent nervous pathways of the lower urinary tract. From Vignoli (2017), with permission

29.3 Functions of the Lower Urinary Tract

29.3.1 Storage

Inhibition or control of voiding occurs within the cerebral cortex, midbrain, and pons. Afferent signals from bladder filling are transmitted to the cortex. The cortex suppresses micturition reflexes. The bladder is filled without detrusor contraction (accommodation). The bladder is in about 99% urine storage mode. During the storage phase, sympathetic activity is mediated through the hypogastric nerve to inhibit contraction of the detrusor. The bladder neck outlet mechanism and the striated muscle of the urethral sphincter and pelvic floor are in a state of contraction to achieve continence. The former



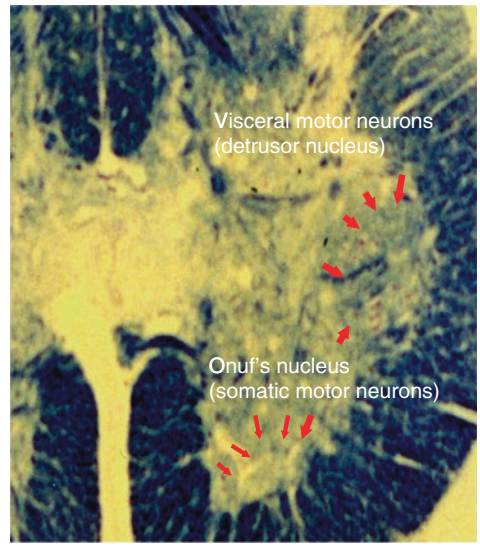


Fig. 29.3 Onuf's nucleus and the detrusor nucleus are located at different sites. The sacral segment with Onuf's nucleus is located in the lower sacral segment, which is slightly lower than the location of the detrusor nucleus

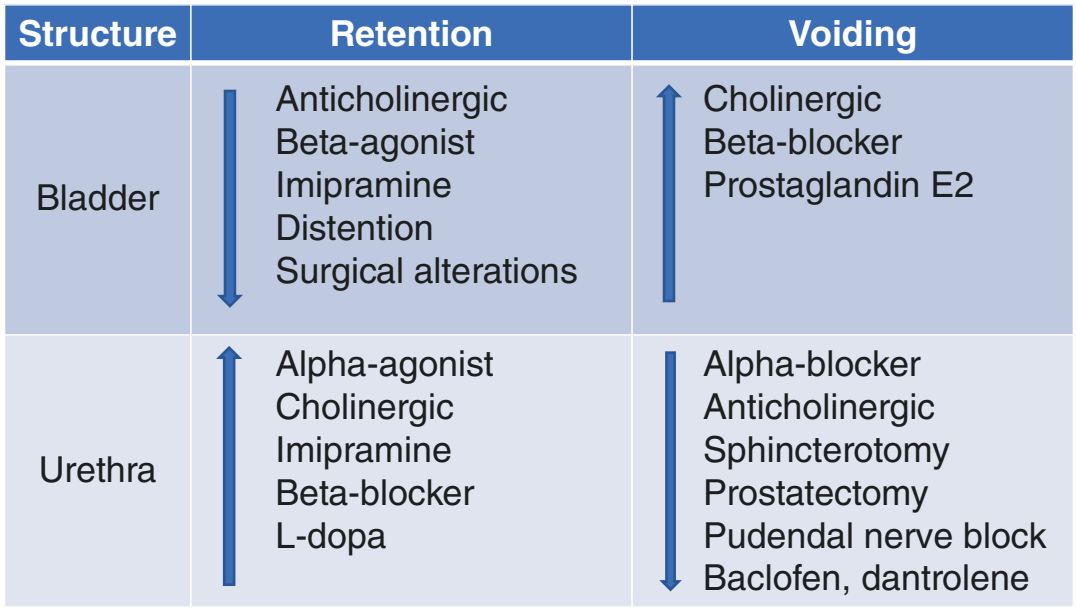


Fig. 29.4 Manipulations to increase or decrease bladder contractility or urethral resistance to achieve a low-pressure voiding system. A decrease in the bladder contractility (left column) promotes retention. The opposite (right column) promotes bladder emptying

will proceed through tonic sympathetic activity originating from the thoracolumbar sympathetic outflow (T12-L2). The latter is formed by the tonic activity via the pudendal nerve from the anterior horn cells in Onuf's nucleus (S2-S4) innervating the striated muscle of the sphincter (Schroder 1981). The parasympathetic activity innervating the detrusor muscle is inhibited by descending inhibitory pathways from the pontine micturition center. Continence is achieved by maintaining the urethra at a higher pressure than the bladder (Roberts 2008). Intravesical pressure during filling should not exceed 10 cmH_2O, despite an increase in volume from 0 to 450–550 mL. This is achieved not only by inhibition of the parasympathetic activity, but also by an active process of detrusor relaxation leading to high or acceptable bladder compliance.

29.3.2 Emptying

Voluntary voiding is a coordination of voluntary and reflex actions starting from the pons to achieve both contraction of the detrusor and relaxation of the sphincter. Relaxation of the external urethral sphincter and bladder neck during the voiding phase is mediated via inhibition of the pudendal nerve and inhibition of the sympathetic activity. The physiological trigger for bladder emptying is a sense of fullness. A-δ myelinated afferent fibers pass from the lower urinary tract to the spinal cord through nerves conveying all three types of afferent fibers: parasympathetic, sympathetic, and somatic fibers. As the bladder sends sensory impulses to the brain through the posterior columns and lateral spinothalamic tracts of the spinal cord, the individual becomes increasingly aware of the necessity to void. The brain signals to the external sphincter whether it is an appropriate place and time to empty the bladder and make the necessary social arrangements. Relaxation of the external urethral sphincter and pelvic floor musculature is the first sign of the onset of voiding. The detrusor contraction occurs after a few seconds. The pontine micturition center allows the sacral micturition center to induce a detrusor contraction mediated by muscarinic receptors (M2, M3).

29.4 Physical and Neurological Examination

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) should be used to properly document the neurological findings of spinal cord injuries. Neurological examination is characterized by the neurological lesions. During a rectal examination, it is important for the examiner to examine sacral sensation, anal reflex, bulbocavernosus reflex, anal sphincter tone, and voluntary control of the anal sphincter. The bulbocavernosus reflex and anal reflex are suitable for assessing the integrity of S2-S4 reflex arc (Vodusek 2003). In addition, examination of the lower extremity motor and sensory functions, especially S1 segmental motor and sensory, and reflexes such as dartos reflex and cremasteric reflex should be included. The voluntary activity of the S1 key muscle also suggests that the urethral sphincter can be functioning. The presence of voluntary activity indicates functioning motor tracts, and the anal reflexes indicate only that the sacral reflex arc is not damaged. The absence of bulbocavernosus reflex and deep tendon reflexes in the lower extremities suggests lower motor neuron lesion bladder dysfunction. The dartos reflex is a somatoautonomic reflex that depends on the sympathetic segment T11-L2. Intact dartos reflex arc reflects the integrity of the afferent and efferent branches of the genitofemoral nerve (T11-L2) and thoracolumbar sympathetic arc (Soler et al. 2017; Yilmaz et al. 2006). Neurological examinations, however, do not always predict the type of bladder dysfunction.

Symptoms of urinary dysfunction include urinary retention and incontinence. Voiding frequency and voiding volume should be assessed. Bowel and sexual functions should usually be impaired concomitantly and assessed. Hand functions and dexterity, mobility, cognitive function, lifestyle, preferences, and available assistance affect the choice of management options. Other urological problems such as benign prostatic hyperplasia, stress incontinence, or urinary tract infection may coexist and should be considered in the evaluation of urinary dysfunction. The presence and frequency of complications, including autonomic dysreflexia and urinary tract infection and stone, associated with bladder dysfunction, should also be assessed.

29.5 Neurogenic Bladder Dysfunction

Different clinical manifestations of neurogenic lower urinary tract dysfunction can occur depending on the neurological level of injury and completeness of the lesion (Panicker et al. 2013). Depending on the neurological status and neurological level of injury, the bladder can become overactive (emptying too frequently/quickly) or underactive (not emptying completely), with urethral complex overactivity (dyssynergia with partial/complete urinary retention) or underperformance (incontinence). Therefore, the pathophysiology of neurogenic bladder should be described as neurogenic detrusor overactivity, neurogenic detrusor underactivity, detrusor-sphincter dyssynergia, and neurogenic sphincter deficiency (Corcos and Przydacz 2018).

Neurogenic detrusor overactivity is an involuntary contraction of the detrusor muscle associated with an increase in bladder pressure during the filling phase of urodynamics (Osman et al. 2014). High intravesical pressures may cause vesicoureteral reflux and may cause adverse effects on the integrity of the upper urinary tract. Neurogenic detrusor underactivity is defined as a contraction of reduced strength and/or duration that results in prolonged emptying of the bladder and/or a failure to achieve complete bladder emptying within a normal period of time during urodynamics (Abrams et al. 2003). Detrusor-external urethral sphincter dyssynergia (detrusor-sphincter dyssynergia) is a dysfunctional coordination condition between the detrusor muscle and the urethral sphincter by simultaneous contraction of the bladder and the external urethral sphincter during the voiding phase, resulting in a functional obstruction (Abrams et al. 2003). Detrusor-sphincter dyssynergia incidence ranges from 20% to 50% among neurogenic bladder patients (Stoffel 2016). These problems result in

high postvoid residual urine and recurrent urinary tract infections. Involvement of the lumbar or sacral spinal cord can result in an acontractile bladder (normal detrusor in the ICS definition) with flaccid urethral sphincter.

The scheme from Madersbacher (Fig. 29.5) represents an attempt to classify various types of neurogenic lower urinary tract dysfunction characterized by detrusor muscle and urethral sphincter function (Jonas et al. 2003). Nevertheless, the clinical manifestations and types of the neurogenic lower urinary tract dysfunction may vary from patient to patient. There are three potential types of detrusor-sphincter dyssynergia: (1) detrusor-external sphincter or skeletal muscle dyssynergia (this means that the external urethral sphincter of the skeletal muscle does not relax when the bladder body contracts), (2) detrusor-internal sphincter dyssynergia in which smooth muscle of the bladder neck and proximal urethra does not relax during contraction of the bladder body, and (3) a combination of (1) and (2).

Because of the complex interactions between the supraspinal and cortical centers mediating the lower urinary tract function through the spinal cord, the same lesion level and degree of sensory or motor completeness may not result in the same type of neurogenic lower urinary tract dysfunction. Changes in the neurological status during the first year after injury may occur, and the pattern of the neurogenic bladder may change. The final type and extent of neurogenic lower urinary tract dysfunction is therefore estimated by follow-up (Kaplan et al. 1991). Differences in video-urody-

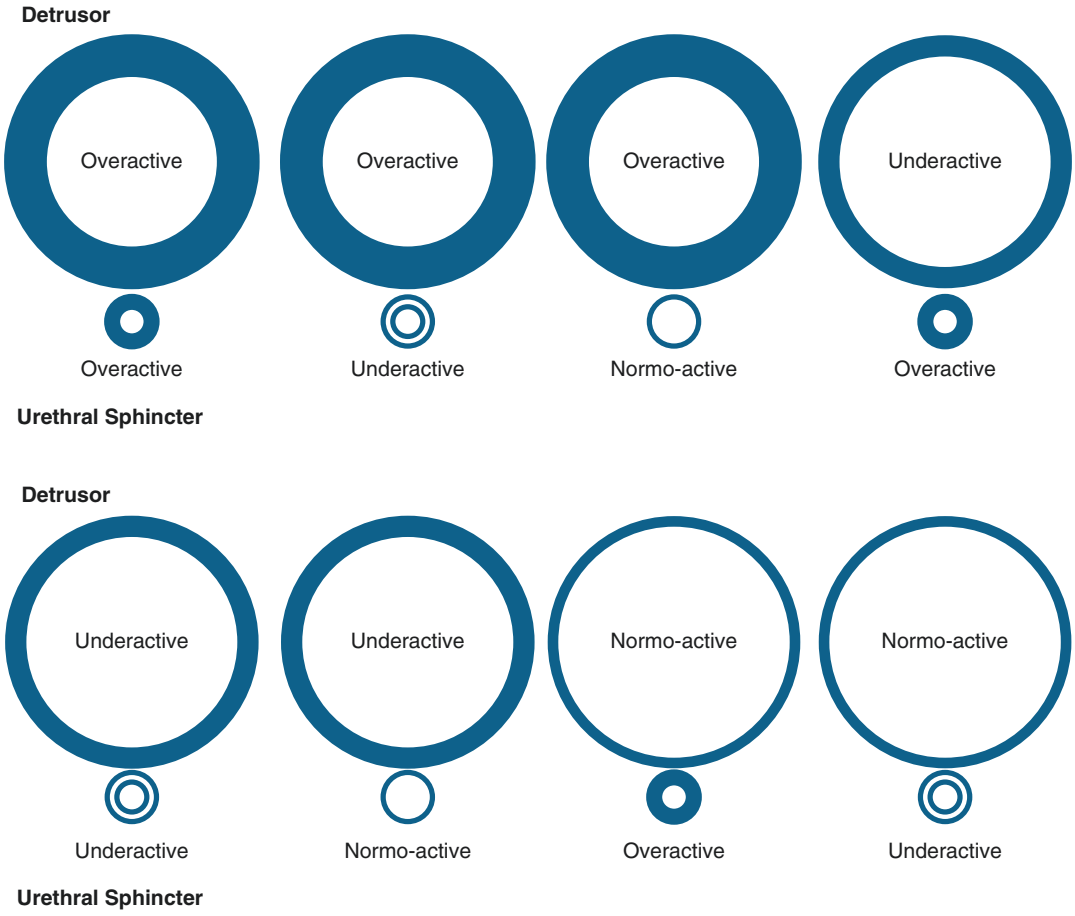


Fig. 29.5 Madersbacher classification system

namic studies may be evident in the characteristics of detrusor overactivity, maximum detrusor pressure during storage phase, or overall bladder compliance (Kaplan et al. 1991). An accurate diagnosis of neurogenic lower urinary tract dysfunction after spinal cord injury should therefore be performed by video-urodynamic study.

Depending on the type of neurogenic bladder, proper treatment is essential for lifelong maintenance of the lower urinary tract in patients with spinal cord injuries. The protection of the upper urinary tract, preservation of kidney function, and being continent are important factors in quality of life and participation of the patients in daily activities. Therefore, regular and careful neurologic and urologic examinations are important in the treatment of patients with spinal cord injuries.

29.5.1 Lower Motor Neuron Lesion Bladder Dysfunction

Bladder dysfunction is closely related to the neurological level of injury and completeness of the lesion. However, neurological examinations and neurological status do not always predict the characteristics of bladder dysfunction. They can evolve over months before they are stabilized. If the lesion contains only the peripheral innervation of the bladder or completely destroys the sacral micturition center, the bladder dysfunction will be a lower motor neuron lesion bladder. This type of bladder dysfunction is associated with hypotonic or atonic detrusor and/or hypo- or acontractile external urethral sphincter. As a result, clinical symptoms include urinary retention with associated overflow incontinence.

29.5.2 Upper Motor Neuron Lesion Bladder Dysfunction (Suprasacral Lesion)

If the lesion is above the sacral micturition center, the result is an upper motor neuron lesion bladder, characterized by a low bladder volume, high detrusor pressures, decreased bladder compliance, and bladder trabeculation. Many patients with spinal cord injuries develop detrusor-sphincter dyssynergia, characterized by cocontraction of the bladder and sphincter.

29.5.3 Assessment

Assessment of the lower urinary tract includes measurement of postvoid residual urine volume, voiding cystourethrogram, urodynamic study or video-urodynamic study, and cystoscopy. If the patient does not have an indwelling catheter, the patient is assessed for bladder emptying by measuring postvoid residual volume. Measurements of postvoid residual urine can be performed using bladder ultrasound (bladder scanner) or catheterization after voiding. Voiding cystourethrogram can evaluate the bladder neck and urethral function during filling and voiding phases, as well as bladder volume, bladder contour, and vesicoureteral reflux. Cystoscopy is used to assess bladder anatomy and identify stones, cystitis, or bladder tumors. Evaluation of the upper urinary tract includes anatomical structures by ultrasound, computed tomography scan, or intravenous pyelogram, as well as renal functions using radionuclide renal scans.

29.5.3.1 Voiding Diary

The voiding diary is intended to record voiding behavior, including intermittent catheterization and fluid intake habits semi-objectively. The voting diary should contain the micturition time including intermittent catheterization, frequency-volume chart, and bladder diary including voiding frequency, incontinence episodes, voiding volumes, and intake volumes. Accurate recording of the voiding diary variables can provide an estimate of functional bladder capacity and can help reveal variations in voided volumes that indicate detrusor overactivity (Amundsen et al. 2007; Wyman et al. 2009). The voiding diary also helps to identify polyuria and nocturnal polyuria and to calculate 24-h and nocturnal total urine volume (Drake 2015).

29.5.3.2 Postvoid Residual Urine Volume

If people with spinal cord injuries do not properly self-void at low pressure, the postvoid residual may not be of great clinical significance as it is mostly voided by intermittent catheterization. However, an increase in postvoid residual suggests complications such as UTI and bladder stones if the bladder is emptied without catheterization. When measuring the postvoid residual urine volume, ultrasound measurement is preferable to catheterization.

29.5.3.3 Urodynamic Studies

Urodynamic studies are important in assessing the nature of voiding function. However, this study should be used with good clinical judgment and may have some limitations. The results of urodynamic studies are very helpful in assessing prognosis of the neurogenic bladder dysfunction and risk of deterioration of the upper urinary tract and provide appropriate follow-up monitoring. It is generally accepted that urodynamic study should be performed to provide an accurate diagnosis of neurogenic bladder dysfunction in people with spinal cord injuries. Urodynamic studies are the current standard for evaluating lower urinary tract function. Urodynamic studies include bladder filling sensation, capacity, compliance, detrusor leak point pressure, maximum detrusor pressure, sphincter activity using usually surface electromyography, urinary flow, ability to empty, and postvoid residual volume (Agrawal and Joshi 2015). Technical recommendations on how to perform urodynamic testing and report findings were set and updated by the International Continence Society in their "Good Urodynamic Practice" in 2017 (Rosier et al. 2017). The first version of the International Spinal Cord Injury Urodynamic Basic Data Set for standardized data collection and reporting of minimum information on urodynamic studies was published in 2008. The second version in 2018 adopted new terminology and included the variable "detrusor function during filling cystometry," "detrusor function during voiding," "detrusor leak point pressure during filling cystometry," "cystometric bladder capacity during filling cystometry," and "urethral function during voiding." The cutoff value for low bladder compliance was changed from 10 mL/cmH_2O to 20 mL/cmH_2O (Pannek et al. 2018) (Fig. 29.6). Continuous blood pressure monitoring is important for people at risk for autonomic dysreflexia during the procedure (Yoon et al. 2018) (Fig. 29.7).

The bladder should be empty at the start of filling. Since fast filling and room-temperature saline can cause bladder instability, a physiological filling rate should be used with body temperature saline solution (Blok et al. 2020). The technique of the filling cystometry, described as continuous fluid filling of the bladder via a transurethral catheter or other route (e.g., suprapubic, Mitrofanoff), is used to mimic the bladder's filling and storage as well as to record the pressure–volume relationship within the bladder. Therefore, cystometry allows for the evaluation of intravesical pressure, bladder wall compliance that is the ability of the bladder to accommodate the increasing volume with low pressure, bladder sensation, and involuntary detrusor contractions. The results obtained may include detrusor overactivity, low bladder compliance resulting in high bladder storage pressure, abnormal bladder sensation, incontinence, and incompetent or relaxing external urethral sphincter (Blok et al. 2020).

A 7F (6-8F) two-channel bladder catheter and 8F rectal catheter are used. Using a thin indwelling catheter, the bladder is filled with saline solution at body temperature with a slow filling rate (<30 mL/min) until the maximum bladder capacity is reached. It is recommended to start filling at a low rate of 10 mL/min or less (Danforth and Ginsberg 2014). Then, the bladder filling can be maintained at a rate of 20–30 mL/min if no increase in detrusor pressure is observed. *Filling rates* are variable and can be slow (10 mL/min), medium (10–100 mL/min), or fast (>100 mL/min). Physiologic filling rate can be calculated at less than 1/4 of the total body weight in mL/min. It has been shown that filling rates of more than 20% of the estimated bladder capacity artificially increase the detrusor pressure (Joseph 1992). At the same time, the intravesical and the intra-abdominal pressure are continuously measured. The measurement of

INTERNATIONAL SPINAL CORD INJURY URODYNAMIC BASIC DATA SET (Version 2.0)

Data collection form

Date performed: YYYYMMDD Unknown

Bladder sensation during filling cystometry:
Normal Increased Reduced Absent Non-specific Unknown

Detrusor function during filling cystometry:
Normal Neurogenic detrusor overactivity Unknown

Maximum detrusor pressure during filling cystometry: _____ cm H2O
Not applicable Unknown

Compliance during filling cystometry: _____ mL/cm H20
Low (< 20 mL/cm H20) Yes No Unknown

Detrusor leak point pressure: _____ cm H2O Unknown

Cystometric bladder capacity: _____ mL Unknown

Detrusor function during voiding:
Normal Underactive detrusor Acontractile detrusor Unknown

Urethral function during voiding:
Normal Detrusor sphincter dyssynergia Non-relaxing urethral sphincter obstruction Unknown

Post void residual volume: _____mL Not applicable Unknown

Fig. 29.6 Data collection form of the International Spinal Cord Injury Urodynamic Basic Data Set (Version 2.0)

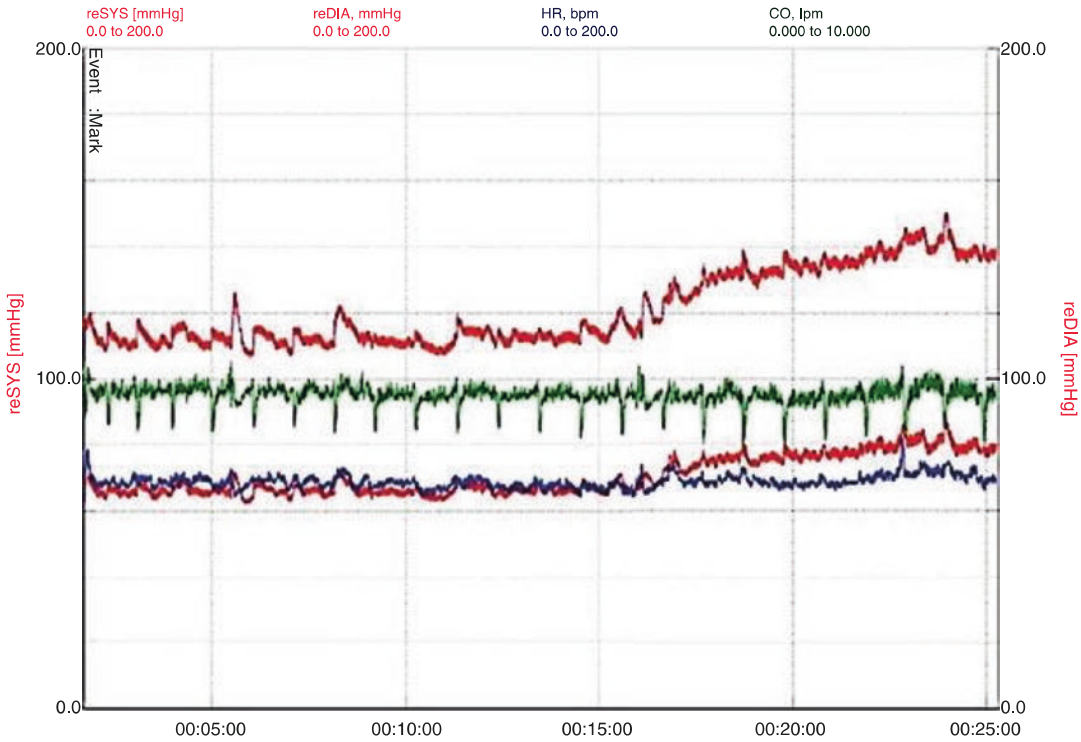


Fig. 29.7 Cardiovascular responses during video-urodynamic study using Finometer™. From Yoon et al. (2018), with permission

abdominal pressure is measured by inserting a rectal balloon catheter. A *detrusor pressure* is obtained by subtracting rectal pressure from intravesical pressure: detrusor pressure = intravesical pressure − rectal pressure (or abdominal pressure). *Detrusor leak point pressure* of 40 cmH_2O is considered as a cutoff value for upper urinary tract failure (Kim et al. 1998). *Detrusor compliance* is calculated by dividing the change in volume (ΔV) by the change in detrusor pressure (ΔPdet) and is expressed in mL/cmH_2O. The current recommendation is to measure compliance between the start of bladder filling and the cystometric capacity (or just before the start of any detrusor contraction that causes significant leakage) (Corcos and Przydacz 2018). Compliance is considered one of the most reproducible and reliable urodynamic measurements (Rovner and Koski 2015).

In addition, the electromyographic activity of the external urethral sphincter muscle or pelvic floor muscle is recorded (McGuire 2010). Even if surface electrodes are commonly used because of the patient fears that a needle electrode will be more accurately inserted into the perineal area. For needle electromyography in women, the needle is inserted perianally or periurethrally to a depth of 10–15 mm. For men, a 50–75 mm needle electrode is needled to reach the external urethral sphincter muscle fibers located distal to the prostate. Procedures for urodynamic study should follow the guidelines for good urodynamic practice (Schäfer et al. 2002) (Fig. 29.8). Figure 29.9 is a case of urodynamic study in T4 AIS A with

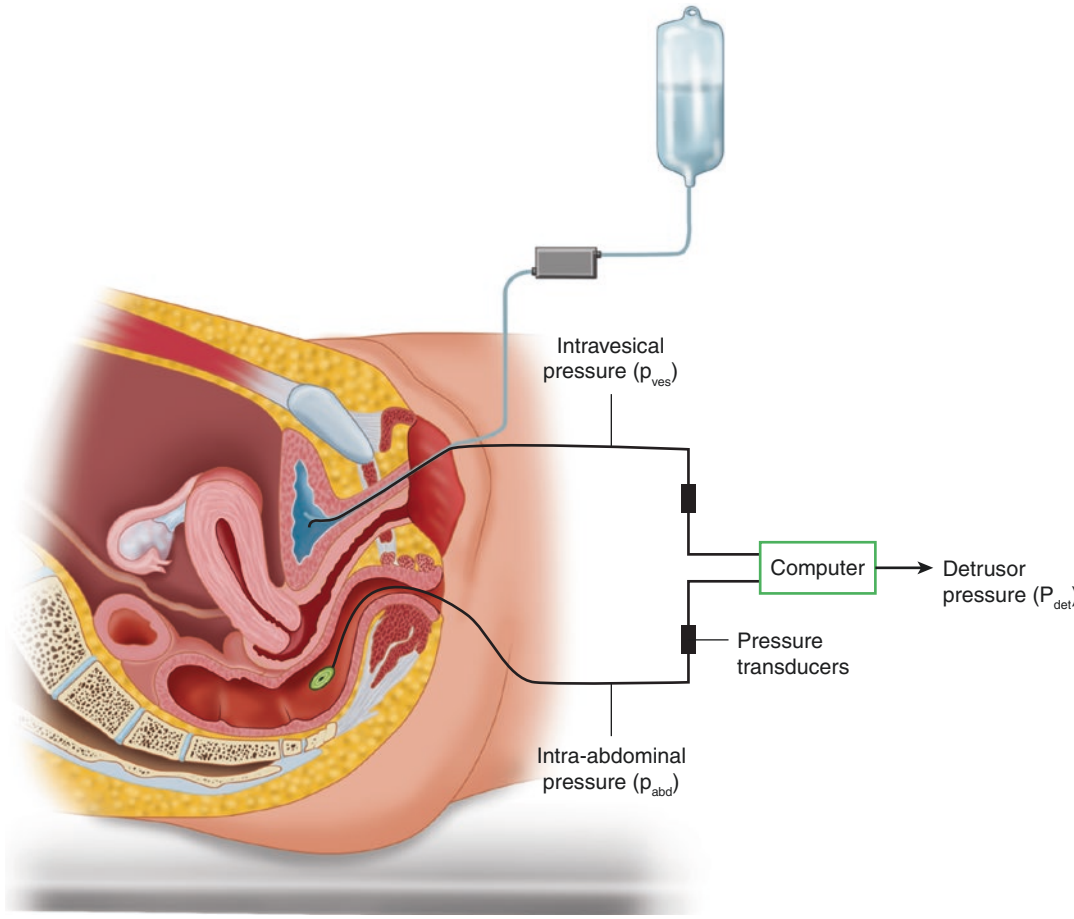


Fig. 29.8 Urodynamic study. The intravesical and intraabdominal pressure and EMG activity of the external urethral sphincter or perineal muscles are continuously measured

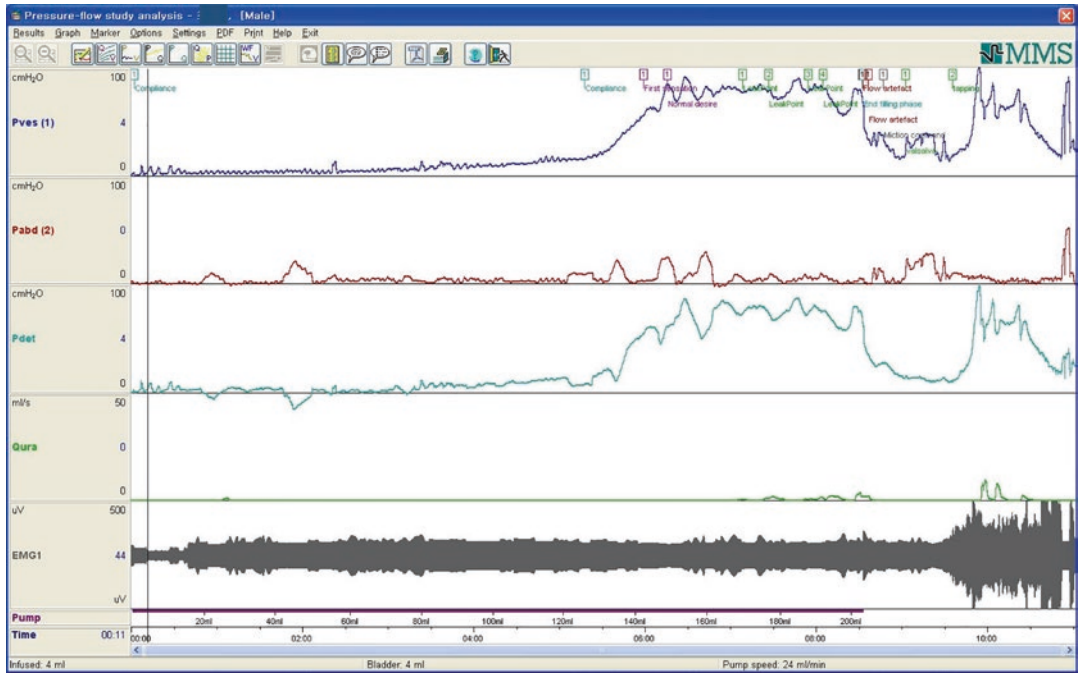


Fig. 29.9 The urodynamic study in a patient with T5 AIS A shows: phasic and terminal detrusor overactivity, low maximum cystometric capacity, high leak point pressure, low detrusor compliance, and detrusor-external sphincter dyssynergia

phasic and terminal detrusor overactivity, low maximum cystometric capacity, high leak point pressure, low detrusor compliance, and detrusor-external sphincter dyssynergia.

The parameters of the urodynamic study according to the goals of neurogenic bladder treatment are as follows: adequate cystometric bladder capacity, 500–600 mL; low detrusor pressure, compliance greater than 10 mL/cmH_2O with no detrusor contractions during filling; and adequate postvoid residual urine, less than 100 mL at low detrusor pressure <60 cmH_2O in males and <30 cmH_2O in females (Biering-Sörensen et al. 2008).

Video-urodynamics combines radiologic imaging with multichannel urodynamics. The use of contrast agents for bladder filling during urodynamics and fluoroscopy allows synchronous and dynamic imaging of the lower urinary tract. This procedure detects secondary changes in the morphology of the lower urinary tract, vesicoureteral reflux, and detrusor-external sphincter or bladder neck dyssynergia. Morphological changes (e.g., vesicoureteral reflux) can also be associated with functional changes (e.g., detrusor overactivity) (Agrawalla et al. 2004).

29.5.3.4 Laboratory Studies for Renal Function

Laboratory studies for renal function include blood urea nitrogen (BUN), creatinine, and cystatin C. Cystatin C has been suggested as a potential alternative to serum creatinine because it potentially has fewer non-GFR determinants. The use of serum cystatin C avoids the limitations related to both diet and muscle mass that affect serum creatinine. Cystatin C as a marker for estimating GFR is independent of gender, age, muscle mass, and cirrhosis and does not need to be corrected for height or weight. Cystatin C may be more accurate than serum creatinine in estimating GFR and is more strongly associated with all-cause mortality and cardiovascular events (Ferguson et al. 2003). For more informa-

tion, see *Chap. 9. Commonly Used Laboratory Tests in the Management of Spinal Cord Injuries*. Bacterial colonization is common; however, it plays little role in routine urine culture.

Cystatin C

Cystatin C, a 13 kDa protein of the cystatin superfamily of cysteine protease inhibitors, is produced at a relatively constant rate by all nucleated cells and is excreted almost exclusively by glomerular filtration. Cystatin C is more sensitive and may be a specific marker than creatinine for assessing impaired renal excretory function (Dharnidharka et al. 2002). Even if serum creatinine is still within normal range, a slight decrease in GFR leads to an increase in cystatin C concentrations.

Glomerular Filtration Rate

GFR is necessary to accurately measure renal excretory function when drugs with a narrow therapeutic index are used and are excreted by the kidney, and when an accurate measurement of kidney function is required in patients with abnormal muscle mass, for example, in people with spinal cord injuries.

Serum Urea

Urea is freely filtered by the glomerulus, with variable reabsorption, which is affected by extracellular volume status. Intravascular volume depletion, diuretics, congestive heart failure, GI bleeding, tetracyclines, and renal failure can cause elevated levels. A disproportionate increase in serum urea compared to creatinine occurs in hypovolemia and GI bleeding. Decreased levels are seen in chronic liver disease and alcohol abuse. Serum urea is a very poor marker of excretory function.

Radionuclide Studies

Various radioisotope markers are available to estimate the GFR. The most commonly used markers are ^{51}Cr EDTA, ^{99m}Tc DTPA (diethylenetriaminepentaacetic acid), iohexol, and ^{125}I iothalamate. ^{51}Cr EDTA is reliable, even with low levels of renal function. Unlike other markers, ^{125}I iothalamate can also be administered subcutaneously, allowing slow equilibration with stable plasma concentrations. ^{99m}Tc DTPA is used in renal isotope scan. It provides an anatomical correlation with renal function, such as information on the relative uptake by each kidney. ^{99m}Tc has a very short half-life and radiation exposure is minimized.

29.6 Medical and Social Concerns

The main goal of medical management for neurogenic bladder dysfunction is to preserve renal function. Repeated upper urinary tract infections and vesicoureteral reflux cause renal scarring and progressive renal failure. In addition, incontinence can cause skin irritation and maceration, which contributes to skin breakdown or delayed healing of the pressure injuries. Bladder dysfunction has significant social consequences (Bauman et al. 2012). Spinal cord injured person often experiences urinary incontinence. Some patients may have to rely on others for catheterization or cleaning of soiled bed linens and clothing. This can lead to personal embarrassment.

29.7 Voiding Methods

Clean intermittent catheterization is considered the method of choice for bladder emptying when neurological or non-neurological causes make normal voiding impossible or incomplete (Wyndaele et al. 2010). Passive voiding by abdominal straining, Valsalva maneuver, or suprapubic compression of the lower abdomen, Credé maneuver, or high-pressure voiding is not recommended because it results in high unphysiological intravesical pressure that endangers the upper urinary tract. Some patients require indwelling transurethral or suprapubic catheter because they are unwilling to perform intermittent catheterization (Dixon et al. 2010). Patients whose bladders are mainly managed with indwelling catheters, either suprapubic catheter or urethral Foley, are at increased risk of loss of compliance over time compared to those managed with clean intermittent catheterization

(Nseyo and Santiago-Lastra 2017). The advantages and disadvantages of each voiding method are summarized in Table 29.2 (Brooks and Kirshblum 2006).

29.7.1 Intermittent Catheterization

There are currently no effective oral medications to improve bladder emptying, and appropriate physical means are required to completely remove the intravesical urine. This can be done either by teaching the patient to perform intermittent catheterization or by a permanent indwelling catheter. The intermittent catheterization, when possible, is desirable for both bladder health and the patient's self-esteem (Consortium of Spinal Cord Medicine 2006). Intermittent catheterization is very useful in the control or alleviation of urinary incontinence and is useful for patients with significant residual urine due to impaired voiding. Patients with poor bladder compliance and detrusor hyperreflexia that impair the function of storage should be given additional anticholinergic drugs or β3-agonist, and intermittent catheterization is required.

Intermittent catheterization is the treatment of choice for patients with significant residual urine or urinary retention (Fig. 29.10). Intermittent catheterization can be performed by the patient or caregiver if intermittent self-catheterization is not possible due to impaired upper extremities, comorbidities, or lack of compliance. Sterile, no-touch intermittent catheterization as a reliable and low-risk alternative to an indwelling catheter was introduced by Sir Ludwig Guttmann (Guttmann and Frankel 1966). Since introduction of clean intermittent catheterization by Lapides in 1972, clean intermittent catheterization has been used extensively in patients with neurogenic bladder. Lapides et al. (1972) proposed a concept of clean rather than sterile intermittent self-catheterization based on the theory that local host resistance, maintenance of a good blood supply to the bladder by avoiding overdistention, was a more important factor in preventing urinary tract infection than the risk of introducing bacteria at the time of catheterization. Since sterile intermittent catheterization is too time-consuming and costly to use as a routine procedure in daily life, clean catheteriza-

Table 29.2 Advantages and disadvantages of bladder management options

Voiding method	Advantages	Disadvantages
Reflex voiding	• Noninvasive	• May generate high pressures • May have high postvoid residual volumes • Need urodynamic study to evaluate pressures generated with voids
Intermittent catheterization	• Allows for catheter-free periods • Improved self-image	• Requires repeated catheterizations • Difficult for patients with poor hand function • Noncompliance with schedule may increase UTIs and generate high volumes and pressures
Indwelling urethral catheter	• Relatively easy for patients and caregivers to maintain • Suitable for patients with poor hand function • Less frequent catheter changes	• Increased UTIs • Increased risk of bladder cancer with long-term (>10 years) use • Risk of urethral erosion • Decreased bladder capacity • Interferes with sexual intercourse
Indwelling suprapubic catheter	• Relatively easy for patients and caregivers to maintain • Suitable for patients with poor hand function • Less frequent catheter changes • Does not interfere with sexual intercourse	• Increased UTIs • Increased risk of bladder cancer with long-term (>10 years) use • Decreased bladder capacity

From Brooks and Kirshblum (2006), with permission

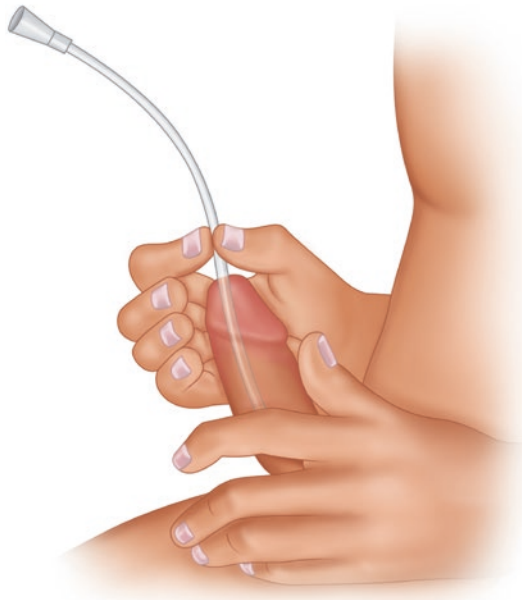


Fig. 29.10 Clean intermittent self-catheterization

tion is the method of choice. There is no high-level evidence of low incidence of complications compared to clean catheterization (Prieto et al. 2014). When used routinely, clean intermittent catheterization is effective in preserving kidney function by preventing overdistention of the bladder and reducing pressures, thereby promoting consistent blood flow to bladder walls. Clean intermittent catheterization improves continence in neurogenic bladder patients, facilitates greater community participation, and decreases home confinement. Patients can successfully learn to perform intermittent catheterization as young as 4 years of age (Lucas 2019).

Intermittent catheterization can be initiated if the patient is medically stable and has a daily urine volume less than 3000 mL. Intermittent catheterization should start at 4 or 6 h intervals. Acceptable catheterization volumes should not exceed 400 mL to 500 mL. Larger amounts can cause bladder distention and excessive intravesical pressure. Patients are advised to adjust their fluid intake adequately to minimize excessive catheterization. A detailed diary of fluid intake and catheter volume should be maintained. To prevent urinary incontinence, patients should limit fluid intake so that the maximum bladder volume does not exceed 500–600 mL in the time between catheterizations.

In most cases, self-catheterization begins on a schedule, such as every 4–6 h during the daytime and 8 h overnight. Intermittent catheterization four times a day is more practical than a strict every 6-h program which may need waking the person during the night. In individuals who cannot perform self-catheterization, finding a caregiver who performs intermittent catheterization during the night may be difficult. The frequency of intermittent catheterization should be individually controlled for catheterization volumes between 300 and 500 mL, continence, and avoidance of autonomic dysreflexia and/or urgency. Individuals performing self-catheterization can use clean technique, not sterile catheterization. The external orifice of the urethra tends to be colonized by normal flora. Despite strict sterile catheterization, these microorganisms can be introduced into the bladder during catheterizations (Barnes et al. 1992).

Clean intermittent catheterization has potential problems including trauma, urinary tract infection, bladder stone, and upper urinary tract deterioration. The most common complication of intermittent catheterization is urinary tract infection. The incidence and prevalence of this complication is difficult to predict because of the different definition criteria in various assessment studies of urinary tract infection (Wyndaele et al. 2012). Avoiding bladder overdistention by performing intermittent catheterization at regular intervals helps prevent urinary tract infection (Wyndaele 2002). Urethral stricture is a common complication in men with intermittent catheterization. In men performing intermittent catheterization, the long-term incidence of urethral stricture was 25% and significantly higher than for men using other bladder evacuation methods. There was no significant difference in the incidence of urethral strictures for effects of tetraplegia or catheter type (Krebs et al. 2015). The use of a water-soluble surgical lubricant or 2% lidocaine gel can reduce urethral trauma.

Chronic bacteriuria is common in patients with intermittent catheterization but does not cause any serious consequences in the urinary tract with no

vesicoureteral reflux. Asymptomatic bacteriuria alone is not an indication for antibiotic treatment. The catheters can be reusable and can be washed with soap and water. Some patients sterilize the catheters for 10 min in boiling water or in the microwave. Hydrophilic catheters were developed with the aim of reducing friction and therefore reducing trauma during the catheterization process. The use of a hydrophilic catheter reduced the risk of urinary tract infection in the acute period and significantly delayed the time to first urinary tract infection compared to an uncoated plastic catheter. Hydrophilic catheters can also be useful for persons with urethral strictures or discomfort during catheterization (Cardenas et al. 2011; Li et al. 2013; Woodbury et al. 2008).

29.7.2 Credé and Valsalva Maneuver

Credé maneuver (Fig. 29.11a) uses suprapubic pressure to express the bladder. Valsalva is a method of using the abdominal muscles and the diaphragm to increase the abdominal pressure. These methods can be considered with lower motor neuron lesion and low outlet resistance or sphincterotomy. These techniques must only be tried in patients with confirmed safe urodynamic parameters and have been associated with poor bladder emptying, subsequent hydronephrosis, and upper tract complications. For these reasons and better documented outcomes with clean intermittent catheterization, these techniques are no longer routinely recommended (Lucas 2019). These methods are generally not recommended as primary methods of bladder emptying, as the bladder is not completely emptied using these techniques. These methods should be avoided with detrusor-sphincter dyssynergia, bladder outlet obstruction, vesicoureteral reflux, or hydronephrosis, as they may worsen with increased abdominal pressure.

29.7.3 Reflex Voiding

Reflex voiding requires various maneuvers performed by the patient or caregiver to evoke an unphysiological sacral reflex to stimulate detrusor fibers in the bladder that allow it to be voided. Maneuvers are unique to each patient, but examples include suprapubic tapping or jabbing, pulling on pubic hair, scratching the thigh, touching the penile skin or clitoris, or anorectal manipulation (Lucas 2019). Reflex voiding (Fig. 29.11b) may be useful for males with suffi-

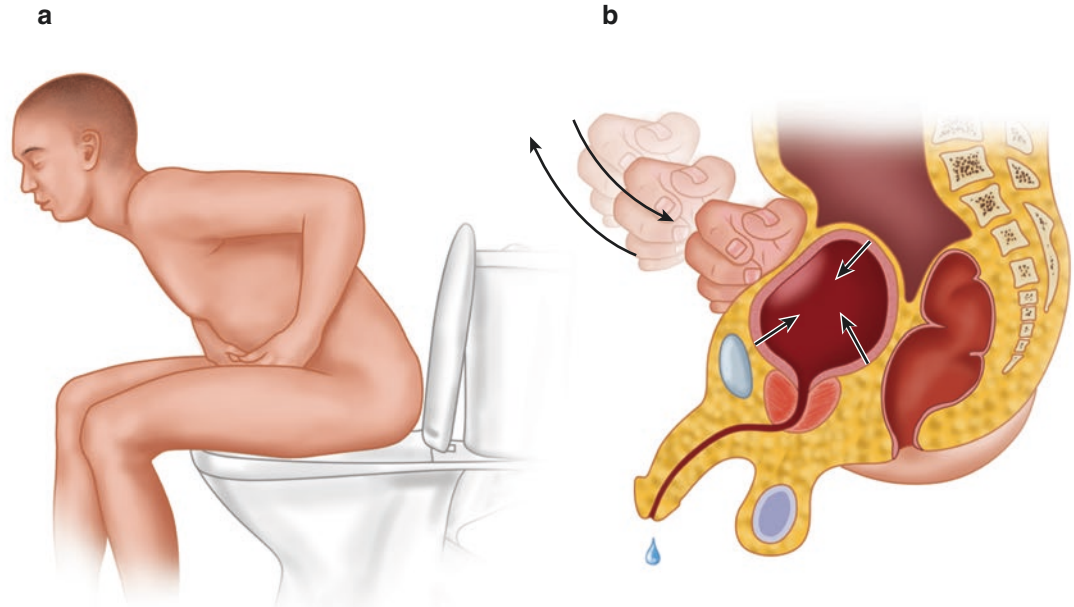


Fig. 29.11 High-pressure voiding. (**a**) Credé maneuver, (**b**) reflex voiding

cient detrusor contraction who have sufficient hand skills or willing caregiver to put on condom catheter and empty leg bag, the ability to maintain a condom catheter in place, small bladder capacity, small postvoid residual volume, and low-pressure voiding. A variety of options can be considered to ensure low-pressure voiding during reflex voiding. Nonsurgical options to consider include α-blockers or botulinum toxin to the sphincter to reduce detrusor-sphincter dyssynergia. Surgical options include sphincterotomy or endourethral stent to ensure low pressure.

Complications of reflex voiding include condom catheter leakage and/or failure, penile skin breakdown, poor bladder emptying, urinary tract infection, upper tract damage if high bladder pressure is not treated, and autonomic dysreflexia in patients with neurological level of injury at T6 or above.

29.7.4 Indwelling Catheter

Placement of an indwelling urethral catheter is a common practice for patients in the acute stage following a spinal cord injury, allowing for close monitoring of a patient's fluid balance. Urethral catheters must be inserted under sterile conditions. A less ideal alternative to intermittent catheterization is an indwelling catheter, such as a urethral Foley or suprapubic catheter. An indwelling catheter is intended for individuals who are unable to perform or unwilling to participate in an intermittent catheterization program. Individuals who have vesicoureteral reflux or who has significant incontinence refractory to other treatment strategies may benefit from an indwelling catheter (Belman 1995; Dixon et al. 2010). People with spinal cord injuries who require indwelling catheters for long-term bladder management can still benefit from the addition of antimuscarinic medication. The use of the antimuscarinic oxybutynin in people with spinal cord injuries and chronic indwelling catheters was associated with better bladder compliance and less hydronephrosis (Goetz and Klausner 2014; Kim et al. 1997).

Indwelling catheters have long-term risks such as vesicoureteral reflux, hydronephrosis, urethral incompetence and leakage, severe autonomic dysreflexia, bladder calculi, labial erosion, hypospadias, and bladder cancer. There were no significant differences in the incidence of long-term complications related to renal function, bladder stones, urinary tract infection, and bladder cancer between suprapubic catheters and transurethral indwelling catheters in patients with spinal cord injuries (Katsumi et al. 2010). The risk for bladder stones is about 25%, whereas the risk for stone recurrence in patients with transurethral catheter is increased compared to those with suprapubic catheter (Bartel et al. 2014). In transurethral catheters, percentage of urethral and scrotal complications is higher. When using suprapubic catheters, the routine use of anticholinergic medication and clamping of the catheter is not required to maintain detrusor compliance and renal function (Pannek et al. 2010; Rigby 2009).

Indwelling catheters should be changed every four weeks (Rushing 2006). A suprapubic catheter is preferred as it decreases the incidence of urethral trauma, epididymitis, and prostatitis. Sexual intercourse is easier with a suprapubic catheter than with urethral catheter (Feifer and Corcos 2008). Individuals with both urethral and suprapubic catheters increase the risk of transitional cell and squamous cell carcinoma of the bladder. Therefore, cystoscopy is recommended every two years (Robinson 2008). In the past, clamping of the urethral or suprapubic catheter has been advocated and used on the assumption that there may be a splinting effect that prevents the bladder contracture. However, this intervention is not recommended because it can lead to overdistention of the bladder, contribute to a urinary tract infection, and cause autonomic dysreflexia. Irrigation was often performed by people with spinal cord injuries who use chronic indwelling catheters for long-term bladder management. In addition, people with intermittent catheterization have sometimes been given bladder irrigation with antimicrobial agents. However, the guidelines do not recommend routine use of this irrigation because there is no evidence to reduce catheter-associated urinary tract infection, and the practice of irrigation may itself increase the risk of catheter-associated urinary tract infection (Hooton et al. 2010). Moreover, there is no difference in effectiveness between saline and other

irritants including antibiotic solution, at reducing bacteriuria (Waites et al. 2006).

29.7.5 Sacral Root Stimulation and Rhizotomy

Patients with complete spinal cord injuries may use a sacral anterior root stimulation to allow voiding, but sacral posterior root rhizotomy is often required to suppress detrusor and sphincter overactivity. Nowadays, sacral anterior root stimulation is rarely used because the patient reluctantly undergoes concomitant dorsal rhizotomy, which is a destructive and irreversible procedure that causes the loss of reflex sexual function and reflex defecation.

29.8 Management

There are several methods for detrusor relaxation, including drug treatment, botulinum toxin injection in the detrusor, and surgical procedures. Recent trends in neurogenic bladder management in patients with spinal cord injuries have changed over the past 30 years (Fig. 29.12). The management goal of neurogenic bladder is to increase bladder compliance and reduce detrusor pressure during urine storage. Because intermittent catheterization is the choice of voiding method, there is less interest in medical interventions that promote voiding by reducing the bladder outflow resistance.

Bladder management in spinal cord injury depends on the characteristics of the lower urinary tract dysfunction and needs to be individualized through appropriate education. At some point after spinal cord injury, the ultimate goal and main focus of neurogenic lower urinary tract dysfunction treatment are protection of renal function. Depending on the level and completeness of the lesion, several types of neurogenic lower urinary tract dysfunction occur. Initially, after spinal cord injury, during the spinal shock phase, there is an acontractile bladder. Several days to several weeks later, various types of neurogenic bladder can occur. An acontractile bladder usually does not require any treatment other than evacuation at regular intervals through self-catheterization or intermittent catheterization. Patients with detrusor overactivity usually require treatment to reduce the elevated detrusor pressure during storage, which increases bladder capacity and leads to continence and protects renal function.

The first urological evaluation should be performed as soon as possible within the first two weeks of the primary rehabilitation phase. Bladder management should be established for the first rehabilitation phase of the patient who can remove the indwelling catheter after acute treatment. It is advisable to review the medical history and perform an ultrasound examination of the lower and upper urinary tracts to rule out structural and pathological findings that may interfere certain treatment options. After the spinal shock phase, detrusor activity may recur in association with incontinence and pressure-related renal damage. Therefore, the first video-urodynamic assessment should be performed within the first 8 weeks after injury.

Depending on the type of neurogenic lower urinary tract dysfunction and the initial treatment, a second urodynamic examination is recommended after 8–12 weeks of the initial test. This test is important for assessing the treatment effect in established urologic treatment or for the early detection of signs of clinically asymptomatic neurogenic detrusor overactivity. The results of the second urodynamic study will be useful as an additional urodynamic study at the end of the primary rehabilitation phase at 6 months.

High detrusor pressure during storage phase due to low bladder compliance or detrusor overactivity associated with detrusor-sphincter dyssynergia is the main risk factor for the deterioration of renal function (Gerridzen et al. 1992). The main goal of the bladder management is to maintain the low detrusor pressure during urine storage and emptying of the bladder (Perkash 1993). Other important goals are to achieve urinary continence, to prevent recurrent urinary tract infection, to allow the patient to manage the bladder independently, and to adapt bladder management to the general condition of the patient. To achieve these goals, an appropriate bladder management during the acute phase and throughout the primary rehabilitation is important. Urodynamic evaluation is essential for treatment adaptation and risk assessment. Treatment should never be initiated or applied exclusively on the basis of clinical symptoms. In addition, bladder management for patients with spinal cord injuries should not only be selected based on the urody-

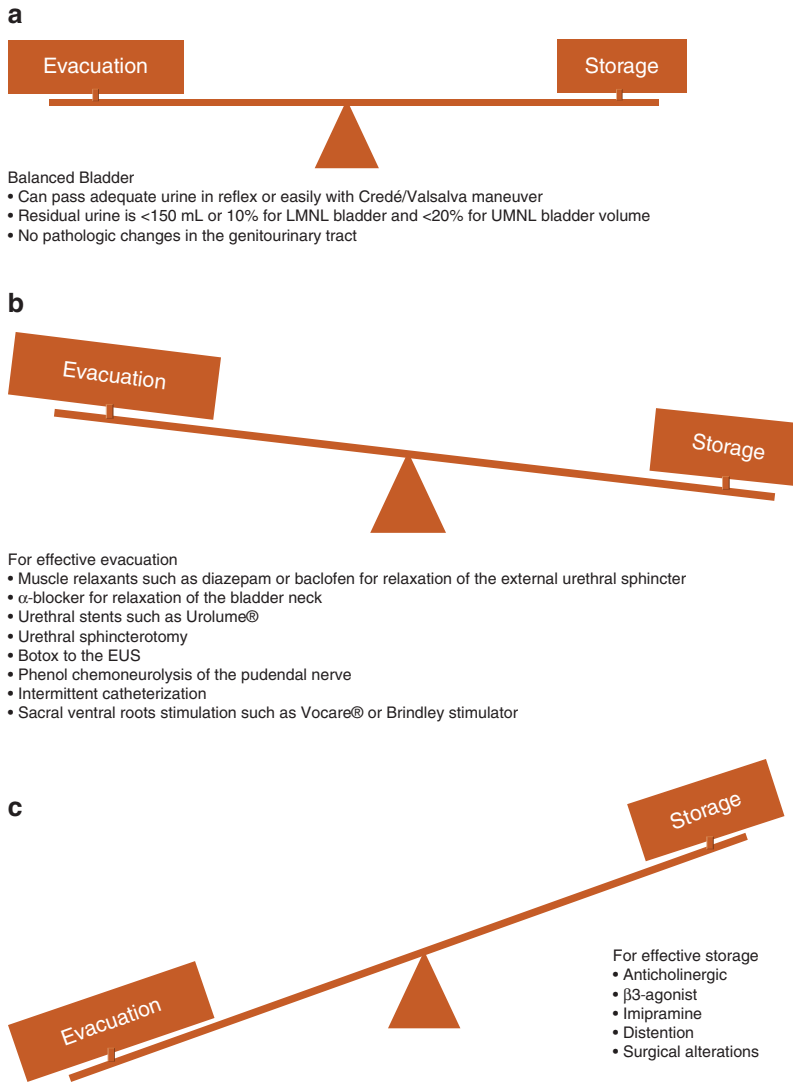


Fig. 29.12 Over the past 30 years there have been changes in the management of neurogenic bladder in people with spinal cord injuries. Assessment and treatment have been modified depending on which of the two functions involves storing and voiding urine and which is the primary function of the bladder. When the treatment goal of neurogenic bladder dysfunction was bladder balance (a), more emphasis was placed on urethral voiding, and assessment and treatment placed more emphasis on management of lower urinary system outflow (b). The current treatment goal is to increase detrusor compliance for preserving the upper urinary tract system, and the treatment goal is to decrease detrusor activity, and intermittent catheterization is recognized as the method of choice for voiding in neurogenic bladder dysfunction

namic data, but all psychological and sociological factors must be included in all decisions.

The primary goal of the bladder management in the acute phase is to ensure a low-pressure urinary drainage without significant residual urine less than 20% of the maximum bladder capacity. Patients with detrusor leak point pressure less than 40 cmH_2O have a lower risk for upper urinary tract injury than those with detrusor leak point pressure above 40 cmH_2O (McGuire et al. 1981). Early bladder management immediately following spinal cord injury usually uses an indwelling catheter, transurethral. In case of secondary complications such as urethral strictures or recurrent urinary tract infection, transurethral catheters should be removed and replaced with alternative drainage system including suprapubic catheter as soon as possible. Today, intermittent catheterization is recommended as the standard first-line treatment in patients with most types of neurogenic bladder.

29.8.1 Neurogenic Bladder Management Routines

Immediately after spinal cord injury, an indwelling catheter is the most practical and safe bladder management. A closed system of drainage should be used, being careful not to lift the drainage bag above the individual's body and keep the catheter straight and allow free-flowing. Once medical stability is achieved and the person becomes more active, bladder management options need to be addressed. The person should be informed about options available and encouraged to actively participate as long as they are comfortable with bladder management. Options include intermittent catheterization, continued use of an indwelling catheter, and surgical diversion procedures. Before commencing bladder management for the neurogenic bladder, a complete urologic profile should be done to help ensure successful bladder management for the individual. A complete urologic profile is recommended on an annual basis to prevent genitourinary complications.

The Foley catheter is removed in the morning to switch to intermittent catheterization. Fluid intake is limited during the night before the removal of the catheter. Fluid restrictions of 2 L per day are often applied to individuals using intermittent catheterization. In addition, persons may need to restrict fluid intake before bedtime. The person is placed in a fluid restriction of 1800–2000 mL: 400 mL at breakfast, lunch, and dinner and 200 mL at 10:00 AM, 4:00 PM, and 8:00 PM. Intermittent catheterization is scheduled every 4 h. Many persons need to catheterize one or more times during the night, especially when significant postural diuresis occurs. Limited fluid intake helps prevent overdistention of the bladder. In addition, the urine-specific gravity and electrolytes including serum sodium are recommended to assess on a weekly basis during rehabilitation stay.

Other options for long-term bladder management include the use of an indwelling catheter, either urethral or suprapubic. Although the indwelling catheter cannot be considered the ideal medical management, it may be the best option for some people due to some factors. If the individual has a high cervical cord injury and there is a lack of a consistent, reliable primary caregiver who can perform intermittent catheterization, an indwelling catheter may be the answer. The most important consideration is what is most realistic for the individual to make him as an independent and functional as possible. Choosing a urethral or a suprapubic catheter is not always easy for the individual. The advantages of a suprapubic catheter are as follows: a large catheter can be used; easy to change; greater sexual freedom; and not developing urethral complications such as a penile-scrotal fistula or urethral stricture. The indwelling catheters must remain and be secured by appropriate taping of the catheters (Fig. 29.13).

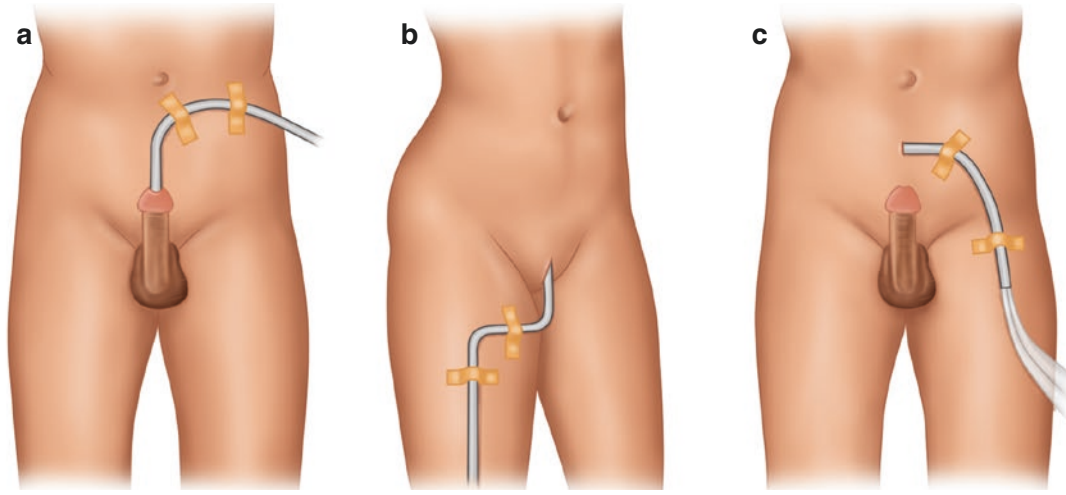


Fig. 29.13 Proper taping of indwelling catheters: (**a**) male, (**b**) female, and (**c**) suprapubic catheter

29.8.2 Pharmacological Management

29.8.2.1 Treatment for Upper Motor Neuron Lesion Bladder

Normal bladder contraction is mediated by the release of acetylcholine at the postganglionic parasympathetic receptor site. The drugs used to reduce bladder contractility can be categorized as anticholinergics, tricyclic antidepressants, β-agonists, and musculotropics. High detrusor pressures are associated with detrusor overactivity or low bladder compliance and often combined with detrusor-sphincter dyssynergia. Antimuscarinic drugs (Table 29.3) are the first-line treatment to reduce neurogenic detrusor overactivity (Andersson 2011). It is important to lower the detrusor pressure during storage because the protection of the upper urinary tract is the main goal of antimuscarinic treatment. Drugs with anticholinergic properties decrease detrusor tone and increase bladder capacity. This intervention may reduce vesicoureteral reflux and uninhibited bladder contractions.

The efficacy and safety of antimuscarinic agents, such as oxybutynin, trospium chloride, tolterodine, and propiverine, for the long-term treatment of neurogenic detrusor overactivity are well established. Therapeutic compliance is an important issue, as the antimuscarinic treatment of neurogenic detrusor overactivity in patients with spinal cord injuries lasts commonly lifelong (Appell 1997; Cameron 2010). Patients with spinal cord injuries tend to require higher doses of antimuscarinic drugs than people with idiopathic detrusor overactivity, which in turn may lead to more severe side effects that can lead to discontinuation of treatment (Kessler et al. 2011). There is no antimuscarinic drug that is clearly superior to others in terms of efficacy–side effect ratio. Therefore, individualized treatment is mandatory (Groen et al. 2016). Evaluation of treatment efficacy must be based on urodynamic studies and not just on the symptoms. There are only a few studies on the results of antimuscarinic treatment of neurogenic detrusor overactivity based on urodynamic assessments in patients with spinal cord injuries (Cameron 2010; Chancellor et al. 2006).

Table 29.3 Commonly used antimuscarinic drugs for neurogenic detrusor overactivity

Drugs	Dose (mg)	Usual frequency
Oxybutynin (Ditropan®)		
Immediate release	2.5–5	2–3 times a day
Controlled release	5–20	Once daily
Transdermal patch	36 (releasing approximately 3.9 mg oxybutynin/24 h	Replace once every 3–4 days
Propiverine (Detrunorm®)		
Immediate release	15	1–3 times a day
Controlled release	30	Once daily
Tolterodine (Detrol®)		
Immediate release	2–4	1–2 times a day
Controlled release	4	Once daily
Solifenacin (VESIcare®)		
Controlled release	5–10	Once daily
Darifenacin (Enablex®, Emselex®)		
Controlled release	7.5–15	Once daily
Fesoterodine (Toviaz®)		
Controlled release	4–8	Once daily
Trospium chloride (Sanctura®)		
Immediate release	20	Twice daily, before food
Controlled release	60	Once daily

It is important to know that patients with neurogenic detrusor overactivity due to spinal cord injury may need to be treated with high-dose antimuscarinic therapy, which may increase the dose of a single drug or a combination of other drugs to increase high-dose therapy efficiency without significantly increasing side effects (Amend et al. 2008; Horstmann et al. 2006). In terms of side effects of antimuscarinic agents, dry mouth is consistently the most common complaint. Gastrointestinal side effects (constipation, megacolon, decreased GI motility), blurred vision, cardiac adverse events including heart rate increase and prolonged QT interval, and cognitive impairment are commonly reported (Kessler et al. 2011). Intravesical instillation of oxybutynin solution has been used to minimize systemic absorption and associated side effects of antimuscarinics. Intravesical instillation of oxybutynin (0.1–0.25%) is a safe and effective alternative for

patients who cannot tolerate oral oxybutynin (Amark et al. 1998; Cameron et al. 2009). Bladder instillation is performed using crushed tablets diluted in water or saline and instilled in the bladder after catheterization to retain it.

Mirabegron is the first of a new class of drugs. Beta3-agonists stimulate β3-adrenergic receptors in the detrusor muscles to improve bladder relaxation during bladder filling. Mirabegron can increase bladder capacity without blocking contractibility. Doses of 25 and 50 mg are well tolerated and are associated with significant improvements in incontinence episodes and micturition frequency (Herschorn et al. 2013). Mirabegron was introduced for the treatment of non-neurogenic overactive bladder (Bragg et al. 2014). This drug is empirically used for overactive neurogenic bladder in people with spinal cord injuries. However, it has not been approved for neurogenic detrusor overactivity. For more information on bladder medication, see *Chap. 10. Pharmacokinetics and Pharmacotherapeutics in Spinal Cord Injuries*.

For micturition, the detrusor pressure is required to exceed the bladder outlet pressure. In some persons with spinal cord injuries, it may not be possible to void because of increased internal sphincter tone. Medications and procedures can lead to a successful decrease in outlet obstruction and enable voiding (Novara et al. 2006). Alpha-adrenergic antagonists such as prazosin, terazosin, doxazosin, or tamsulosin can decrease the bladder neck tone. These medications can cause significant hypotension, and the doses should be carefully titrated. Other adverse effects of α-adrenergic antagonists include fatigue and aggravation of ejaculatory impairment. Baclofen, diazepam, and dantrolene may be considered to reduce the external sphincter tone, but these medications are usually not successful. In male patients, tone of the external sphincter may be decreased with transurethral or transperineal injection of botulinum toxin into the external urethral sphincter or pudendal nerve block using phenol solution (Ko and Kim 1997). However, these procedures are not recommended for women because they may lead to incontinence. In fact, the current goal of neurogenic bladder management is mainly emphasized by the low maximum detrusor pressure and the high detrusor compliance; the interest in the management of the structure for urine outflow is comparatively less. Commonly used pharmacological agents for neurogenic bladder dysfunction, including antimuscarinic agents and α-blockers, are summarized in Table 29.4.

29.8.2.2 Treatment of Lower Motor Neuron Lesion Bladder

This type of bladder will result in two possible clinical scenarios. If the tone of sphincter decreases but the tone of detrusor is normal or compromised, the person will have continuous incontinence. A condom catheter will be satisfactory for male patients. In a female patient, an indwelling catheter will be required. Theoretically, the use of α-adrenergic drugs such as ephedrine and pseudoephedrine may increase the internal sphincter bladder neck tone. However, α-adrenergic drugs do not seem to actually achieve socially acceptable continence. If the sphincter is able to maintain acceptable continence, intermittent catheterization is recommended if the detrusor tone is diminished and the individual cannot micturate. Another alternative is bladder evacuation with the Valsalva maneuver or Credé maneuver. Indwelling catheters are less satisfactory treatment for this bladder dysfunction.

There are no drugs with proven efficacy for treating detrusor underactivity. Parasympathomimetic or cholinergic agonist drugs such as bethanechol chloride are not effective in increasing detrusor tone and do not improve residual urine and/or voiding dysfunction (Light and Scott 1982).

29.8.2.3 Infravesical Obstruction

The nonselective (phenoxybenzamine) and selective (tamsulosin, terazosin) α-blockers lead to limited efficacy for functional voiding obstruction resulting in a reduction of residual urine and a decrease in maximum detrusor pressure during voiding (Linsenmeyer et al. 2002). As their clinical efficacy may vary considerably, their use in the treatment of infravesical obstruction should be assessed individually.

29.8.2.4 Botulinum Toxin A for Detrusor Overactivity

If the first-line therapy of detrusor overactivity with antimuscarinics is not effective or cannot be tolerated due to side effects, injection of botuli-

Table 29.4 Commonly used pharmacological agents for neurogenic bladder dysfunction

Class	Drugs	Therapeutic effects	Common adverse effects
Muscarinic acetylcholine antagonists (anticholinergic or antimuscarinic agents)	• Oxybutynin • Tolterodine • Fesoterodine • Darifenacin • Trospium	Improve urine storage by relaxing detrusor tone	• Dry mouth • Constipation • Dry eyes • Blurred vision • Dyspepsia • Confusion
Beta3-selective adrenoreceptor agonist	• Mirabegron	Improve urine storage by targeting the main adrenoreceptor involved in detrusor muscle relaxation	• Milder side effects versus anticholinergic medications • Mean rise in blood pressure • Not recommended for patients with uncontrolled hypertension
Alpha-adrenoreceptor antagonist (alpha-blocker)	• Terazosin • Doxazosin • Tamsulosin	Improve urine flow by reducing outlet resistance	• Nasal congestion • Postural hypotension • Dizziness
Botulinum toxin A	• Botox	Injections into detrusor muscle decrease detrusor overactivity or injections at external sphincter enhance voiding	• Urinary retention • UTIs • Repeat injections for therapeutic effect

num toxin A in the detrusor muscle may increase the bladder capacity and decrease the elevated detrusor pressure. In the case of a neurogenic detrusor overactivity, 200 IU of botulinum toxin A is acceptable, but the dosage used ranges between 100 IU and 300 IU. The effect lasts between 6 and 12 months on average.

29.8.2.5 Bladder Augmentation

If conservative or minimally invasive detrusor relaxation treatments have not been unsuccessful, augmentation cystoplasty is a surgical option to obtain adequate bladder capacity and low intravesical pressure. It should be avoided in patients with compromised renal function since they are more susceptible to fluid and electrolyte imbalances. Severe abdominal adhesion or pelvic irradiation is also contraindications of this procedure.

29.9 Urinary Tract Infection

Urinary tract infections are the most common infections in patients with spinal cord injuries that lead to serious morbidity. Urinary tract infection in patients with spinal cord injuries occurs 1.5–2.5 episodes per patient per year. This has been identified as the main cause of readmissions of patients with spinal cord injuries. Approximately 5–10% of patients admitted to hospital are infected during their hospitalization (Noreau et al. 2000). One-fifth of the hospital readmissions were due to urinary tract infection with an average hospital stay of 15.5 days (DeJong et al. 2013). Urinary tract infection is one of the most important complications of neurogenic bladder dysfunction after spinal cord injury. Urinary tract infections cause serious consequences, including frequent recurrences, pyelonephritis with sepsis, renal damage, and complications caused by constant or repetitive use of antimicrobial agents, including multi-class antibiotic resistance and *Clostridium difficile* colitis (Flores-Mireles et al. 2015). High intravesical pressure, postvoid residual, and incontinence are the main consequences of urinary tract infection. In addition, the potential complications of neurogenic bladder dysfunctions (vesicoureteral reflux, stone formation, incomplete emptying of the bladder) and the methods of urinary drainage (intermittent or indwelling catheters, urinary diversion) contribute to urinary tract infections. Among the causative factors in urinary tract infections, indwelling urinary catheterization is the most common risk factor for complicated urinary tract infections (Flores-Mireles et al. 2019).

Urinary tract infections are usually caused by the endogenous flora of the host, which overcomes other competing normal flora and host defense mechanisms. Colonization is the growth of microorganisms in the urine without tissue invasion. In contrast, a urinary tract infection is the microbial colonization of urine with associated tissue invasion of the uroepithelium. Increased postvoid residual urine volumes promote the growth of bacteria. Intermittent catheterization programs can also introduce bacterial flora from the urethra to the bladder (D'Hondt and Everaert 2011).

The pathologic condition of the urinary tract after spinal cord injury depends on the status of the bladder. Neurogenic dysfunction of the bladder and necessary instrumentations result in damage of the normal anatomic and physiologic defense mechanisms to remove bacteria and maintain sterility of the urinary system. Urinary stasis contributes significantly to the increased risk of infection in this population. If the bladder is frequently emptied properly, the residual organisms do not have a chance to multiply before washout occurs. A large residual volume increased intravesical pressure, which keeps the bacteria in solution from the phagocytic action of the bladder wall, which interferes with blood flow to the bladder wall. Mucosal ischemia that is associated with high-pressure voiding and poor compliance of the bladder wall can promote tissue invasion.

The patients with spinal cord injuries are also likely to be exposed to instrumentations. In hospitalized catheterized patients with an open urine collection system, the incidence of the asymptomatic microbial disease is 100% of the patients within 3–4 days. Catheterization, intermittent catheterization or indwelling Foley catheterization, and other instrumentations introduce organisms located at the external urethral meatus or skin into the bladder. In above 50% of the spinal cord injured patients, the same microorganisms are isolated from the anterior urethra and from the bladder (Barnes et al. 1992). The distal urethra is colonized by skin flora, which is

dominated by Gram-positive cocci and diphtheroids. Lactobacilli are common organisms in females. Most urinary tract infections in people with spinal cord injuries are caused by bowel flora, most commonly Gram-negative bacilli and enterococci. In the individuals with neurogenic bladder, the microorganisms isolated from the skin flora include species such as *Enterobacteriaceae*, *Pseudomonas*, *Acinetobacter*, and *Enterococcus,* which are spread from feces (D'Hondt and Everaert 2011; Taylor and Waites 1993). In addition, the same types of microorganisms as those from various areas of the skin, including perineal, peripubic, and perianal regions, are isolated in urine (Hamamci et al. 1998). The catheter insertion is considered to result in a significant increase in bladder colonies, approximately 10 times the number of bladder colonies (Hamamci et al. 1998). The spectrum of pathogens that cause catheter-associated urinary tract infection is considerably broader than that caused by uncomplicated urinary tract infection. In addition to *Escherichia coli* (75–85%), which accounts for the vast majority of uncomplicated urinary tract infection in the general population, pathogens including *Klebsiella* species, *Pseudomonas* species, *Proteus* species, *Serratia* species, *Enterococcus* species, *Citrobacter* species, *Acinetobacter* species, and *Staphylococcus* species are responsible for a much higher percentage of urinary tract infection in individuals with spinal cord injury ((Flores-Mireles et al. 2019).

Patients with spinal cord injuries which cause urinary tract infection often have atypical or nonspecific symptoms. The specificity of individuals with spinal cord injuries is that there is usually asymptomatic bacteriuria and the sensory disorder leads to the lack of clear symptom of urinary tract infection. The clinician should carefully evaluate the patient to determine whether a positive urine culture is an infection or is an asymptomatic bacteriuria. Dysuria or suprapubic discomfort cannot occur due to a disturbed sensation. Patients may only report generalized malaise. The most common signs and symptoms of suspected urinary tract infection in patient with spinal cord injury are fever (D'Hondt and Everaert 2011). However, fever should not be attributed to urinary tract infection if the only positive point is bacteriuria unless other possible causes of fever are excluded. Approximately 45% of febrile conditions in patients with spinal cord injuries are thought to be due to urinary tract infection (Montgomerie et al. 1989). New urinary incontinence may occur, including leaking around an indwelling catheter, increased residual volumes, increased spasticity, cloudy or strong-smelling urine and changes in urinary pH, or hematuria. Occasionally, urinary retention occurs. Increased spasticity may occur in the lower abdomen or the legs. Localizing symptoms, such as a new incontinence between catheterizations, can provide an indication of the condition, but it does not always exist. The patient with spinal cord injury above the T6 neurological level of injury may more frequently present with symptoms of autonomic dysreflexia such as headache, sweating, and flushing, if urinary tract infection is complicated. Sometimes, especially in older patients or those with previous cognitive impairment, increased confusion may be a significant feature.

29.9.1 Diagnosis

Classically, the diagnosis of urinary tract infection is based on the combination of urinary symptoms, such as dysuria, urinary frequency, urgency, etc., markers of inflammation, such as pyuria, and a positive urine culture (Forster and Pohl 2019). Major laboratory tests for the neurogenic bladder dysfunction include routine blood chemistries including electrolyte, blood urea nitrogen, creatinine, hemoglobin, leukocyte count, and C-reactive protein; urine analysis (urinalysis); and urine culture and sensitivity testing. The most important diagnostic tests for urinary tract infection are urine analysis and urine culture. If a urinary tract infection is suspected, a complete urine analysis should be performed. Turbid, malodorous urine with a dense precipitate may be evidence of pyuria or infection, but it can also be normal. Infection with urea-splitting (urease-producing) organism produces alkaline urine. However, a change in urine pH is usually not a significant diagnostic finding. The urine culture should be performed before starting antibiotics administration. A blood culture can be performed if there is a suspicion of systemic infection. Additional laboratory tests are complete blood counts including differential counts, blood urea nitrogen, serum creatinine, and cystatin C.

There is no universally accepted definition of urinary tract infection. The National Institute on Disability and Rehabilitation Research consensus conference recommended a standard definition of urinary tract infection in the patient with spinal cord injuries using urine culture data, urinalysis, and clinical symptoms including fever (NIDRR 1992). For urine culture data, the cutoff was based on bladder management, including individuals with indwelling catheters, those who perform clean intermittent catheterization, and patients with condom catheter ranging from $\geq 10^2$ to $\geq 10^4$ colony-forming units (CFU). The most widely accepted definition defines urinary tract infection in patients with neurogenic lower urinary tract dysfunction as the new onset of sign/symptom associated with laboratory findings of a urinary tract infection (bacteriuria, leukocyturia, and positive urine culture) (Groen et al. 2016; Drekonja and Johnson 2008). The most commonly used microscopic criteria for the diagnosis of urinary tract infection are significant bacteriuria with greater than or equal to 10^5 CFU/mL without a catheter and greater than or equal to 10^2 CFU/mL in catheter-associated urinary tract infection. The Infectious Disease Society of America used the data to propose $\geq 10^3$ as the cutoff because it balances sensitivity with meaningful detection. Although there are catheter-associated urinary tract infections, many clinicians consider the presence of symptoms for the diagnosis of urinary tract infection in spinal cord injury, regardless of the number of bacteria in the urine (Hooton et al. 2010).

Asymptomatic bacteriuria is defined as the presence of a significant number of urine microbes (10^5 CFU/ml) in patients without clinical symptoms or signs of infection. Pyuria is defined as the presence of leukocytes in the urine as a good indicator of urinary tract infection in the non-spinal cord injury population. However, it is difficult to interpret the significance of pyuria in patients with spinal cord injury. The irritating effect of a urinary catheter, especially indwelling catheter, on the bladder wall or routine change of catheter results in a significant increase in urinary white cell count without altering the bacterial colony count. Gram-positive microorganisms such as *Staphylococcus epidermidis* and *Streptococcus faecalis* are accompanied by a small number of leukocytes despite the appearance of a large number of colonies, while Gram-negative microorganisms are accompanied by significant pyuria when there are large numbers of colonies (Anderson and Hsieh-Ma 1983). Therefore, the presence of significant pyuria may be a sign of urinary tract infection due to bacterial tissue invasion, but this is not always the case. And the absence of pyuria is less likely to have a urinary tract infection, but it does not rule out it.

An acidic urine inhibits microbial growth. Urinary tract infection is prevented by the washout effect of large volumes of urine. A large flow of fluid interferes with the adherence of microorganisms and dilutes the concentration of microorganisms. However, if large fluid volumes can reduce urine osmolality, it will be beneficial for bacterial growth.

29.9.2 Treatment of Urinary Tract Infection

The majority of patients with spinal cord injuries are intermittently or chronically bacteriuric. Asymptomatic bacteriuria does not require treatment except before instrumentation, as this treatment may increase the risk of more resistant bacterial strains without affecting the risk for symptomatic urinary tract infection (Everaert et al. 2009). Asymptomatic urinary tract infection in patients with high-grade reflux, hydronephrosis, or urea-splitting organisms may consider antibiotic treatment. Treatment and the duration of treatment is not well defined and may be empirical. Urine culture should be done before starting antibiotic treatment. Empiric antibiotic treatment is initiated until results of the culture and then adjusted based on the results of the urine culture and sensitivity.

People with symptomatic urinary tract infection should be treated with the most specific antibiotic treatment for the shortest but sufficient period. Since the urinary catheter surface due to biofilm formation becomes a source of bacterial growth, it is important to remove it and replace it with a new one before treatment of symptomatic infection (Zimakoff et al. 1995). In general, it is advisable to take 5–7 or 7–10 days oral treatment with a single substance. Treatment can be extended to 14 days if clinically associated with urogenital organs, such as pyelonephritis. A urethral Foley catheter

may be temporarily used to avoid bladder distention if it causes intermittent catheterization with unacceptable catheterization volume when fluid intake is excessive. If no response occurs within 48–72 h, cultures are repeated, and imaging studies should be considered to exclude urinary tract pathology.

Organisms of urinary tract infection in patients with spinal cord injury include *Escherichia coli, Klebsiella, Proteus, Providencia, Pseudomonas,* and *Enterococcus*. The flora changes over time due to chronic instrumentation and recurrent antibiotic therapy. The choice of antibiotics should also be effective against Gram-negative organisms. People with mild symptoms may be started on oral antibiotics, often aminoglycosides or fluoroquinolones. Currently, antibiotics, such as trimethoprim sulfamethoxazole, ciprofloxacin, and ampicillin, are the most commonly recommended therapeutics for urinary tract infections (Flores-Mireles et al. 2015). However, increasing antibiotic resistance rate and high recurrence rates threaten to significantly enhance the burden. In the appearance of fungi in urethral cultures, treatment is not required. In this case, local (intravesical) or systemic antifungal treatment is not recommended, and it is recommended to replace the catheter with a new one. If the infection is accompanied by symptoms of the urinary tract infection or the presence of fungus is a symptom of systemic infection, then antifungal treatment is necessary. Symptomatic urinary tract infection in patients with neurogenic bladder should always be treated with the most specific and available narrow-spectrum antibiotics for the shortest possible duration (Dinh et al. 2019). Figure 29.14 shows a treatment algorithm for urinary tract infection in patients with neurogenic bladder.

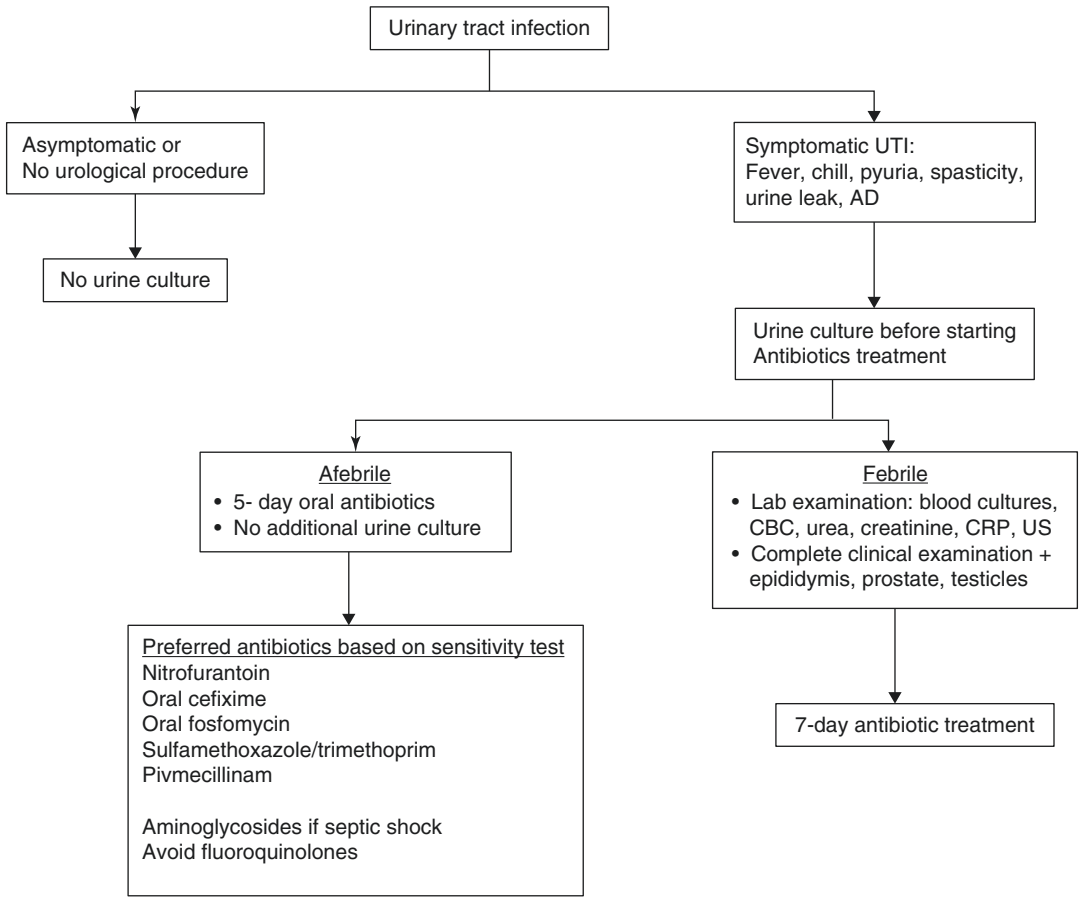


Fig. 29.14 Treatment algorithm for urinary tract infection in patients with neurogenic bladder. Adapted from Dinh et al. (2019)

29.9.3 Recurrent Urinary Tract Infection

Recurrent urinary tract infections are often defined as more than one episode in the last 6 months or more than two episodes in the last 12 months (Aydin et al. 2015). Treatment of predisposing factors of neurogenic low urinary tract dysfunction, e.g., detrusor overactivity, residual urine, or bladder stones, is the first step in preventing recurrent urinary tract infections (Aydin et al. 2015).

29.9.4 Prevention of Urinary Tract Infection

Correct catheterization techniques, the avoidance of large postvoid residual urine, and good hygiene care are very important to prevent urinary tract infection. The use of hydrophilic catheters for intermittent catheterization has been shown to reduce the incidence of urinary tract infection in men. Bladder irrigation using various substances ranging from disinfectants to saline solution is not effective in the prevention (Waites et al. 2006). Prophylactic antibiotics have no long-term effects and often enhance proliferation of resistant organisms or growth of more than one organism. Individuals with spinal cord injuries who use urinary catheters have high rates of bacterial colonization that occur within 30 days of initial catheterization and return to baseline levels after discontinuation of antibiotic therapy (Goetz and Klausner 2014). However, antibiotics are needed before the use of urological instrumentation. The prostate is a potential source for recurrent urinary tract infection in male spinal cord injured patients. In patients with bacterial prostatitis, antibiotic treatment does not eradicate the bacteria (Darouiche and Hull 2012).

The effects of methenamine salts, vitamin C supplements, and cranberry juice or cranberry extracts are unclear and have not been proven. Low-dose, long-term, antibiotic prophylaxis does not reduce the frequency of urinary tract infections but increases bacterial resistance or growth of more than one organism and cannot be recommended (Everaert et al. 2009). A modified use of antibiotic substances for prophylaxis (weekly cycling oral antibiotics) has been introduced, but the results need to be confirmed in future studies (Salomon et al. 2006).

29.10 Vesicoureteral Reflux

Vesicoureteral reflux may cause renal function deterioration by causing recurrent pyelonephritis with scarring and back pressure-related hydronephrosis. Vesicoureteral reflux can be caused by high bladder pressure, changes in the submucosal course of the ureters, recurrent urinary tract infection, or congenital malformations of the ureteral orifice. Management includes measures to lower intravesical pressure and prevent urinary tract infection. In some refractory cases, indwelling catheterization may be indicated to achieve continuous urine flow and reduce bladder pressure (Belman 1995).

The distal part of the ureter enters into the bladder at an oblique angle, and the ureteral meatus opens at the posterolateral portion of the trigone. Increased intravesical pressure will push the submucosal portion of the ureter to the detrusor muscle, thus obliterating the ureter as a functional valve mechanism. The effectiveness of this valve mechanism depends on the ratio of ureteral diameter to the length of the submucosal ureter. As the bladder wall thickens, the oblique angle of the submucosal path of the ureter in the bladder wall becomes perpendicular to the bladder wall, thereby losing the functional valve mechanism. Bladder pressure is transmitted perpendicular to the open ureteral meatus, thereby promoting the vesicoureteral reflux (Darge and Riedmiller 2004; Dixon et al. 1998; Koyanagi and Tsuji 1981).

The bladder can only eliminate urine when the intravesical pressure exceeds the urethral pressure. Therefore, emptying bladder may be incomplete with detrusor-sphincter dyssynergia. The urine remaining in the bladder is the postvoid residual volume. High postvoid residual greater than 100 mL with high intravesical pressure can be associated with vesicoureteral reflux. There is no consensus on absolute intravesical pressure that leads to vesicoureteral reflux. Intravesical pressure of 40 cmH_2O to 60 cmH_2O may be associated with vesicoureteral reflux. The diagnosis of vesicoure-

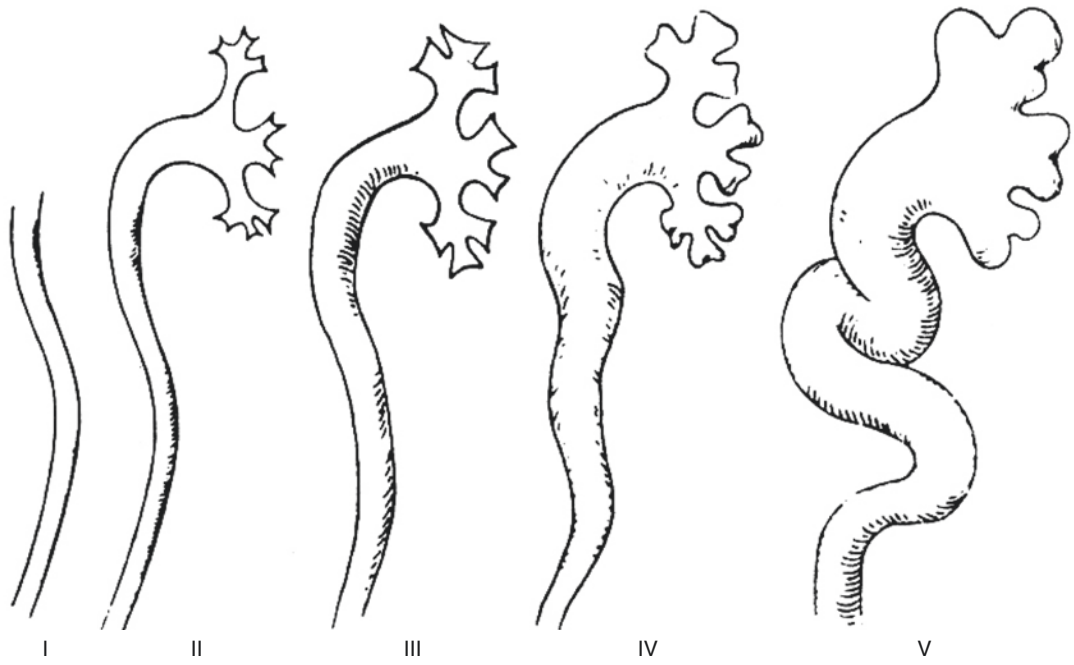


Fig. 29.15 International system of radiographic grading of vesicoureteral reflux. Grade I, into a nondilated ureter; II, into the pelvis and calyces without dilatation; III, mild to moderate dilatation of the ureter, renal pelvis, and calyces with minimal blunting of the calyceal fornices; IV, moderate ureteral tortuosity and dilatation of the pelvis and calyces; V, gross dilatation of the ureter, and calyces, loss of papillary impression, and ureteral tortuosity

teral reflux is confirmed by a voiding cystogram (Cooper et al. 2003). Schematic representations of the international system of radiographic grading of vesicoureteral reflux are shown in Fig. 29.15.

29.11 Urinary Stones

Urinary tract stones are common in patients with spinal cord injuries. The risk of bladder stones after spinal cord injury is about 35%, and the risk of renal stones is between 8% and 10%. Factors that cause bladder stones are urinary stasis and urinary tract infection by urea-splitting organisms (urease-producing organisms), usually *Proteus mirabilis*. Risk factors for upper tract calculi include bladder catheterization, bladder calculi, vesicoureteral reflux, and environmental factors. The urea-splitting organisms increase urine pH and precipitate struvite stones. Alkaline urine caused by the urea-splitting organisms promotes crystallization of magnesium ammonium phosphate (struvite) and calcium phosphate (apatite). Bacteria can adhere to the endothelium of the urinary tract by irritation and inflammation of the urinary endothelium. Struvite and apatite crystals are incorporated into the bacterial biofilm. Urease catalyzes the formation of ammonium and bicarbonates due to decomposition of urea and water. It is believed that the risk of renal stones in the first few months after spinal cord injury is related to hypercalciuria. Other factors, such as urinary retention, also play an important role in early stones. After the first two years of injury, 98% of renal stones consist of either struvite or apatite. Staghorn calculi are stones that occupy the renal pelvis and extend into one or more of the renal infundibula. These are most commonly composed of struvite (Ost and Lee 2006).

The symptoms of urinary stones may be nonspecific in people with spinal cord injuries and may overlap with symptoms of other complications. It is important to consider urinary stones in the differential diagnosis of nonspecific presentations such as increasing spasticity, sweating, and episodes of autonomic dysreflexia. It is especially important for people with recurrent urinary tract infections.

29.12 Malignancy

Overall, the incidence of bladder cancer in patients with neurogenic bladder is relatively rare. Studies on the incidence of bladder cancer in people with neurogenic bladder range from 0.2% to 2%, with many studies showing an incidence of less than 0.5% (Welk et al. 2013). Concerns about malignancy in people with neurogenic bladder are often attributed to the use of chronic indwelling catheters for persistent inflammation. There are several risk factors for inflammation, including recurrent infections, urolithiasis, and chronic indwelling catheterization (Nseyo and Santiago-Lastra 2017). The presence of bladder stones was identified as a risk factor in retrospective review (Stonehill et al. 1996). Yearly screening cystoscopy is recommended for patients with any of the following conditions: gross hematuria, more than 4 episodes of urinary tract infections per year, chronic indwelling catheters, chronic perineal or pelvic pain, abnormal radiographic studies, or colon augments after the patient is older than 50 years (Nseyo and Santiago-Lastra 2017).

29.13 Nocturnal Polyuria

Nocturia, defined as the act of waking up to void during the hours of intended sleep (Hashim et al. 2019), is one of the most common and troublesome lower urinary tract symptoms (Haddad et al. 2020). Abnormal nocturnal urine production often manifests as nocturnal polyuria. Normal people have circadian rhythms in urine production, and daytime urine volume is 2–3 times at night. The periodic rhythm of urine production is mainly influenced by arginine vasopressin. An increase in antidiuretic hormone (ADH) at night leads to a decrease in urine during sleep (Viaene et al. 2019). In patients with spinal cord injuries and the elderly, nocturnal ADH secretion decreases and nocturnal urine increases (Norgaard et al. 2007).

Global polyuria is defined as urine production more than 40 mL/kg/24 h in adults. Nocturnal polyuria accounts for more than 20–33% of daily urine volume (21–35 years >20%, > 60 years >33%) or more than 90 mL/h during the night between 1 AM and 6 AM. In patients with spinal cord injuries, water intake after dinner must be strictly limited to reduce the risk of bladder overdistention, urinary frequency, and urinary incontinence, as well as planned voiding or intermittent catheterization (Viaene et al. 2019; Weiss and Everaert 2019).

Desmopressin is used as oral dose or nasal spray if the urine volume during the night is not controlled by restricting fluid intake (Weiss and Everaert 2019). Desmopressin, an analogue of the natural pituitary hormone vasopressin, has an antidiuretic effect, increasing reabsorption of water by the kidney and temporary decrease in urine production. Desmopressin should be used with caution as hyponatremia and hypokalemia are more likely to occur. Hyponatremia and water intoxication resulting in confusion, headaches, and a general malaise are reported as side effects, but not common. Desmopressin is given 0.1–0.2 mg orally before bedtime or as nasal spray (0.5 mg/5 mL). Once sprayed, desmopressin is sprayed on 10 μg.

29.14 Epididymitis

Epididymitis is common in patients with spinal cord injuries, especially in patients with chronic urethral catheter. Foley catheters can block the ejaculatory ducts with retrograde spread of urethral bacteria, causing epididymitis or orchitis. A typical presentation is enlargement and induration of the testicle and/or epididymis. The scrotum skin may be erythematous or attached to the testicles. Treatment includes appropriate antibiotics and elevation of the testicle. A suprapubic catheter is recommended (Dixon et al. 2010). At least 4 weeks of antibiotics are needed.

29.15 Follow-Up Evaluation

There is no consensus on the appropriate neurourological follow-up, such as frequency of urodynamics, cystoscopy, and renal function

assessment. The treatment of neurogenic bladder in patients with spinal cord injury is not limited to symptoms alone, so regular controls of upper and lower urinary traction function are essential. In patients with spinal cord injuries, video-urodynamic or urodynamic evaluation, bladder ultrasound, and assessment of renal function should be included. Urodynamic examination is standardized; however, the best method for evaluating renal function is controversial. Renal ultrasound is useful for detecting renal scar, stones, or dilatation of the collecting system (Cameron et al. 2012).

The most practical way to measure the functional renal mass in humans is to measure glomerular filtration rate (GFR). This is usually done indirectly by measuring serum creatinine levels. It is clear that serum creatinine alone is not sufficient, as it often depends on reduced muscle mass in patients with spinal cord injury. Therefore, serum creatinine levels underestimate the degree of renal damage. The serum creatinine is a very insensitive indicator for moderate changes in function at the beginning of kidney disease. The GFR should be reduced to about 30% of normal levels before the serum creatinine level exceeds the normal range. Although there is controversy over the benefits of serum cystatin C levels compared to creatinine, most authors regard cystatin C as an excellent method for patients with spinal cord injury (Cameron et al. 2012; Erlandsen et al. 2012).

The following summarized strategy for the evaluation of renal function can be recommended (Cameron et al. 2012; Weidner et al. 2017):

- Within the first 2 weeks after spinal cord injury: renal and bladder ultrasound to assess preexisting morphologic alterations
- After the spinal shock phase (>6 weeks after spinal cord injury): video-urodynamic study, bladder ultrasound, and renal function (serum cystatin C, renal ultrasound)
- 5 months after spinal cord injury: urodynamic study control
- 9–12 months after injury: video-urodynamic or urodynamic study, bladder ultrasound, and renal function (serum cystatin C, renal ultrasound)

If the abovementioned assessment shows favorable urodynamic result (no risk for renal damage, maximum detrusor pressure <40 cmH_2O and a detrusor compliance ≥20 mL/cmH_2O, normal renal function, and normal results on renal ultrasound), annual controls are scheduled for the first 5 years after spinal cord injury. If the control is stable after 5 years, the follow-up intervals can be extended every 2 years. If the results are unfavorable (maximum detrusor pressure ≥40 cmH_2O and a detrusor compliance <20 mL/cmH_2O or impaired renal function or abnormal findings on renal ultrasound) treatment should be initiated and controls should be performed at shorter intervals until favorable results are achieved (Pannek and Kullik 2009).

If clinical symptoms, such as recurrent urinary tract infections, urinary incontinence, autonomic dysreflexia, decreased bladder capacity, or difficulties in catheterization, are present, a neurological evaluation should be performed as soon as possible. Depending on the symptoms, it should include urodynamic assessment, ultrasound, and cystoscopy, if feasible, and treatment should be initiated. For patients with indwelling catheters and bladder augmentation, it is advisable to perform them at regular intervals after 5 years.

29.16 Special Considerations of the Urological Management in Elderly Patients with Spinal Cord Injuries

Incidence of both traumatic and nontraumatic spinal cord injuries in the elderly is increasing (NSCISC 2021). Mortality increases with increasing age, but there is a decreasing trend in mortality among the elderly patients with spinal cord injuries. Improvements in health care and nutrition have helped patients with spinal cord injuries live longer. Changes in health, comorbidities, cognition, and dexterity with age have an impact on function and are important considerations in the management of the elderly patients with spinal cord injuries. Treatment decisions are

therefore more complex, as these changes and the associated polypharmacy must be taken into account (Chan et al. 2018).

29.16.1 Upper Urinary Tract Changes with Aging

In elderly people with spinal cord injuries, renal function can deteriorate due to aging and/or associated with neurogenic bladder dysfunction and its consequences such as reflux, obstruction, or urinary stones (Chan et al. 2018). Using cystatin C as a measure of renal function in an older population with spinal cord injuries, renal impairment was found in 8% of cases after an average of 18.9 years after injury (Choi et al. 2015).

Renal stones are common in people with spinal cord injuries due to calcium mobilization from bones, reduced exercise and mobility, and recurrent urinary traction infections with urea-splitting organisms. Patients aged 61 or older at the time of injury were 16.8 times more likely to have renal stones than patients aged 16–30 years (DeVivo et al. 1984). During the first year after spinal cord injury and in people aged 45 or older, there was a significant increased risk of renal stones (Chen et al. 2000). Patients with spinal cord injuries remain at risk of developing renal stones over time.

29.16.2 Lower Urinary Tract Changes with Aging

Urological problems may occur independent of the spinal cord injury, however, may precede the injury, and may complicate management issues. Age-related changes in the lower urinary tract, such as benign prostatic hypertrophy resulting in outlet obstruction, decrease in detrusor contractile function, and changes in the pelvic floor, can cause lower urinary tract dysfunction in elderly patients with spinal cord injuries (Chan et al. 2018). Maximum detrusor pressure is lower over the subsequent four decades of surveillance. Bladder management can change with age. While age is not a specific barrier to intermittent catheterization, there are several factors that may preclude this method of bladder management in elderly patients with spinal cord injuries or who may require intermittent catheterization by the caregiver. Trunk stability, upper limb function, motivation and cognitive function, and adequate vision are important considerations for intermittent catheterization. For patients who do not want or cannot perform intermittent catheterization independently, an indwelling catheter helps with bladder emptying and incontinence. Elderly patients may prefer a suprapubic catheter over intermittent catheterization for convenience and for improvement of quality of life (Chan et al. 2018).

References

Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. 2003;61:37–49.

Agrawal M, Joshi M. Urodynamic patterns after traumatic spinal cord injury. J Spinal Cord Med. 2015;38:128–33.

Agrawalla S, Pearce R, Goodman TR. How to perform the perfect voiding cystourethrogram. Pediatr Radiol. 2004;34:114–9.

Amark P, Eksborg S, Juneskans O, et al. Pharmacokinetics and effects of intravesical oxybutynin on the paediatric neurogenic bladder. Br J Urol. 1998;82:859–64.

Amend B, Hennenlotter J, Schafer T, et al. Effective treatment of neurogenic detrusor dysfunction by combined high-dosed antimuscarinics without increased side-effects. Eur Urol. 2008;53:1021–8.

Amundsen CL, Parsons M, Tissot B, et al. Bladder diary measurements in asymptomatic females: functional bladder capacity, frequency, and 24-hr volume. Neurourol Urodyn. 2007;26:341–9.

Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. J Neurotrauma. 2004;10:1371–83.

Anderson J, Bradley W. Bladder and urethral innervation in multiple sclerosis. J Urol. 1976;48:239–43.

Anderson RU, Hsieh-Ma ST. Association of bacteriuria and pyuria during intermittent catheterization after spinal cord injury. J Urol. 1983;130:299–301.

Andersson KE. Antimuscarinic mechanisms and the overactive detrusor: an update. Eur Urol. 2011;59:377–86.

Appell RA. Clinical efficacy and safety of tolterodine in the treatment of overactive bladder: a pooled analysis. Urology. 1997;50:90–6.

Aydin A, Ahmed K, Zaman I, et al. Recurrent urinary tract infections in women. Int Urogynecol J. 2015;26:795–804.

Barnes DG, Timoney AG, Moulas G, et al. Correlation of bacteriological flora of the urethra, glans and perineum with organisms causing urinary tract infection in the spinal injured male patient. Paraplegia. 1992;30:851–4.

Bartel P, Krebs J, Wöllner J, et al. Bladder stones in patients with spinal cord injury: a long-term study. Spinal Cord. 2014;52:295–7.

Bauman WA, Korsten MA, Radulovic M, et al. 31st g. Heiner Sell lectureship: secondary medical consequences of spinal cord injury. Top Spinal Cord Inj Rehabil. 2012;18:354–78.

Belman AB. A perspective on vesicoureteral reflux. Urol Clin N Am. 1995;22:139–50.

Biering-Sörensen F, Craggs M, Kennelly M, et al. International urodynamic basic spinal cord injury data set. Spinal Cord. 2008;46:513–6.

Blok B, Castro-Diaz D, Popolo GD, et al. EAU guidelines on neuro-urology. 2020. https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Neuro-Urology-2020.pdf. Last assessed 10 Oct 2021.

Bragg R, Hebel D, Vouri SM, et al. Mirabegron: a beta-3 agonist for overactive bladder. Consult Pharm. 2014;29:823–37.

Brooks M, Kirshblum S. Spinal cord injury. In: Cooper G, editor. Essential physical medicine and rehabilitation. Totowa: Humana Press; 2006.

Burnstock G. The changing face of autonomic neurotransmission. Acta Physiol Scand. 1986;126:67–91.

Cameron AP. Pharmacologic therapy for the neurogenic bladder. Urol Clin North Am. 2010;37:495–506.

Cameron AP, Clemens JQ, Latini JM, et al. Combination drug therapy improves compliance of the neurogenic bladder. J Urol. 2009;182:1062–7.

Cameron AP, Rodriguez GM, Schomer KG. Systematic review of urological followup after spinal cord injury. J Urol. 2012;187:391–7.

Capoor J, Stein AB. Aging with spinal cord injury. Phys Med Rehabil Clin N Am. 2005;16:129–61.

Cardenas DD, Moore KN, Dannels-McClure A, et al. Intermittent catheterization with a hydrophilic-coated catheter delays urinary tract infections in acute spinal cord injury: a prospective, randomized, multicenter trial. PM R. 2011;3:408–17.

Chan LW, Griebling TL, Arnold EP, et al. Special considerations in the urological management of the older spinal cord injury patient. World J Urol. 2018;36:1603–11.

Chancellor MB, Anderson RU, Boone TB. Pharmacotherapy for neurogenic detrusor overactivity. Am J Phys Med Rehabil. 2006;85:536–45.

Chen Y, DeVivo MJ, Roseman JM. Current trend and risk factors for kidney stones in persons with spinal cord injury: a longitudinal study. Spinal Cord. 2000;38:346–53.

Choi HM, Oh D-J, Sung BM. Neurogenic bladder and chronic kidney disease in spinal cord injury patients. Nephrol Dial Transpl. 2015;30(Suppl 3):164.

Consortium for Spinal Cord Medicine. Bladder management for adults with spinal cord injury. Clinical practice guidelines for health care professionals. Washington, DC: Paralyzed Veterans of America; 2006.

Cooper CS, Madsen MT, Austin JC, et al. Bladder pressure at the onset of vesicoureteral reflux determined by nuclear cystometrogram. J Urol. 2003;170:1537–40.

Corcos J, Przydacz M. Consultation in neurourology. A practical evidence-based guide. Cham: Springer; 2018.

D'Hondt F, Everaert K. Urinary tract infections in patients with spinal cord injuries. Curr Infect Dis Rep. 2011;13:544–51.

Danforth TL, Ginsberg DA. Neurogenic lower urinary tract dysfunction: how, when, and with which patients do we use urodynamics? Urol Clin North Am. 2014;41:445–52.

Darge K, Riedmiller H. Current status of vesicoureteral reflux diagnosis. World J Urol. 2004;22:88–95.

Darouiche RO, Hull RA. Bacterial interference for prevention of urinary tract infection. Clin Infect Dis. 2012;55:1400–7.

de Groat WC, Fraser MO, Yoshiyama M, et al. Neural control of the urethra. Scand J Urol Nephrol Suppl. 2001;207:35–43.

DeJong G, Tian W, Hsieh CH, et al. Rehospitalization in the first year of traumatic spinal cord injury after discharge from medical rehabilitation. Arch Phys Med Rehabil. 2013;94:S87–97.

DeVivo MJ, Fine PR, Cutter GR, et al. The risk of renal calculi in spinal cord injury patients. J Urol. 1984;131:857–60.

Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. Am J Kidney Dis. 2002;40:221–6.

Dinh A, Davido B, Duran C, et al. Urinary tract infections in patients with neurogenic bladder. Med Mal Infect. 2019;49:495–504.

Dixon JS, Jen PY, Yeung CK, et al. The vesico-ureteric junction in three cases of primary obstructive megaureter associated with ectopic ureteric insertion. Br J Urol. 1998;81:580–4.

Dixon L, Dolan LM, Brown K, et al. RCT of urethral versus suprapubic catheterization. Br J Nurs. 2010;19(18):S7–13.

Drake MJ. Management and rehabilitation of neurologic patients with lower urinary tract dysfunction. Handb Clin Neurol. 2015;130:451–68.

Drekonja DM, Johnson JR. Urinary tract infections. Prim Care. 2008;35:345–67.

Erlandsen EJ, Hansen RM, Randers E, et al. Estimating the glomerular filtration rate using serum cystatin C levels in patients with spinal cord injuries. Spinal Cord. 2012;50:778–93.

Everaert K, Lumen N, Kerckhaert W, et al. Urinary tract infections in spinal cord injury: prevention and treatment guidelines. Acta Clin Belg. 2009;64:335–40.

Feifer A, Corcos J. Contemporary role of suprapubic cystostomy in treatment of neuropathic bladder dysfunction in spinal cord injured patients. Neurourol Urodyn. 2008;27:475–9.

Ferguson TW, Komenda P, Tangri N. Cystain C as a biomarker for estimating glomerular filtration rate. Curries Opin Nephrol Hypertens. 2003;24:295–300.

Flores-Mireles AL, Walker JN, Caparon M, et al. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015;13:269–84.

Flores-Mireles A, Hreha TN, Hunstad DA. Pathophysiology, treatment, and prevention of catheter-associated urinary tract infection. Top Spinal Cord Inj Rehabil. 2019;25:228–40.

Forster CS, Pohl H. Diagnosis of urinary tract infection in the neuropathic bladder: changing the paradigm to include the microbiome. Top Spinal Cord Inj Rehabil. 2019;25:222–7.

Gerridzen RG, Thijssen AM, Dehoux E. Risk factors for upper tract deterioration in chronic spinal cord injured patients. J Urol. 1992;147:416–8.

Goetz LL, Klausner AP. Strategies for prevention of urinary tract infections in neurogenic bladder dysfunction. Phys Med Rehabil Clin N Am. 2014;25:605–18, viii

Gormley EA. Urologic complications of the neurogenic bladder. Urol Clin North Am. 2010;37:601–7.

Groen J, Pannek J, Castro Diaz D, et al. Summary of European Association of Urology (EAU) guidelines on neurourology. Eur Urol. 2016;69:324–33.

Guttmann L, Frankel H. The value of intermittent catheterization in the early management of traumatic paraplegia and tetraplegia. Paraplegia. 1966;4:63–8.

Haddad R, Denys P, Arlandis S, et al. Nocturia and nocturnal polyuria in neurological patients: from epidemiology to treatment. A systematic review of the literature. Eur Urol Focus. 2020;6:922–34.

Hamamci N, Dursun E, Akbas E, et al. A quantitative study of genital skin flora and urinary colonization in spinal cord injured patients. Spinal Cord. 1998;36:617–20.

Hashim H, Blanker MH, Drake MJ, et al. International Continence Society (ICS) report on the terminology for nocturia and nocturnal lower urinary tract function. Neurourol Urodyn. 2019;38:499–508.

Herschorn S, Barkin J, Castro-Diaz D, et al. A phase III, randomized, double-blind, parallel-group, placebo-controlled, multicentre study to assess the efficacy and safety of the beta3 adrenoceptor agonist, mirabegron, in patients with symptoms of overactive bladder. Urology. 2013;82:313–20.

Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010;50:625–63.

Horstmann M, Schaefer T, Aguilar Y, et al. Neurogenic bladder treatment by doubling the recommended antimuscarinic dosage. Neurourol Urodyn. 2006;25:441–5.

Jonas U, Castro-Diaz D, Bemelmans BLH, et al. Neurogenic voiding dysfunctions (NVD). Eur Urol. 2003;44:I–XV.

Joseph DB. The effect of medium-fill and slow-fill saline cystometry on detrusor pressure in infants and children with myelodysplasia. J Urol. 1992;147:444–6.

Kaplan SA, Chancellor MB, Blaivas JG. Bladder and sphincter behavior in patients with spinal cord lesions. J Urol. 1991;146:113–7.

Katsumi HK, Kalisvaart JF, Ronningen LD, et al. Urethral versus suprapubic catheter: choosing the best bladder management for male spinal cord injury patients with indwelling catheters. Spinal Cord. 2010;48:325–9.

Kessler TM, Bachmann LM, Minder C, et al. Adverse event assessment of antimuscarinics for treating overactive bladder: a network meta-analytic approach. PLoS One. 2011;6:e16718.

Kim YH, Bird ET, Priebe M, et al. The role of oxybutynin in spinal cord injured patients with indwelling catheters. J Urol. 1997;158:2083–6.

Kim YH, Kattan MW, Boone TB. Bladder leak point pressure: the measure for sphincterotomy success in spinal cord injured patients with external detrusor-sphincter dyssynergia. J Urol. 1998;159:493–6.

Ko HY, Kim KT. Treatment of external urethral sphincter hypertonicity by pudendal nerve block using phenol solution in patients with spinal cord injury. Spinal Cord. 1997;35:690–3.

Koyanagi T, Tsuji I. Study of ureteral reflux in neurogenic dysfunction of the bladder: the concept of a neurogenic ureter and the role of the periureteral sheath in the genesis of reflux and supersensitive response to autonomic drugs. J Urol. 1981;126:210–7.

Krebs J, Wöllner J, Pannek J. Urethral strictures in men with neurogenic lower urinary tract dysfunction using intermittent catheterization for bladder evacuation. Spinal Cord. 2015;53:310–3.

Lapides J, Diakno AC, Silber SJ, et al. Clean, intermittent self-catheterization in the treatment of urinary tract disease. J Urol. 1972;107:458–61.

Li L, Ye W, Ruan H, Yang B, et al. Impact of hydrophilic catheters on urinary tract infections in people with spinal cord injury: systematic review and meta-analysis of randomized controlled trials. Arch Phys Med Rehabil. 2013;94:782–7.

Light JK, Scott FB. Bethanechol chloride and the traumatic cord bladder. J Urol. 1982;128:85–7.

Linsenmeyer TA, Horton J, Menevento J. Impact of alpha 1-blockers in men with spinal cord injury and upper tract stasis. J Spinal Cord Med. 2002;25:124–8.

Lucas E. Medical management of neurogenic bladder for children and adults: a review. Top Spinal Cord Inj Rehabil. 2019;25:195–204.

McGuire EJ. Urodynamics of the neurogenic bladder. Urol Clin North Am. 2010;37:507–16.

McGuire EJ, Woodside JR, Borden TA, et al. Prognostic value of urodynamic testing in myelodusplastic patients. J Urol. 1981;126:205–9.

Miller ER. Physiology of the lower urinary tract. Urol Clin North Am. 1996;23:171–5.

Montgomerie JZ, Guerra DA, Schick DG, et al. Pseudomonas urinary tract infection in patients with spinal cord injury. J Am Paraplegia Soc. 1989;12:8–10.

National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham: National Spinal Cord Injury Statistical Center; 2021.

NIDRR. The prevention and management of urinary tract infections among people with spinal cord injuries. National Institute on Disability and Rehabilitation Research consensus statement. January 27-29, 1992. J Am Paraplegia Soc. 1992;15:194–204.

Noreau L, Proulx P, Gagnon L, et al. Secondary impairments after spinal cord injury. Am J Phy Med Rehabil. 2000;79:526–35.

Norgaard JP, Hashim H, Malmberg L, et al. Antidiuresis therapy: mechanism of action and clinical implications. Neurourol Urodyn. 2007;26:1008–13.

Novara G, Galfano A, Ficarra V, et al. Anticholinergic drugs in patients with bladder outlet obstruction and lower urinary tract symptoms: a systematic review. Eur Urol. 2006;50:675–83.

Nseyo U, Santiago-Lastra Y. Long-term complications of the neurogenic bladder. Urol Clin North Am. 2017;44:355–66.

Osman NI, Chapple CR, Abrams P, et al. Detrusor underactivity and the underactive bladder: a new clinical entity? A review of current terminology, definitions, epidemiology, aetiology, and diagnosis. Eur Urol. 2014;65:389–98.

Ost MC, Lee BR. Urolithiasis in patients with spinal cord injuries: risk factors, management, and outcomes. Curr Opin Urol. 2006;16:93–9.

Panicker JN, De Seze M, Fowler CJ. Neurogenic lower urinary tract dysfunction. Handb Clin Neurol. 2013;110:209–20.

Pannek J, Kullik B. Does optimizing bladder management equal optimizing quality of life? Correlation between health-related quality of life and urodynamic parameters in patients with spinal cord lesions. Urology. 2009;74:263–6.

Pannek J, Göcking K, Bersch U. To clamp or not to clamp? Bladder management by suprapubic catheterization in patient with neurogenic bladder dysfunction. World J Urol. 2010;28:637–41.

Pannek J, Kennelly M, Kessler TM, et al. International Spinal Cord Injury urodynamic basic data set (version 2.0). 2018. https://www.iscos.org.uk/uploads/2019.04.12_International_SCI_Uro.0)_final.pdf

Perkash I. Long-term urologic management of the patient with spinal cord injury. Urol Clin North Am. 1993;20:423–34.

Prieto J, Murphy CL, Moore KN, et al. Intermittent catheterization for long-term bladder management. Cochrane Database Syst Rev. 2014;9:CD006008.

Pullen AH, Tucker D, Martin JE. Morphological and morphometric characterisation of Onuf's nucleus in the spinal cord in man. J Anat. 1997;191:201–13.

Rigby D. An overview of suprapubic catheter care in community practice. Br J Community Nurs. 2009;14:278, 280, 282–4.

Roberts MM. Neurophysiology in neurourology. Muscle Nerve. 2008;38:815–36.

Robinson J. Insertion, care and management of suprapubic catheters. Nurs Stand. 2008;23(8):49–56.

Rosier PFWM, Schaefer W, Lose G, et al. International continence society good urodynamic practices and terms 2016: urodynamics, uroflowmetry, cystometry, and pressure-flow study. Neurourol Urodyn. 2017;36:1243–60.

Rovner ES, Koski ME, editors. Rapid and practical interpretation of urodynamics. New York: Springer; 2015.

Rushing J. Caring for your patient's suprapubic catheter. Nursing. 2006;36:32.

Salomon J, Denys P, Merle C, et al. Prevention of urinary tract infection in spinal cord injured patients: safety and efficacy of a weekly oral cyclic antibiotic (WOCA) programme with a 2 year follow-up—an observational prospective study. J Antimicrob Chemother. 2006;57:784–8.

Samson G, Cardenas DD. Neurogenic bladder in spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:255–74.

Schäfer W, Abrams P, Liao L, et al. International Continence Society. Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies. Neurourol Urodyn. 2002;21:261–74.

Schroder HD. Onuf's nucleus X: a morphological study of a human spinal nucleus. Anat Embryol (Berl). 1981;162:443–53.

Soler JM, Previnaire JG, Amarenco G. Dartos reflex as autonomic assessment in persons with spinal cord injury. Spinal Cord Ser Cases. 2017;3:17097.

Stoffel JT. Detrusor sphincter dyssynergia: a review of physiology, diagnosis, and treatment strategies. Transl Androl Urol. 2016;5:127–35.

Stonehill WH, Dmochowski RR, Patterson AL, et al. Risk factors for bladder tumors in spinal cord injury patients. J Urol. 1996;155:1248–50.

Taylor TA, Waites KB. A quantitative study of genital skin flora in male spinal cord-injured outpatients. Am J Phys Med Rehabil. 1993;72:117–21.

Viaene A, Denys MA, Goessaert AS, et al. Evaluation of the occurrence and diagnose definitions for nocturnal polyuria in spinal cord injured patients during rehabilitation. Eur J Phys Rehabil Med. 2019;55:40–6.

Vignoli G. Urodynamics: a quick pocket guide. Switzerland: Springer; 2017.

Vodusek DB. Bulbocavernous reflex revisited. Neurourol Urodyn. 2003;22:681–2.

Waites KB, Canupp KC, Roper JF, et al. Evaluation of 3 methods of bladder irrigation to treat bacteriuria in persons with neurogenic bladder. J Spinal Cord Med. 2006;29:217–26.

Weidner N, Rupp R, Taney KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.

Weiss JP, Everaert K. Management of nocturia and nocturnal polyuria. Urology. 2019;133S:24–33.

Welk B, McIntyre A, Teasell R, et al. Bladder cancer in individuals with spinal cord injuries. Spinal Cord. 2013;51:516–21.

Woodbury MG, Hayes KC, Askes HK. Intermittent catheterization practices following spinal cord injury: a national study. Can J Urol. 2008;15:4065–71.

Wyman JF, Burgio KL, Newman DK. Practical aspects of lifestyle modifications and behavioural interventions in the treatment of overactive bladder and urgency urinary incontinence. Int J Clin Pract. 2009;63:1177–91.

Wyndaele JJ. Complications of intermittent catheterization: their prevention and treatment. Spinal Cord. 2002;40:536–41.

Wyndaele JJ, Kovindha A, Madersbacher H, et al. Neurologic urinary incontinence. Neurourol Urodyn. 2010;29:159–64.

Wyndaele JJ, Brauner A, Geerlings SE, et al. Clean intermittent catheterization and urinary tract infection: review and guide for future research. BJU Int. 2012;110:E910–7.

Yilmaz U, Yang CC, Berger RE. Dartos reflex: a sympathetically mediated scrotal reflex. Muscle Nerve. 2006;33:363–8.

Yoon JA, Shin YB, Shin MJ, et al. Cardiovascular monitoring during video urodynamic studies in persons with spinal cord injury. Am J Phys Med Rehabil. 2018;97:1–6.

Zimakoff JD, Pontoppidan B, Larsen SO, et al. The management of urinary catheters: compliance of practice in Danish hospitals, nursing homes and home care to national guidelines. Scand J Urol Nephrol. 1995;29:299–309.

Recommended Additional Reading

Blaivas J, Chancellor M, Weuss J, et al. Atlas of urodynamics. 2nd ed. Oxford: Blackwell Publishing; 2007.

Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation, Phys Med Rehabil Clin N Am. Philadelphia, PA: Elsevier; 2014.

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Chapple CR, MacDiarmid SA, Patel A. Urodynamics made easy. 3rd ed. Philadelphia, PA: Elsevier; 2009.

Corcos J, Przydacz M. Consultation in neurourology. A practical evidence-based guide. Cham: Springer; 2018.

Corcos J, MacDiarmid S, Heesakkers J, editors. Overactive bladder: practical management. Oxford: John Wiley & Son, Ltd.; 2015.

Corcos J, Ginsberg D, Karsenty G, editors. Textbook of the neurogenic bladder. 3rd ed. Boca Raton, FL: CPC Press; 2016.

Noback CR, Strominger NL, Demarest RJ, Ruggiero DA. The human nervous system: structure and function. 6th ed. Totowa, NJ: Humana Press; 2005.

Preston RA. Acid-base, fluids and electrolytes: made ridiculously simple. 2nd ed. Miami, FL: MedMaster, Inc.; 2011.

Rovner ES, Koski ME, editors. Rapid and practical interpretation of urodynamics. New York: Springer; 2015.

Vignoli G. Urodynamics: a quick pocket guide. Switzerland: Springer; 2017.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

Neurogenic Bowel Dysfunction and Gastrointestinal Complications

30

Neurogenic bowel dysfunction remains a major life-limiting problem and has also long been known as an area of poor self-care after spinal cord injury. Impairments in sensation of need for defecation, of volitional control, and the potential for constipation and fecal incontinence cause distress, impact social function, and present management challenges (Glickman and Kamm 1996). Management goals include optimal social function, especially minimizing incontinence and interference with living activities, and prevention of complications such as abdominal pain, impaction, bowel obstruction, and hemorrhoids (Lavis and Goetz 2019). Gastrointestinal problems in both the acute and chronic phases of spinal cord injury are a major cause of gastrointestinal morbidity. Gastrointestinal problems are a large cause of rehospitalization among people with spinal cord injuries, accounting for 11% of readmissions in an Australian study (Middleton et al. 2004).

The control of the gastrointestinal system involves complex interactions between autonomic and somatic innervation that ultimately act at the level of the intrinsic enteric nervous system. After spinal cord injury, this fine control mechanism is interrupted to varying degrees dependent upon the level and extent of the spinal cord injury (Chung and Emmanuel 2006). In assessing and managing neurogenic bowel in people with spinal cord injuries, precise variables associated with bowel dysfunction should be evaluated. Important historical bowel variables include premorbid bowel habits, current frequency of bowel movements, level of assistance needed (e.g., FIM score), frequency of characteristics of incontinent episodes, effects on social function such as leaving the house, stool consistency (e.g., Bristol stool scale score), medications/supplements, diet, fluid intake, and changes in bowel function from previous visits. Sensation of need for a bowel movement, ability to prevent stool leakage (continence), and voluntary anal sphincter contraction are relevant measures of autonomic and motor function (Goetz et al. 2018; Lavis and Goetz 2019).

Patients with spinal cord injuries need a bowel program that allows socially acceptable continence and prevents fecal impaction. The functions of the gastrointestinal tract depend on enteric, parasympathetic, and sympathetic neural control. In addition, the gastrointestinal tract is the largest endocrine organ in the body, secreting enteric peptides to regulate local gastrointestinal homeostasis and regulating homeostasis of the organism through its action on the brain. The main functions of the gastrointestinal tract are to digest and absorb nutrients, maintain proper fluid balance, and store and pass nondigested substances. The colon, the rectum, and the internal anal sphincters form an integrated unit for the

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final digestion, storage, transport, and gastrointestinal removal. Normal stool continence depends on complex interactions between the consistency of stools, colorectal transit time, rectal tone, anorectal sensibility, tone of the puborectalis and anal sphincter muscles, and voluntary contraction of the external anal sphincter muscle (Johns et al. 2021).

Neurogenic bowel dysfunction in spinal cord injuries refers to the colonic dysfunction that occurs as reduced colonic transit, constipation, disordered evacuation reflexes, and potential incontinence following disruption of normal control. In addition to defecation problem due to neurogenic bowel dysfunction, gastrointestinal problems associated with the upper gastrointestinal tract include dysphagia, gastroesophageal reflux, gastric ulcer and gastritis, superior mesenteric artery syndrome, gallbladder disease, and pancreatitis (Gondim et al. 2010). Nutritional homeostasis after major injuries is often associated with more favorable results by the timing and route of nutritional supplementation (Rowan et al. 2004).

With the resolution of the spinal shock phase, the neurological level and severity of spinal cord injury have a significant impact on gastrointestinal dysfunction (Bauman et al. 2012). Functional gastrointestinal disturbances lead to a variety of symptoms, including delayed gastric emptying, early satiety and nausea, bloating, abdominal pain, and diminished propulsive transit throughout the length of the gastrointestinal tract. Decreased swallowing reflexes and esophageal sphincter tone may also lead to reflux of gastric contents and aspiration pneumonia. Spinal cord injury at any level affects distal bowel function with constipation, difficulty in evacuation, decreased anorectal sensation, and overflow incontinence. These are common issues that negatively affect quality of life and reduce social integration and independence (Banwell et al. 1993). Autonomic dysreflexia, which is triggered by gastrointestinal problems such as fecal impaction and acute abdomen, may be a potentially life-threatening complication in some patients (Table 30.1).

Table 30.1 Common gastrointestinal causes of autonomic dysreflexia

Potential causes irritating the abdominal wall or viscera	
Gastric ulcer	Hepatitis
Duodenal ulcer	Bowel obstruction
Cholecystitis	Superior mesenteric artery
GB stone	syndrome
Visceral	Tight clothing
masses	Abdominal binder
Gastroenteritis	Malfunctional ostomies, tube, or
Pancreatitis	drainage
Constipation	GI interventional procedures
Hemorrhage	Rectal foreign body

30.1 Functional Anatomy and Physiology of the Bowel

The gastrointestinal system consists of the oropharynx, esophagus, stomach, small intestine, colon, and rectum. All parts of the gastrointestinal system are formed by a similar pattern with mucosa, submucosa, circular and longitudinal muscle layers, and an outer serosal covering layer. Between the muscular layers and beneath the mucosa are collections of nerve cells that form plexuses (the submucosal Meissner's and muscular Auerbach's plexuses) that are involved in controlling intestinal peristalsis and secretion. Dependent upon their position in the gastrointestinal tract, these layers vary in thickness and complexity. Related secretory structures include the liver, gallbladder, and pancreas. The main purpose of the gastrointestinal system is to provide fluids, nutritions, and electrolytes to the body. The average daily intake of 800 gm of food and 1200 mL of water is mixed with about 7 L of secretions from the salivary glands, stomach, gallbladder, pancreas, and intestines, resulting in absorption of about 8.85 L of the mixture and finally excretion of 150 gm of fecal waste (Vander et al. 1985).

30.1.1 Colon and Anorectum

The colon is a closed tube that is bound proximally by the ileocecal valve and distally by the anal sphincter. The lower gastrointestinal tract consists of (1) the right colon, which reabsorbs

water and electrolytes, and (2) the left colon (descending and sigmoid colon) which acts as a storage space with the anorectum and allows the socially acceptable elimination of the desiccated feces. Main functions of the colon include (1) absorption of water and electrolytes from the ingested food that is mixed with gastric secretions that pass into the small intestine and into the large intestine and (2) storage of fecal matter until it can be expelled (Guyton and Hall 2006). The colon also helps the growth of beneficial bacteria, secretes mucus to lubricate the stool, and pushes the stool out of the body through the rectum and anus.

The main function of the rectum and anus is the maintenance of fecal continence. At the distal rectum is the anal canal formed from anal mucosa overlying two layers of muscle, the internal and external anal sphincters. The mechanical barrier of the anorectal continence mechanism consists of the internal anal sphincter muscle, the striated muscle of the external sphincter, and the puborectalis muscle (Fig. 30.1). The internal anal sphincter is formed from a condensation of the inner circular smooth muscle and is therefore not under voluntary control. The internal anal sphincter muscle is a continuation of the circular muscle layer of the rectum. It is under reflex control of the enteric nervous system and the sacral spinal cord. The external anal sphincter is made up of a circumferential voluntary striated muscle band, which is continuous with the pelvic floor. The upper part of the anal canal is also surrounded by the puborectalis muscle. At rest, the activities of the internal anal sphincter and the puborectalis sling provide the majority of continence. The tonic activity of the smooth muscle internal sphincter maintains a resting high-pressure zone in the anal canal and prevents the passage of stool. Tonic contraction of the internal anal sphincter provides 80% of the resting anal pressure (Schweiger 1979). These sphincters work in conjunction with the puborectalis muscle. The puborectalis muscle forms a sling around the anal canal and pulls the anal canal typically to an acute angle of less than 100° (anorectal angle), sealing the anal canal from the rectum and providing mechanical resistance against distal propulsion of feces (Schuster 1975; Henry and Thomson 1984) (Fig. 30.2).

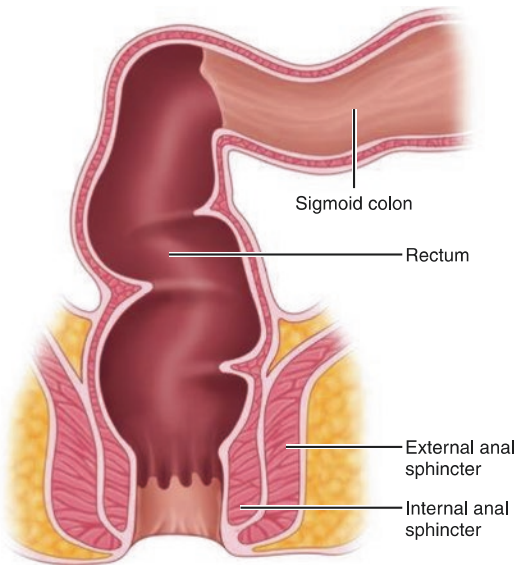

Fig. 30.1 Anal sphincters. The internal anal sphincter is contiguous with the distal end of the circular smooth muscle layer of the colon. Tonic contraction of the internal anal sphincter generates the majority of the resting anal tone. Adapted from Green and Olson (1996)

As the stool enters the rectum and distends the rectal vault, the smooth muscle of the internal sphincter relaxes reflexively through the rectoanal inhibitory reflex, allowing the stool to descend to the proximal anal canal. Stretch of the rectal wall by stool initiates the defecation reflex through a reflex arch between the rectum and the sacral spinal cord. The rectoanal inhibitory reflex is a locally mediated spinal response in which the pudendal nerve transmits the sensory inputs to the spinal cord segments (L4-S1) and also returns to the external anal sphincter via the pudendal nerve. The anal canal is densely innervated by sensory receptors that induce reflexive contractions of the external anal sphincter and prevent the stool from descending further into the anal canal. Defecation can be interrupted by voluntary contraction of the external anal sphincter.

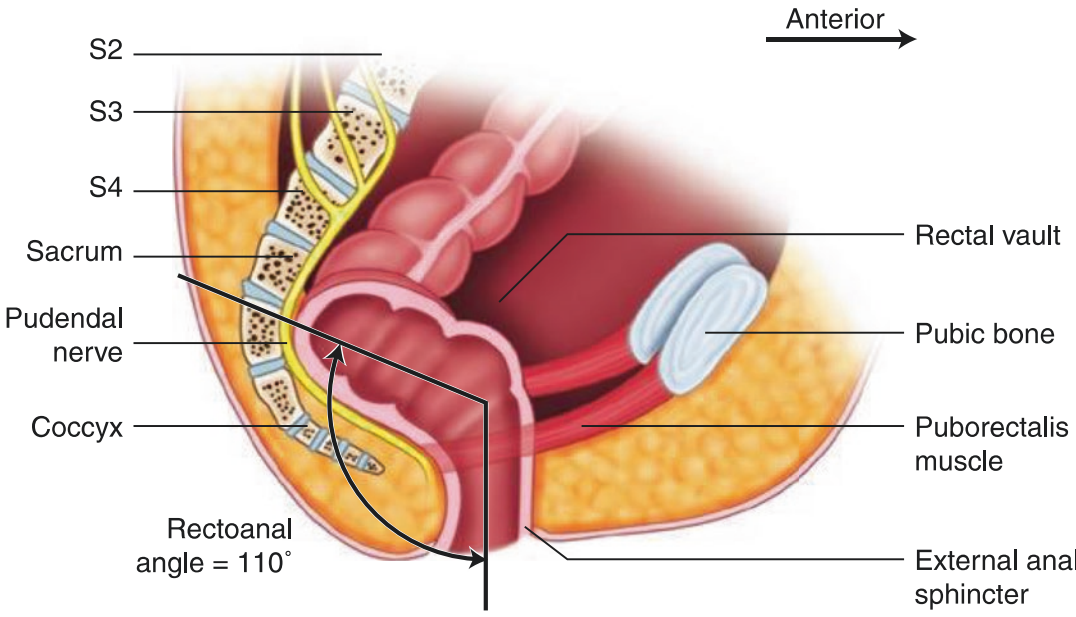

Fig. 30.2 Mechanism of continence. The puboanal angle formed by the tonic contraction of the puborectalis impairs the passage of stool from the rectal vault into the anal canal. Adapted from Green and Olson (1996)

Table 30.2 The innervation of the colon

Segments		Innervations	Nerves	Functions
Extrinsic component	Cranial nerve X, S2-S5	Parasympathetic	• Vague nerve to splenic flexure • Pelvic nerve to splenic flexure-anal sphincter	• Increased peristalsis and motility • Increased secretions • Relaxation of smooth muscle sphincter
	T10-L2 (T5-L3)	Sympathetic	• Hypogastric nerve	• Decreased peristalsis and motility • Decreased secretions • Contraction of smooth muscle sphincter
	S2-S4	Somatic	• Pudendal nerve	• Contraction of EAS and pelvic floor musculature
Intrinsic component		• Myenteric (Auerbach) plexus • Submucosal (Meissner) plexus		• Rhythmic contractility to assist stool propulsion • Controls intestinal secretion and absorption

30.1.2 Neural Innervations

The neural regulation of the gastrointestinal system is both intrinsic and extrinsic, and although the intrinsic component may work independently of the extrinsic component, the extrinsic component is essential for normal function (Table 30.2).

30.1.2.1 Intrinsic Innervation

The intrinsic component of the gastrointestinal nervous system is commonly referred to as the enteric nervous system and can function without extrinsic regulation (Fig. 30.3). The intrinsic innervation of the gastrointestinal tract consists of two separate but integrated networks of ganglia

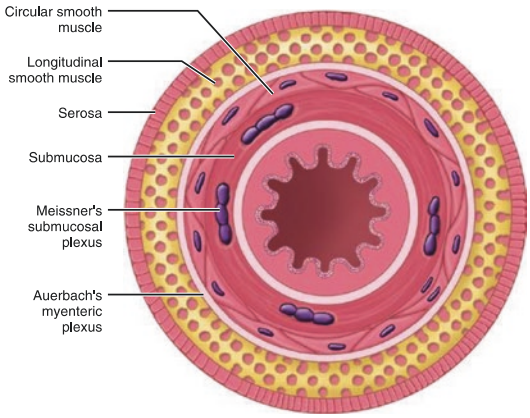

Fig. 30.3 Enteric nervous system. Adapted from Ugalde et al. (1996)

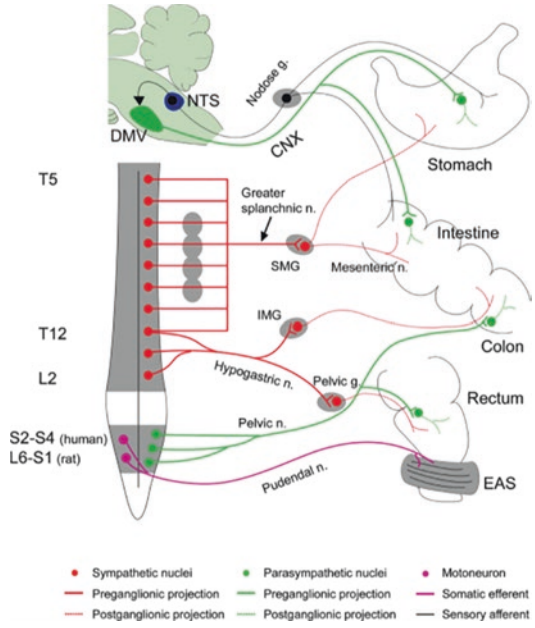

Fig. 30.4 Neural pathways with sympathetic and parasympathetic nervous system to the gastrointestinal tract. *NTS* nucleus tractus solitarii, *DMV* dorsal motor nucleus of vagus, *EAS* external anal sphincter, *SMG* superior mesenteric ganglion, *IMG* inferior mesenteric ganglion, *G* ganglion, *n* nerve. Adapted from Hou and Rabchevsky (2014)

and neuronal processes, the submucosal and myenteric plexuses, which contain the neural circuits that have an independent reflex function and a quasi-autonomous control of the gastrointestinal tract. The colon is made up of smooth muscles that are aligned in an inner circular layer and an outer longitudinal layer. Between these layers Auerbach's plexus (myenteric ganglia) and Meissner's plexus (submucosal ganglia) lie, which are part of the intrinsic innervation of the colon. The Auerbach's plexus lies between the 2 smooth muscle layers and mainly have a motor function, and Meissner's plexus mainly serves a sensory function. Both plexus groups are interconnected by interneurons and function as a single functional unit. The Auerbach's plexus is well developed, consists of unmyelinated fibers and postganglionic parasympathetic cell bodies and lies between the longitudinal and circular muscles and coordinates peristalsis. Stimulation of the Auerbach's plexus increases the intestinal activity, including increased contractile force and velocity to assist stool propulsion throughout the colon. The Meissner's plexus plays an important role in coordination of the intestinal wall movements as well as digestive juice secretion. The Meissner's plexus lies on the luminal side of the circular muscle in the submucosa together with connective tissue, glands, and small vessels. It conveys local sensory and motor responses to Auerbach's plexus and to the central nervous system (Stiens et al. 1997). Unlike the small intestine, the mobility of the colon is irregular and more dependent on extrinsic innervation of the autonomic nervous system to determine the speed and extent of peristalsis and to coordinate evacuation.

30.1.2.2 Extrinsic Innervation

The extrinsic innervation of the colon is accomplished by autonomic and somatic innervation (Fig. 30.4). Sympathetic innervation projects through the hypogastric nerve via the superior mesenteric, inferior mesenteric, and celiac ganglia. The sympathetic supply to the right colon originates at the lateral columns of the lower 6–8 thoracic segments (T5–T12) of the spinal cord. The sympathetic supply to the left colon and upper rectum originates in the lateral columns of the upper three lumbar segments (L1–L3) of the spinal cord. The parasympathetic supply to the colon and anorectum consists of both cranial

(vague nerve) and sacral (pelvic nerve) divisions. The parasympathetic innervation to the right colon is carried by the dorsal motor nucleus of the vagus nerve. The parasympathetic innervation pathways to the left colon (the splenic flexure of the colon) and the distal part of the colon and the whole rectum (the anorectum) originate from the sacral parasympathetic centers S2–S4 or S2–S5 of the spinal cord. Somatic nerve supply comes from the pudendal nerve (S2–S4), which supplies the external anal sphincter and the pelvic floor musculature (Enck et al. 2006).

Sympathetic stimulation leads to decrease in peristalsis and gut motility, and decreased secretion, and contracts the internal anal sphincter. The increased parasympathetic tone results in increases in contractility, mobility, tone of the colon, secretion, and relaxation of the involuntary internal anal sphincter.

Sympathetic Innervation

In general, sympathetic stimulation slows digestion by reducing motility and secretions of the gastrointestinal tract. The sympathetic nervous system arises from the thoracolumbar segments (T5-L3), with cell bodies of the preganglionic fibers lying in the intermediolateral column (lateral horn) of the spinal cord. The preganglionic fibers leave the spinal cord via ventral roots and tend to be relatively short as they leave via white rami (myelinated) before entering the paravertebral ganglia of the sympathetic chain. At the sympathetic chain, they can synapse on postganglionic fibers and synapse in a more peripherally located prevertebral ganglia such as the celiac and superior mesenteric ganglia, or terminal ganglia such as the inferior mesenteric plexus (Ugalde et al. 1996). The former innervates nearly the entire length of the gastrointestinal tract, from the stomach to the ileum, while the superior mesenteric ganglion projects to the ascending and transverse colon. In addition, sympathetic nerve fibers of the splenic flexure and rectum are originated within L1-L3 segments of the spinal cord. These fibers extend to form the inferior mesenteric plexus and the hypogastric plexus. At the level of the hypogastric plexus, sympathetic fibers are connected by the sacral parasympathetic nerve (Lomax et al. 2010). The internal anal sphincter has a sympathetic supply from the inferior mesenteric ganglion via the hypogastric nerves. Sympathetic tone is excitatory to the internal sphincter musculature and helps to maintain continence (Chung and Emmanuel 2006). Like the parasympathetic preganglionic neurons, the sympathetic preganglionic neurons are cholinergic. However, the sympathetic postganglionic neurons are primarily noradrenergic.

Parasympathetic Innervation

The paraspinal nervous system promotes digestion and motility of gastrointestinal tract. The parasympathetic nervous system arises from the cranial (cranial nerves III, VII, IX, and X) and sacral (S2-S4,5) segments of the neuraxis and, in contrast to the sympathetic nervous system, tends to have long preganglionic and short postganglionic fibers. Cranial nerve X (vagus) of the cranial nerves carries fibers that arise in the dorsal motor nucleus of cranial nerve X and synapse at superficial and deep cardiac and pulmonary plexuses and at the Auerbach's and Meissner's plexus in the gastrointestinal tract. These plexuses transmit parasympathetic impulses along postganglionic fibers, which ultimately innervate smooth muscle and glands to increase gastrointestinal motility and digestion from the esophagus up to the level of the splenic flexure of the colon (Hou and Rabchevsky 2014; Ugalde et al. 1996). While vasovagal reflex circuit regulates digestive processes from the oral cavity to the transverse colon, the degree of vagal control is reduced caudally (Altschuler et al. 1993). In general, vagal input is terminated at the second segment of the transverse colon, and the portions of the gastrointestinal tract that form the distal transverse colon receive parasympathetic input (nervi erigentes) from the intermediate gray columns of S2-S4 via the pelvic nerve. Parasympathetic innervation is important for relaxation of the internal anal sphincter and for increasing motility of the sigmoid colon and rectum. Acetylcholine is the neurotransmitter of the parasympathetic preganglionic neurons and acts by binding to nicotinic receptors.

Somatic Innervation

Somatic control of the gastrointestinal tract is limited to the ingestion of food and liquids into the oropharynx and esophagus, as well as the exit of fecal waste from the rectal vault. Somatic control of the external anal sphincter is important in maintaining fecal continence. The pudendal nerve consists of the sacral root (S2-S4) and supplies the external anal sphincter with somatic innervation. In addition, fibers from S4 innervate the levator ani muscles (iliococcygeus, pubococcygeus, and puborectalis) via the levator ani nerves. Defecation occurs in response to distention of mechanoreceptors within the rectal mucosa, which stimulate afferent response that is transmitted to the spinal cord and cerebral cortex. Afferent signals caused by rectal distention are transmitted along the autonomic pathways to stimulate reflex rectal contraction and internal anal sphincter relaxation. Voluntary relaxation of the external anal sphincter and levator ani can result in expelling feces from the rectal vault (Ugalde et al. 1996).

30.1.3 Colonic Reflexes

It is important to understand the underlying mechanisms and relevance of spinal cord injury since colonic reflexes play an important role in pathophysiology and are the basis of various aspects of bowel management after spinal cord injury. Gastrocolic (cholinergic), colocolonic (myenteric plexus), and rectocolic (pelvic nerve) reflexes stimulate colon motility. The gastrocolic reflex leads to increased small bowel and colonic propulsive motility, and is mediated by neural and endocrine mechanisms (Chung and Emmanuel 2006). By ingesting food or a caloric drink approximately 30 min before bowel management is planned, reflex colonic contractions can aid stool emptying (Longo et al. 1995). Fatty foods tend to have larger and longer action on the reflex compared to protein or carbohydrate-dominant foods. The rectocolic reflex is a pelvic reflex that is triggered by mechanical or chemical stimulation in the rectum or anus. It also produces colonic peristalsis that brings the stool down to the rectum. The stool entering the rectum can then trigger the rectoanal inhibitory reflex, a reflex relaxation of the internal anal sphincter in response to rectal distension that allows expulsion of stool from the rectum through proximal contraction and distal relaxation, resulting in caudal propagation. Voluntary contractions of the external anal sphincter and puborectalis muscle contraction prevent defecation and maintain continence in the presence of rectal contraction. This is also called holding reflex.

30.1.4 Defecation

The defecation usually begins when stool is pushed into the rectum by peristalsis. The rectoanal inhibitory reflexes reduce tone of the internal anal sphincter and dilate the rectum. The amount of stool expands the rectal wall as well as the puborectalis muscles and stimulates the urge to defecate. Voluntary relaxation of the external anal sphincter and the puborectalis muscle allows passage of the stool to straighten the anorectum. The stool is pushed out with Valsalva maneuver, followed by persistent peristalsis and increased abdominal pressure.

30.2 Neurogenic Bowel Dysfunction

There are similarities between the genitourinary and gastrointestinal tracts in terms of the smooth internal and striated external sphincters, innervation, blood supply, and the response to cholinergic and adrenergic stimuli. Therefore, people with a micturition dysfunction associated with neurogenic bladder may also have problems with dysfunctional bowel problems. Spinal cord injury affects bowel activity through a variety of mechanisms including temporary loss/depression of reflex activity (spinal shock), effects on colorectal compliance and motility, increased colonic transit time, and changes in anal sphincter control (Stiens et al. 1997). Patients with supraconal lesions have increased tone of the distal colon and rectum, while transit time throughout the

Table 30.3 Differentiation of motor function characteristics between UMNL and LMNL neurogenic bladders

UMNL neurogenic bladder	LMNL neurogenic bladder
Positive anal reflex	No anal reflex
Positive bulbocavernosus reflex	Absent bulbocavernosus reflex
Injury above conus medullaris	Injury to conus medullaris or cauda equina

UMNL upper motor neuron lesion, *LMNL* lower motor neuron lesion

colorectum is prolonged. In contrast, patients with conal or cauda equina lesions have a flaccid, hypotonic distal colon, and rectum with significantly prolonged transit of the distal colon and rectum. Both groups have significantly reduced emptying of the rectosigmoid at defecation (Goetz et al. 2018). The characteristics of motor function between the upper motor neuron neurogenic bladder and the lower motor neuron neurogenic bladder are summarized in Table 30.3.

Patients with spinal cord injuries usually lose the ability to cope with rectal fullness and voluntary control of the external anal sphincter. Depending on the level and completeness of the injury, two types of colonic disorders can occur. Lesions above the conus medullaris have an upper motor neuron bowel. The external anal sphincter cannot be relaxed voluntarily and the pelvic floor muscle becomes spastic. However, neural connections between the spinal cord and the colon as well as the myenteric plexus can preserve and evacuate the stool by reflex activity. In lesions below the conus medullaris, there is a lower motor neuron bowel. The myenteric plexus regulates the movement of stool but tends to be very slow. Most spinal cord injuries cause constipation and sometimes fecal impaction. Fecal incontinence is relatively uncommon (Ebert 2012).

30.2.1 Upper Motor Neuron Lesion Neurogenic Bowel

Upper motor neuron type bowel dysfunction resulting from a lesion above the conus medullaris (supraconal spinal cord injury) slows entire bowel transit time, as well as increased colonic wall and external anal sphincter muscle tone. Rectal hypertonia can cause decreased compliance and predisposes to reflex defecation and incontinence (Preziosi and Emmanuel 2009). The resulting slow entire bowel transit leads to constipation, which is often exacerbated by changes in puborectalis muscle function. Evacuation of feces is achieved by triggering reflex defecation either by mechanical (digitation) or chemical means (suppositories or enemas) (Chung and Emmanuel 2006).

30.2.2 Lower Motor Neuron Lesion Neurogenic Bowel

Lesions of the conus medullaris, cauda equina, or pelvic nerves cause lower motor neuron type bowel dysfunction with reduced parasympathetic and somatic tone of the internal and external anal sphincters. The smooth muscle tone of the descending colon and rectosigmoid apparatus are also reduced, so there is no extrinsic reflex peristalsis and feces propulsion. The sensory limbs of the pelvic floor reflex arc are also anatomically damaged, leaving only enteric-mediated reflexes. Therefore, unlike upper motor neuron bowel dysfunction, lower motor neuron bowel may lead to overflow incontinence, flaccid paralysis associated with a lower motor neuron lesion, passive incontinence, and leakage (Krogh et al. 2001). Regardless of the mechanism, the potential for fecal incontinence can cause serious anxiety in individuals and can lead to social isolation. Manual removal of stool, assisted by increases in intra-abdominal pressure, such as with a Valsalva maneuver, is the mainstay of management of such individuals (Chung and Emmanuel 2006).

30.2.3 Assessment

A neurological examination of spinal cord injury based on ISNCSCI should be performed to understand the expected type of neurogenic bladder dysfunction. The major components of the patient's history include premorbid

gastrointestinal function and health status, current bowel program, current bowel symptoms, defecation frequency and duration, stool character (Bristol Stool Scale) (Fig. 30.5), and medication use (Table 30.4). Diet, fluid intake, activity levels, and history of autonomic dysreflexia should be assessed. In addition, a systemic assessment of bowel function should be performed, including time of day, frequency, need for assistance, duration, facilitation techniques, type of rectal stimulation, medications for bowel function, stool characteristics (volume, consistency, color, mucus, presence of blood), and presence or absence of desire to have a bowel movement (Krogh et al. 2017).

The International Spinal Cord Injury Bowel Function Basic Data Set (Version 2.0) is a standardized assessment tool. Version 2.0 consists of 16 items that describe background information on bowel function and details on neurogenic bowel dysfunction and bowel management (Krogh et al. 2017). The International Standards to document Autonomic Function following SCI (ISAFSCI), second edition, contain the following assessment points for the bowel functions: bowel emptying, awareness of bowel fullness, and ability to prevent bowel leakage (Wecht et al. 2021). The Neurogenic Bowel Dysfunction (NBD) Score can also be calculated quickly and is used to assess the severity of neurogenic bowel dysfunction and response to treatment (Krogh et al. 2006): a severe NBD score is ≥14, moderate an NBD score of 10–13, minor an NBD score of 7–9, and very minor an NBD score of 0–6.

Patient should also be evaluated for difficulties in defecation, including delayed or painful evacuations, constipation, diarrhea, and unplanned evacuations or fecal incontinence.

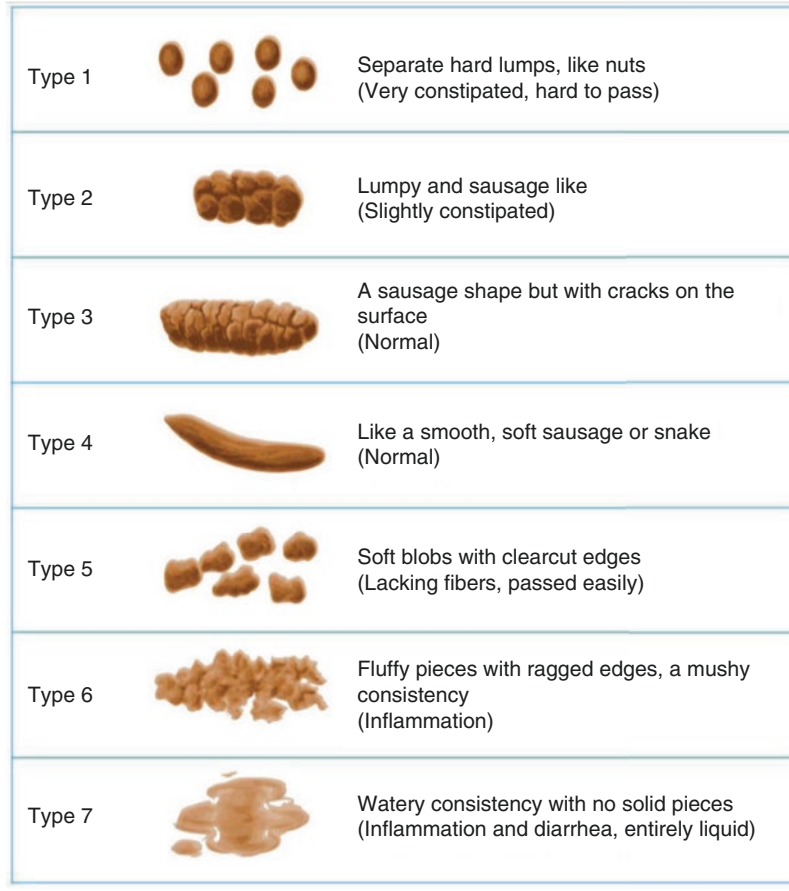

Fig. 30.5 Bristol Stool Scale

Table 30.4 Medications containing constipating or diarrheal effects

Drugs with Constipating Effects
Analgesics (including non-steriodal anti-inflammatory drugs)
Antacids (e.g., aluminum and calcium compounds)
Anticolinergics (e.g., Oxybutynin, Ditropan®)
Anticonvulsants (e.g., oxcarbazepine, Trileptal®)
Antidepressants (e.g., selective serotonin reuptake inhibitors)
Antihypertensives (e.g., clonidine, Catapres®)
Antimotility (e.g., Loperamide, Imodium®)
Anti-Parkinsonism (e.g., Sinemet, Carbidopa, Lodosyn®)
Antispastic (e.g., Clonide, Catapres®)
Diuretics (e.g., hydrochlorothiazide)
Hematinics (e.g., Iron)
Laxatives (long-term use)
Opiates (e.g., Morphine, Codeine)
Psychotherapeutic drugs (e.g., Thioridazine, Mellaril®)
Drugs with Diarrheal Effects
Antacids containing magnesium
Antibiotics
Antidepressant (e.g., Sertraline, Zoloft®)
Antihypertension (e.g., Captopril, Capoten®)
Chemotherapy drugs
Nonsteroidal anti-inflammatory drugs (Ibuprofen, and Motrin®)

From Gulick and Namey (2012)

Symptoms of autonomic dysreflexia are sometimes caused by constipation or other complications of the neurogenic bowel. Fecal impaction or other abdominal pathologies may indicate atypical or nonspecific symptoms such as anorexia and nausea.

30.2.3.1 Physical Examination

International Standards to document Autonomic Function after Spinal Cord Injury (ISAFSCI), second edition, recommended measures of autonomic control of the distal bowel: sensation of the need to empty the bowels and ability to prevent bowel leakage (Wecht et al. 2021). The anocutaneous reflex mediated by the pudendal nerve, S2-S4, is examined by stroking the mucocutaneous junction of the anus with a safety pin or pulling perianal hair. It should be tested on both sides. Perianal pin prick sensation should be checked. Digital rectal examinations should be performed to evaluate the presence of deep anal pressure, voluntary anal contraction, and bulbocavernosus reflex, the presence of the palpable ridge of the puborectalis muscular sling, and the presence of stool, hemorrhoids, or masses. Abdomen examinations include examinations for percussion, auscultation of bowel sounds, distention, hernia, and palpation for any hard stool, tenderness, or masses.

30.2.3.2 Diagnostic Tests

An abdominal radiograph may show feces and abnormal gaseous patterns. For colorectal cancer screening, occult blood tests in stool must be performed. However, hemorrhoids can lead to false-positive results. Colonoscopy is another cancer screening option. To test for unexplained diarrhea, stool examination for leukocytes, pathogens, and *Clostridium difficile* toxin may be required. Colonic transit test involves ingestion of radiopaque markers with one or more subsequent abdominal X-rays that track the passage of the markers along the colon. Colon transit time can be calculated from the distribution of markers in the right, transverse, and rectosigmoid segments of the colon (Wald et al. 2014). Anorectal manometry is useful in assessing rectal sensation, basal anal sphincter tone, and the ability to volitionally increase the anal sphincter tone. A high-resolution probe with sensors can measure puborectalis and anal sphincter pressures at rest, with squeeze, during a cough maneuver, and during attempted defecation, rectal sensation, compliance, and the presence of the rectoanal inhibitory reflex (Johns et al. 2021).

30.2.4 Management of Neurogenic Bowel Dysfunction

30.2.4.1 Neurogenic Bowel Management Routines

A bowel program is the treatment plan that aims to minimize or eliminate the occurrence of unplanned or difficult evacuations; to evacuate stool at a regular, predictable time within 60 min of bowel care; and to minimize gastrointestinal complications (Johns et al. 2021). The goals of the treatment plan should be individualized for each patient, depending on the neurological

impairment, lifestyle, patient needs, activity level, socioeconomic status, and level of assistance. Before starting the bowel program, premorbid and current bowel function should be evaluated. Preexisting conditions, such as laxative dependency, autonomic neuropathy, irritable bowel syndrome, or inflammatory bowel disease, can alter bowel transit time. These diseases may also reduce the effectiveness of bowel care medications (Chen and Nussbaum 2000).

For most patients, a complete bowel evacuation every other day is satisfactory. The lower the frequency of bowel movement, the more likely fecal impaction. For most tetraplegic patients, caregivers are needed to complete the bowel regimen. Also, defecation may take up 2 h to complete. Therefore, bowel program must be scheduled at convenient times for both the patient and caregiver (Chen and Nussbaum 2000). When starting a bowel program, it is advantageous to start with an empty intestine. A plain X-ray of the abdomen is useful. In the case of constipation, an enema should precede the beginning of the bowel program. Medications that reduce bowel mobility, such as tricyclic agents and narcotics, should be minimized. Broad-spectrum antibiotics can change gut flora and cause diarrhea.

Recommendations for optimizing diet and fluids are the most commonly used management protocol. Proper fluid intake of 2500–3000 mL per day is ideal and essential for good bowel programs. The recommended fluid intake should be consistent with the bladder management program. Proper diet is an essential prerequisite for a successful bowel management. The diet should contain a sufficient fluid and fiber, as loose stools are more likely to shorten bowel transit time. There are several types of fibers that have different effects on the gastrointestinal tract. The specific effect depends on the degree of water solubility. In the colon, fibers tend to shorten transit time, provide bulk to stool, facilitate the transit through the colon, and increase frequency of bowel movements. This effect is more pronounced with coarse fibers. Another benefit of a high-fiber diet is a feeling of fullness that can limit the intake of high-fat diet. A total of 15 gm of dietary fiber per day is ideal with a variety of sources. With a high-fiber diet, patients should be carefully observed for intolerable symptoms such as acceptable flatulence, marked increase in stool volume, and abdominal distention (Krassioukov et al. 2010). Poor control of flatus and fecal leakage can lead to physical, psychological, sexual, and social problems (DeLisa and Kirshblum 1997). Effective bowel management strategies to address and prevent these symptoms are important for the well-being of people with spinal cord injuries. A pyramid in Fig. 30.6 shows a generally accepted hierarchy of neurogenic bladder management.

Adverse effects and unexpected complications are common during bowel care program. Vigilance for the problems should be given. Anticholinergics used in the treatment of neurogenic bladder dysfunction, opiates, and

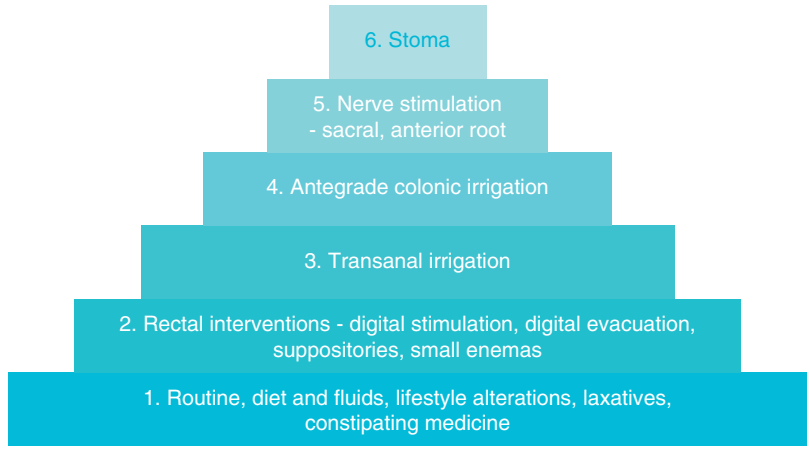

Fig. 30.6 A generally accepted hierarchy of neurogenic bowel management. Adapted from MASCIP (2012). https://www.mascip.co.uk/wp-content/uploads/2015/02/CV653N-Neurogenic-Guidelines-Sept-2012.pdf

antispasticity medications slow bowel transit and dry stool, making constipation worse. Broad-spectrum antibiotics can cause diarrhea by altering the balance of commensal enteric flora in the intestine. Anal digitation, evacuation, and rectal medication administration can cause local trauma irritating hemorrhoids and predisposing to anal fissure and solitary rectal ulcer formation (Chen and Nussbaum 2000).

The goal for people with upper motor neuron bowel dysfunction is a soft but formed stool or Bristol Stool Scale of 3–4. The goal for persons with lower motor neuron bowel should be a firm formed stool or Bristol Stool Scale of 2–3.

30.2.4.2 Bowel Care Schedule

It is necessary to consistently determine the schedule of bowel movements based on factors influencing defecation, preinjury patterns of defecation, attendant care, personal goals, and lifestyle considerations. Bowel care should be done at the same time of the day. To avoid chronic colorectal distention, at least every 2 d is recommended. The goal is to have the bowel program complete within 45–60 min. The bowel program should begin with acute care and last until the end of their life. Simplification of the program may be considered, if there is no unexpected evacuation and elimination is consistent. It is important to evaluate the effectiveness of the program and its compliance with treatment, and modify the program as needed. In general, at least 3–5 cycles of bowel care are required to assess the suitability of each revision before any additional treatment changes.

Gastrocolic and rectocolic reflexes may be useful for the management of bowel and upper motor neuron bowel dysfunction. Gastrocolic reflex is a normal phenomenon that leads to defecation after meals. Patients with spinal cord injuries should be brought to the toilet within 1 h after a meal. The rectocolic reflex may be affected by digital stimulation of the rectum and slow clockwise movement of the digit. Triggering of defecation is performed, if necessary, by digital stimulation, glycerin suppositories, or bisacodyl suppositories. They are often given 20–30 min after a meal to use the gastrocolic reflex (Fig. 30.7). Patients try defecation after 10 min. Seating should be taken for effective bowel care

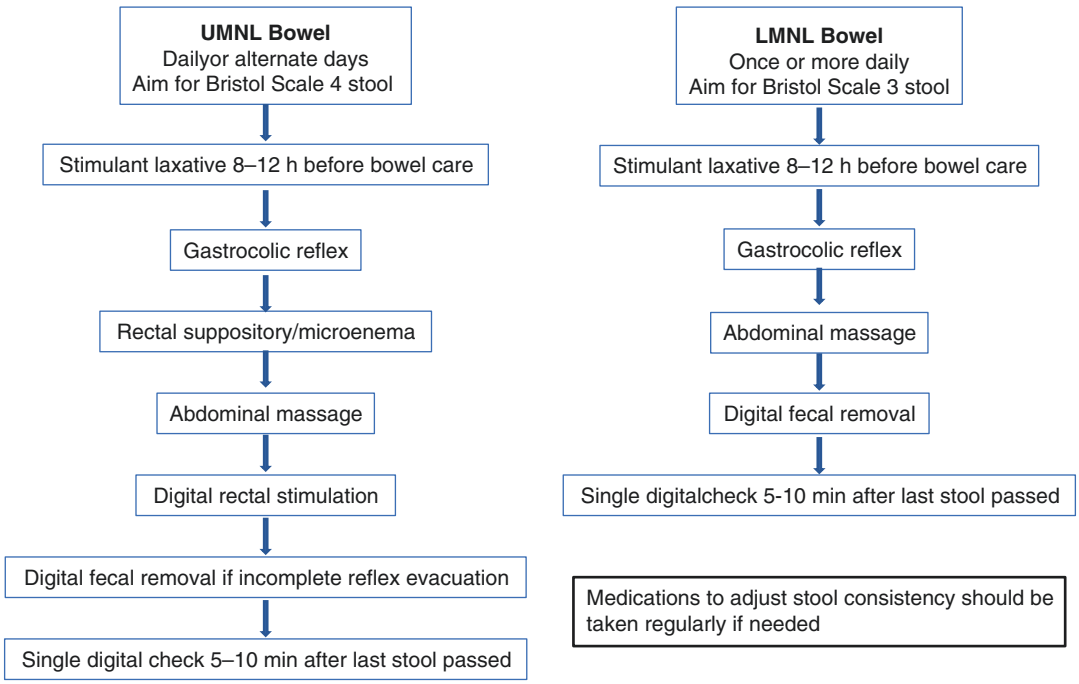

Fig. 30.7 Schematic representation of neurogenic bowel care

if the use of gravity and mechanical advantages of the abdominal muscle to promote bowel movement in the sitting position is feasible (Consortium of Spinal Cord Medicine 2020).

30.2.4.3 Digital Rectal Stimulation and Manual Evacuation of Stool

Mechanical rectal stimulation is used to trigger anorectal reflexes to increase motility and relax sphincters in reflexic neurogenic bladder dysfunction. Digital rectal stimulation is one of the most commonly used mechanical rectal stimulation in patients with reflexic neurogenic bladder dysfunction (Consortium of Spinal Cord Medicine 2020). Complications associated with mechanical rectal stimulation include autonomic dysreflexia, hemorrhoids, abdominal distension, and anal fissures.

Digital stimulation or suppositories are often ineffective in triggering stool evacuation because of the disturbed rectocolic reflexes in patients with areflexic bowel. Manual evacuation of the stool is required daily or more often to reduce incontinence during scheduled evacuation. Manual stool evacuation is indicated as a treatment for areflexic bowel management and fecal impaction. Manual evacuation is performed with the affected individual side-lying in bed or positioned on a padded commode if prescribed to be performed in an upright position. Manual evacuation may need to be performed daily or more frequently in areflexic neurogenic bladder dysfunction (Consortium of Spinal Cord Medicine 2020).

30.2.4.4 Medications

Drugs used to modify bowel habits include stool softeners, bulk formers, colonic stimulants, colonic irritants, and prokinetic agents (Gulick and Namey 2012) (Table 30.5). Medication use for bowel care should be individualized. Stool softeners, such as decussate, should be the first-line medication to prevent the formation of hard stools. Stool softeners function by permitting passage of water into the stool, softening fecal material, and facilitating its movement. Oral stimulants (Senna or bisacodyl) are irritants that stimulate the myenteric plexus, promoting peristaltic movement (Gor et al. 2016). Oral stimulant laxatives can cause all of the side effects of cramps, diarrhea, and dehydration. Their chronic use can lead to colonic mucosal staining due to macrophage phagocytosis of pigments derived from laxatives. Glycerin and bisacodyl suppositories may be useful adjunctive agents in a bowel regimen. Rectal chemical stimulants, containing glycerin alone or in combination with other agents, are commonly used to facilitate the contraction and secretion processes in the colon due to ease of administration and timing of effects. Enemas should not be part of a regular bowel program, but these agents are useful for providing a clear gut before starting the bowel program or before treating constipation.

30.2.4.5 Others

Transanal irrigation offers another nonsurgical technique that is considered well tolerated. Transanal irrigation is a process that facilitates the evacuation of feces from the bowel by introducing water or other liquid into the bowel through the anus in an amount sufficient to reach beyond the rectum. This infused water distends the rectal wall and stimulates the stretch receptors to stimulate bowel movements (Wilson 2017).

Many surgical interventions have been identified for more intractable bowel dysfunction. Antegrade continence enemas require a necessary surgical procedure as described by Malone and colleagues (Melone et al. 1990). Colostomy or ileostomy allows for easier management and a high degree of satisfaction (Boucher et al. 2019; Hocevar and Gray 2008).

In all treatments, persons with injuries above T6 must always be careful to trigger autonomic dysreflexia in the management of the neurogenic bowel if they are poorly or aggressively managed (Faaborg et al. 2014).

30.2.4.6 Proper Positioning for Defecation

The best position for defecation is sitting with hips and knees flexed on a commode. If possible, it is necessary to slightly raise the feet so that the knees are slightly higher than the hips. In this

Table 30.5 Medications used for bowel care

Medication	Action	Precautions or contraindications
Bulk forming	Contain natural and semisynthetic hydrophilic polysaccharides and cellulose derivatives that dissolve in the intestinal fluid to facilitate passage of the intestinal contents and stimulate peristalsis. Does not affect absorption of nutrients.	Abdominal cramping and flatulence may occur. Avoid taking a bulking agent within 1 to 3 h of taking other medications. Drink at least 8 oz of fluid with each dose. Acts within 12 to 24 h.
Methylcellulose, Citrucel®		
Carboxymethyl cellulose sodium		
Malt soup extract, Malsupex®		
Partially hydrolyzed guar gum Benerfiber®		
Polycarbophil, FiberCort®		
Emollients/Stool softeners	Increase the wetting efficiency of intestinal fluid, promotes a softer stool, and help prevent painful defecation and straining.	May cause diarrhea and mild abdominal cramping. Avoid use if nausea, vomiting, or abdominal pain exists. Acts within 24 to 72 h.
Docusate sodium, Colace®		
Docusate calcium		
Docusate potassium		
Lubricants	Soften fecal contents by coating them, thus preventing colonic absorption of fecal water.	Excessive use may impair absorption of vitamins A, D, E, and K. Acts in 6 to 8 h.
Mineral Oil		
Saline Laxatives (Osmotics)	Produce both secretory and motor reactions that draw water into the intestine, to increase intraluminal pressure which in turn increases intestinal motility.	Indicated for acute evacuation of the bowel. Take on an empty stomach as food will delay its action. May cause abdominal cramping, diuresis, nausea, vomiting, and dehydration. Acts within 30 min to 3 h.
Magnesium citrate, Citroma®		
Magnesium hydroxide, Milk of magnesium®		
Magnesium sulfate, Epson Salts®		
Polyethylene Glycol, MiraLAX®		
Lactulose		
Stimulants	Increase the propulsive peristaltic activity of the intestine by local irritation of the mucosa or by a more selective action on the intramural nerve plexus of intestinal smooth muscle, thus increasing motility. Stimulate secretion of water and electrolytes in either the small or large intestine or both.	Used for simple constipation, but not to be used for more than 1 week unless ordered by a physician. May cause severe cramping, electrolyte and fluid deficiencies, enteric loss of protein, malabsorption resulting from excessive hypermotility and catharsis, and hypokalemia. Usually acts within 6 to 12 h or may require up to 24 h.
Senna, Senokot®		
Bisacodyl		
Castor oil		
Suppositories	A hyperosmotic laxative that irritates the lining of the intestine. Draws water into the rectum to stimulate a bowel movement. Has a direct stimulating effect on the network of nerves in the large intestine. Provides lubrication to promote elimination of stool.	Do not use if abdominal pain, feel sick, or have vomiting.
Glycerin		Take plenty of fluids while taking the medication. Usually acts within 30 min.
Dulcolax		
Enemas	Lubricates the colon and allows for added cleansing. Pulls water from the body into the bowel which helps to soften the stool and cause a bowel movement.	Enema solutions can cause fluid and electrolyte disturbances in the blood if used on a chronic basis. May cause anal irritation, diarrhea, gas, nausea, stomach, cramps. Acts within 5 to 15 min.
Mineral oil		
Fleet enema		

From Gulick and Namey (2012)

position, the acute angle of the anal canal created by the puborectalis sling can be straight. The less optimal position is the left lateral position in bed. This position allows gravity to help the stool flow and maximizes the mechanical advantage of the abdominal muscles. Care should be taken to avoid pressure injuries during the bowel evacuation program in the bed or on a commode.

In summary, the basic bowel care plan for new patients with spinal cord injuries is as follows (Nesathurai 2000):

- Complete history and physical examination.
- Determine goals of bowel program (frequency, timing, location).
- Minimize medications that may decrease bowel motility.
- Recommend diet high in fibers, fruits, and vegetables.
- Minimize fatty foods and dairy products, which may impair gut motility.
- KUB to ensure unobstructed bowel.
- Introduce stool softener.
- Place patient on commode after breakfast to manipulate gastrocolic reflex.
- Encourage defecation in sitting position, not in bed.
- If no bowel movement, then perform rectal stimulation. If this is unsuccessful, consider suppository.
- If no bowel movement after the third day, give enema and consider adding a second adjunctive medication.

30.3 Other Gastrointestinal Problems

30.3.1 Fecal Impaction

The goal of a good bowel program is to prevent fecal impaction that is characterized by absence or reduction of defecation. In some cases, there may be overflow diarrhea. Fecal impaction can lead to autonomic dysreflexia or perforated viscus. If impacted stools are present in the rectum, manual disimpaction should be attempted. Anesthetic jelly should be used to prevent autonomic dysreflexia. If the impaction is more proximal, an enema or an effective oral stimulant may be indicated. Repeated fecal impactions associated with multiple episodes of autonomic dysreflexia may indicate ileostomy or colostomy.

30.3.2 Constipation

Constipation is defined by the presence of infrequent bowel habits (<3 bowel movements per week), hard stools, excessive straining, a sense of anorectal blockage, and a sense of incomplete evacuation during defecation (Longstreth et al. 2006). Constipation is the most frequent complication in all stages of recovery in spinal cord injuries. The frequency of constipation is affected by the level of injury, with up to three-quarters of tetraplegics being affected, falling to a third in paraplegics with lesions between the T10 and L2 cord segments (De Looze et al. 1998). Contributing factors include immobility, delayed colonic transit time, loss of gastrocolic reflex, absence of abdominal pressure on Valsalva maneuver due to absent or weak abdominal muscles, loss of rectal vault sensation, and interference with the supraspinal defecation center. Patients must be asked for any medications that they currently are taking to determine if any of them have constipating and/or diarrheal effect (Table 30.4).

A balanced diet, adequate fluid, and fiber intake are important components in the management and prevention of constipation. Bowel program includes exercise and a high-fiber diet (fruits and vegetables) and meals that lessen constipation (banana, potato, and processed cheese). Increased activity is useful by mechanical stimulation of peristalsis. Bulk forming agents such as psyllium seed or methylcellulose can provide additional fibers. If additional medication is required, regular doses of magnesium citrate or hyperosmotic (lactulose) laxative can be given. These agents increase luminal fluid secretion and provide an osmotic load that stimulates motility. Avoid stimulant laxatives such as senna, cascara, or bisacodyl, as they may impair colonic motility for prolonged use. Bulk forming agents and laxatives administered at least 8 h prior to intended bowel care are useful. Rectal stimulation with glycerin suppositories or mild enemas triggers reflex sigmoid contractions with relaxation of the anal sphincter and facilitates bowel movements (Chatoor and Emmnauel 2009).

30.3.3 Gastroesophageal Reflux

The incidence of gastroesophageal reflux disease in patients with spinal cord injuries was reported to be approximately 22% (Singh and Triadafilopoulos 2000). The incidence of gastroesophageal reflux and hiatal hernia in individuals with more than 5 years of spinal cord injury increased (Gore et al. 1981). Gastroesophageal reflux disease is a clinical syndrome caused by reflux of stomach contents including acid and pepsin into the esophagus. Normal functions are dependent on the lower esophageal sphincter and diaphragm, which act as barriers preventing reverse movement of stomach contents into the esophagus.

Gastroesophageal reflux occurred by 3 mechanisms: (1) transient lower esophageal sphincter relaxations, (2) abdominal straining, and (3) free reflux across a patulous low esophageal sphincter (Dodds et al. 1982). Decrease in the gastroesophageal sphincter tone, increased acid secretion, supine recumbency, immobilization, and medications may cause gastroesophageal reflux after spinal cord injury. The syndrome is manifested clinically by symptoms of heartburn, epigastric or substernal pain, dysphagia, nocturnal cough, aspiration pneumonia, or hiccoughs. Drugs that decrease lower esophageal sphincter pressure include anticholinergics, tricyclic antidepressants, theophylline, diazepam, and calcium channel blockers. Other major factors affecting the lower esophageal sphincter tone include obesity, smoking, and delayed gastric emptying.

When the patient has a medical history of gastroesophageal reflux, several diagnostic tests are available to determine the presence or absence of gastroesophageal reflux and its complications. If the diagnosis of gastroesophageal reflux disease is unclear and empiric therapy with proton pump inhibitors fails, assessment of pH monitoring and evaluation of obstruction, anatomical deformity causing disruption of the gastroesophageal tract, and hiatal hernia may be considered (Armstrong et al. 2005; Singh and Triadafilopoulos 2000). The diagnostic tools include a barium swallow radiographic examination, esophagoscopy, esophageal manometry, and Bernstein test (acid perfusion test).

Treatment of gastroesophageal reflux and reflux esophagitis is aimed at improving esophageal acid clearance of the esophagus, reducing the acidity of refluxed material, and increasing gastroesophageal junction competence (Sontag 1990). Treatment of gastroesophageal reflux should be emphasized with elimination and correction of predisposing factors such as postural maneuvers elevating the head of the bed 6–8 inches, discontinuation of drugs decreasing lower esophageal sphincter, and weight loss. Antacids, H2 antagonists, and proton pump inhibitors inhibit gastric acid secretion and relieve symptoms. Bethanechol (25 mg qid) and dopamine antagonists improve esophageal clearance and increase pressure of the lower esophageal sphincter.

30.3.4 Acute Abdomen and Gastrointestinal Bleeding

Typical findings of an acute intra-abdominal process in patients with spinal cord injuries can be missing or misleading. Because of delayed diagnosis and misdiagnosis, the mortality rate is 10–15% in these patients (Charney et al. 1975). Diagnosis and management are based on an understanding of the level of spinal cord injury and whether this is complete or incomplete. The causes of acute abdomen in patients with spinal cord injuries are listed in Table 30.6.

Proper prophylaxis of stress ulcers can reduce the incidence of gastritis leading to bleeding. Upper gastrointestinal bleeding occurs in 5–20% of patients with acute spinal cord injuries (El Masri et al. 1982). Gastrointestinal bleeding after spinal cord injury is usually associated with gastroduodenal ulcers (Juler and Eltorai 1985; Walters and Silver 1986). Peptic ulcers are often reported after traumatic injuries requiring intensive care. Gastrointestinal bleeding is more common in patients with cervical or high thoracic cord injuries and increases in frequency in complete injuries (Kiwerski 1986; Solerstrom and Ducker 1985).

Symptoms of gastrointestinal bleeding in chronic or acute diseases are often insidious, and

Table 30.6 Causes of acute abdomen in patients with spinal cord injuries

Cause	Disease
GI bleeding	Gastric perforation, ulcer perforation, hemorrhagic gastritis, esophageal bleeding
Infection, inflammation	Appendicitis, cholecystitis, pancreatitis
Peritonitis	Intestinal perforation, bladder rupture
Intraabdominal abscess	Liver abscess, intrapelvic abscess, pancreatic abscess
Urological disease	Pyelonephritis, cystitis, bladder stone, ureter stone, renal stone, renal abscess
Bowel obstruction	Gastroduodenal obstruction, small bowel obstruction, large bowel obstruction
Aortic dissection	Aortic dissection
IVC filter migration	IVC filter migration
Intestinal infarction	Mesenteric venous thrombosis, mesenteric artery occlusion
Severe paralytic ileus	Paralytic ileus

there are no early symptoms. Hemodynamic instability and cardiopulmonary dysfunction are common presentations. Upper gastrointestinal bleeding classically shows hematochezia and black tarry stool; if it is massive, it can also show bright red blood per anus. Lower gastrointestinal bleeding is classically accompanied by maroon stools (right side of the colon), bright red blood per rectum (left side of the colon), and melanic (rectocecal). Gastrointestinal bleeding due to perforation in spinal cord injuries may not be detected at first until apparent hemodynamic instability appears (Leramo et al. 1982). The provocating factors are multifactorial and include stress hormone-mediated ulceration, diminished supraspinal controls leading to unopposed parasympathetic dysfunction, gastric vascular changes, oxidative stress, as well as the controversial use of steroids for treatment of spinal cord injury (Solerstrom and Ducker 1985). Gastrointestinal bleeding rate in spinal cord injury was 2.77% with 33% mortality while receiving high-dose steroids (Khan et al. 2014). Aspirin and nonsteroidal anti-inflammatory drugs can cause gastritis and anticoagulants, particularly full-dose heparin may initiate or exacerbate bleeding in the patients with gastritis.

Patient care for spinal cord injury with gastrointestinal bleeding is similar to other patients with intensive care. Hemodynamic stability and attention to cardiopulmonary monitoring are necessary. Blood pressure should be maintained, and coagulopathy should be corrected. Identification of the location of bleeding can be categorized as upper and lower gastrointestinal sources. If upper gastrointestinal bleeding is suspected, upper gastrointestinal endoscopy is the test of choice. If lower gastrointestinal bleeding is suspected, fiber-optic flexible colonoscopy should be selected as the first diagnostic tool. Treatment is currently being conducted on anatomic location and pathogenesis underlying gastrointestinal bleeding. The most important treatment for bleeding from stress gastritis is prevention. Lowering the gastric acidity and maintaining intragastric pH 4–5 or higher can prevent bleeding. Prophylactic administration of antacids, histamine-2 receptor antagonists, or proton pump inhibitors for the first 4 weeks after spinal cord injury are widely used in intensive care units, and this particular complication is minimized. The use of prolonged proton pump inhibitors is associated with an increased incidence of *Clostridium difficile* infection.

30.3.5 Gallbladder Disease

Patients with spinal cord injuries may have an increased prevalence of gallbladder disease. Cholelithiasis is more common in patients with spinal cord injuries. In the study, gallstone morbidity in patients with spinal cord injuries increased threefold compared to the control group (Apstein and Dalecki-Chippenfield 1987) and 25% in male patients with chronic spinal cord injuries (Rotter and Larrain 2003). Although the reasons for the increase in cholelithiasis are not well known, there is a possibility of decreased gallbladder motility and bile stasis due to impaired sympathetic innervation, altered enterohepatic circulation of bile acids, and changes in biliary lipid excretion. Acute pancreatitis may

result from spasm of the sphincter Oddi secondary to parasympathetic predominance. High doses of steroids can increase risk.

Clinical presentation may not show typical symptoms or signs due to sensory loss. Patients with cervical or high thoracic injuries may have atypical symptoms, such as increased spasticity, abdominal spasms, autonomic dysreflexia, and referring pain to the shoulder.

30.3.6 *Clostridium Difficile* Infection

The common cause of inpatient diarrhea is antibiotic therapy. *Clostridium difficile* infection is a major cause of hospital infections and is becoming more common and more serious. The use of antibiotics has been the most prevalent and modifiable risk factor for *C. difficile* intestinal colonization and infection. Other risk factors of *C. difficile* include exposure to healthcare facilities; older age; greater severity of underlying illness; immune suppression; use of antacids, proton pump inhibitors, and H2 receptor blockers; and tubal feeding (Freeman et al. 2010; Shaughnessy et al. 2013). A study of rehabilitation hospital in patients with diarrhea identified *C. difficile* as the cause in 25% (Yablon et al. 1993). Recurrent *C. difficile* after successful treatment is also becoming increasingly common and difficult to treat. Recurrence occurs in up to 20% of patients with *C. difficile*, of whom 45% have a second recurrence, and some will experience multiple recurrences (Johnson 2009).

The clinical manifestations of *C. difficile* infection range from asymptomatic, to mild or moderate diarrhea, to fulminant and sometimes fatal pseudomembranous colitis. Testing for *C. difficile* should be performed on unformed, diarrheal stool. Empirical therapy without diagnostic testing should be avoided. Patients diagnosed with *C. difficile*-associated diarrhea should discontinue all concomitant antimicrobial agents unless they are used to treat the *C. difficile* infection. For proper management, strict infection control guidelines had to be implemented. Hand hygiene with soap and water is preferred over alcohol-based hand sanitizers because *C. difficile* spores are resistant to killing by alcohol (Cohen et al. 2010). The most commonly used antimicrobials to treat *C. difficile* infection are metronidazole and vancomycin. Fidaxomicin (Dificid®) is a new macrocytic antibiotic against *C. difficile* (Juang and Hardesty 2013). Symptomatic *C. difficile* infection, a mild or moderate disease, is usually administered oral metronidazole or oral vancomycin for 10 days. Oral metronidazole, 500 mg three times daily or 250 mg four times daily, and oral vancomycin, 125 mg four times daily, show similar efficiencies. Metronidazole is the preferred treatment. Asymptomatic patients should not be tested or treated routinely (Cohen et al. 2010).

30.3.7 Superior Mesenteric Artery Syndrome

Superior mesenteric artery syndrome is also referred to as cast syndrome, arteriomesenteric duodenal compression syndrome, and Wilkie's syndrome. Superior mesenteric artery syndrome is rare and may be consistent with celiac axis compression syndrome due to mesenteric ischemia caused by celiac axis compression. The pathophysiology of superior mesenteric artery syndrome is associated with compression of the third portion of the duodenum by the superior mesenteric artery owing to loss of the fat layer between those two structures, which causes obstruction of the proximal duodenal outflow. The duodenum passes through the superior mesenteric artery and the abdominal aorta (Fig. 30.8). A narrow angle of about 45° is expected between these two vessels, which is described as an anatomic condition for compression of the duodenum when precipitating factors occur. Already narrow angles and compressing the duodenum may cause superior mesenteric artery syndrome. Other reported anatomic conditions include reduced fat cushion between the duodenum and vessels resulted from weight loss, abdominal compression by body jacket, prolonged supine lying, shorter height, and stiffness of the thoracic curve.

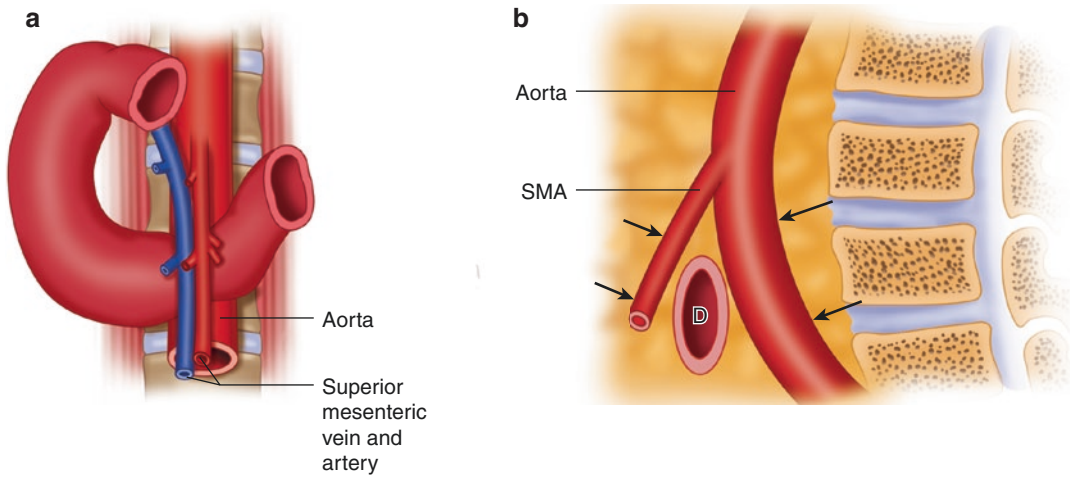

Fig. 30.8 (**a**) Diagram of the anatomy of the third part of the duodenum and (**b**) its relationship to the aorta, vertebrae, and superior mesenteric vessels. Adapted from Ahmed and Taylor (1997)

There are reports of both congenital and acquired factors. Congenital factors that alter the angular relationship between the duodenum and the blood vessels are prone to compress. Acquired factors include BMI ≤8; severe rapid loss of mesenteric fat; abdominal wall weakness; prolonged colon transit time, which can lead to constipation; and postsurgical complications after abdominal or spinal surgery in which anatomical alteration can lead to the superior mesenteric artery syndrome (Table 30.7).

Symptoms of superior mesenteric artery syndrome include general discomfort, no bowel movement for several days, diffuse abdominal discomfort, autonomic dysreflexia, or unexplained increase of tone or spasms after a meal or binge drinking (Roth et al. 1991). History includes postprandial nausea and vomiting, early satiety, and indistinct chest discomfort. The only symptoms can be general fatigue and poor oral intake. In severe cases, abnormal vital signs include fever and hemodynamic instability. Physical examination findings include flushing, sweating, distended abdomen, and abnormal bowel sounds. Abdominal palpation can cause localizing or diffuse pain or be negative. Neurological examinations may increase tone or muscle spasms.

Table 30.7 Predisposing causes of superior mesenteric artery syndrome

Chronic wasting disease
Spinal cord injury
Cerebral palsy
Amyotrophic lateral sclerosis
Drug abuse
Dietary disorders
Malabsorption
Anorexia nervosa
Trauma
Brain injury
Bum
Multiple injuries
Postoperative conditions
Spinal instrumentation, scoliosis surgery, body casting
Aortic aneurysm repair
Nissen fundoplication
Anatomy and congenital anomalies
High insertion of the ligament of Treitz
Intestinal malrotation
Peritoneal adhesion
Low origin of the superior mesenteric artery
Increased lumbar lordosis
Intestinal malrotation
Focal lesions
Dissecting aortic aneurysm
Tumor growth in the mesenteric root
Prevertebral abscess

Basic assessment includes initial basic studies such as complete blood count, chemistries, and flat and upright abdominal films. Barium study shows a cutoff between the third and fourth portion of the duodenum in the supine position.

A lumbosacral corset that pushes the abdomen upward, positioning with the head elevated after meals, frequent small meals, and replacement of weight loss are essential for management of the superior mesenteric artery syndrome. First-line treatment is medical treatment, which includes decompressing the dilated gastric region with nasogastric tube and bowel rest with nutrition delivered parenterally. Upright positioning for meals and side lying after eating help widen the aorto-mesenteric angle (Balmasesa et al. 1987). Surgical treatment is to investigate and relieve the cause of the compression, such as abdominal mass, aneurysms, spinal deformities, and other pathological conditions. Laparoscopic duodenojejunostomy may be a selected surgical procedure. It is necessary to individualize the intervention for patients (Merrett et al. 2009).

30.3.8 Hemorrhoids

Hemorrhoids are usually caused by an increase in rectal pressure and are often associated with prolonged efforts to remove hard stools. Suppositories, enemas, or digital stimulation can aggravate hemorrhoids. Symptoms include bleeding, pain, and autonomic dysreflexia. Effective treatment includes maintaining soft stools and regular bowel movements. Topical steroid ointment and medicated suppositories are effective in the treatment of this issue. If hemorrhoids do not respond to these interventions, surgical consultation is needed.

30.4 Lifespan Care of Neurogenic Bowel Dysfunction

As with the general population, maintaining activity and optimal health also contributes to achieving regular and predictable bowel emptying. Establishing and maintaining a regular bowel regulation can reduce risk of chronic gastrointestinal problems such as fecal impaction, hemorrhoids, gastroesophageal reflux, diverticulosis, and so on. Patients with spinal cord injuries live longer and suffer from many diseases, including duodenal ulcers and diverticulitis. Patients may also develop malignancies in the upper and lower gastrointestinal tracts (Walker-Dalton 1995). Physicians should screen all patients over the age of 50 years, including people with spinal cord injury, for colorectal cancer screening with stool occult blood tests and colonoscopy.

References

Ahmed AR, Taylor I. Superior mesenteric artery syndrome. Postgrad Med J. 1997;73:776–8.

Altschuler SM, Escardo J, Lynn RB, et al. The central organization of the vague nerve innervating the colon of the rat. Gastroenterology. 1993;104:502–9.

Apstein MD, Dalecki-Chippenfield K. Spinal cord injury is a risk factor for gallstone disease. Gastroenterology. 1987;92:966–8.

Armstrong D, Marshall JK, Chiba N, et al. Canadian consensus conference on the management of gastroesophageal reflux disease in adults-update 2004. Can J Gatroenterol. 2005;19:15–35.

Balmasesa MT Jr, Gordon C, Cunningham ML, et al. Superior mesenteric artery syndrome after resection of an arteriovenous malformation in the cervical cord. Am J Gastroenterol. 1987;82:896–9.

Banwell IC, Creasey GH, Aggarwal AM, et al. Management of the bowel in patients with spinal cord injury. Urol Clin N Am. 1993;20:517–26.

Bauman WA, Korsten MA, Radulovic M, et al. 31st g. Heiner sell lectureship: secondary medical consequences of spinal cord injury. Top Spinal Cord Inj Rehabil. 2012;18:354–78.

Boucher M, Dukes S, Bryan S, et al. Early colostomy formation can improve independence following spinal cord injury and increase acceptability of bowel management. Top Spinal Cord Inj Rehabil. 2019;25:23–30.

Charney KJ, Juler GL, Comarr AE. General surgery problems in patients with spinal cord injuries. Arch Surg. 1975;110:1083–8.

Chatoor D, Emmnauel A. Constipation and evacuation disorders. Best Pract Res Clin Gastroenterol. 2009;23:517–30.

Chen D, Nussbaum SB. The gastrointestinal system and bowel management following spinal cord injury. Phys Med Rehabil Clin N Am. 2000;11:45–56. viii

Chung EA, Emmanuel AV. Gastrointestinal symptoms related to autonomic dysfunction following spinal cord injury. Prog Brain Res. 2006;152:317–33.

Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). Infect Control Hosp Epidemiol. 2010;31:431–55.

Consortium of Spinal Cord Medicine. Management of neurogenic bowel dysfunction in adults after spinal cord injury. Clinical practice guideline for health care professionals. Washington, DC: Paralyzed Veterans of America; 2020.

De Looze D, Van Laere M, De Muynck M, et al. Constipation and other chronic gastrointestinal problems in spinal cord injury patients. Spinal Cord. 1998;36:63–6.

DeLisa JA, Kirshblum S. A review: frustrations and needs in clinical care of spinal cord injury patients. J Spinal Cord Med. 1997;20:384–90.

Dodds WJ, Dent J, Hogan WJ, et al. Mechanisms of gastroesophageal reflux in patients with reflux esophagitis. N Engl J Med. 1982;307:1547–52.

Ebert E. Gastrointestinal involvement in spinal cord injury: a clinical perspective. J Gastrointestin Liver Dis. 2012;21:75–82.

El Masri WE, Cochrane P, Silver JR. Gastrointestinal bleeding in patients with acute spinal injuries. Injury. 1982;14:162–7.

Enck P, Greving I, Klosterhalfen S, et al. Upper and lower gastrointestinal motor and sensory dysfunction after human spinal cord injury. Prog Brain Res. 2006;152:373–84.

Faaborg PM, Christensen P, Krassioukov A, et al. Autonomic dysreflexia during bowel evacuation procedures and bladder filling in subjects with spinal cord injury. Spinal Cord. 2014;52:494–8.

Freeman J, Bauer MP, Baines SD, et al. The changing epidemiology of *Clostridium difficile* infections. Clin Microbiol Rev. 2010;23:529–49.

Glickman S, Kamm MA. Bowel dysfunction in spinal-cord-injury patients. Lancet. 1996;347:1651–3.

Goetz LL, Emmanuel A, Krogh K. International standards to document remaining autonomic function in persons with SCI and neurogenic bowel dysfunction: illustrative cases. Spinal Cord Ser Cases. 2018;4:1.

Gondim FA, de Oliveira GR, Thomas FP. Upper gastrointestinal motility changes following spinal cord injury. Neurogastroenterol Motil. 2010;22:2–6.

Gor RA, Katorski JR, Elliott SP. Medical and surgical management of neurogenic bowel. Curr Opin Urol. 2016;26:369–75.

Gore RM, Mintzer RA, Calenoff L. Gastrointestinal complication of spinal cord injury. Spine (Phil Pa 1976). 1981;6:538–44.

Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.

Gulick E, Namey M. Bowel dysfunction in persons with multiple sclerosis. In: Catto-Smith AG, editor. Constipation. London: IntechOpen; 2012. https://doi.org/10.5772/29317. Available from: https://www.intechopen.com/books/constipation-causes-diagnosis-and-treatment/constipation-and-fecal-incontinence-among-persons-with-multiple-sclerosis-a-review-pertaining-to-pre.

Guyton AC, Hall JE. The autonomic nervous system and the adrenal medulla. Propulsion and mixing of food in the alimentary tract. In: Textbook of medical physiology. Philadelphia, PA: Elsevier & Saunders; 2006. p. 748–60. 781–806.

Henry MM, Thomson JP. The anal sphincter. Scand J Gastroenterol Suppl. 1984;93:53–7.

Hocevar B, Gray M. Intestinal diversion (colostomy or ileostomy) in patients with severe bowel dysfunction following spinal cord injury. J Wound Ostomy Continence Nurs. 2008;35:159–66.

Hou S, Rabchevsky AG. Autonomic consequences of spinal cord injury. Compr Physiol. 2014;4:1419–53.

Johns J, Krogh K, Rodriguez GM, et al. Management of neurogenic bowel dysfunction in adults after spinal cord injury: clinical practice guideline for health care providers. Top Spinal Cord Inj Rehabil. 2021;27:75–151.

Johnson S. Recurrent *Clostridium difficile* infection: a review of risk factors, treatments, and outcomes. J Infect. 2009;58:403–10.

Juang P, Hardesty JS. Role of fidaxomicin for the treatment of Clostridium difficile infection. J Pharm Pract. 2013;26:491–7.

Juler GL, Eltorai IM. The acute abdomen in spinal cord injury patients. Paraplegia. 1985;23:1118–23.

Khan MF, Burks SS, Al-Khayat H, et al. The effect of steroids on the incidence of gastrointestinal hemorrhage after spinal cord injury: a case-controlled study. Spinal Cord. 2014;52:58–60.

Kiwerski J. Bleeding from the alimentary canal during the management of spinal cord injury patients. Paraplegia. 1986;24:92–6.

Krassioukov A, Eng JJ, Claxton G, et al. Neurogenic bowel management after spinal cord injury: a systematic review of the evidence. Spinal Cord. 2010;48:718–33.

Krogh K, Christensen P, Laurberg S. Colorectal symptoms in patients with neurological diseases. Act Neurol Scand. 2001;103:335–43.

Krogh K, Christensen P, Sabroe S, et al. Neurogenic bowel dysfunction score. Spinal Cord. 2006;44:625–31.

Krogh K, Emmanuel A, Perrouin-Verbe B, et al. International spinal cord injury bowel function basic data set (version 2.0). Spinal Cord. 2017;55:692–8.

Lavis T, Goetz LL. Comprehensive care for persons with spinal cord injury. Phys Med Rehabil Clin N Am. 2019;30:55–72.

Leramo OB, Tator CH, Hudson AR. Massive gastroduodenal hemorrhage and perforation in acute spinal cord injury. Surg Neurol. 1982;17:186–90.

Lomax AE, Sharkey KA, Furness JB. The participation of the sympathetic innervation of the gastrointestinal tract in disease states. Neurograstoenterol Motil. 2010;22:7–18.

Longo WE, Woolsey RM, Vernava AM, et al. Cisapride for constipation in spinal cord injured patients: a preliminary report. J Spinal Cord Med. 1995;18:240–4.
Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology. 2006;130:1480–91.
Melone PS, Ransley PG, Kiely EM. Preliminary report: the antegrade continence enema. Lancet. 1990;336(8725):1217–8.
Merrett ND, Wilson RB, Cosman P, et al. Superior mesenteric artery syndrome: diagnosis and treatment strategies. J Gastrointest Surg. 2009;13:287–92.
Middleton JW, Lim K, Taylor L, et al. Patterns of morbidity and rehospitalisation following spinal cord injury. Spinal Cord. 2004;42:359–67.
Multidisciplinary Association of Spinal Cord Injury Professionals (MASCIP). Guidelines for management of neurogenic bowel dysfunction in individuals with central neurological conditions. 2012. https://www.mascip.co.uk/wp-content/uploads/2015/02/CV653N-Neurogenic-Guidelines-Sept-2012.pdf. Accessed December 1 2021.
Nesathurai S, editor. The rehabilitation of people with spinal cord injury. 2nd ed. London: Blackwell Science; 2000.
Preziosi G, Emmanuel A. Neurogenic bowel dysfunction: pathophysiology, clinical manifestations and treatment. Expert Rev Gastroenterol Hepatol. 2009;3:417–23.
Roth EJ, Fenton LL, Gaebler-Spira DJ, Frost FS, et al. Superior mesenteric artery syndrome in acute traumatic quadriplegia: case reports and literature review. Arch Phys Med Rehabil. 1991;72:417–20.
Rotter KO, Larrain CG. Gallstones in spinal cord injury (SCI): a late medical complication? Spinal Cord. 2003;41:105–8.
Rowan CJ, Gillanders LK, Paice RL, et al. Is early central feeding safe in patients who have suffered spinal cord injury? Injury. 2004;35:238–42.
Schuster MM. The riddle of the sphincters. Gastroenterology. 1975;69:249–62.
Shaughnessy MK, Amundson WH, Kuskowski MA, et al. Unnecessary antimicrobial use in patients with current or recent Clostridium difficile infection. Infect Control Hosp Epidemiol. 2013;34:109–16.
Singh G, Triadafilopoulos G. Gastroesophageal reflux disease in patients with spinal cord injury. J Spinal Cord Med. 2000;23:23–7.
Solerstrom CA, Ducker TB. Increased susceptibility of patients with cervical cord lesions to peptic gastrointestinal complications. J Trauma. 1985;25:1030–8.
Sontag SJ. The medical management of reflux esophagitis. Role of antacids and acid inhibitions. Gastroenterol Clin N Am. 1990;19:683–712.
Stiens SA, Bergman SB, Goetz LL. Neurogenic bowel dysfunction after spinal cord injury: clinical evaluation and rehabilitative management. Arch Phys Med Rehabil. 1997;78:S86–S102.
Ugalde V, Litwiller SE, Gater DR Jr. Bladder and bowel anatomy for the physiatrist. Phys Med Rehabil State Art Rev. 1996;10:547–68.
Vander AJ, Sherman JH, Luciano D. The digestion and absorption of food. In: Human physiology: the mechanisms of body function. 4th ed. New York: McGraw-Hill; 1985. p. 459–503.
Wald A, Bharucha AE, Cosman BC, et al. ACG clinical guideline: management of benign anorectal disorders. Am J Gastroenterol. 2014;109:1141–57.
Walker-Dalton LM. Bowel care: implementing changes toward quality improvement. SCI Nurs. 1995;12:8–9.
Walters K, Silver JR. Gastrointestinal bleeding in patients with acute spinal injuries. Int Rehabil Med. 1986;8:44–7.
Wecht JM, Krassioukov AV, Alexander M, et al. International standards to document autonomic function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.
Wilson M. A review of transanal irrigation in adults. Br J Nurs. 2017;26:846–56.
Yablon SA, Krotenberg R, Fruhmann K. Clostridium difficile-related disease: evaluation and prevalence among inpatients with diarrhea in two freestanding rehabilitation hospitals. Arch Phys Med Rehabil. 1993;74:9–13.

Recommended Additional Reading

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Eltorai IM, Schmit JK, editors. Emergencies in chronic spinal cord injury patients. New York: Eastern Paralyzed Veterans Association; 2001.
Robertson D, Bigaaioni I, Burnstock G, et al. Primer on the autonomic nervous system. 3r ed. London: Elsevier; 2011.
Schweiger M. Method for determining individual contributions of voluntary and involuntary anal sphincters to resting tone. Dis Colon Rectum. 1979;22:415–6.
Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.
Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

Neurogenic Sexual Dysfunction in Spinal Cord Injuries

31

Sexuality is a universal and integral part of the human experience, both in good health and poor health, and persists in individuals well beyond reproductive years (Davidson and Phillips 2017). Sex is a person's most fundamental need, and it is also a highly personalized experience. Sexual drive and sex are the products of not only biological desires, but also a person's sexual experience and a harmonic integration of culture and spirit. Sexual dysfunction is a disorder in all facets of sexual activity and can occur in many ways in patients with disabilities. It ranges from the "low level" of altered function in the sexual organs to the "highest level" of person's trust. All medical expertise is based primarily on the medical mechanical problems of penile erectile and ejaculatory dysfunction. The main problems of sexual dysfunction occur only when the patient approaches. For people with spinal cord injuries, sexual function has been identified as a priority for recovery. Recovery of sexual function is extremely important and constitutes an area of unmet need for people with spinal cord injuries. It would be the highest priority for people with paraplegia and the second highest priority in people with tetraplegia after recovering arm and hand function (Anderson 2004; Kennedy et al. 2006). Sex is no longer considered as relatively unimportant for the majority of people with spinal cord injuries. Sexuality is a complex issue, and although we know our patients well, we often do not progress beyond the medical problem of erection, fertility, or contraception. For biologically effective sexual activity, an erection should occur with predictability, and vaginal lubrication based on adequate sexual arousal should facilitate comfortable sexual intercourse. While orgasm is not a prerequisite to a rewarding sexual experience, having a reliable orgasm with reliability after spinal cord injury is a bonus (Elliott 2006).

In general, sexual satisfaction decreases in people with spinal cord injuries (Alexander et al. 1993; Reitz et al. 2004). However, sexuality after spinal cord injury remains a central motivating factor in life (Reitz et al. 2004). The age group of the majority of spinal cord injury patients is a sexually active age, and sexual interest may be high, so sexual problems in patients with spinal cord injuries cannot be overlooked. As life expectancy after spinal cord injury increases, the importance in rehabilitation has gradually shifted to improving quality of life. To achieve this goal, the rehabilitation team must address issues related to sexuality during the acute and chronic phases of spinal cord injuries. Sexual dysfunction (sexual desire, genital arousal, orgasm, and pain with sex), change in sensation, and autonomic dysreflexia can be present in both sexes after spinal cord injury. Autonomic dysreflexia typically occurs in individuals with an injury at or above T6. Sexuality in spinal cord injuries, as well as the medical and neurogenic problems of the sexual organs, is associated with many components,

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including body control, trunks stability, and the presence of spasticity (Consortium for Spinal Cord Medicine 2010).

31.1 Neurophysiology of Sexual Responses

Erection is a neurovascular phenomenon that occurs under neurological-hormonal control. Sensory inputs from the eyes and skin refer to a certain area within the hypothalamus, where appropriate signals are relayed to the penis. The upper centers that regulate the erectile function in the brain are located in the cortex and the hypothalamus. The lower centers are located in the spinal cord. Erections can be psychogenic or reflexogenic. Depending on the source of their induction and the main affected erection center, the erection differs from reflexogenic and psychogenic ones. Normally, these two mechanisms are synergistic.

The psychogenic, sympathetic erection center is located at the T11–T12 to L2–L3 of the spinal cord, and the reflexogenic, parasympathetic erection center is located at the S2–S4 of the spinal cord. Psychogenic erections involve more complex pathways. Psychogenic erection that predominates in humans is the result of sexual desires from images, fantasies, and thoughts related to previous sexual experiences. In psychogenic erections, various visual, auditory, tactile, and/or imaginative afferent stimuli are processed through central pathways. Having traveled in different pathways, these fibers travel in the hypogastric nerve to reach the pelvic plexus, where the effect is integrated with parasympathetic function. The sympathetic nervous system, which works with the parasympathetic system, therefore plays an important role in psychogenic erection (Everaert et al. 2010). Reflexogenic erection results from somatesthetic stimulation and may be independent of sexual arousal. The parasympathetic erection center also contains somatic fibers. The afferents are the pudendal nerve, which carries sensory afferents from the genitals, and the efferent pathway is through the pelvic nerve (Fig. 31.1). The major neurotransmitter involved in parasympathetic stimulation is nitric oxide (NO). NO is released by parasympathetic stimulation to activate guanylyl cyclase to convert guanosine monophosphate (GMP) to cyclic GMP (cGMP), which acts as a potent vasodilator. Phosphodiesterase 5 mediates in reverting cGMP to GMP. A phosphodiesterase inhibitor (PDE5I) inhibiting this process has been developed and used as a therapeutic agent for erectile dysfunction. Ejaculation consists of emission and expulsion. Emission involves contractions of the internal reproductive organs, releasing their content into the prostatic urethra to form the semen. Expulsion is accompanied by a rhythmic contraction of the perineal muscles. Emission is controlled by TL innervation and receives inputs from the sacral pathway that activates the sympathetic splanchnic nerves synapsing in the celiac and mesenteric ganglia with the hypogastric nerves innervating the internal reproductive organs (Courtois and Cordeau 2022). The ejaculation phase is coordinated by a spinal generator of ejaculation (SGE) in the L3–L4 segments (Chéhensse et al. 2017; Truitt and Coolen 2002) to coordinate the events from the sensory inputs of erection to the intraspinal connections between the sacral and TL pathways to emission and expulsion (Borgdorff et al. 2008; Truitt and Coolen 2002).

The female sexual response has been classically described as having four phases: arousal, plateau, orgasm, and resolution. The arousal phase consists of clitoral erection, congestion of the labia majora and minora, and vaginal lubrication. These reactions are controlled by reflexes that are synaptically connected via the dorsal clitoral nerve in the S2–S4 with the parasympathetic preganglionic pelvic nerve, which runs through the utero-vaginal plexus, and synapsing with the postganglionic cavernous nerves (Fig. 31.2). Vaginal lubrication results from vasodilation and vasocongestion of the vaginal epithelium. This is followed by the plateau phase with maximal congestion of the clitoral structure and contraction of the suspensory ligament embedding the clitoral glans under its prepuce.

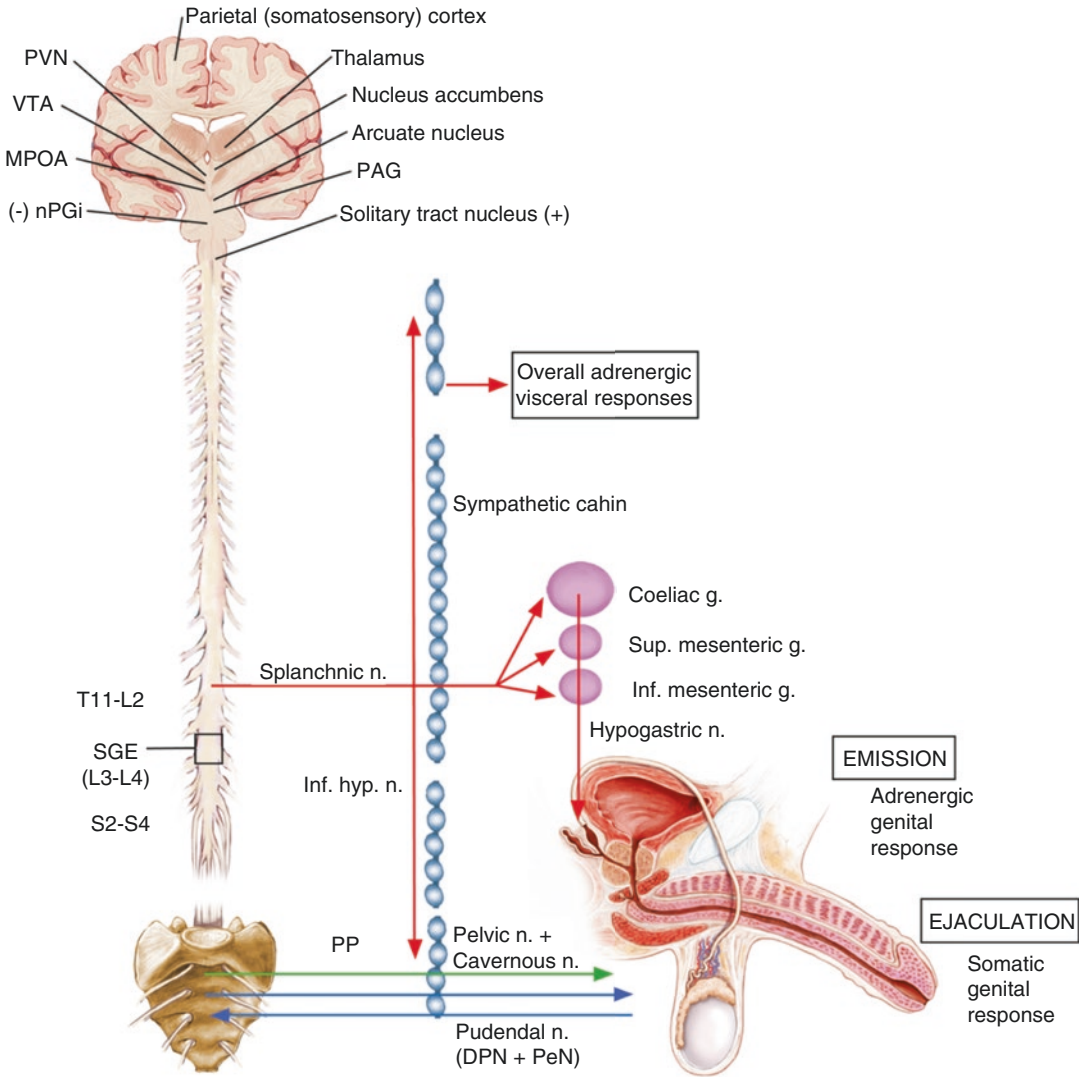

Fig. 31.1 Innervation of the male sexual organs. The sequence of events between erection, emission, and ejaculation is coordinated by the spinal generator of ejaculation (SGE) located in the L3–L4 of the spinal cord. *DPN* Dorsal penile nerve, *MPOA* medial preoptic area of the hypothalamus; *g.* ganglia, *hyp.* hypogastric, *Inf.* inferior, *n.* nerve, *nPGi* nucleus paragigantocellularis, *PAG* periaqueductal gray, *PeN* perineal nerve, *PP* pelvic plexus, *PVN* paraventricular nucleus, *sup.* superior, *VTA* ventrotegmental area. From Courtois and Cordeau (2022), with permission

Sexual arousal can also be activated by psychogenic stimuli that feed into the sacral pathway or synapse with the TL pathway, travel through the paravertebral sympathetic chain, and feed into the utero-vaginal plexus (Courtois and Cordeau 2022). It is believed that the neural pathways controlling climax in females are identical to emission and ejaculation, that is, involve the simultaneous activation of the hypogastric nerves and sympathetic chain.

Neural innervation associated with sexual function and sexual responses in men and women is summarized in Tables 31.1 and 31.2, respectively.

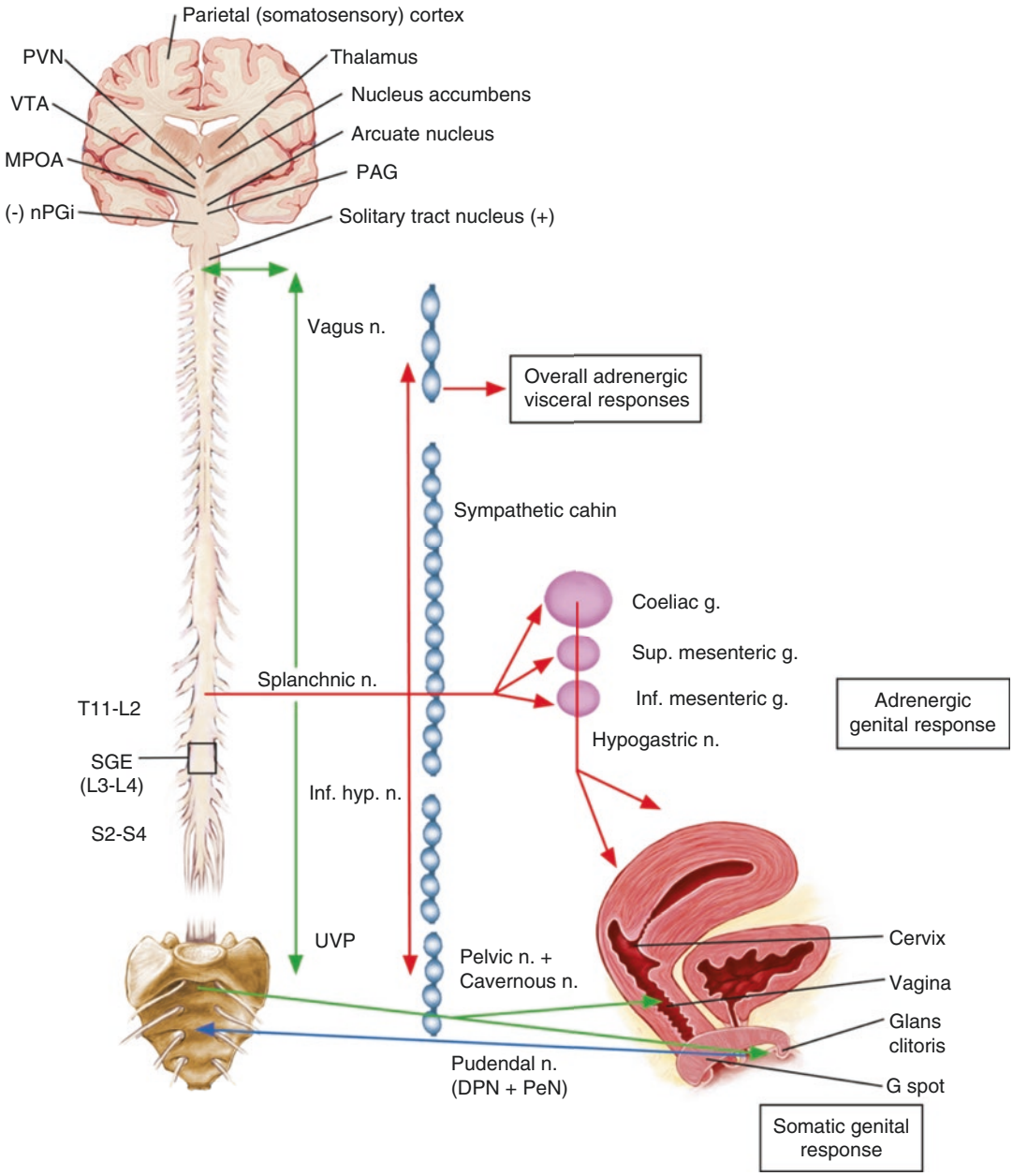

Fig. 31.2 Innervation of the female sexual organs. The spinal generator of ejaculation (SGE), which is also identified in females, may presumably participate in the coordination of events. *DPN* Dorsal penile nerve, *g.* ganglia, *hyp.* hypogastric, *Inf.* inferior, *MPOA* medial preoptic area of the hypothalamus, *n.* nerve, *nPGi* nucleus paragigantocellularis, *PAG* periaqueductal gray, *PeN* perineal nerve, *PVN* paraventricular nucleus, *sup.* superior, *UVP* uterovaginal plexus, *VTA* ventrotegmental area. From Courtois and Cordeau (2022), with permission

Table 31.1 Neural innervation of sexual function

Segments	Innervations	Nerves	Male responses	Female responses
S2–S4	Parasympathetic	Pelvic nerve	• Erection • Reflexogenic or psychogenic	• Genital arousal • Engorgement
T10–L2	Sympathetic	Hypogastric nerve	• Ejaculation • Psychogenic erection with conjunction of parasympathetic	• Psychogenic arousal • Lubrication

Table 31.2 Sexual responses in men and women

Physiologic changes	Male	Female
Genital arousal	• Erection • Increased blood flow to the penis • Decreased outflow from the penis • Erectile tissue relaxation	• Increased blood flow to the vagina and clitoris • Clitoral erection • Vaginal lubrication
Orgasm	• Ejaculation • Emission: contraction of ductus deferens, seminal vesicles, prostate, urethra • Expulsion: rhythmic contractions of perineal muscles and smooth muscles of the urethra	• Rhythmic contraction of the vagina, uterus, and anal sphincter

31.2 Physical Examinations and Assessment of Sexual Dysfunction in Spinal Cord Injuries

The physical examination shows clinical signs contributing to the diagnostic approach of erectile dysfunction. When examining the external genitalia, a neurological examination should also be included. The goal of the physical examination is to identify the level of lesion, depending on the sacral and the thoracolumbar origin of the nervous system of the external genital organs. Assessment of the sensation of the genitalia, the perineum, and the perianal region is essential for evaluation of the parasympathetic erectile center, as the somatic sensation of these areas is reflected in the S2–S4 segments of the spinal cord. By evaluating the reflex of the cremaster muscle (cremasteric reflex), we can evaluate the L1–L2 reflex arc. By evaluating the reflexes of rectus abdominis, we can evaluate the T9–T12 reflex arcs, and the bulbocavernosus reflex is suitable to evaluate the integrity of S2–S4 reflex arc (Vodusek 2003). The dartos reflex is a somatoautonomic reflex that depends on the sympathetic segment T11–L2. Intact dartos reflex arc reflects the integrity of the afferent and efferent branches of the genitofemoral nerve (T11–L2) (Soler et al. 2017; Yilmaz et al. 2006). In addition, deep tendon reflexes of the lower extremities can evaluate the lumbar and upper sacral segments of the spinal cord.

International Standards to Document Autonomic Function after Spinal Cord Injury (ISAFSCI), Second Edition, recommended measures of autonomic control of the sexual function: psychogenic arousal, reflex genital arousal, orgasm, and ejaculation (Wecht et al. 2021).

31.3 Psychological Considerations

With the direct effect of spinal cord injury on sexual response, other factors may have a significant effect on sexual function: pain, spasticity, difficulty positioning, impaired hand function, neurogenic bowel and bladder-related issues, and psychological/emotional issues related to depression, self-esteem, or relationships. Adaptation to spinal cord injury is a progressive process that extends over a longer period. Successful sexual adaptation is affected by many factors such as time of injury, quality of social support, physical

health, gender, and severity of the injury. To achieve satisfactory sexual adjustment, patients with spinal cord injuries must learn to use their new sexual abilities as opposed to the past.

After traumatic injury, people usually experience a period of reduced sexual drive and activity. Libido may not be affected by spinal cord injury, but can be reduced by depression, trauma of the injury, or medications. People with spinal cord injuries who have been injured for the first time may deny the importance of sexual problems. Others may be reluctant to discuss sexual matters for cultural or personal reasons. Other patients may have a period of sexual acts during rehabilitation, such as unacceptable sexually explicit language, inappropriate physical contact with staff, etc.

In acute rehabilitation phase, sensitive discussions about sexuality are appropriate. People with spinal cord injuries can learn about issues such as dating, efficiency, relationships, parenting, and physical appearance. Erection, lubrication, sensation, orgasm, ejaculation, fertility, and sexuality related to bladder and bowel function are other interesting topics. Although the patient does not engage in discussions about the sexual matters, it is important that the members of the rehabilitation team provide basic information (Elliott 2006).

A bladder or bowel accident can occur at any time during sexual activity or social events. The embarrassment, shame, and humiliation associated with incontinence cause excessive anxiety and are often considered as a major cause of social isolation or the termination of a relationship. To minimize unexpected incontinence, the bladder should be emptied before sexual activity. If Foley catheter presents, it can be taped to the side of the penis with a condom placed over the catheter. Women can have a sexual intercourse despite having a Foley catheter by taping the catheter to the abdomen. Despite the best management program, sexual stimulation can cause urinary and/or fecal incontinence. Fluids should be limited during the hours prior to sexual activity. Towels should be available to manage episodes of urinary or fecal incontinence.

31.4 Male Sexuality

31.4.1 Erection

Erectile and ejaculatory functions are complex physiological activities requiring interaction between the vascular, venous, and endocrine systems. Erections are controlled by the parasympathetic nervous system, while ejaculation is controlled by the sympathetic nervous system. In the simplest terms, erection is controlled by a reflex arc, which is mediated in the sacral spinal cord. The reflexes include afferent and efferent limbs. The afferent limb consists of somatic afferent fibers from the genital areas that enter the sacral spinal cord through the pudendal nerve. The efferent limbs are parasympathetic fibers derived from the sacral spinal cord. These fibers traverse the cauda equina and exit through the S2–S4 nerve roots. The postganglionic parasympathetic fibers secrete nitric oxide, which relaxes the smooth muscle of the corpus cavernosum and increases blood flow perfusion to the penile arteries. As a result, the penile vasculature is engorged with blood resulting in erection. This reflex is modulated by higher brainstem and subcortical and cortical centers. In addition, erectile function is affected by hormonal factors such as testosterone (Wespes et al. 2006).

31.4.2 Ejaculation

Ejaculation is the culmination of male sexual activity and is mainly controlled by the sympathetic nervous system. Similar to the sympathetic distribution of the bladder, the fibers come from the thoracolumbar spinal cord and into the sympathetic chain. These fascicles then travel through the splanchnic nerves into the hypogastric plexus. After synapses in the inferior mesenteric ganglion, postganglionic fibers travel through the hypogastric nerves to supply the vas deferens, seminal vesicles, and ejaculatory ducts in the prostate.

Ejaculation is a neurologically more complicated phenomenon and is based on the coordination of the sympathetic system (T11–L2), the

parasympathetic nervous systems (S2–S4), and the somatic nervous system through the pudendal nerve (S2–S5). Semen ejection is caused by rhythmic contraction of the urethral smooth muscle via the sympathetic innervation and ischiocavernosus and bulbocavernosus muscles of the somatic innervation.

31.5 Female Sexuality

The physiology of the female sexual activity has not been studied as the male sexual activity. Sexual satisfaction of women, however, depends on a complex interaction of the endocrine and nervous systems. Sexual arousal is the result of psychogenic and physical stimulation. This excitement manifests itself in vaginal lubrication and tension of the vaginal introitus. Stimulation of the genital region, including the clitoris, labia majora, and labia minora, causes afferent signals to travel through the pudendal nerve in the S2–S4 segments of the spinal cord. These fibers interact with efferent parasympathetic fibers that project through the pelvic nerve. As a result, the arteries of the perineal muscles dilate, and the vaginal introitus is tightened. In addition, the parasympathetic fibers cause Bartholin's glands to secrete mucus to aid vaginal lubrication.

Female orgasm is characterized by the rhythmic contraction of the pelvic structures. Female orgasm also leads to cervical dilatation, which can promote sperm transport and fertility.

31.6 Erectile Dysfunction and Management

The cause of erectile dysfunction in men with spinal cord injuries is varied. Although erection is the result of physiologically parasympathetic innervation of the penis, many other factors, including vascular dysfunctions, medication, depression, or stress, can contribute to erectile dysfunction. Psychogenic erections are usually preserved in patients with spinal cord injuries below L3. Reflexogenic erections are usually not possible in patients with S2–S4 injuries due to damage of lower motor neurons (Konstantinidis 2012).

Men with upper motor neuron lesions usually preserve reflexogenic erections with a minimal capacity for psychogenic erections. More than 90% of men with complete and incomplete upper motor neuron lesions can achieve reflexogenic erections, but less than 10% in men with complete upper motor neuron injuries and 50% of patients with incomplete upper motor neuron lesion can achieve psychogenic erections (Jones et al. 2008). Although the majority of men with upper motor neuron lesions are able to obtain reflexogenic erections, they are often poorly sustained and often not rigid enough to achieve successful intercourse. In patients with complete lower motor neuron lesions, 12% can achieve reflexogenic erections, and about 25% achieve psychogenic erections (Jones et al. 2008).

All patients with erectile dysfunction require general considerations regarding blood pressure, lipid profile, hormonal status, diabetes mellitus, medications (antispasmodics, antidepressants, and antihypertensives), and stopping of smoking. On the other hand, most of the patients with spinal cord injuries are young men with active sexual function before they are damaged, and the cause of erectile dysfunction is mostly neurogenic. These patients sometimes have a psychogenic component and rarely have other organic causes such as vascular insufficiency.

There are several treatment options available to treat erectile dysfunction, including oral phosphodiesterase 5 (PDE-5) inhibitors, vacuum erection devices, intraurethral alprostadil, vasoactive intracavernosal injections, and penile implants. The first line of treatment includes oral PDE-5 inhibitors and vacuum devices. In the second line of treatment, there are penile injections and transurethral application of vasoactive substances. Finally, there is the implantation of penile prosthesis in the third line of treatment (Ramos and Samso 2004).

31.6.1 Phosphodiesterase Type 5 (PDE-5) Inhibitors

The first-line treatment usually consists of oral phosphodiesterase inhibitors that utilize the nitric oxide-cGMP (cyclic guanosine monophosphate) pathway. This pathway relaxes cavernosal smooth muscle allowing for increased blood flow and thus inducing erection. Sildenafil (Viagra®), tadalafil (Cialis®), and vardenafil (Levitra®) have been shown to be comparably effective and satisfactory in the treatment of erectile dysfunction in men with spinal cord injuries (Rizio et al. 2012). The overall efficacy was similar for all the drugs (85% for sildenafil, 74% for vardenafil, and 72% for tadalafil). The duration of erections was also similar for all (26–34 min). The higher dose of the drug was required in 45% in the group of sildenafil, compared with over 70% of the patients in the other two groups (Konstantinidis 2012). About 50% of men with complete lesions needs >50 mg, whereas only one-third of men with incomplete lesions need to increase the dose of the drug (Schmid et al. 2000).

Tadalafil is more effective than sildenafil, especially for patients with lower motor neuron lesions (Del Popolo et al. 2004). Spinal cord injury usually requires higher dosages than in the general population. PDE5 inhibitors should be avoided in patients with retinitis pigmentosa and concomitant use of nitrates and alpha blockers (Hough et al. 2020). Contraindications for PDE-5 inhibitors are not different from those in able-bodied men. However, men with autonomic dysreflexia due to spinal cord injury tend to be treated with nitrates, so special advice should be given not to use these drugs to avoid severe complications (Giuliano et al. 2007). It is contraindicated in patients taking nitroglycerin. In addition, when using the antihypertensive agent because of autonomic dysreflexia, be sure to use PDE-5 inhibitors within 48 h, and in the elderly, the residual efficacy of PDE-5 inhibitors persists for 72 h.

Men with tetraplegia or high-level paraplegia should be advised the possibility of postural hypotension several hours after administration. These drugs are rapidly absorbed after oral administration and taken approximately 60 min before the expected sexual activity. They are most effective for men who are able to achieve reflex erections. Intracorporeal injections produced a more rigid erection, but sildenafil appeared to be more satisfactory than intracorporeal injections and vacuum constriction devices.

31.6.2 Intracavernosal Injections

The injection takes place between the 1st and 3rd or between the 9th and 11th hours of the penile shaft. A gentle massage of the area helps to absorb the medication. The erection starts 5–10 min later, and it is independent of sexual arousal. Patients with spinal cord injuries are more likely to have priapism, possibly due to excessive release of neurotransmitters that promote erection or due to sympathetic hypertonia. For these reasons, low doses of vasoactive drugs are used at the beginning of the treatment, and the dose is titrated for each patient. The overall rate of men with satisfactory erections in a meta-analysis of other studies was 90% of the users of intracavernosal injections (Deforge et al. 2006). Intracorporeal injections of prostaglandin E1 (alprostadil), papaverine, phentolamine, or a combination of these agents (often referred to as bi-, tri-, or quad-mix) can induce an erection at rates of up to 90% in the upper motor neuron and lower motor neuron lesions. Side effects include hypotension, hemorrhage, bruising, injection site pain and fibrosis, and priapism (Monga et al. 1999). Initially, patients received low doses of the pharmacological agent, and the dose is increased until a satisfactory erection is achieved for intercourse. Sometimes, a mixture of the agents is prescribed. Erections should not last longer than 4 h. Self-administration may be difficult with poor hand function.

Priapism is a long-lasting erection induced by PDE-5 inhibitors or intracavernosal injection and is more common in patients with spinal cord injuries than in the general population. If the erection lasts more than 2 h, the patient needs an urgent treatment. The treatment is done using an 18G needle into the corpora cavernosa and removing

the blood and perfusing with physiological saline. If the erection persists, 10–20 mg of epinephrine mixed with 1 mL saline is injected into the corpora cavernosa. There is a risk of increased blood pressure or autonomic dysreflexia during the procedure.

31.6.3 Vacuum Erection Device

The vacuum device is a cylinder with an open edge. The penis is placed through the open edge inside the device. When pumping, the inside of the cylinder becomes a vacuum. The negative pressure causes the blood to fill the corpora cavernosa, causing an erection. After erection, a ring that is tightly placed around the base of the penis is required for maintaining the erection. The higher complication rate of vacuum device in men with spinal cord injuries has to do with the absence of sensations in the area, so that a very tight ring that remains for a long time can cause tissue ischemia and necrosis without any pain or discomfort. The tension ring should not be left on for longer than 30 min. The appropriate advice for the users using the device is to observe the general use of the product and to avoid the very high negative pressure and the long-lasting strangulation of the penile shaft. Satisfaction with the use of the vacuum device is lower than expected (Denil et al. 1996). Individuals who use a vacuum device report that the base of the penis looks weak despite the rigid penile shaft. Petechiae and premature loss of erection (venous leak) have been reported.

31.6.4 Intaeurethral Alprostadil (Medicated Urethral System for Erection, MUSE)

The communication between the corpora cavernosa and the corpus spongiosum has been the basis for the application within the urethra of vasoactive drugs. Alprostadil (PGE1) was used for this purpose. The method of action is the same as intracavernosal injections without needles and punctures. There is an applicator which brings the drug into the urethra. In patients with spinal cord injuries, the outcome was not as satisfactory as using intracavernosal injections (Bodner et al. 1999). It is often less effective in patients with complete spinal cord injuries.

31.6.5 Penile Prosthesis

1. Infection, extruded rods, erosion, and pain are possible side effects of penile prosthesis. Removal of the penile prosthesis damages the cavernosal bodies, so intracavernosal injection or PDE5 inhibitors are usually not effective.

31.7 Sexual Arousal in Males and Females with Spinal Cord Injuries

Even though the quality or sustainability of erections is often compromised, more than 80% of men can regain some erectile function after spinal cord injury within 2 years after injury. The effects of spinal cord injury on sexual function can be understood based on the neurophysiology. A complete spinal cord injury affecting the sacral S2–S4 level leads to loss of reflexogenic erection in men. Reflexogenic erections are spared in spinal cord injury above the sacral level. Reflexogenic erections, which require the integrity of parasympathetic erectile center (S2–4), have been observed in people with spinal cord injuries. These arise after irritation of the skin or mucosa below the level of the lesion. Manipulations, such as rubbing of the thighs or nipples, squeezing of the glans, suprapubic percussion, and irritation of the anal region, proved to be more effective than masturbation or any other stimulation of the genitalia (Derry et al. 2002; Monga et al. 1999; Saenz de Tejada et al. 2005). Psychogenic erections are generally absent in spinal cord injury at T10 or above but are often preserved with injury below T10–L2. Similar generalizations also apply to the effect of spinal cord injury on reflexogenic and psychogenic lubrication in women (Table 31.3). In women, the arousal phase of sexual response is

Table 31.3 Sexual reactions of men and women dependent on the neurological level of spinal cord injury

Sexual responses		Neurological level of injury				
		Above T10	T10–T11	T12–L1	Conus medullaris	Cauda equina
Male	Psychogenic erection	Absent	Partial	Partial	Present	Present
	Reflex erection	Present	Present	Present	Present/absent	Absent
	Ejaculation	Possible	Without control	Partial	Absent	Absent
	Sensory of testis	Absent	Absent	Partial	Present	Present
Female	Psychogenic lubrication	Absent	Partial	Partial	Present	Present
	Reflex lubrication	Present	Present	Present	Present/absent	Absent

characterized by lubrication of the vagina; swelling of the clitoris; increases in heart rate, respiratory rate, and blood pressure; facial flushing; and other symptoms and signs. In women with complete UMN injuries affecting the sacral segments, the ability for reflex, but not psychogenic, lubrication should be maintained. Women with incomplete UMN injuries affecting the sacral segments are believed to be able to maintain reflex lubrication and psychogenic lubrication (Bérard 1989).

Lesions higher than T11 level are combined with erection of both corpora cavernosum and corpus spongiosum, while lesions below this level exclude the participation in the erection of the corpus spongiosum (Biering-Sorensen and Sonksen 2001). This erection (reflexogenic erection only, with no psychogenic erection) is usually sufficient for penetration, but it has short duration. Reflexogenic erections are maintained in 95% of patients with all injuries over the sacral center, while this percentage is up to 25% in lower level lesions. Reflex genital arousal has been associated with preservation of intact reflex function such as bulbocavernosus reflex and anal reflex in the S2–S4 dermatomes. Incomplete spinal cord injury patients have a greater incidence of reflexogenic and psychogenic erections and ejaculation in men and genital lubrication and orgasm in women.

Psychogenic erections were observed in 60% of patients with intact sympathetic erectile center (T11–L2) and lesion below the L2 level. Sensory preservation of T10–L2 dermatomes is associated with preservation of psychogenic arousal, as indicated by genital engorgement in women and erections in men. Psychogenic erections, as mentioned above, are independent from direct physical stimulation and are the result of visual or acoustic stimuli, dreams, fantasies, or memories. These erections are usually of poor quality and of short duration. Objectively, it is more of a swelling of the penis rather than a hard erection, which rarely allows penetration (Chapelle et al. 1980; Courtois et al. 1999; Derry et al. 2002; Smith and Bodner 1993). A mixed erection occurs when the spinal cord injuries are between the two centers. These erections occur after a psychological stimulus and are sustained or even are intensified by a physical stimulus, or they are prolonged reflexogenic erections that are enhanced by a strong sexual desire.

Nocturnal erections have also been recorded in men with spinal cord injuries. These erections usually occur during the REM phase of sleep. The comparison between the erections of tetraplegics and paraplegics showed that tetraplegic men had better erections than paraplegic patients in terms of hardness and duration. In addition, thoracic spinal lesion is associated with poor nocturnal erections comparing with cervical spinal injuries (Suh et al. 2003). Patients with lesions above the T6 level often present the phenomenon of autonomous dysreflexia, which involves reflecting increased sympathetic tone at the level below the lesion.

Men and women with spinal cord injuries often have no sensation in traditional erogenous areas such as the genitals and nipples. Stimulation of these areas can result in penile erections or vaginal lubrication, but not necessarily sexual pleasure. However, other areas that are not normally recognized as erogenous areas, such as the ears, eyelids, and neck, can be excited to become sexually aroused (Elliott 2006). Some people find that the skin surfaces at or around the neurological level have increased tactile sexual response.

Overall, the ability to spontaneously ejaculate after spinal cord injury is less than 10% of men with complete spinal cord injury. Ejaculation in men with complete spinal cord injury above T10 is rare. Ejaculation can occur in up to 20% of men with complete spinal cord injuries below T10 level, usually in patients with preserved psychogenic erection. Positive signs of the ability to ejaculate after spinal cord injury, either by self or partner stimulation, include incomplete injury, degree of genital sensation, voluntary anal control, and the presence of a strong bulbocavernosus reflex.

31.7.1 Sexual Dysfunction in Males with Spinal Cord Injuries

For men with spinal cord injuries, there may be reflexogenic or psychogenic erections. Reflexogenic erections are secondary to manual stimulation of the genital region. Psychogenic erections lead to a cortical modulation of the sacral arc resulting from erotic stimuli. Generally, erections with incomplete injuries are more likely than complete injuries. Sometimes, men with spinal cord injuries can only maintain an erection while the penis is stimulated and the quality of the erection is insufficient for satisfactory penetration. Therefore, the erection must be augmented with medications, devices, or a penile implant to satisfy the sexual function.

Ejaculation is a more complicated neurological process and is more profoundly affected by spinal cord injury. Coordinated efforts of the sympathetic, parasympathetic, and somatic nervous systems result in ejaculation (Benevento and Sipski 2002). The ability to ejaculate is less common than an erection. The ejaculation rate varies according to the neurological level of injury and nature of the neurological injury. Men with all levels of spinal cord injury can ejaculate in 12–15%. The ejaculation rate in complete upper motor neuron lesions is estimated to be 20%. Despite difficulties with ejaculation, up to 42% of men with various levels and completeness of spinal cord injury have reported orgasm (Alexander et al. 1993). In the cases of incomplete upper motor neuron lesions, the ejaculation rate is estimated to be slightly higher at 32%. Many men who are able to ejaculate experience retrograde ejaculation into the bladder. Some people may experience dribbling of semen. The experience of orgasm in men with spinal cord injuries is variable. Some persons describe a primarily emotional event. Others experience generalized muscle relaxation or a pleasant feeling in the pelvis or at the sensory level. Other men report that the orgasm after the injury no longer exists.

31.7.2 Sexual Dysfunction in Females with Spinal Cord Injuries

In women with spinal cord injuries, there are a number of physical and psychological barriers to sexual activity due to spasticity, bladder management with fear of incontinence, low self-esteem, difficulty meeting a partner, and a lack of confidence in sexual abilities and abilities to satisfy a partner (Anderson 2004; Kreuter et al. 2011).

Most women with spinal cord injuries can achieve some vaginal lubrication. This lubrication can be mediated by reflexogenic or psychogenic factors (Sipski et al. 1995a). Individuals with incomplete upper and lower motor neuron injuries are more likely to have satisfactory lubrication. If vaginal lubrication is not satisfactory, a water-soluble lubricant can be used. Sildenafil may be beneficial for women with spinal cord injuries by increasing perineal blood flow and increasing vaginal lubrication. Genital arousal in women can be achieved through psychogenic or reflexogenic pathways and is decreased in 25–50% women with spinal cord injuries (Sipski 1991a; Sipski et al. 2001). Reflex genital arousal in manual genital stimulation is associated with intact reflex function in the S2–S4 dermatomes (Anderson et al. 2007). In women with complete spinal cord injuries above T6, psychogenic arousal can occur in the absence of genital vasocongestion. About 50% of women report development of a new area of arousal above the level of injury, including the head, neck, and torso (Komisaruk et al. 2004). It is believed that the

vagus nerve may serve as a genital sensory pathway that bypasses the spinal cord and transmits afferent vagino-cervical activity that can lead to orgasm (Sipski et al. 1997; Whipple and Komisaruk 1997).

Spared pin prick sensory function in the T11–L2 dermatomes in women with spinal cord injuries has been associated with the ability to have psychogenic genital vasocongestion (psychogenic arousal) and a greater degree of genital responsiveness than patients with minimal or no sensory preservation in those dermatomes (Sipski et al. 1995a; Sipski et al. 1997).

Most women with spinal cord injuries report the ability to have penetrating sexual intercourse. Factors that interfere with sexual intercourse are level of injury, pain, spasticity, and autonomic dysreflexia during sexual activity (Whipple and Komisaruk 1997). More than 50% of women with spinal cord injuries have frequent sexual activities, and almost half of all women with spinal cord injuries can achieve orgasm, even if the time required for orgasm is prolonged compared to women without spinal cord injuries (Sipski et al. 1995b). The ability to reach orgasm is associated with the presence of genital sensation and spasticity. Women with intact bulbocavernosus and/or anal reflexes usually have an orgasm, while women without S2–S5 sensation or bulbocavernosus and anal reflexes (lower motor neuron lesions) decrease significantly.

31.8 Cardiovascular Responses Associated with Sexual Activity in Spinal Cord Injuries

Cardiovascular autonomic function plays a crucial role in enabling sexual activity and determining sexual function. In addition, it increases blood flow to the cavernous tissue to enable physical sexual intercourse and has an integrated function in determining muscle activity according to genital arousal and exercise intensity related to sexual activity. In people with spinal cord injuries, the autonomic function is changed to varying degrees. Therefore, autonomic dysreflexia, low resting blood pressure, and orthostatic hypotension can be barriers or consequences of sexual behavior.

Sexual activity in the general population found moderate increases in heart rate and systolic and diastolic blood pressure, approximately 2–4 METs of metabolic demand (Bohlen et al. 1984; Palmeri et al. 2007). The peak blood pressure occurs at the beginning of orgasm plateau and falls to the baseline level 10 min after orgasm (Xue-Rui et al. 2008). Cardiovascular response to sexual activity in people with spinal cord injuries is more difficult to predict and shows more unstable pattern than in the general population. People with lesions above T6 are more susceptible to episodes of autonomic dysreflexia, and sexual stimulation can be a potent trigger for this phenomenon (McBride et al. 2003). Interestingly, the self-stimulation showed no typical autonomic dysreflexia in spinal cord injuries above T6 (Sipski et al. 2006).

31.9 Fertility in Patients with Spinal Cord Injuries

31.9.1 Male Fertility

Male infertility after spinal cord injury is characterized by erectile and ejaculatory dysfunction as well as low semen quality (Brackett et al. 2010). Deterioration of semen characteristics occurs very early after spinal cord injury (Das et al. 2006) and mainly affects sperm motility and viability (Patki et al. 2008). The majority of men with spinal cord injuries cannot ejaculate during sexual intercourse with successful ejaculations in approximately 5% of men with complete upper motor neuron lesion and 18% of those with lower motor neuron lesions (Colpi et al. 2004; Sonksen and Ohl 2002). Successful ejaculation rates are higher in people with incomplete injuries.

Most men with spinal cord injuries have difficulty in conceiving children without some assistance, with less than 10% of couples achieving successful spontaneous pregnancies (Alexander et al. 2017; Brown et al. 2006). Retrograde ejaculation, repeated urinary tract infections, and

altered testicular temperature may contribute to infertility. Men with spinal cord injuries have been shown to have adequate numbers of spermatozoa but abnormally low sperm motility and viability (Aikman et al. 2018; Ibrahim et al. 2016). The causes of decreased motility and viability of sperm after spinal cord injury are still controversial (Ibrahim et al. 2016). In patients with spinal cord injuries, the frequency of retrograde ejaculation is high because the bladder neck does not close properly. Adrenergic agonists such as midodrine or pseudoephedrine may also be used to reduce retrograde ejaculation if necessary (Dimitriadis et al. 2010).

Spermatogenesis and epididymal function are sensitive to temperature, and prolonged sitting in a wheelchair can lead to increased scrotal temperature and thus to dyspermia (Brindley 1982). However, men with ambulatory spinal cord injuries also have poor sperm quality. It is therefore unlikely that an elevated scrotal temperature after spinal cord injury contributes to dyspermia (Brackett et al. 1994). The seminal fluid of men with spinal cord injuries may even be toxic to sperm as it can inhibit the sperm motility of fertile men. In addition, the abnormal sperm transport and storage due to autonomic nervous system dysfunction (mainly sympathetic) following spinal cord injury may also contribute to dyspermia (Patki et al. 2008).

Due to the ejaculatory dysfunction, over 90% of men with spinal cord injuries require assisted ejaculation to obtain a sperm sample (Brackett et al. 2010). To get sperm in men who do not ejaculate, penile vibratory stimulation and, if this fails, electroejaculation can be attempted. Penile vibratory stimulation is the first-line method for assisted ejaculation, followed by transrectal electrical stimulation for nonresponders. The combined success rate of these two methods is between 80 and 90%. Penile vibratory stimulation consists of placing a vibratory on the dorsum or frenulum of the glans penis, and the mechanical stimulation by the vibration generates the ejaculatory reflex to induce ejaculation (Bird et al. 2001; Kafetsoulis et al. 2006). This method is more effective in men with a level of injury T10 or above as compared to men with a level of injury T11 or below (Bird et al. 2001). Penile vibratory stimulation can induce autonomic dysreflexia. The majority of responders will ejaculate within 2 minutes of starting the stimulation. Electroejaculation can be used in people who do not respond to penile vibratory stimulation and applies electric current delivered through a probe placed into the rectum, which stimulates nerves leading to semen emission.

There are several surgical techniques that can be used to obtain sperm if above methods are unsuccessful. These include testicular sperm extraction, testicular sperm aspiration, microsurgical epididymal sperm aspiration, percutaneous epididymal sperm aspiration, and aspiration of sperm from the vas deferens. Once the ejaculate is obtained from the male, determination of the total sperm count and quality is undertaken. Depending on the sperm count and viability, there are different options for intravaginal insemination (IVI) and/or intrauterine insemination (IUI) or in vitro fertilization (IVF). If conventional method of IVF is not sufficient because of insufficient motility of the sperm to attempt fertilization, an intracytoplasmic sperm injection (ICSI), a single sperm injection into a single egg, can be performed.

31.9.2 Menstruation, Birth Control, and Female Fertility

31.9.2.1 Menstruation

A spinal cord injury does not affect fertility in women returning from menstruation. Immediately following spinal cord injury, amenorrhea occurs in 85% of women with cervical and high thoracic injuries and 50–60% women overall. It is thought to be a temporary increase in prolactin, and a recurrence of ovulation can be demonstrated (Reame 1982). Amenorrhea that lasts between 3 and 24 months has been reported among women with spinal cord injuries (Bughi et al. 2008; Jackson and Wadley 1999). Within 6 months and 1 year after injury, 50–90% of women return to their menstruation. The completeness of injury does not affect the menstrual cycle. Women with spinal cord injuries have menopause at the same

age as women without spinal cord injuries. When normal menstruation returns, women with spinal cord injuries may become pregnant with similar success rates as the general population (Craig 1994; Nygaard et al. 1990; Smeltzer 2007).

31.9.2.2 Birth Control

Birth control methods should be consulted with a gynecologist, including risk of thromboembolism compared to the benefits of each option. The risk of thromboembolism in oral contraceptive may increase in recumbent individuals. It should be remembered that medications such as antibiotics can reduce the efficacy of contraceptives. Oral contraceptives containing only progesterone are safer than medications containing both estrogen and progesterone. If the risk of thromboembolism is high, estrogen-based contraceptives should not be used. Progesterone preparations usually have a lower risk of thrombosis. Progesterone-only pills, transdermal patches, and intramuscular medroxyprogesterone injections might be preferable alternatives, although all hormonal forms of contraception have well-described side effect profiles (Pereira 2003). Oral contraceptive pills and hormonal preparations must be avoided in women within 1 year of injury, those who smoke, and those who have a history of cardiovascular issues (Hough et al. 2020).

Contraceptive sponges, cervical caps, and diaphragms can be difficult for patients to insert without assistance. Intrauterine device (IUD) is generally not recommended and is associated with an increased incidence of pelvic inflammatory disease. Untreated pelvic inflammatory disease can lead to autonomic dysreflexia. In addition, women with spinal cord injuries may not be aware that the device has been moved from the cervix.

31.9.2.3 Preconceptual Consideration

In women with spinal cord injuries, fertility is not impaired. Spinal cord injury has many potential effects on female sexuality, including changes in self-image, decreased sensation, and physical limitations. Despite these challenges, many women resume sexual activity after spinal cord injury (Jackson and Wadley 1999; Sipski 1991b). Preconceptual counseling is important for women with spinal cord injuries considering having a child. The following checklist provides an overview of the important aspects to be considered preconceptually and during pregnancy (Bertschy et al. 2020): (1) neurological, psychological, and orthopedic stability; (2) review and pause medication if necessary; (3) substitute folic acid (4 mg per day); (4) check urinary and bowel management; and (5) check for implants.

31.9.2.4 Medication Control

Medications should be carefully controlled with regard to the safety of the fetus (Table 31.4). Most of the anticonvulsants and commonly used medications in spinal cord injuries, including baclofen, are not safe for the fetus and should not be used (Mitra et al. 2015). However, for patients with severe autonomic dysreflexia or severe spasticity, it may be used with caution with the consent of the patient. A special awareness of the dangers of tobacco and alcohol is also needed. Women with spinal cord injuries are at greatest risk of anemia during pregnancy. If the hemoglobin level is less than 9 gm/dL, take an iron medicine. However, iron may aggravate constipation and cause autonomic dysreflexia. Anemia also increases the risk of pressure injuries. Anemia should be treated before birth to avoid blood transfusions during the delivery process. If anticoagulation is necessary, use heparin or low-molecular-weight heparin or an IVC filter. Warfarin is thought to have crossed the placenta and may cause congenital anomalies (Greer 1999).

There is no reliable data on the prescription of anticholinergics to pregnant women with spinal cord injuries. These drugs should be avoided in the first trimester. Intramuscular botulinum toxin injections into the detrusor muscles before pregnancy can be an option to compensate for the lack of bladder-relaxing effect of anticholinergics or antimuscarinics (Bertschy et al. 2020). A 200 U botulinum toxin A injection into the detrusor is an officially approved therapy for spinal cord injury below the cervical spinal cord beyond pregnancy. There is still an off-label use for cer-

Table 31.4 Effects on pregnancy and lactation of commonly used medications in women with spinal cord injuries

Medication	Pregnancy effects	Lactation effects
Baclofen	• Teratogenesis: no data in human, some abnormalities detected in animal models	• 0.1% of maternal dose in milk
Dantrolene	• Little data exists; has been given without adverse effects in the peripartum period to prevent malignant hyperthermia	• No data
Diazepam	• Teratogenesis—facial clefts in animals; no good evidence of anomalies but not in humans • Fetal—third trimester chronic use associated with floppy infant syndrome and diazepam withdrawal syndrome • Neurobehavioral—effects noted in rats but not in humans	• Diazepam can accumulate in breast-fed infants as well • Repeated use in nursing mothers is not recommended • Relatively contraindicated, short-term use only
Tizanidine	• Slowed development in animal studies • No human information	• It is possible, yet unknown, where this drug accumulates in breast milk
Oxybutynin	• Teratogenesis—anomalies seen in animals given doses toxic to the mothers	• Should not be used
Prazosin	• Teratogenesis—not seen in animals; fetal and maternal toxicity at high doses in animals • Fetal—used with apparent safety for hypertension in few patients	• Accumulates to a small amount in breast milk
Ciprofloxacin	• Fetal—arthropathy in animals; use not recommended in pregnant women	• Recently considered compatible with breastfeeding
Nitrofurantoin	• No animal or human abnormalities reported	• Approved for use during breastfeeding
Ampicillin	• No abnormalities reported	• Compatible with breastfeeding
Trimethoprim-sulfamethoxazole	• Some abnormalities in animals, but none reported in humans • Do not use near delivery due to risk of serious jaundice	• Can use during breastfeeding except when baby is premature, jaundiced, or G6PD deficiency
Gabapentin	• No information available	• Unknown whether and to what degree it is found in breast milk
Calcium channel blockers (Nifedipine)	• Some abnormalities in animals	• Compatible with breastfeeding

vical spinal cord injuries. The effect of botulinum toxin A on the bladder lasts 6–9 m. Therefore, the overactivity of the detrusor can be adequately suppressed, at least for part of the pregnancy (Bertschy et al. 2020; Yuan et al. 2017).

Drugs used to reduce spasticity are among the most commonly used drugs in spinal cord medicine. Due to serious side effects of baclofen, tizanidine, dantrolene, and diazepam, these substances are not recommended during pregnancy and should only be used in exceptional situations. Diazepam can be used in the short term for select individuals, but increases the risk of floppy infant syndrome (Bertschy et al. 2020).

Pregabalin and gabapentin are mainly used to treat neuropathic pain. There are insufficient data on the use of these substances in pregnant women. However, the use of pregabalin reported an increased risk of severe malformations. The use of pregabalin should only be considered if the potential benefit to the mother is significantly higher than the potential risk to the fetus (Bertschy et al. 2020). During pregnancy, paracetamol is considered the analgesic and antipyretic of first choice. To avoid the risk of hepatotoxicity, the maximum daily dose should not exceed 4 gram. Among NSAIDs ibuprofen and diclofenac can be used in the first two trimesters. However, they are contraindicated in the last trimester because of the possibility of premature closure of the ductus arteriosus. Fetal renal failure and oligohydramnios are commonly reported complications resulting from the use of all

Table 31.5 Differential diagnosis of autonomic dysreflexia during labor vs. preeclampsia

	Autonomic dysreflexia	Preeclampsia
Lesion level	Often above lesion level T6	Independent of lesion level
Blood pressure	Attacking and extremely intensive	Slowly increasing
Heart rate	Bradycardic or tachycardic	Mostly normofrequency
Symptoms	Synchronous with uterine contractions	Independent of uterine contractions
Urine dipstick	Positive for norepinephrine[a]	Positive for protein
Uric acid, liver functions, platelets	Normal laboratory values	Elevated uric acid or lover functions, decreased platelets
Proteinuria	No	Yes (>300 mg/24 h)
Clinical observation	Flushing, sweating, pounding headache, and increased reflexes	Edema, continuous headache, flickering vision, pain in upper abdomen, and increased reflexes
Serological peculiarities	Atypical	Possible, for example, with HELLP (hemolysis, elevated liver enzymes, low platelets, uric acid↑, transaminase↑, thrombocyte↓, and haptoglobin↓)
Treatment	Remove offending stimulus, acute antihypertensive therapy	Intravenous $MgSO_4$

From Bertschy et al. (2020) and Pereira (2003), with permission
[a]Not helpful in acute setting

NSAIDs in the last trimester (Bertschy et al. 2020).

Antibiotic therapies for urinary tract infections are often required during pregnancy in women with spinal cord injuries. Due to the increased risk of multidrug-resistant germs, a urine culture should always be collected and a susceptibility test initiated before starting antibiotic treatment. The decision to initiate an antibiotic therapy must always be strict and tailored to the individual. Beta-lactam antibiotics should be the first choice and nitrofurantoin the second, but the latter should not be used in the third trimester (Bertschy et al. 2020).

31.9.2.5 Pregnancy, Labor, and Birth

Pregnancy presents potential problems, including development of pressure injuries, recurrent urinary tract infections, increased spasticity, decreased lung function, leg edema, constipation, and other biomechanical issues (Hough et al. 2020). Preterm labor rates are slightly increased in women with spinal cord injuries (Camune 2013; Pereira 2003). Because uterine innervation is between T10 and T12, patients with lesions above T10 may not be aware of uterine contractions or fetal movements. Autonomic dysreflexia may develop during labor (Baker and Cardenas 1996; McGregor and Meeuwsen 1985). Preeclampsia can be difficult to distinguish from autonomic dysreflexia during labor (Bertschy et al. 2020; Pereira 2003) (Table 31.5). Recognition and prevention of autonomic dysreflexia during labor and delivery in women with spinal cord injuries are critically important. Autonomic dysreflexia usually occurs in association with uterine contractions. However, if the autonomic dysreflexia is diagnosed, epidural anesthesia is the treatment of choice and should be continued at least 12 h after delivery or until autonomic dysreflexia is resolved. The spinal cord injury physician should closely support the patient in cooperation with the obstetrician (Ghidini and Simonson 2011). Because of the high risk of premature labor, the cervical dilatation and prenatal care should be monitored from 28 weeks of pregnancy. A number of changes related to pregnancy can lead to a loss of independence. Worsening spasticity of the abdominal or adductor muscles, reported by one-fifth of women with spinal cord injuries who experience pregnancy, in addition to the weight gain and carpal tunnel syndrome that are common during

pregnancy even in women without spinal cord injuries, may lead to difficulty in transferring or propelling a wheelchair at the end of pregnancy in up to half of women with spinal cord injuries (Ghidini et al. 2008; Jackson and Wadley 1999). During the second and third trimester, pregnant women may have difficulty in performing functional tasks previously completed independently. Transfer may require the assistance of a caregiver, and a power wheelchair may be necessary for mobility. Possible health conditions and their management during pregnancy of women with spinal cord injuries are summarized in Table 31.6.

The spontaneous vaginal delivery rate was reported in 37%, with an additional 31% of deliveries by assisted vaginal deliveries, the remaining

Table 31.6 Possible health conditions and their management during pregnancy in women with spinal cord injuries

	First trimester	Second trimester	Third trimester	Management
Vegetative	Autonomic dysreflexia	Autonomic dysreflexia	Autonomic dysreflexia	Elevate upper body
				Eliminate trigger stimulus
				Antihypertensives
Bladder	Urinary tract infection (UTI)	UTI	UTI	UTI prophylaxis after pyelonephritis
		Urinary incontinence	Urinary incontinence	↑Catheterization frequency
	Urinary incontinence	Pyelonephritis	Pyelonephritis	Consider an indwelling catheter for a short period
		Urinary calculus	Urinary calculus	
Bowel	Obstipation	Obstipation	Obstipation	Adjust nutrition and drinking habits
			Bowel management influenced by pressure on bowel	Adapt bowel management to medication and stool consistency
			Positioning for defecation	Consider additional assistance
Skin		↑Risk of pressure injuries	↑Risk of pressure injuries	↑Pressure relief
				↑Frequency of skin checks
				↓Transfers
				Consider adaptation of aids (cushion, mattress, shower bench or chair)
Weight		↑Weight	↑Weight	Healthy nourishment
Mobility			Reduced mobility and altered body mechanics may need to be adjusted	Consider changes in daily wheelchair (positioning of axles, anti-tip bars)
			↑Fatigue	Consider hiring an electric wheelchair for a short period
			↑Dependency in daily activities and dressing	Practice situations before baby belly grows (put a ball under t-shirt)
				Consider additional time in daily life
Spasticity			↑Spasticity	Consider physiotherapy
				Avoid situations that cause spasms
Respiratory function			Limited breathing and vital capacity	Breathing physiotherapy
			Decreased effective coughing capacity	Breath support by overpressure inhalation or CPAP application
				Ingestion of secretolytics

32% being delivered by cesarean delivery. The rate of spontaneous vaginal delivery is higher in patients with below T6, while patients with higher-level injuries are more likely to develop autonomic dysreflexia and require assisted deliveries (Hughes et al. 1991). Postpartum patients should be carefully evaluated for bladder distension. If the bowel regimen needs to be resumed and constipation requires manual evacuation, topical anesthesia should be used. Prophylaxis of thromboembolism in patients with spinal cord injuries during the puerperium is controversial and management should be individualized (Pereira 2003).

31.10 Sexual Activity of Spinal Cord Injuries in Practice

Most men with spinal cord injuries resume sexual activity within 1 year of injury. However, the frequency of sexual activity has been shown to decrease after injury. Fifty-two percent of men had sex 2–3 times per week before injury, compared to 30% after injury. Forty-eight percent of men had sex once a week or less before the injury, compared to 70% after injury (Alexander et al. 1993). In addition, 99% of men reported penile-vaginal intercourse as their preferred sexual activity before injury, compared to only 16% of men after injury. Most men preferred oral sex, kissing, and hugging after injury (Alexander et al. 1993). The reduced frequency of female masturbation has been noted after injury (Comarr and Vigue 1978).

To minimize unexpected incontinence, the bladder needs to be emptied before sexual activity. If the urethral Foley catheter presents, it can be taped to the side of the penis with a condom placed over the catheter. Women may have sexual intercourse despite having a Foley catheter by securing it to the abdomen. Despite the best management program, sexual stimulation can cause urinary and/or fecal incontinence. Fluids should be limited during the hours before sexual activity (Elliott 2006). Towels must be available to manage episodes of urinary or fecal incontinence.

References

Aikman K, Oliffe JL, Kelly MT, et al. Sexual health in men with traumatic spinal cord injuries: a review and recommendations for primary health-care providers. Am J Men Health. 2018;12:2044–54.

Alexander CJ, Sipski ML, Findley TW. Sexual activities, desire and satisfaction in males pre- and post-spinal cord injury. Arch Sex Behav. 1993;22:217–28.

Alexander MS, Aisen CM, Alexander SM, et al. Sexual concerns after spinal cord injury: an update on management. NeuroRehabilitation. 2017;41:343–57.

Anderson KD. Targeting recovery: priorities of the spinal cord-injured population. J Neurotrauma. 2004;21:1371–83.

Anderson KD, Borisoff JF, Johnson RD, et al. Spinal cord injury influences psychogenic as well as physical components of female sexual ability. Spinal Cord. 2007;45:349–59.

Baker ER, Cardenas DD. Pregnancy in spinal cord injured women. Arch Phys Med Rehab. 1996;7:501–7.

Benevento BT, Sipski ML. Neurogenic bladder, neurogenic bowel, and sexual dysfunction in people with spinal cord injury. Phys Ther. 2002;82:601–12.

Bérard EJ. The sexuality of spinal cord injured women: physiology and pathophysiology: a review. Paraplegia. 1989;27:99–112.

Bertschy S, Schmidt M, Fiebag K, et al. Guideline for the management of pre-, intra-, and postpartum care of women with a spinal cord injury. Spinal Cord. 2020;58:449–58.

Biering-Sorensen F, Sonksen J. Sexual function in spinal cord lesioned men. Spinal Cord. 2001;39:455–70.

Bird VG, Brackett NL, Lynne CM, et al. Reflexes and somatic responses as predictors of ejaculation by penile vibratory stimulation in men with spinal cord injury. Spinal Cord. 2001;39:514–9.

Bodner DR, Haas CA, Krueger B, et al. Intraurethral alprostadil for treatment of erectile dysfunction in patients with spinal cord injury. Urology. 1999;53:199–202.

Bohlen JG, Held JP, Sanderson MO, et al. Heart rate, rate-pressure product, and oxygen uptake during four sexual activities. Arch Intern Med. 1984;144:1745–8.

Borgdorff AJ, Bernabé J, Denys P, et al. Ejaculation elicited by microstimulation of lumbar spinothalamic neurons. Eur Urol. 2008;54:449–56.

Brackett NL, Lynne CM, Weizman MS, et al. Scrotal and oral temperatures are not related to sperm quality of serum gonadotropin levels in spinal cord-injured men. J Androl. 1994;15:614–9.

Brackett NL, Lynne CM, Ibrahim E, et al. Treatment of infertility in men with spinal cord injury. Nat Rev Urol. 2010;7:162–72.

Brindley GS. Deep scrotal temperature and the effect on it of clothing, air temperature, activity, posture and paraplegia. Br J Urol. 1982;54:49–55.

Brown DJ, Hill ST, Baker HW. Male fertility and sexual function after spinal cord injury. Prog Brain Res. 2006;152:427–39.

Bughi S, Shaw SJ, Mahmood G, et al. Amenorrhea, pregnancy and pregnancy outcomes in women following spinal cord injury: a retrospective cross-sectional study. Endocrin Ract. 2008;14:437–41.

Camune BD. Challenges in the management of the pregnant woman with spinal cord injury. J Perinat Neonatal Nurs. 2013;27:225–31.

Chapelle PA, Durand J, Lacert P. Penile erection following complete spinal cord injury in man. Br J Urol. 1980;52:216–9.

Chéhensse C, Facchinetti P, Bahrami S, et al. Human spinal ejaculation generator. Ann Neurol. 2017;81:35–45.

Colpi G, Weidner W, Jungwirth A, et al. EAU guidelines on ejaculatory dysfunction. Eur Urol. 2004;46:555–8.

Comarr AE, Vigue M. Sexual counseling among male and female patients with spinal cord and/or cauda equina injury. Part II. Results of interview and neurological examinations of females. Am J Phys Med. 1978;57:215–27.

Consortium for Spinal Cord Medicine. Sexuality and reproductive health in adults with spinal cord injury: a clinical practice guideline for health-care professionals. J Spinal Cord Med. 2010;33:281–336.

Courtois F, Cordeau D. Sexual dysfunction in neurological disorders. In: Jankovic J, Mazziotta JC, Pomeroy SL, et al., editors. Bradley and Daroff's neurology in clinical practice. 8th ed. Philadelphia: Elsevier; 2022.

Courtois FJ, Goulet MC, Charvier KF, et al. Posttraumatic erectile potential of spinal cord injured men: how physiologic recordings supplement subjective reports. Arch Phys Med Rehabil. 1999;80:1268–72.

Craig DI. Spinal cord injury and pregnancy: the stories of two women. SCI Nurs. 1994;11:100–4.

Das S, Soni BM, Sharma SD, et al. A case of rapid deterioration in sperm quality following spinal cord injury. Spinal Cord. 2006;44:56–8.

Davidson R, Phillips A. Cardiovascular physiology and responses to sexual activity in individuals living with spinal cord injury. Top Spinal Cord Inj Rehabil. 2017;23:11–9.

Deforge D, Blackmer J, Garritty C, et al. Male erectile dysfunction following spinal cord injury: a systematic review. Spinal Cord. 2006;44:465–73.

Del Popolo G, Marzi VL, Mondaini N, et al. Time/duration effectiveness of sildenafil versus tadalafil in the treatment of erectile dysfunction in male spinal cord injured patient. Spinal Cord. 2004;42:644–8.

Denil J, Ohl DA, Smythe C. Vacuum erection device in spinal cord injured men: patient and partner satisfaction. Arch Phys Med Rehabil. 1996;77:750–3.

Derry F, Hultling C, Seftel AD, et al. Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. Urology. 2002;60(2 Suppl 2):49–57.

Dimitriadis F, Karakitsios K, Tsounapi P, et al. Erectile function and male reproduction in men with spinal cord injury: a review. Andrologia. 2010;42:139–65.

Elliott SL. Problems of sexual function after spinal cord injury. Prog Brain Res. 2006;152:387–99.

Everaert K, de Waard WI, Van Hoof T, et al. Neuroanatomy and neurophysiology related to sexual dysfunction in male neurogenic patients with lesions to the spinal cord or peripheral nerves. Spinal Cord. 2010;48:182–91.

Ghidini A, Simonson M. Pregnancy after spinal cord injury: a review of the literature. Top Spinal Cord Inj Rehabil. 2011;16:93–103.

Ghidini A, Healey A, Andreani M, et al. Pregnancy and women with spinal cord injuries. Acta Obstet Gynecol Scand. 2008;87:1006–10.

Giuliano F, Sanchez-Ramos A, Löchner-Ernst D, et al. Efficacy and safety of tadalafil in men with erectile dysfunction following spinal cord injury. Arch Neurol. 2007;64:1584–92.

Greer IA. Thrombosis in pregnancy: maternal and fetal issues. Lancet. 1999;353:1258–65.

Hough S, Cordes CC, Goetz LL, et al. A primary care provider's guide to sexual health for individuals with spinal cord injury. Top Spinal Cord Inj Rehabil. 2020;26:144–51.

Hughes SJ, Short DJ, Usherwood M, et al. Management of pregnant women with spinal cord injuries. Br J Obstet Gynecol. 1991;98:513–8.

Ibrahim E, Lynne CM, Brackett NL. Male fertility following spinal cord injury: an update. Andrology. 2016;4:13–26.

Jackson AB, Wadley V. A multicenter study of women's self-reported reproductive health after spinal cord injury. Arch Phys Med Rehabil. 1999;80:1420–8.

Jones ML, Leslie DP, Bilsky G, et al. Effects of intrathecal baclofen on perceived sexual functioning in men with spinal cord injury. J Spinal Cord Med. 2008;31:97–102.

Kafetsoulis A, Brackett NL, Ibrahim E, et al. Current trends in the treatment of infertility in men with spinal cord injury. Fertil Steril. 2006;86:781–9.

Kennedy P, Lude P, Taylor N. Quality of life, social participation, appraisals and coping post pinal cord injury: a review of four community samples. Spinal Cord. 2006;44:95–105.

Komisaruk BR, Whipple B, Crawford A, et al. Brain activation during vaginocervical self-stimulation and orgasm in women with complete spinal cord injury: fMRI evidence of mediation by the vagus nerves. Brain Res. 2004;1024:77–88.

Konstantinidis C. Chapter 7. Erectile dysfunction in paraplegic males. In: Nunes K, editor. Erectile dysfunction-disease-associated mechanisms and novel insights into therapy. London: InTechOpen; 2012. p. 127–43. http://www.intechopen.com/books/erectile-dysfunction-disease-associated-mechanisms-and-novel-insights-into-therapy.

Kreuter M, Taft C, Siösteen A, et al. Women's sexual functioning and sex life after spinal cord injury. Spinal Cord. 2011;49:154–60.

McBride F, Quah SP, Scott ME, et al. Tripling of blood pressure by sexual stimulation in a man with spinal cord injury. J R Soc Med. 2003;96:349–50.

McGregor JA, Meeuwsen J. Autonomic hyperreflexia: a mortal danger for spinal cord injured women in labor. Am Obstet Gynecol. 1985;151:330–3.

Mitra M, Clements KM, Zhang J, et al. Maternal characteristics, pregnancy complications, and adverse birth outcomes among women with disabilities. Med Care. 2015;53:1027–32.

Monga M, Bernie J, Rajasekaran M. Male infertility and erectile dysfunction in spinal cord injury: a review. Arch Phys Med Rehabil. 1999;80:1331–9.

Nygaard I, Bartscht KD, Cole S. Sexuality and reproduction in spinal cord injured women. Obstet Gynecol Surg. 1990;45:727–32.

Palmeri ST, Kostis JB, Casazza L, et al. Heart rate and blood pressure response in adult men and women during exercise and sexual activity. Am J Cardiol. 2007;100:1795–801.

Patki P, Woodhouse J, Hamid R, et al. Effects of spinal cord injury on semen parameters. J Spinal Cord Med. 2008;31:27–32.

Pereira L. Obstetric management of the patient with spinal cord injury. Obstet Gynecol Surv. 2003;58:678–87.

Ramos AS, Samso JV. Specific aspects of erectile dysfunction in spinal cord injury. Int J Impot Res. 2004;16(Suppl 2):S42–5.

Reame NE. A prospective study of the menstrual cycle and spinal cord injury. Am J Phys Med Rehabil. 1982;71:15–21.

Reitz A, Tobe V, Knapp PA, et al. Impact of spinal cord injury on sexual health and quality of life. Int J Impotence Res. 2004;16:167–74.

Rizio N, Tran C, Sorenson M. Efficacy and satisfaction rates of oral PDE5 is in the treatment of erectile dysfunction secondary to spinal cord injury: a review of literature. J Spinal Cord Med. 2012;35:219–28.

Saenz de Tejada I, Angulo J, et al. Pathophysiology of erectile dysfunction. J Sex Med. 2005;2:26–39.

Schmid DM, Schurch B, Hauri D. Sildenafil in the treatment of sexual dysfunction in spinal cord-injured male patients. Eur Urol. 2000;38:184–93.

Sipski ML. Spinal cord injury: what is the effect on sexual response? J Am Paraplegia Soc. 1991a;14:40–3.

Sipski ML. The impact of spinal cord injury on female sexuality, menstruation and pregnancy: a review of the literature. J Am Paraplegia Soc. 1991b;14:122–6.

Sipski M, Alexander CJ, Gómez-Marín O. Effects of level and degree of spinal cord injury on male orgasm. Spinal Cord. 2006;44:798–804.

Sipski ML, Alexander CJ, Rosen RC. Physiologic parameters associated with psychogenic sexual arousal in women with complete spinal cord injuries. Arch Phys Med Rehabil. 1995a;76:811–8.

Sipski M, Alexander CJ, Rosen RC. Orgasm in women with spinal cord injuries: a laboratory assessment. Arch Phys Med Rehabil. 1995b;76:1097–102.

Sipski ML, Alexander CJ, Rosen RC. Physiologic parameters associated with sexual arousal in women with incomplete spinal cord injuries. Arch Phys Med Rehabil. 1997;78:305–13.

Sipski ML, Alexander CJ, Rosen RC. Sexual arousal and orgasm in women: effects of spinal cord injury. Ann Neurol. 2001;49:35–44.

Smeltzer SC. Pregnancy in women with physical disabilities. J Obstet Gynecol Neonatal Nurs. 2007;36:88–96.

Smith EM, Bodner DR. Sexual dysfunction after spinal cord injury. Urol Clin North Am. 1993;20:535–42.

Soler JM, Previnaire JG, Amarenco G. Dartos reflex as autonomic assessment in persons with spinal cord injury. Spinal Cord Ser Cases. 2017;3:17097.

Sonksen J, Ohl DA. Penile vibratory stimulation and electroejaculations in the treatment of ejaculatory dysfunctions. Int J Androl. 2002;25:324–32.

Suh DD, Yang CC, Clowers DE. Nocturnal penile tumescence and effects of complete spinal cord injury: possible physiologic mechanisms. Urology. 2003;61:184–9.

Truitt WA, Coolen LM. Identification of a potential ejaculation generator in the spinal cord. Science. 2002;297:1566–9.

Vodusek DB. Bulbocavernosus reflex revisited. Neurourol Urodyn. 2003;22:681–2.

Wecht JM, Krassioukov AV, Alexander M, et al. International standards to document autonomic function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.

Wespes E, Amar E, Hatzichristou D, et al. EAU guidelines on erectile dysfunction: an update. Eur Urol. 2006;49:806–15.

Whipple B, Komisaruk BR. Sexuality and women with complete spinal cord injury. Spinal Cord. 1997;35:136–8.

Xue-Rui T, Ying L, Da-Zhong Y, et al. Changes of blood pressure and heart rate during sexual activity in healthy adults. Blood Press Monit. 2008;13:211–7.

Yilmaz U, Yang CC, Berger RE. Dartos reflex: a sympathetically mediated scrotal reflex. Muscle Nerve. 2006;33:363–8.

Yuan H, Cui Y, Wu J, et al. Efficacy and adverse events associated with use of onabotulinum toxin a for treatment of neurogenic detrusor overactivity: a meta-analysis. Int Neurourol J. 2017;21:53–61.

Recommended Additional Reading

Cardenas DD, Hooton TM. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Kennedy P, editor. The Oxford handbook of rehabilitation psychology. Oxford: Oxford University Press; 2012.

Leyson JFJ, editor. Sexual rehabilitation of the spinal-cord-injured patient. Clifton: Humana Press; 1991.

Noback CR, Strominger NL, Demarest RJ, Ruggiero DA. The human nervous system: structure and function. 6th ed. Totowa, NJ: Humana Press; 2005.

Robertson D, Bigaaioni I, Burnstock G, et al. Primer on the autonomic nervous system. 3rd ed. London: Elsevier; 2011.

Vodu Šek DB, Boller F. Neurology of sexual and bladder disorders. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 130. London: Elsevier; 2015.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

Pressure Injuries in Spinal Cord Injuries

32

Pressure injuries are a common, costly, and potentially life-threatening complication in people with spinal cord injuries, complicating the rehabilitation process and interfering with participation in activities. On the other hand, the most common preventable medical complication of patients with spinal cord injury is the development of pressure injuries. Pressure injury is a devastating complication of spinal cord injury with a high risk of infection, osteomyelitis, sepsis, and death. It also decreases community integration and quality of life. Diseases of the genitourinary system were the leading cause of rehospitalization in most years following the injury. Pressure injuries are the second most common cause of rehospitalization in patients with spinal cord injuries, ranging from 11.3% for 1 year after the injury to 20.8% for 20 years after injury (NSCISC 2021). In the nineteenth century, pressure ulcers were called bedsore or decubitus ulcer, but after World War II, Sir Ludwig Guttmann and Donald Munro developed management of spinal cord injuries; there has also been a breakthrough in the treatment of pressure ulcers. The terms bedsore or decubitus ulcer are not appropriate because patients using wheelchairs have a high frequency of ischial ulcers, and the pressure ulcer does not occur only in the bed or lying posture. Thus, the term pressure sore or pressure ulcer has generally been accepted as the terminology. The National Pressure Injury Advisory Panel (NPIAP, formerly NPUAP) defines a pressure ulcer as a localized injury to the skin and/or underlying tissue, usually over a bony prominence as a result of pressure or pressure associated with shear. The NPIAP changed the term for pressure ulcers and updated the definitions for the stages of pressure ulcers (NPUAP 2016; Ayello et al. 2018; The editors of Nursing 2017). The term "pressure injury" replaces "pressure ulcer" in the NPIAP Pressure Injury Staging System.

Among patients 1 year after the injury, 25.1% reported the occurrence of pressure injuries since discharge from rehabilitation. The prevalence of pressure ulcer increased in the years following the injury (NSCISC 2021) (Fig. 32.1). The spinal cord injury population is at great risk for pressure injuries. Up to 80% of patients with spinal cord injuries will experience pressure injury during their lifetime, and 30% are expected to experience recurrent pressure injuries (Caliri 2005; Chen et al. 2005). A pressure injury can seriously decrease functional independence. In addition, the financial burden on the healthcare systems is enormous. The vigilance of clinicians is necessary to prevent pressure injuries. When a pressure injury occurs, management strategies can promote healing and reduce the incidence of complications.

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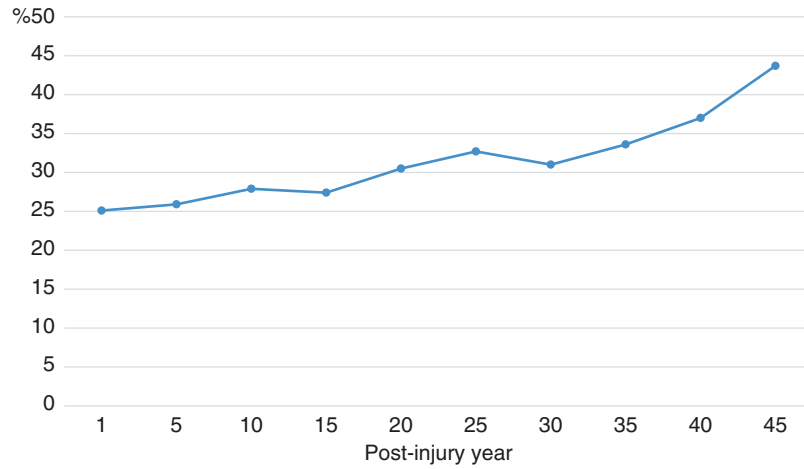

Fig. 32.1 Pressure injury occurrence by post-injury year

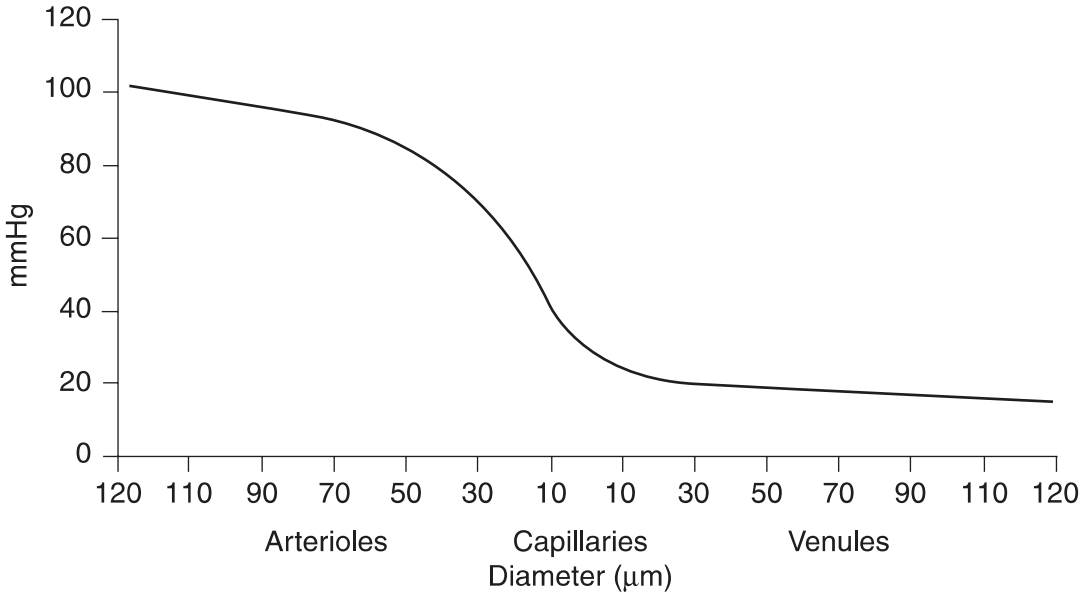

Fig. 32.2 Pressure in various components of the tissue microcirculation. From Young and Woolsey (1995)

32.1 Pathophysiology of Pressure Injuries

When pressure greater than the arterial end pressure, 32 mmHg or more, is applied to the local tissues and the inflammatory response and higher metabolic demand cause hypoxia of the local tissue, resulting in pressure injuries (Fig. 32.2). The tissue metabolic reactions may be reversed if the external pressure applied above the arterial end pressure is removed, but the progression of pressure injuries is irreversible if pressure over 70 mmHg is applied for more than 2 h. However, irreversible tissue necrosis can be avoided if intermittent pressure relief is applied even if an external pressure of 240 mmHg or more is applied.

Pressure ulcer is distinguished from neurotrophic, venous, arterial, vasculitic, and neoplastic ulcers. If the soft tissue is compressed between the bone and a subjacent hard surface, blood flow is blocked, and tissue death occurs. The minimum

time required for tissue death can be 1–2 h (Daniel et al. 1985). The amount of dead tissue reaches its maximum next to the bone and the least at the skin surface, creating a volcano-shaped defect with a bone at the base (Nola and Vistnes 1980).

Pressure injury can be caused by localized damage of the skin and/or underlying soft tissue, usually over a bony prominence or medical or other device-related problems. The sites of the bony prominence are the most exposed to pressure ulceration. When seated in a wheelchair, the ischial tuberosities are at greatest risk, while in side lying, the greater trochanters are in danger; and in the supine position, the sacrum, heels, and occiput may develop pressure-related lesion. The ischial tuberosity is uncovered by the inferior edge of the gluteus maximus muscle in the seated position when it is great at risk for pressure injury. Common areas include the occiput, scapula, sacrum, ischial tuberosity or ischial bursae, greater trochanter, and heel. The most frequently affected area during the acute phase is the sacrum followed by the heels and ischium. At one year, the most common sites are the sacrum, ischium, heels, and trochanters. Two years after injury, the most common sites are the ischium, sacrum, and trochanters (Meijer et al. 1994; Michael 1991).

Pressure injuries are caused by extrinsic and intrinsic factors. Extrinsic factors are the external conditions that contribute to the formation of pressure injury, including excessive pressure, shear, friction, and maceration. The injury occurs as a result of intense and prolonged pressure or pressure with shear forces. There is an inverse relationship between the amount of pressure and the duration of the pressure required to induce an ulcer. Intense pressure over a short period of time can cause damage as lower-intensity pressure over a long period of time (Barnett and Ablarde 1995; Patterson and Fisher 1986). If the tissue pressure exceeds the capillary closing pressure, a progressive tissue ischemia leading to cellular death will occur. When pressure is applied on a body surface, the greatest pressure is on the tissues overlying the bone, and the muscle is more sensitive to the effects of pressure than the skin. That is, the muscle is damaged first because of its higher metabolic requirements. Pressure injuries occur in the muscles between the skin and the bones.

Intrinsic factors are the individual's own conditions and include demographic and psychosocial variables: poor nutrition, spasticity, contractures, heterotopic ossification, recurrent urinary tract infection, urinary or fecal incontinence, altered consciousness, substance abuse, tobacco and alcohol, medication intake, and medical comorbidities such as cardiac disease, diabetes mellitus, vascular disease, immune deficiency, and malignancy. Depression is also a known risk factor for developing pressure injuries, and hospitalization for pressure injuries in the patient with spinal cord injuries and depression can lead to a suicide attempt (Dorsett and Geraghty 2008).

Adequate nutrition is not only an important factor in maintaining the vitality of undamaged tissue but also in tissue recovery. Initially, a high-protein diet is required to balance weight loss and prevent protein deficiency and anemia. If the patient has an open pressure injury, the problem of protein deficiency deteriorates due to the continual loss of protein from this ulcer area. Drugs, alcohol, nicotine, and caffeine affect the nutritional state of the patient. Nicotine and caffeine cause vasoconstriction, which decreases oxygenation and nutrition supply to the tissues.

Ischemia is generally recognized as an important factor in the occurrence of pressure injuries. If the forces on an area of the body are great enough for a sufficient time, the capillary blood flow is blocked to prevent cellular metabolism and cause tissue necrosis. When the developed forces concentrate in a very small area, the pressure in this area is highest. Intense pressures applied over a short period of time can be as damaging as lower pressures applied over a prolonged period of time (Patterson and Fisher 1986). In addition, higher pressures develop at the circumstance of a wound than in the wound itself. If the applied pressure exceeds normal capillary pressure, tissue injuries will occur. Microscopic changes can occur in the skin with only 1 h of continuous pressure of 60 mmHg (Patterson and Fisher 1986). Actual pressure necrosis can occur

at a continuous pressure of 30 mmHg, even if the tissue is normal or denervated. The capillary perfusion pressure is 20–30 mmHg, from 14 mmHg on the venous side to 35 mmHg on the arterial side. The body is contoured due to irregular surface skeleton and different consistencies and thicknesses of other soft tissues. When the patient is supine, the highest pressure exerts over the sacrum, and if the patient lies on one side, the pressure exerts over the trochanteric area. The greatest pressure when the patient is sitting is in the ischial tuberosities. When the patient's head and upper trunk are lying at an angle of 30–60°, the sacral region is more heavily loaded than the flat supine position.

In supine position, a pressure of 40–60 mmHg is applied to the sacrum, buttock, heel, and occiput, and 50 mmHg of pressure is applied to the knee and chest in the prone position. If the foot is not supported by the footplate, 40–60 mmHg pressure is applied to the sciatic notch and femur, but 100 mmHg pressure is applied to the ischial tuberosity when the foot is placed on the floor or footplate. The capillary hydrostatic pressure in the normal state is 15–30 mmHg, especially 40–75 mmHg in the bony protrusion.

Shear is a tangential force that acts on the surface of the skin and occurs when the underlying tissue moves and the skin does not move. When external pressure is exerted on the bone, the tissues over the bone are flattened and laterally displaced. The displacement of the tissues induces a shearing force. When pressure is applied to the skin, particularly over a bony prominence, the skin and underlying soft tissues are distorted. In Fig. 32.3, the horizontal lines just below the bony prominence come closer together to indicate tissue compression. Elsewhere, particularly under the bony prominence, the lines are also elongated, indicating tensile (stretching) and shear (distorting) stresses (International Review 2010). That is, even the application of vertical pressure creates tensile and shear stresses even within the tissues near bony prominence (Reger et al. 2007). Sliding in bed when bed changes, poor turning and transfer techniques, and sliding instead of lifting increase shear. Spasticity can increase the effect of shear because the extremities can repeatedly slide over one surface or be pressed directly against another part for an extended period of time. Shearing forces between the skin and bones can lead to angulation and stretching of the blood vessels, which impairs blood circulation. Friction injury is similar to shearing. The skin is abraded on the underlying bone and subcutaneous structures. Cell damages caused by friction are the result of thermal injury

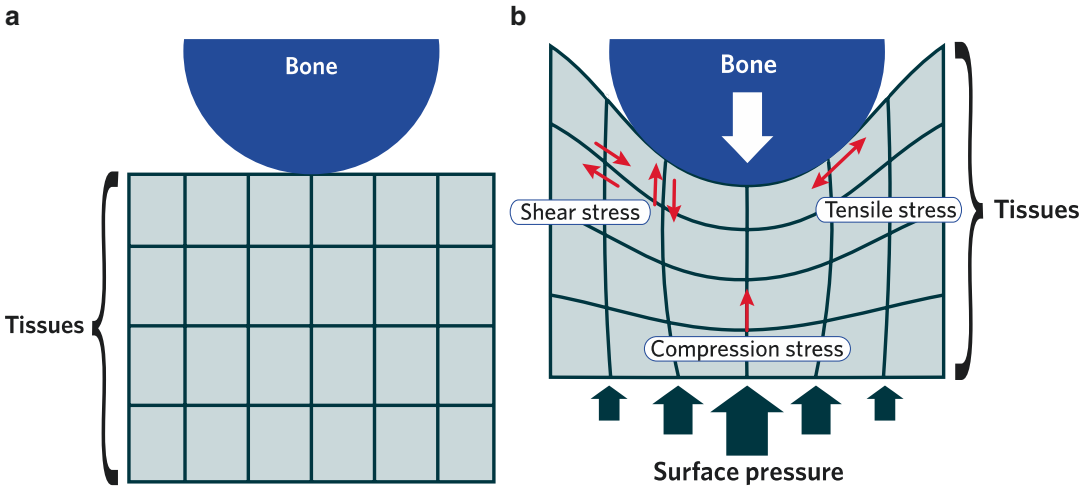

Fig. 32.3 Tissue distortion due to pressure. (**a**) No pressure on the tissue, (**b**) When only pressure is applied perpendicularly, tensile and shear stresses also occur within the tissues near the bony prominences. Adapted from International Review (2010)

(Dinsdale 1974). Maceration is softening of the skin by moisture. Maceration is caused by prolonged contact with urine, feces, sweat, or the combination of those substances and is directly related to the occurrence of skin damage. A warm, moist environment is an optimal medium for bacterial growth, and skin softened by constant moisture is less resistant to the forces of direct pressure and friction than dry skin. Temperature rise is a factor in skin damage. An increase in skin temperature by 1.0 °C results in a 10% increase in tissue metabolism and an equal increase in oxygen demand for tissues already compromised vascularity.

Long-standing ulcer over 20 years can develop to Marjolin's ulcer, a type of squamous cell carcinoma. Marjorin's ulcers are present with increased discharge and wart-like growth of the wound base (Berkwits et al. 1986).

32.2 Staging and Assessment of Pressure Injuries

Many risk factors are involved in the formation of pressure injuries. Age, duration of injury, marital status, economic level, demographic factors such as race, and sociopsychological factors such as behavioral disorder and cognitive status are involved (Byrne and Salzberg 1996). Biochemical measurements reflect nutritional status such as prealbumin (19.5–35.8 mg/dL), albumin, and hemoglobin. Among biochemical indicators reflecting nutritional status, prealbumin is used as a sensitive index to assess nutritional status because of a short half-life of 2–3 days (Posthauer et al. 2015).

The Braden Scale is commonly used as a tool for risk assessment. Other measures as a risk assessment tool are the Salzberg Scale and Norton Scale. Braden Scale is the most commonly used tool to assess the risk of pressure injuries, although this is not the best assessment tool for patients with spinal cord injuries. The Braden Scale consists of four steps for six items (sensory perception, moisture, activity, mobility, nutrition, and friction and shear) with 1 for the highest risk and 4 for the lowest risk, except for the friction and shear phenomenon in three stages, and the score is distributed in 6–23 points. The lower the score, the greater the risk of pressure injuries. A score of 19–23 is no risk, and a score of 9 or less is a very high risk. 11–19 points are managed as subjects with compression ulcers. Other tools are Norton Scale and Salzberg Scale.

The National Pressure Injury Advisory Panel (NPIAP) changed its terminology regarding pressure ulcers and updated the definitions for the stages of pressure injury (NPUAP 2016; Ayello et al. 2018; The editors of Nursing 2017). The term "pressure injury" replaces "pressure ulcer" in the NPIAP Pressure Injury Staging System. In addition to the terminology changes, Arabic numbers are now used in the names of the stages instead of Roman numerals, and the term "suspected" has been removed from the deep tissue injury definition. Additional definitions of pressure injuries to the six stages include "medical device-related pressure injury" and "mucosal membrane pressure injury" (The editors of Nursing 2017) (Table 32.1).

Refer to NPIAP for full definitions of the different stages of pressure injuries, which were revised in 2016 (Edsberg et al. 2016; NPUAP 2016; https://cdn.ymaws.com/npiap.com/resource/resmgr/online_store/npiap_pressure_injury_stages.pdf) (Table 32.2).

Table 32.1 Different stages of NPUAP pressure injury

Stage I
• Non-blanchable erythema
• Skin intact
Stage II
• Possible blister formation
• Partial-thickness skin damage
Stage III
• Subcutaneous fat exposed
• Full-thickness skin loss
Stage IV
• Exposed muscles, bones, tendons, or vital organs
• Skin, subcutaneous and possibly more tissue loss
Unstageable
• Entire wound base covered by slough and/or eschar
• Full-thickness skin loss
Deep tissue injury
• Unknown level of tissue injured below skin
• Skin intact

From Boyko et al. (2018), with permission

Table 32.2 Definition of NPIAP pressure injury stages

Category	Description
Stage 1 Pressure Injury Non-blanchable erythema of intact skin	Intact skin with a localized area of non-blanchable erythema, which may appear differently in darkly pigmented skin. Presence of blanchable erythema or changes in sensation, temperature, or firmness may precede visual changes. Color changes do not include purple or maroon discoloration; these may indicate deep tissue pressure injury.
Stage 2 Pressure Injury Partial-thickness skin loss with exposed dermis	Partial-thickness loss of skin with exposed dermis. The wound bed is viable, pink or red, moist, and may also present as an intact or ruptured serum-filled blister. Adipose (fat) is not visible and deeper tissues are not visible. Granulation tissue, slough, and eschar are not present. These injuries commonly result from adverse microclimate and shear in the skin over the pelvis and shear in the heel. This stage should not be used to describe moisture associated skin damage (MASD) including incontinence associated dermatitis (IAD), intertriginous dermatitis (ITD), medical-adhesive related skin injury (MARSI), or traumatic wounds (skin tears, burns, abrasions).
Stage 3 Pressure Injury Full-thickness skin loss	Full-thickness loss of skin, in which adipose (fat) is visible in the ulcer and granulation tissue and epibole (rolled wound edges) are often present. Slough and/or eschar may be visible. The depth of tissue damage varies by anatomical location; areas of significant adiposity can develop deep wounds. Undermining and tunneling may occur. Fascia, muscle, tendon, ligament, cartilage, and/or bone are not exposed. If slough or eschar obscures the extent of tissue loss, this is an Unstageable Pressure Injury.
Stage 4 Pressure Injury Full-thickness skin and tissue loss	Full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage, or bone in the ulcer. Slough and/or eschar may be visible. Epibole (rolled edges), undermining and/or tunneling often occur. Depth varies by anatomical location. If slough or eschar obscures the extent of tissue loss, this is an Unstageable Pressure Injury.
Unstageable Pressure Injury Obscured full-thickness skin and tissue loss	Full-thickness skin and tissue loss in which the extent of tissue damage within the ulcer cannot be confirmed because it is obscured by slough or eschar. If slough or eschar is removed, a Stage 3 or Stage 4 pressure injury will be revealed. Stable eschar (i.e., dry, adherent, intact without erythema or fluctuance) on the heel or ischemic limb should not be softened or removed.
Deep Tissue Pressure Injury Persistent non-blanchable deep, red, maroon, or purple discoloration	Intact or non-intact skin with localized area of persistent non-blanchable deep red, maroon, purple discoloration or epidermal separation revealing a dark wound bed or blood-filled blister. Pain and temperature change often precede skin color changes. Discoloration may appear differently in darkly pigmented skin. This injury results from intense and/or prolonged pressure and shear forces at the bone and muscle interface. The wound may evolve rapidly to reveal the actual extent of tissue injury, or may resolve without tissue loss. If necrotic tissue, subcutaneous tissue, granulation tissue, fascia, muscle, or other underlying structures are visible, this indicates a full-thickness pressure injury (Unstageable, Stage 3, or Stage 4). Do not use DTPI to describe vascular, traumatic, neuropathic, or dermatologic conditions.
Additional pressure injury definitions	
Medical device related pressure injury: This describes an etiology	Medical device related pressure injuries result from the use of devices designed and applied for diagnostic or therapeutic purposes. The resultant pressure injury generally conforms to the pattern or shape of the device. The injury should be staged using the staging system.
Mucosal membrane pressure injury	Mucosal membrane pressure injury is found on mucous membranes with a history of a medical device in use at the location of the injury. Due to the anatomy of the tissue these ulcers cannot be staged.

Pressure Injury A pressure injury is a localized damage to the skin and underlying soft tissue usually over a bony prominence or related to medical or other devices. The injury can present as intact skin or an open ulcer and may be painful. The injury occurs as a result of intense and/or prolonged pressure or pressure in combination with shear. The tolerance of soft tissue for pressure and shear may also be affected by microclimate, nutrition, perfusion, comorbidities, and condition of the soft tissue.

Stage 1 Pressure Injury: Non-Blanchable Erythema of Intact Skin Intact skin with a localized area of non-blanchable erythema, which may appear differently in darkly pigmented skin. Presence of blanchable erythema or changes in sensation, temperature, or firmness may precede visual changes. Color changes do not include purple or maroon discoloration; these may indicate deep tissue pressure injury.

Stage 2 Pressure Injury: Partial-Thickness Skin Loss with Exposed Dermis Partial-thickness loss of skin with exposed dermis. The wound bed is viable, pink or red, moist, and may also present as an intact or ruptured serum-filled blister. Adipose (fat) is not visible, and deeper tissues are not visible. Granulation tissue, slough, and eschar are not present. These injuries commonly result from adverse microclimate and shear in the skin over the pelvis and shear in the heel. This stage should not be used to describe moisture associated skin damage (MASD) including incontinence associated dermatitis (IAD), intertriginous dermatitis (ITD), medical-adhesive related skin injury (MARSI), or traumatic wounds (skin tears, burns, abrasions).

Stage 3 Pressure Injury: Full-Thickness Skin Loss Full-thickness loss of skin, in which adipose (fat) is visible in the ulcer and granulation tissue and epibole (rolled wound edges) are often present. Slough and/or eschar may be visible. The depth of tissue damage varies by anatomical location; areas of significant adiposity can develop deep wounds. Undermining and tunneling may occur. Fascia, muscle, tendon, ligament, cartilage, and/or bone are not exposed. If slough or eschar obscures the extent of tissue loss, this is an unstageable pressure injury.

Stage 4 Pressure Injury: Full-Thickness Skin and Tissue Loss Full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage, or bone in the ulcer. Slough and/or eschar may be visible. Epibole (rolled edges), undermining and/or tunneling often occur. Depth varies by anatomical location. If slough or eschar obscures the extent of tissue loss, this is an unstageable pressure injury.

Unstageable Pressure Injury: Obscured Full-Thickness Skin and Tissue Loss Full-thickness skin and tissue loss in which the extent of tissue damage within the ulcer cannot be confirmed because it is obscured by slough or eschar. If slough or eschar is removed, a stage 3 or stage 4 pressure injury will be revealed. Stable eschar (i.e., dry, adherent, intact without erythema or fluctuance) on the heel or ischemic limb should not be softened or removed.

Deep Tissue Pressure Injury: Persistent Non-Blanchable Deep Red, Maroon, or Purple Discoloration Intact or non-intact skin with localized area of persistent non-blanchable deep red, maroon, purple discoloration or epidermal separation revealing a dark wound bed or blood-filled blister. Pain and temperature change often precede skin color changes. Discoloration may appear differently in darkly pigmented skin. This injury results from intense and/or prolonged pressure and shear forces at the bone–muscle interface. The wound may evolve rapidly to reveal the actual extent of tissue injury or may resolve without tissue loss. If necrotic tissue, subcutaneous tissue, granulation tissue, fascia, muscle, or other underlying structures are visible, this indicates a full-thickness pressure injury (unstageable, stage 3 or stage 4). Do not use deep tissue pressure injury to describe vascular, traumatic, neuropathic, or dermatologic conditions.

Additional definitions of pressure injury are:

Medical Device-Related Pressure Injury This describes an etiology.

Medical device-related pressure injuries result from the use of devices designed and applied for diagnostic or therapeutic purposes. The resultant pressure injury generally conforms to the pattern or shape of the device. The injury should be staged using the staging system.

Mucosal Membrane Pressure Injury Mucosal membrane pressure injury is found on mucous

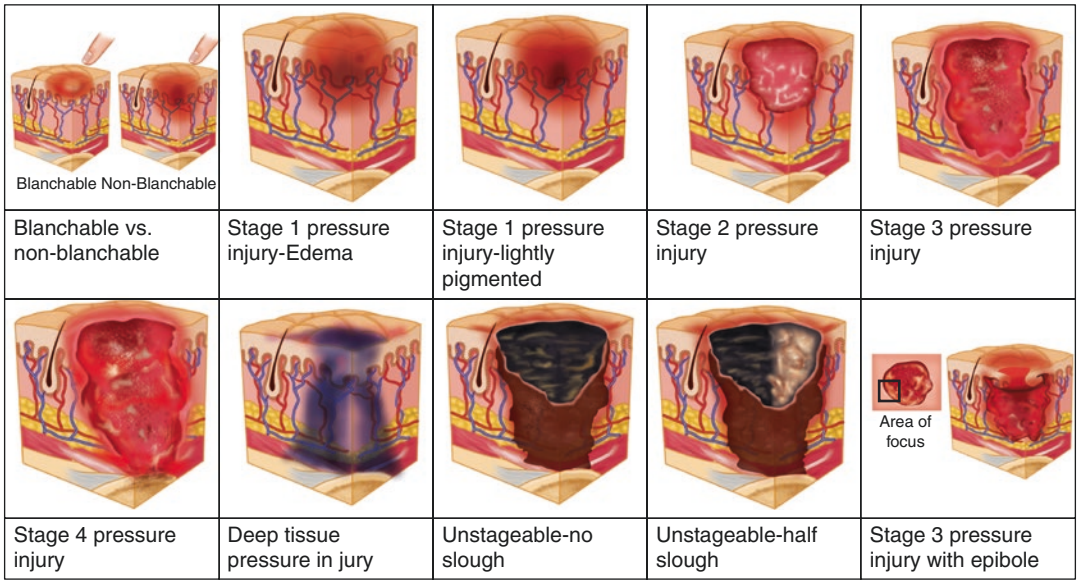

Fig. 32.4 Pictorial illustration of each stage of pressure injuries

membranes with a history of a medical device in use at the location of the injury. Due to the anatomy of the tissue, these ulcers cannot be staged.

Figure 32.4 shows a pictorial illustration of each stage of pressure injuries.

In order to determine the appropriate treatment of an open wound, a decision on the cause must first be made. Depending on location and appearance, an assessment of pressure injury should be made to determine the depth and the nature of the material at the wound base. Depth is determined by debridement. Good documentation of clinical findings of pressure injury allows an accurate assessment of lesion improvement or deterioration. Assessment and documentation of the pressure injuries should include location of the wound, the appearance and color of wound base and margins, size (length, width, and depth), NPIAP stage, presence of eschar, slough, granulation tissue, epithelialization, appearance of wound margins, undermining/sinus formation, exudate, tissue and drainage odor, evidence of infection, surrounding tissue, state of periwound tissue, and healing status. CT or MRI can help to determine the depth and severity of a pressure injury or osteomyelitis. A sinogram can be helpful in assessing sinus formation or undermining. The healing or progression of the pressure injury should be documented by an objective assessment.

Reevaluation and monitoring of pressure injuries are needed to determine proper management. In addition to a wound measurement, a photographic recording helps to document the course of the wounds. The Pressure Ulcer Scale for Healing (PUSH) is used to assess and follow-up the pressure injuries based on wound size (length and width), amount of exudate, and tissue type (NPUAP 1998; https://cdn.ymaws.com/npiap.com/resource/resmgr/online_store/push_tool_information_form.pdf).

32.3 Beds for Pressure Injuries

Proper beds may prevent and treat pressure injuries. Static support surfaces, such as foam or static air mattresses, are an appropriate choice for persons with adequate bed mobility, which can be positioned without weight bearing on a wound. At least the static support surface should have 1 in. cushion between any bony prominence and the bed frame. Specialized beds are available for allowing maximal pressure distribution, such as low-air-loss bed and air-fluidized bed. The low-air-loss bed consists of series of 18–20 air-filled

sacks, each of which can be individually pressurized, allowing body weight to shift from one body part to another. The air-fluidized bed consists of a container filled with tiny ceramic beads, in which air is continually forced out by a blower.

Dynamic support surfaces, such as water, gel, or alternating pressure pads, can be used for individuals who compromise bed mobility and are at high risk of pressure injuries. These support surfaces are also suitable for patients with stage 1 or 2 pressure injuries. Low-air-loss and air-fluidized beds are used when a patient has already suffered from a large-sized stage 3 or 4 pressure injuries and dynamic support surface could not be improved.

32.4 Pressure Injury Prevention

Prevention measures include examining the skin over bony prominences at least daily, regular shifting body weight in bed and wheelchair, keeping the skin clean and dry in case of incontinence, and individually prescribed wheelchair and pressure redistribution cushion or power tilt/recline mechanism, ensuring all equipment maintained properly, nutrition to maintain appropriate body weight, avoiding smoking, and limiting alcohol intake. Comprehensive training and education programs for patients with spinal cord injuries and their family and caregivers are very important, including information on etiology, risk factors, proper positioning, equipment, complications, and principles of wound prevention, skincare, treatment, and time to find and request medical attention (Kosiak 1961; NPUAP 2016; https://cdn.ymaws.com/npiap.com/resource/resmgr/online_store/1a._pressure-injury-preventi.pdf) (Table 32.3).

Minimizing extrinsic factors such as pressure, shear, maceration, and friction can reduce the rate of pressure injury formation. If the patient is bedridden, the entire skin surface should be examined daily. Patients lying on a regular mattress should be repositioned at least every 2 h. Although there is no clear consensus on the fre-

Table 32.3 Pressure injury prevention points: From NPIAP (2016)

Pressure injury prevention points
Risk Assessment
1. Consider bedfast and chairfast individuals to be at risk for development of pressure injury.
2. Use a structured risk assessment, such as the Braden Scale, to identify individuals at risk for pressure injury as soon as possible (but within 8 hours after admission).
3. Refine the assessment by including these additional risk factors: A. Fragile skin B. Existing pressure injury of any stage, including those ulcers that have healed or are closed C. Impairments in blood flow to the extremities from vascular disease, diabetes, or tobacco use D. Pain in areas of the body exposed to pressure
4. Repeat the risk assessment at regular intervals and with any change in condition. Base the frequency of regular assessments on acuity levels: A. Acute care ……. Every shift B. Long-term care … Weekly for 4 weeks, then quarterly C. Home care ……. At every nurse visit
5. Develop a plan of care based on the areas of risk, rather than on the total risk assessment score. For example, if the risk stems from immobility, address turning, repositioning, and the support surface. If the risk is from malnutrition, address those problems.
Skin Care
1. Inspect all of the skin upon admission as soon as possible (but within 8 hours).
2. Inspect the skin at least daily for signs of pressure injury, especially non-blanchable erythema.
3. Assess pressure points, such as the sacrum, coccyx, buttocks, heels, ischium, trochanters, elbows and beneath medical devices.
4. When inspecting darkly pigmented skin, look for changes in skin tone, skin temperature, and tissue consistency compared to adjacent skin. Moistening the skin assists in identifying changes in color.
5. Cleanse the skin promptly after episodes of incontinence.

(continued)

Table 32.3 (continued)

Pressure injury prevention points
6. Use skin cleansers that are pH balanced for the skin.
7. Use skin moisturizers daily on dry skin.
8. Avoid positioning an individual on an area of erythema or pressure injury.
Nutrition
1. Consider hospitalized individuals to be at risk for undernutrition and malnutrition from their illness or being NPO for diagnostic testing.
2. Use a valid and reliable screening tool to determine risk of malnutrition, such as the Mini Nutritional Assessment.
3. Refer all individuals at risk for pressure injury from malnutrition to a registered dietitian/nutritionist.
4. Assist the individual at mealtimes to increase oral intake.
5. Encourage all individuals at risk for pressure injury to consume adequate fluids and a balanced diet.
6. Assess weight changes over time.
7. Assess the adequacy of oral, enteral, and parenteral intake.
8. Provide nutritional supplements between meals and with oral medications, unless contraindicated.
Repositioning and Mobilization
1. Turn and reposition all individuals at risk for pressure injury, unless contraindicated due to medical condition or medical treatments.
2. Choose a frequency for turning based on the support surface in use, the tolerance of skin for pressure, and the individual's preferences.
3. Consider lengthening the turning schedule during the night to allow for uninterrupted sleep.
4. Turn the individual into a 30-degree side lying position, and use your hand to determine if the sacrum is off the bed.
5. Avoid positioning the individual on body areas with pressure injury.
6. Ensure that the heels are free from the bed.
7. Consider the level of immobility, exposure to shear, skin moisture, perfusion, body size and weight of the individual when choosing a support surface.
8. Continue to reposition an individual when placed on any support surface.
9. Use a breathable incontinence pad when using microclimate management surfaces.
10. Use a pressure redistributing chair cushion for individuals sitting in chairs or wheelchairs.
11. Reposition weak or immobile individuals in chairs hourly.
12. If the individual cannot be moved or is positioned with the head of the bed elevated over 30º, place polyurethane foam dressing on the sacrum.
13. Use heel offloading devices or polyurethane foam dressing on individuals at high risk for heel ulcers
14. Place thin foam or breathable dressings under medical devices.
Education
1. Teach the individual and family about risk for pressure injury.
2. Engage individual and family in risk reduction interventions

https://cdn.ymaws.com/npiap.com/resource/resmgr/online_store/1a._pressure-injury-preventi.pdf

quency and duration of weight shifts in wheelchairs, it is recommended that weight shifts be performed every 15 min for more than 2 min to allow for adequate tissue perfusion (Consortium of Spinal Cord Medicine 2014; Makhsous et al. 2007). Tetraplegics can relieve pressure on the buttocks by leaning forward or to one side followed by the other. With a tilt weight shift without a reclining mechanism, a minimum of 45° is required for adequate pressure distribution (Jones et al. 2007). Careful and skilled transfers can minimize shear and friction. Care should be taken that shearing does not occur too much when the caregiver moves the patient in bed. Spasticity may increase shear forces and should be managed appropriately.

Weight shifts are important to relieve pressure on the wounds. A push-up pressure relief while seated in a wheelchair relieves the pressure on the buttocks but requires sufficient strength of the upper extremities and can lead to overuse problems in the upper extremities. A forward lean can

unweight ischial tuberosities. A side lean can be done to unweight the contralateral side of the buttock. Proper wheelchair cushion is important. Donut-shaped cushions should not be used because of venous congestion.

In summary, prevention strategies include routine daily skin monitoring, turn and positioning every 2 h; minimizing friction, shear, and moisture; padding bony prominences; early safe mobilization; and proper nutrition (Groah et al. 2015).

32.5 Treatment of Pressure Injuries

32.5.1 Basic Nonsurgical Care: Cleaning, Debridement, and Dressing

32.5.1.1 Cleaning and Debridement

The two main conditions for curing pressure injuries are to keep them pressure-free and clean. The general treatment principle of pressure injury is pressure relief. It is also important to eliminate the reversible underlying predisposing condition; avoid friction, shear, and tissue maceration; keep the wound bed moist; manage excessive drainage; and debride devitalized tissue (Ho and Bogie 2007) (Table 32.4). Comorbid medical problems that affect wound healing should be treated. Smoking cessation is essential for wound healing. Bladder and bowel incontinence should be controlled as this is the cause of maceration of wounds and surrounding tissues. To reduce the progression of the pressure injury wound, the extrinsic factors that contributed to wound formation must be identified and treated. If the wound is clean, moist, and debrided, healing is promoted. The ideal dressing for the pressure injuries should keep the wound bed moist and the surrounding skin dry (Ho and Bogie 2007; Huang et al. 2015).

When the wound is clean, healing can be facilitated by the creating of a tissue growth environment. Necrotic tissue and infection prevent wound healing, so wound of pressure injury should be cleaned. Necrotic tissue can be

Table 32.4 Treatment principles of pressure injuries

1. Assess and document wound (size, stage, wound bed appearance, wound edges, exudates, necrosis, odor, signs of infection, surrounding skin, undermining, sinus formation, tunneling, and degree of granulation tissue epithelialization)
2. Eliminate direct pressure over the pressure injury through positioning techniques and appropriate support surfaces. Limit time in chair if pressure injury is on the ischial tuberosities
3. Observe and document wound healing progress
4. Avoid antiseptics (povidone-iodine, H_2O_2, etc.) and cleansers with nontoxic dilutions
5. Keep periwound skin dry, control exudates, and eliminate dead space
6. Use dressings that keep pressure injury bed moist to allow for optimal cell migration, proliferation, and revascularization
7. Clean wound at every dressing change using minimal mechanical force
8. Create optimum wound environment by using modern dressings (hydrocolloids, hydrogels, foams, alginates, soft silicone) rather than gauze
9. Consider adjunctive therapies (i.e., electrical stimulation, negative-pressure wound therapy, etc.) to enhance healing for appropriate wounds
10. Consider a 2-week trial of topical antibiotics (neomycin, bacitracin, or polymyxin B) for clean, nonhealing injuries
11. Consider an infection if nonhealing wound, and if so, manage with wound cleansing, systemic antibiotics, and debridement after diagnosis is made
12. Ensure adequate nutritional intake
13. Remove necrotic tissue by techniques that may include mechanical, autolytic (applying a moisture-retentive dressings, such as a hydrocolloid, or the use of hydrogels to moisturize the devitalized tissue), enzymatic (e.g., use of collagenase), biologic (use of sterilized eggs of *Lucilia sericata* commonly known as *maggot therapy*), pulsatile high-pressure lavage, or conservative sharp or surgical debridement

From Weidner et al. (2017)

removed mechanically, chemically, or surgically from pressure injuries. In general, a combination of the three methods for debridement is used. Management strategies for common pressure injuries can be divided into local and systemic therapies. Local therapies performed at the pressure injury site include mechanical and chemical treatments. Mechanical methods include wound cleansing, debridement, and dressing. Systemic treatment includes intravenous antibiotics as well as caloric and vitamin supplementation.

A pressure injury wound should be cleansed regularly. Normal saline is an excellent cleansing agent. Irrigation of the wound reduces surface bacteria and tissue trauma (RNAO 2016). A sufficient amount of at least 100–150 mL of solution is required to completely irrigate the entire wound surface. Irrigation with a syringe with 19-gauge needle or catheter to produce gentle pressure (8–15 psi) without trauma is the method of choice for cleansing wounds. Cleansing is very important in removing necrotic tissue and removing exudates and remaining dressing materials. Antiseptic agents, such as iodine-based solution, povidone, or hydrogen peroxide, are not recommended as they have a germicidal effect that interferes with wound healing (Reddy et al. 2008). If chosen, the antiseptic agents should be used for a short period of time and discontinued when superficial critical colonization is no longer a clinical concern, once healing has progressed, or shortly after the person experiences any antiseptic-related adverse events. Unmanaged biofilm increases wound inflammation, which leads to the breakdown of the newly formed extracellular matrix and promotes wound chronicity.

Wounds with devitalized tissue require debridement. Debridement is a technique used to remove non-viable tissue from pressure injuries and prepare the wound bed for further intervention. It is important to remove necrotic tissue as part of wound-bed preparation prior to treatment/management, as necrotic tissue can cause infection, inflammation, and delayed wound healing. Non-viable tissue is usually "moist, yellow, green, tan, or gray and may become thick and leathery with dry black or brown eschar" (RNAO 2016). The use of debridement depends on clinical need, person-centered concerns such as autonomic dysreflexia, bleeding, or pain, available resources, medical training/qualifications. Types of debridement include surgical/sharp, conservative sharp, autolytic, enzymatic, larval, and mechanical debridement. In general, debridement can be performed at the bedside. The pressure injuries should be cleansed before and after debridement. The methods of debridement are summarized in Table 32.5.

Sharp debridement (sharp surgical debridement) is used to remove the necrotic debris in presence of eschar. Sharp debridement is the most invasive and quickest form of debridement. It involves removing non-viable and minimal viable tissue using sharp instruments such as a scalpel and/or scissors. Surgical debridement extends to viable tissue and causes pain and bleeding, which may require general, intralesional, or local topical anesthesia. Conservative sharp debridement includes "the use of scalpels, curettes, scissors, forceps and rongeurs to remove devitalized tissue without pain or bleeding." It differs from surgical debridement in that viable tissue is not excised. This type of debridement is used to control infection in non-healable wounds and to reduce the load of necrotic tissue as part of wound-bed preparation in healable wounds. Debridement should be avoided if a stable, dry, nonfluctuant eschar on the heels or in areas of poor tissue coverage over bony prominences (Rosin et al. 2020). Surgical debridement is mandatory if the ulcer is covered by a hard black eschar that blocks the wound from any other type of treatment. Surgical debridement with scalpel or scissors should be conservative, and only obviously necrotic tissue should be removed. Wound bacteriology is determined at debridement. After debridement, when the wound is clean, it is covered with saline solution. The liquid is applied to wrap gauze in all large wounds (Regan et al. 2009).

Autolytic debridement occurs when a synthetic dressing is used to cover the wound. This

Table 32.5 Methods of debridement

Types of debridement	Purpose	Comments
1. Absorptive		
Dextranomer granules	Secreting ulcers	
Activated charcoal	Secreting ulcers	Beneficial effect against Pseudomonas strains and methicillin-resistant *Staphylococcus aureus*
2. Chemical		
Enzymatic	Ulcers with slough	
Mild acidic preparations	Ulcers with slough	
3. Autolytic	Ulcers with slough	Hydrogel dressings are used to induce autolytic debridement
4. Maggot therapy	Ulcers with slough with/without purulent secretions	
5. Mechanical		
Hydrodebridement and "wet to moist" dressing	To soften slough or dry necrotic tissue	Avoid prolonged soaking
Repeated saline irrigation	To remove purulent or seropurulent secretions with liquefying slough	Irrigation should be done gently
"Wet to dry" dressing	Necrotic tissue with exudate	Healthy tissues may be damaged
Scrubbing	To remove necrotic tissue	Should be avoided
6. Surgical	For solid or semi-solid necrotic material that can be handled effectively with a scalpel or forceps	Contraindicated when bleeding disorders are suspected.

Adapted from Shai and Maibach (2005)

facilitates the natural enzymes produced by the skin to self-ingest the devitalized tissue. Collagenase compounds are chemical debriding agents that can be applied to wound. This method is contraindicated for infected wounds. These agents can damage viable tissue and should be discontinued immediately if the wound is clean. Mechanical debridement includes packing the wound with saline-soaked gauze allowed to dry for 6–8 h and then removed (wet-to-dry gauze dressing). Necrotic tissue attached to the gauze is removed. Other mechanical methods include whirlpool therapy, wound irrigation, dextranomers, and negative-pressure wound therapy. Ulcers with a small surface outlet and a large underlying cavity, such as ischial pressure injury, should be packed with saline-soaked gauze so that the wound heals from the bottom up. If the surface outlet closes first, the cavity can become an abscess. Special precautions should be taken during the debridement of wounds of patients receiving anticoagulant therapy and those at high risk of autonomic dysreflexia (Frisbie 1986; Yarkony 1994).

32.5.1.2 Dressing

Many dressing materials have been introduced. The dressing materials/modalities currently available require the physician to have a better understanding of the wound healing process, differentiating between the various dressing materials, and identifying the conditions for which each class of dressing should be used (Shai and Maibach 2005). Dressings were designed to maintain an optimal microenvironment for healing processes and high wound humidity. The dressing should control the exudates, eliminate dead space, keep the wound bed moist, and keep the surrounding skin dry. There are many dressing materials available commercially. However, there is little evidence to support the superiority of a particular brand. Dressings are used to protect the wound from contamination or additional trauma, to provide compression of swelling of the wound, to absorb exudate, to remove necrotic tissue, and to apply medications (Boyko et al. 2018). The goals of dressing are keeping the wound bed continuously moist and the surrounding skin dry. The choice of dressings is partly

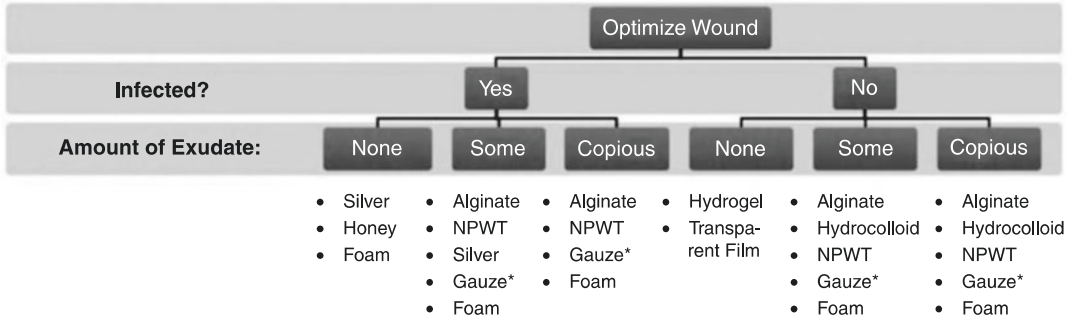

Fig. 32.5 Algorithm for help in choosing an appropriate class of dressings for pressure injury management. *Gauze dressings can be used if limited options available require more frequent dressing changes. From Boyko et al. (2018), with permission

determined by the experiences and preferences of the practitioner depending on the wound condition (Boyko et al. 2018; Sunn 2014) (Fig. 32.5). Each product has advantages and disadvantages, and no single dressing is suitable for all wounds (Table 32.6).

The four main classes of dressings proposed by the FDA are: non-resorbable gauze/sponge, occlusive, hydrogel, and hydrophilic/absorptive. *Gauze/sponge dressings* are used primarily to cover a wound surface area after application of topical preparations such as antibacterial creams. An occlusive or moisture-retentive dressing ensures adequate moisture vapor permeability within the wound's environment and thus provides ideal conditions for wound healing.

Subtypes of occlusive dressings are thin films, hydrocolloid dressings, and foam dressings. In its basic form, an occlusive dressing is composed of a synthetic polymer such as polyethylene or polyurethane, with or without an adhesive backing. *Films* were developed as the first occlusive dressings, followed by more complex products such as hydrocolloid dressings and foam dressings. Films are composed of a thin polyurethane film that is permeable to moisture vapor and gases, but impermeable to fluid and bacteria (Shai and Maibach 2005). Most films are adhesive and can therefore also be applied as a secondary dressing applied over other topical preparations. *Hydrocolloid dressings* contain hydrocolloidal hydrophilic particles (mainly sodium carboxy methyl cellulose) that are gel-forming. Other substances may be included such as gelatin or pectin. When hydrocolloids dressings are applied to an ulcer surface, the hydrocolloid substance interacts with the wound's fluid, resulting in a characteristic gelatinous yellow mass over the wound. This gelatinous mass helps create a moist environment and facilitates autolytic debridement, granulation tissue formation, and epithelialization. The gelatinous mass is between the dressing and the wound bed. Thus, when the dressing is removed or changed there is no damage to superficial tissues within the ulcer bed, including as the granulation tissue and the new regenerative epithelium. The accepted indications for hydrocolloid dressings are mild to moderate exudating wounds, burn wounds, and donor sites. The use of hydrocolloid dressings on infected or necrotic wounds is definitely contraindicated. *Foam dressings* are made of a polymeric material, such as polyurethane, that is made to contain air bubbles. The spaces embedded within the dressing material can absorb fluids. Since most of the foam dressings are occlusive, the indication is similar to that for hydrocolloids.

Hydrogels consists of a three-dimensional matrix of hydrophylic polymers such as carboxymethylcellulose (Intrasite gel®) or polyethylene oxide (Vigilon®), combined with a high water

Table 32.6 Advantages and disadvantages of commonly used dressing products for pressure injuries

Dressing category	Indications	Advantages	Disadvantages	Considerations
Gauze dressings	• Exudative wound • Wounds with dead space, sinus, tunneling • Wounds with exudate and necrotic tissue	• Good mechanical debridement • Cost-effective filler for large wounds	• Delayed healing • Require secondary dressing	• If too wet, dressings will macerate surround skin • Good for packing dead space • Need frequent dressing change
Transparent films Clear, adhesive, semipermeable membrane dressing	• Stage I and II ulcers • For autolytic debridement • Cover for hydrophilic powder or hydrogels	• Promote autolytic debridement • Minimize friction • Impermeable to external fluid or bacteria	• Nonabsorptive • Not for fragile surrounding skin or infected wounds	• Avoid in wounds with infection, copious drainage or tracts • Tegaderm, Opsite, DermaFilm, Polyskin, Cutifilm, Epiview
Hydrocolloids Adhesive wafers containing hydrophilic/ absorptive particles	• Protection of partial-thickness wounds • Autolytic debridement of necrosis or slough • Wounds with mild exudate	• Maintain a moist wound • Nonadhesive to healing tissue • Comfortable • Minimal to moderate absorption	• Not for heavy exudate, sinus tracts, or infection • Odor and yellow drainage on removal	• Change every 3–7 days • Avoid for infection or tracts • Comfeel, Duoderm, Tegasorb, Restore, Hydrocol, Ultec, Replicare
Foams Semipermeable membranes, hydrophilic or hydrophobic	• Partial- and full-thickness wounds	• Nonadherant • Provide some padding	• Not for dry eschar or wounds with no exudate	• Protect intact surround skin with skin sealant to prevent maceration • Polymem, Contreet, Allevyn, Lyofoam, Mediplex, Xtrasorb, Biatain, Curafoam, Tielle, 3M Foam, Hydrasorb
Hydrogels Gels or sheet forms	• Partial- and full-thickness wounds • Wounds with necrosis and slough	• Fill dead space • Rehydrate dry wound bed • Minimal to moderate absorption	• Requires a secondary dressing • Not for heavy exudation • May macerate surrounding skin	• Sheet form can promote pseudomonas and yeast • Dressing changes every 8–48 hours • Use skin barrier to decrease surrounding skin maceration • Curasol, Aquasorb, Carrasyn, Aquaflo, Curafil, Duoderm hydroactive gel, Purilon gel
Alginates Rope or pad forms	• Large amounts of exudate • Wounds with exudate and necrosis • Infected and noninfected exudating wounds	• Absorb 20 times their weight in drainage • Fill dead space • Supports debridement in exudate wound	• Require secondary dressing • Not for dry or light exudate • Can dry wound bed	• Sorban, Seasorb, Algisite, Acticoat, Melgisorb, Algiderm, Nu-derm, Curasorb, Tegagen alginate dressing

content, usually more than 90%. Hydrogel dressings can also be considered for softening black, dry necrotic material, due to their hydrating properties. However, a beneficial effect, if any, is expected to occur relatively slowly. Other forms of debridement, such as surgical debridement, should be considered when treating dry, black necrotic material on an wound bed.

Hydrophilic dressings are designed to absorb exudate. The main representatives of hydrophilic dressings are alginate dressing, dextranomer hydrophilic granules, or activated charcoal dressing. *Alginate dressings* consist of polysaccharide fiber that contain alginic acids, which are obtained from various species of seaweed. The fibers absorb the ulcer exudate to form a highly absorbent hydrophilic gel. This interaction results in a moist wound environment that can provide appropriate conditions for autolytic debridement. Alginate dressings are indicated for moderate to heavy exudating cutaneous ulcers. *Dextranomer hydrophilic preparations* contain microspheres, i.e., granules with a diameter of 0.1–0.3 mm in dry form, which consist of the dextranomer hydrophilic polysaccharide. Upon contact with liquid, the granules absorb water and swell to saturation. *Activated charcoal* is bound to a semipermeable membrane. These dressings protect the ulcer from external infection and trauma. Dressings that combine activated charcoal and silver (0.15%) have been developed, i.e., silver-impregnated activated charcoal dressings (Shai and Maibach 2005).

Negative-pressure wound therapy (NPWT, vacuum wound therapy) devices include occlusive dressing and a suction pump that creates negative pressure on the wound. NPWT distributes negative pressure (a continuous or cyclic force of −125 mmHg) across a wound surface to promote healing of clean stage 3 and 4 pressure injuries. The negative pressure in the wound bed is proposed to facilitate wound healing by increasing blood flow, reducing local tissue edema, decreasing bacterial colonization, and promoting granulation tissue formation and mechanical wound closure (Dumurgier et al. 1991).

32.5.1.3 Infected Pressure Injury Wound

Uninfected wounds promote healing. There are two types of infections: superficial critical colonization (localized infection) and deeper and surrounding infection (systemic infection). The preferred treatment for wounds exhibiting superficial critical colonization is local (topical) antimicrobial agents, whereas systemic antibiotics and debridement should be considered for deeper and surrounding bacterial infections to facilitate wound healing (RNAO 2016).

Topical antimicrobials are generally not recommended for the treatment of locally infected pressure injuries because of the risk of antibiotic resistance, hypersensitivity, inability to penetrate deeper pressure injuries, and uncontrolled systemic absorption of the medication when applied to larger wounds. If a wound does not heal and there is a clinical suspicion of wound infection, a topical antibiotics trial for two weeks may be considered. Wound cultures are of questionable value, as they may reflect colonization and not the pathological organism. Ointments are non-water soluble and can cause damage to wound drainage and should be used with caution. If the wound does not respond to topical antibiotics, systemic antibiotics may be considered. Systemic antibiotics are generally justified only when there is bacteremia, sepsis, advancing cellulitis, or osteomyelitis. Swab cultures are not useful for determining whether a pressure injury is infected and only reflect the bacteria on the wound surface. Tissue biopsy or wound bacteriology at debridement can determine if there are bacteria within the tissue, and wound healing may be impaired if the number of bacteria is greater than 105. Progressive cellulitis is an invasive tissue infection and must be treated with appropriate antibiotics.

Approximately 25% of nonhealing pressure injuries have underlying osteomyelitis. Osteomyelitis is sometimes difficult to diagnose. If the bone feels gritty or soft when probing during a clinical assessment and the pressure injury has either failed to heal or has reopened with treatment, osteomyelitis should be suspected.

Imaging with radiographs, three-phase bone scan with SPECT, MRI with contrast, or tagged white blood cell (WBC) scan with SPECT are useful diagnostic tools. Definitive diagnosis is based on bone biopsy and culture (Rosin et al. 2020). The most common organisms isolated from pressure injuries are *Proteus mirabilis*, group D *streptococci, E. coli, Staphylococcus, Pseudomonas* species, and *Corynebacterium* organisms. Treatment of osteomyelitis includes appropriate antibiotics for 6–12 weeks or surgery.

32.5.1.4 Nutrition

The most important cause of wound healing is nutrition. Useful assessment for nutritional status includes the total lymphocyte count, serum albumin and prealbumin, and transferrin levels, and urine nitrogen study. Proper caloric intake is necessary for the human body to function. Energy requirements are a product of the body's basal energy expenditure. This can be calculated using the Harris–Benedict formula (see Chap. 28). Protein requirement also ranges from 1 to 2 g/kg of body weight per day (Mandt et al. 1992). The goal is to meet nutritional requirements for normal wound healing without overfeeding (Mandt et al. 1992). Evaluation of the patient's current nutritional status often includes clinical laboratory tests such as albumin or prealbumin. Fifty percent of serum protein synthesized by the liver is albumin, the most abundant plasma protein. Yet, serum albumin levels are not valuable indicators of nutritional status in the marasmic and critically ill patient (Bass and Phillips 2007). The transferrin level should be greater than 180 mg/dL and the lymphocyte count greater than 1500/μL. The 24-h urinary nitrogen determinations are useful for determining protein requirement and balance. Blood screening for nutritional barriers to wound healing is presented in Table 32.7. Vitamin C, vitamin A, and zinc supplementation is helpful for wound healing. Iron, folate, and vitamin B12 supplementation helps to optimize erythropoiesis in the anemic patient (Dhall et al. 2013) (Table 32.8).

Table 32.7 Blood screening for nutritional barriers to wound healing

Suggested blood screen	Screening for	Normal values
CBC	Hemoglobin (g/dL)	14–18 (male), 12–16 (female)
Iron status screening: ferritin, serum iron, % saturation, TIBC (toral iron binding capacity)	Ferritin (μg/L)	41–300
	Serum iron (Fe) (μmol/L)	11–32
	Sat %	0.20–0.65
	TIBC (μmol/L)	45-82
CRP, ESR: inflammation/infection, anemia of chronic disease	CRP (mg/L)	<0.8
	ESR (mm/h)	<6 ≤10
Prealbumin, albumin: severity of illness, risk for malnutrition	Prealbumin (mg/dL)	18–40
	Albumin (g/dL)	3.9–5.0
BUN, creatinine: assess for dehydration and renal function	BUN (mg/dL)	6–25
	Creatinine (mg/dL)	≤1.3
Fasting blood glucose and HgbA1C: assess for hyperglycemia/diabetes	FBG (mg/dL)	100–125
	HgbA1C	4–6%
Thyroid function: assess for hypothyroidism	TSH (mU/L)	0.4–5.0

Table 32.8 Dietary supplement helpful for wound healing

Nutrition	Benefit	Dose
Calories	• aids in tissue defense and wound repair	• 31–34 calories/kg/d of IBW
Protein	• necessary for collagen synthesis	• 1.25–1.5 gm/kg/d of IBW
Vitamin C	• aids in collagen synthesis	• 500–1000 mg qd
Vitamin A	• for stimulation of epithelial tissue	• 20,000–25,000 IU qd
Iron	• required for oxygen transport • cofactor for collagen synthesis	• Ferrous sulfate 300 mg tid or • Ferrous gluconate 650 mg tid
Zinc oxide	• cofactor for collagen synthesis	• 25–50 mg qd

Recommended dietary supplements include a combination of arginine, zinc, and vitamin C, which can be obtained through food and/or special nutrition supplements. The recommended dietary intake for people with pressure injures is: 30–35 kcal/kg/body weight, protein 1.25–1.5 g protein/kg/body weight, arginine 4.5 g/day, ascorbic acid 500 mg/day, fluid 1 mL/kcal/day, and zinc. Proteins are particularly important for wound healing because they have the ability to promote positive nitrogen balance and improve healing rates. Protein is an important nutrient in the healing of pressure injuries, but people need to be evaluated for their ability to tolerate high-protein supplementation. Renal function should be evaluated to ensure that the recommended amount of protein does not affect renal function. Arginine, an amino acid, is effective in healing pressure injuries. It has generally been shown to affect tissue repair following trauma by reducing the time required to achieve complete healing of pressure injury with arginine supplementation.

In summary, the treatment strategies are as follows: accurately determined wound stage; minimizing pressure time, shear, friction, and moisture; adequate bed surface; optimal caloric and protein intake, zinc, vitamin C, and vitamin A supplementation; cleansing wound regularly; gentle debridement; treat infection; dressing should be moist and fill empty space; skin around wound to be dry; and if necessary, surgical consultation (Dhall et al. 2013; Dinsdale 1974).

32.5.2 Pressure Injury Management in Practice

Stage 1 pressure injuries are characterized by non-blanchable erythema when pressed, but the lesions must be touched and palpated for examination, not just with the naked eye. The treatment of stage 1 pressure injuries is aimed at preventing further ulceration. Appropriate pressure relief and posture should be used for each part of the heel, ischial tuberosity, and sacrum. The sacrum should be placed on the bedside to side, and the head should not be raised more than 30 degrees. Stage 1 pressure injuries should be carefully monitored for "deep tissue pressure injury."

A stage 2 pressure injury is sometimes recognized as a pressure injury when it progresses to a stage 2 pressure injury and is easily confused with dermatitis or abrasion due to moisture. It is usually wiped with saline, and collagenase is used once every other day. When using collagenase, preparations containing silver should not be used as they deactivate collagenase. A dry collagen dressing may also be used or dry hydrofiber dressing in case of a large amount of exudate.

In stage 3 pressure injury, dead tissues should be scraped or debrided with scissors, blades, etc., and then treated with negative-pressure wound therapy. When the depth of the wound gradually decreases up to 0.1–0.3 cm, the wound is treated with the same method as the treatment of stage 2 pressure injury.

In the case of stage 4 pressure injury, the dead tissue is debrided, and when it is suspected of an infected wound, it is dressed with cadexomer iodine, deeply filled with hydrofiber and an adhesive dressing. The wound dressing is done daily or every other day. If there is suspicion of osteomyelitis, MRI should be used for diagnosis. In case of osteomyelitis, a bone biopsy can be performed as needed. The principle is to treat with negative-pressure wound therapy during the appropriate antibiotic treatment. Negative-pressure wound treatment is changed once or twice a week. Otherwise, the treatments are based on a stage 3 wound, and if the wound becomes shallow enough, the patient should be treated according to the stage 2 wound treatment. The treatment of unstageable pressure injuries is performed in the same way as stage 4 pressure injuries. The unstageable pressure injuries begin with an antimicrobial dressing using hydrofiber. Each time the dressing is done, the dead tissue is debrided.

The dressing principle and recommended dressing products for each stage of pressure injury are summarized in Table 32.9.

Table 32.9 Dressing principle and recommended dressing products for each stage of pressure injury

Category	Dressing	Products
Stage I Non-blanchable erythema	Offloading	Special beds/mats Transparent films, hydrocolloids
Stage II Partial-thickness skin loss	Offloading, collagenase, adherent dressing, foam dressing	Transparent films, hydrocolloids, hydrogels, Foams, alginates
Stage III Full-thickness skin loss	Offloading, negative pressure wound therapy, collagen dressing, skin substitutes	Negative pressure wound therapy (NPWT), hydrogels, foams, alginates
Stage IV Full-thickness tissue loss	Offloading, negative pressure wound therapy, sharp debridement, collagen dressing, skin substitutes	NPWT, hydrogels, foams, alginates
Unstageable Depth unknown	Offloading, sharp debridement, cadexomer iodine dressing, silver dressing	
Deep tissue injury Depth unknown	Offloading	Special beds/mats

32.5.3 Surgical Management

Although there is no consensus on the extent and condition of pressure injuries to be operated on, unlike in the general population, patients with spinal cord injuries have an increased risk of additional pressure injuries in the course of their life; tissue preservation in the areas of prevalent pressure injuries as possible should be considered. Therefore, it is important to minimize the scope of surgery. Regardless of the severity of the pressure injuries, it is necessary to determine the operation after observing the improvement with conservative treatment for at least 2 weeks.

32.5.3.1 Reconstruction

When performing musculocutaneous flaps, only a limited number of patients can be performed and may affect the outcome when the patient is repeatedly subjected to pressure injuries. Musculocutaneous and fasciocutaneous flaps are the procedure of choice for patients with spinal cord injury, who require surgical closure of the pressure injury. Temporary diverting colostomy may be considered if there is fecal incontinence that disturbs the wound, or if it is suspected to interfere with postoperative healing of pressure injuries over the sacrum and ischial tuberosities (Kruger et al. 2013). Prophylactic ischiectomy is not recommended. Ischiectomy does not prevent recurrence of the pressure injury on the area.

32.5.3.2 Postoperative Care

Postoperatively, strict bed rest is prescribed on a low-air-loss mattress or an air-fluidized bed to maintain pressure off the surgical site as much as possible. For treatment of the sacrum or ischial tuberosity, the head of the bed should not be elevated to greater than 15°. This position increases the shearing force on the repaired wound site. There is no consensus on the required immobilization duration post-flap, which varies based on the size of the flap as well as the individual protocols and ranges from 2 to 6 weeks. The minimum postoperative bed confinement is 2 weeks, followed by gradual remobilization in the rehabilitation setting. Patients in bed rest receive passive physiotherapy of unaffected joints, intermittent pneumatic compression of the legs to prevent thromboembolism, and bladder drainage using indwelling urethral catheter. The personal bowel program starts on the third postoperative day. When ready for sitting, the patient is transferred to bed and examined the range of motion of the joints and orthostatic hypotension. The patient may begin to sit for 10–15 min intervals with careful attention to surgical wound healing when the patient becomes tolerable to passive range of motion of the hips up to 90° flexion with no stress to the surgical wound. Full sitting tolerance is achieved 6–7 weeks after surgery.

32.6 Marjolin's Ulcer

Marjolin's ulcer may occur in wounds that have been open for long periods, usually 20 or more years. The diagnosis is suspected by the growth of exophytic tumor at the wound edges, although this does not always occur. Biopsy of suspicious areas in chronic wounds is appropriate (Berkwits et al. 1986). A common diagnosis is squamous cell carcinoma. Treatment is wide resection and flap reconstruction of the defect. The prognosis is not good. Most patients die of metastatic cancer within 2 years despite adequate local control.

References

Ayello EA, Belmore B, Smart H, et al. Survey results from the Philippines: NPUAP changes in pressure injury terminology and definitions. Adv Skin Wound Care. 2018;31:601–6.

Barnett RI, Ablarde JA. Skin vascular reaction to short durations of normal seating. Arch Phys Med Rehabil. 1995;76:533–40.

Bass MJ, Phillips LG. Pressure sores. Curr Probl Surg. 2007;44:101–43.

Berkwits L, Yarkony GM, Lewis V. Marjolin's ulcer complicating a pressure ulcer: case report and literature review. Arch Phys Med Rehabil. 1986;67:831–3.

Boyko TV, Longaker MT, Yang GP. Review of the current management of pressure ulcers. Adv Wound Care (New Rochelle). 2018;7:57–67.

Byrne DW, Salzberg CA. Major risk factors for pressure ulcers in the spinal cord disabled: a literature review. Spinal Cord. 1996;34:255–63.

Caliri MHL. Spinal cord injury and pressure ulcers. Nurs Clin North Am. 2005;40:337–47.

Chen Y, Devivo MJ, Jackson AB. Pressure ulcer prevalence in people with spinal cord injury: age-period-duration effects. Arch Phys Med Rehabil. 2005;86:1208–13.

Consortium of Spinal Cord Medicine. Pressure ulcer prevention and treatment following spinal cord injury. A clinical practice guideline for health care professionals. 2nd ed. Washington, DC: Paralyzed Veterans of America; 2014.

Daniel RK, Wheatley D, Priest D. Pressure sores and paraplegia: an experimental model. Ann Plast Surg. 1985;15:41–9.

Dhall SS, Hadley MN, Aarabi B, et al. Nutritional support after spinal cord injury. Neurosurgery. 2013;72:255–9.

Dinsdale SM. Decubitus ulcers: role of pressure and friction in causation. Arch Phys Med Rehabil. 1974;55:147–52.

Dorsett P, Geraghty T. Health-related outcomes of people with spinal cord injury: a 10 year longitudinal study. Spinal Cord. 2008;46:386–91.

Dumurgier C, Pujol G, Chevalley J, et al. Pressure sore carcinoma: a late but fulminant complication of pressure sores in spinal cord injury patient: case reports. Paraplegia. 1991;29:390–5.

Edsberg LE, Black JM, Goldberg M, et al. Revised national pressure ulcer advisory panel pressure injury staging system: revised pressure injury staging system. J Wound Ostomy Continence Nurs. 2016;43:585–97.

Frisbie JH. Wound healing in acute spinal cord injury: effect of anticoagulation. Arch Phys Med Rehabil. 1986;67:311–31.

Groah SL, Schladen M, Pineda CG, et al. Prevention of pressure ulcers among people with spinal cord injury: a systematic review. PM R. 2015;7:613–36.

Ho CH, Bogie K. The prevention and treatment of pressure ulcers. Phys Med Rehabil Clin N Am. 2007;18:235–53.

Huang L, Woo KY, Liu LB, et al. Dressings for preventing pressure ulcers: a meta-analysis. Adv Skin Wound Care. 2015;28:267–73.

International Review. Pressure ulcer prevention: pressure, shear, friction and microclimate in context. A consensus document. London: Wounds International; 2010.

Jones KR, Fennie K, Lenihan A. Evidence-based management of chronic wounds. Adv Skin Wound Care. 2007;20:591–600.

Kosiak M. Etiology of decubitus ulcers. Arch Phys Med Rehabil. 1961;42:19–29.

Kruger EA, Ires M, Ngann Y, et al. Comprehensive management of pressure ulcers in spinal cord injury: current concepts and future trends. J Spinal Cord Med. 2013;36:572–85.

Makhsous M, Priebe M, Bankard J, et al. Measuring tissue perfusion during pressure relief maneuvers: insights into preventing pressure ulcers. J Spinal Cord Med. 2007;30:97–507.

Mandt J, Teasley-Strausburg K, Shronts E. Nutritional requirements. In: Teasley-Strausburg K, editor. Nutritional support handbook. Cincinnati: Harvey Whitney Books; 1992.

Meijer JH, Germs PH, Schneider H, et al. Susceptibility to decubitus ulcer formation. Arch Phys Med Rehabil. 1994;75:318–23.

Michael K. Prevention and rehabilitation of pressure ulcers. Adv Skin Wound Care. 1991;4:60–9.

National Pressure Ulcer Advisory Panel. Pressure ulcer stage revised by NPUAP. Washington, DC: NPUAP; 2016. http://www.npuap.org/resources/educational-and-clinical-resources/pressure-injury-staging-illustrations/, http://www.npuap.org/resources/educational-and-clinical-resources/npuap-pressure-injury-stages/.

National Pressure Ulcer Advisory Panel (NPUAP) Pressure ulcer scale for healing, PUSH tool version 3.0.

(1998). http://www.npuap.org/resources/educational-and-clinical-resources/push-tool/ push-tool/.
National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham, AL: National Spinal Cord Injury Statistical Center; 2021.
Nola GT, Vistnes LM. Differential response of skin and muscle in the experimental production of pressure sores. Plast Reconstr Surg. 1980;66:728–33.
Patterson RP, Fisher SV. Sitting pressure-time patterns in patients with quadriplegia. Arch Phys Med Rehabil. 1986;67:812–4.
Posthauer ME, Banks M, Dorner B, et al. The role of nutrition for pressure ulcer management: national pressure ulcer advisory panel, European pressure ulcer advisory panel, and pan pacific pressure injury alliance white paper. Adv Skin Wound Care. 2015;28:175–88.
Reddy M, Gill SS, Kalkar SR, et al. Treatment of pressure ulcers: a systematic review. JAMA. 2008;300:2647–62.
Regan MA, Teasell RW, Wolfe DL, et al. A systematic review of therapeutic interventions for pressure ulcers after spinal cord injury. Arch Phys Med Rehabil. 2009;90:213–31.
Reger SI, Ranganathan VK, Sahgal V. Support surface interface pressure, microenvironment, and the prevalence of pressure ulcers: an analysis of the literature. Ostomy Wound Manage. 2007;53:50–8.
Registered Nurses' Association of Ontario (RNAO). Assessment and management of pressure injuries for the interprofessional team. 3rd ed. Toronto, ON: Registered Nurses' Association of Ontario; 2016.
Rosin NR, Tabibi RS, Trimbath JD, et al. A primary care provider's guide to prevention and management of pressure injury and skin breakdown in people with spinal cord injury. Top Spinal Cord Inj Rehabil. 2020;26:177–85.
Shai A, Maibach HI. Wound healing and ulcers of the skin. Diagnosis and therapy-the practical approach. New York: Springer; 2005.
Sunn G. Spinal cord injury pressure ulcer treatment: an experience-based approach. Phys Med Rehabil Clin N Am. 2014;25:671–80.
The editors of nursing. Pressure ulcers get new terminology and staging definitions. Nursing. 2017;47:68–9.
Weidner N, Rupp R, Taney KE, editors. Neurological aspects of spinal cord injury. Cham: Springer; 2017.
Yarkony GM. Pressure ulcers: a review. Arch Phys Med Rehabil. 1994;75:908–17.
Young RR, Woolsey RM, editors. Diagnosis and management of disorders of the spinal cord. Philadelphia, PA: W.B. Saunders; 1995.

Recommended Additional Reading

Bader D, Bouten C, Colin D, et al. Pressure ulcer research. Current and future perspectives. Heidelberg: Springer-Verlag; 2005.
Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.
Kumar S. Ergonomics for rehabilitation professionals. New York: CRC Press; 2008.
Romanelli M, Clark M, Gefen A, et al., editors. Science and practice of pressure ulcer management. London: Springer; 2018.
Thomas DR, Compton GA, editors. Pressure ulcers in the aging population. A guide for clinicians. London: Humana Press; 2014.

Abnormal Thermoregulation in Spinal Cord Injuries

33

Core body temperature (central temperature) is strictly maintained around 37 °C by the autonomic nervous system, called the thermoneutral zone. Heat production must exactly balance heat loss. Thermoregulation is the ability to precisely control core body temperature within a relatively narrow range despite exposure to a wide range of environmental temperature challenges (Wecht et al. 2021). The human body is equipped with a sensory system that can sense whether body temperature rises or falls (Mitchell and Laburn 1985). The hypothalamus integrates information from the temperature sensor and maintains temperature homeostasis through its thermoregulatory function. Certain areas within the hypothalamus, periaqueductal gray, and medullary nucleus raphe pallidus form the autonomic network to control temperature. Input is derived from peripheral (skin cold and warm sensors) and central receptors (warm-sensitive neurons within the preoptic-anterior hypothalamus). Thermoregulation and fever are mediated primarily through the hypothalamus and its effector mechanisms. Spinal cord injuries result in altered control of various physiologic mechanisms, including thermoregulation. Spinal cord injury leads to reduced afferent input to the thermoregulatory brain areas and a disruption of both vasomotor control and sweating capacity below the level of injury (Price and Trbovich 2018). Injuries above T6 are often associated with temperature fluctuations, hypothermia, and hyperthermia (Phillips et al. 1998; Wecht et al. 2015).

Core body temperature is regulated by a homeostatic process controlled primarily in the preoptic area of the anterior hypothalamus. Temperature dysregulation is defined as a person's inability to maintain core body temperature within the normal range (37 ± 0.6 °C) despite having no signs of illness or infection (Sessler 2009). Afferent information from thermoreceptors located throughout the body are transmitted mainly through the spinal cord to the temperature regulatory centers, which in turn activate mechanisms to produce or dissipate heat to maintain core temperature within normal physiological range (Tan and Knight 2018). People with high-level spinal cord injuries are less able to maintain their normal core body temperature when exposed to extreme environmental temperatures; those who do not have the ability to maintain a constant core body temperature regardless of ambient temperature refer to "poikilotherms" (Attia and Engel 1983; Downey et al. 1967). This ability is severely impaired after interrupting the efferent pathway to the hypothalamus (Schmidt and Chan 1992).

33.1 Anatomy and Physiology of Thermoregulation

The human body has a sensory system that detects changes of body temperature. Information from temperature receptors, which are widely

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distributed in many tissues, is transmitted to the hypothalamus through the spinothalamic tracts, where autonomic responses are coordinated, and to the cerebral cortex, where behavioral responses are coordinated. When body temperature tends to rise, typical responses seek cooler environments, shedding clothes, peripheral vasodilatation, and sweating. On the other hand, if body temperature tends to fall, typical responses are seeking warmth, putting on more clothes, peripheral vasoconstriction, and shivering, all responses that reduce heat loss or increase internal heat generation (Mitchell and Laburn 1985). The autonomic nervous system maintains internal body temperature with a strict range of around 37 °C. Eccrine sweating is the primary mechanism for evaporative heat loss to maintain thermoregulation in humans. Elevated core temperature triggers warm-sensitive neurons in the preoptic area of the hypothalamus to activate sweating pathways that descend to the thoracic spinal cord to synapse on preganglionic sympathetic neurons in the intermediolateral cell column to exist in segmental pathways. The preoptic area of the hypothalamus coordinates the activation of the mechanisms of heat dissipation or heat retention and thermogenesis (Pallubinsky et al. 2019). Postganglionic unmyelinated C fibers traverse the gray ramus, combine with peripheral nerves, and travel to the skin, where they innervate predominantly cholinergic sweat glands (Coon and Cheshire 2020).

Thermoregulation is the ability to maintain body temperature homeostasis by balancing heat production and heat loss. Although a typical resting core body temperature for humans is approximately 37 °C, the human internal temperature can fluctuate between 0.2 °C and 1.0 °C due to changes in the circadian rhythm over a 24 h period or during hormonal changes in the menstrual cycle (Minson and Brunt 2016). The human body has a remarkable ability to maintain a constant core temperature despite changes in ambient temperature. A normal unclothed adult can adjust the core temperature within 0.6 °C between 13 °C and 60 °C ambient temperatures in dry air. The ambient temperature range in which the normal body temperature is maintained as the metabolic process and evaporative process is called the thermoneutral zone (Pallubinsky et al. 2019), approximately between 27 °C and 33 °C for a naked adult (Fig. 33.1). If heat loss or heat gain exceeds the control mechanism, hypothermia and hyperthermia will occur.

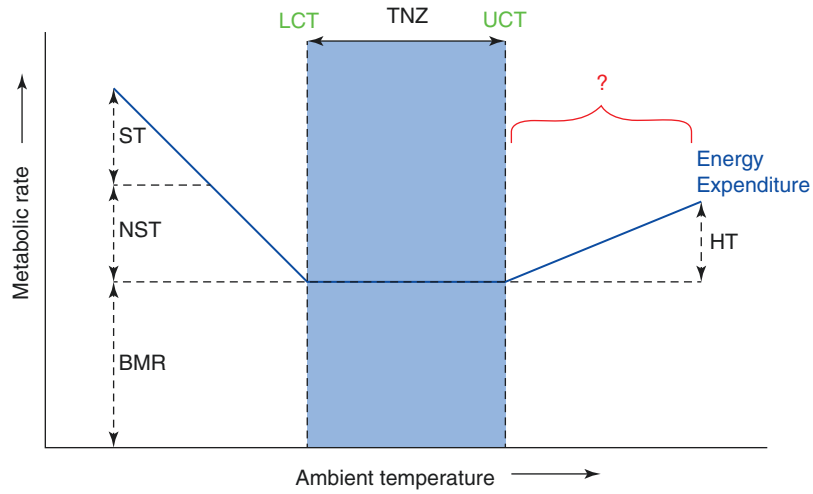

Fig. 33.1 The thermoneutral zone. The thermoneutral zone (TNZ) reflects the ambient temperature range wherein the energy expenditure is at basal level (basal metabolic rate, BMR) and there are no thermoregulatory changes in metabolic rate (*NST* non-shivering thermogenesis, *ST* shivering thermogenesis, *HT* heat-related thermogenesis). *LCT* lower critical temperature, *UCT* upper critical temperature. From Pallubinsky et al. (2019), with permission

Many sympathetic functions, including those that are particularly concerned with cutaneous blood flow and body temperature regulation, are controlled by the hypothalamus. The descending pathways synapse in the intermediolateral columns of T1-L2 segments of the spinal cord. Cutaneous blood flow, sweating, and piloerection depend on the activity of the sympathetic nervous system. The heat-sensitive temperature sensors are located mainly in the preoptic region of the anterior hypothalamus. The hypothalamus normally interprets afferent information about external and internal body temperature and integrates thermoregulatory responses to maintain body temperature within a narrow range. The skin also has warmth receptors, but relatively few compared to the numerous cold receptors. Other cold-sensitive receptors are likely located in the hypothalamus, midbrain, spinal cord, and other internal structures (Schmidt and Chan 1992). The hypothalamic noradrenergic and cholinergic efferents control vasomotor responses, sudomotor or sweating function, as well as shivering and piloerection. When the core temperature of the body is lowered, sympathetic noradrenergic efferents cause shivering, piloerection, and vasoconstriction to produce heat. As the core temperature rises, vasodilation and sweating occur, resulting in a cooling effect. Piloerection, which depends on the sympathetic activity of hypothalamic stimulation, increases insulation in mammals but is only vestigial in humans.

Details of the sympathetic distribution associated with temperature regulation are given in Table 33.1. The sympathetic nerve fibers which serve for sweating and vasomotor function pass in distance fiber tracts in the medulla and spinal cord. Thus, it is possible that an irregular trauma to the spinal cord, or a local cord lesion or other causes, produces dissociation of vasomotor function from sweating. The regulation of heat loss in humans depends mainly on cutaneous vasomotor activity and sweating along with a conscious regulation of insulation. Cutaneous vasomotor activity is dependent on the dual control of a reflex and a core temperature receptor mechanism. Vasomotor activity is influenced by central and skin temperatures. The normal reflex, which causes vasodilatation when the trunk is heated, is prevented when the cord temperature is low, the critical level being 36.5–36.8 °C. The reflex is also progressively inhibited if the initial skin

Table 33.1 Sympathetic innervation subserving temperature regulation

Structures	Efferent pathways			Main function
	Location of cell body in spinal cord and course of preganglionic neurons	Site of ganglionic synapse	Course of postganglionic fibers	
Head and neck				
Blood vessels	T1–T4 to cervical sympathetic chain	All cervical, internal carotid, and vertebral ganglia	In perivascular plexuses accompanying various branches of carotid and vertebral arteries	Vasoconstriction
Sweat glands	T2–4(5)* to cervical sympathetic chain	Cervical ganglia	With external carotid artery (supraorbital with internal)	Sweating (eccrine)
Upper extremities	T2–8(9)* to upper thoracic and cervical sympathetic chain	Middle and stellate ganglia, T2 and T3 ganglia	Rami communicantes to roots of brachial plexus, then to branches of plexuses	Vasoconstriction Sweating (eccrine) Pilomotion
Trunk	T4–10(11)* to sympathetic chain	Thoracic and lumbar ganglia	Approximately segmental distribution	Vasoconstriction Sweating (eccrine) Pilomotion
Lower extremities	T10–12, L1, 2(3)* to sympathetic chain	L1–5, S1–S3 paravertebral ganglia	Gray rami communicantes to lumbar and sacral plexuses: direct branches to perivascular plexuses	Vasoconstriction Sweating (eccrine) Pilomotion

( )*, These segments are inconstant

temperature on the trunk is below 33 °C. Active vasodilation and sweating are mediated by sympathetic cholinergic nerves that release acetylcholine and an unknown cotransmitter to mediate sweating and active vasodilation, respectively (Kellogg et al. 1995; Minson and Brunt 2016). Vasoactive intestinal peptide (VIP) and nitric oxide (NO) can be the cotransmitter.

Sweating is the most effective method of heat dissipation in humans. Sweating causes heat loss through evaporation and is very effective when the humidity in the air is not high. Sweating helps lower core body temperature when it rises above thermoneutral zone. This can happen due to environmental heat exposure or decreased heat dissipation (e.g., excessive clothing or bed coverings) or as a result of increased heat production (e.g., excessive muscular activity) (Struhal et al. 2017). There are two histologically distinct types of sweat glands: the eccrine and the apocrine glands. The eccrine glands are located over most of the body surface and affect temperature regulation. The eccrine glands have a roughly segmental distribution and are innervated by postganglionic sympathetic fibers with acetylcholine as a chemical transmitter. Sweat glands of palms and soles do not participate in heat dissipation. The apocrine glands, often involved in emotional sweating, have a limited distribution and are found particularly in the axillae, the anogenital region, and around the nipples. The apocrine glands are stimulated by circulating humoral agents, principally adrenaline.

Normal metabolism generates heat, and if the heat production of the body is increased, for example, by exercise, it must be dissipated by additional heat loss through cutaneous vasodilatation or sweating. Various drugs, such as atropine, amphetamine, ecstasy (MDMA), cocaine, penicillins, cephalosporins, phenytoin, or amphotericin B, can trigger release of cytokines, facilitating hyperthermia or triggering fever (Sessler 2009). In cold environment, however, increased internal heat production may be required to maintain body temperature, and this is achieved by increased involuntary activity in skeletal muscles that causes shivering. Shivering provides powerful protection against hypothermia, but when the core temperature falls below about 30 °C, many body functions, including shivering, begin to fail, and the body tends to cool down rapidly. Although metabolism can be significantly increased during shivering in normal person, the increase in individual with spinal cord injury is much lower.

33.2 Disorder of Thermoregulation in Spinal Cord Injuries

Core body temperature remains relatively stable in normal people. However, patients with spinal cord injuries have wide variation of their core temperature due to a disruption on the nervous pathways in the temperature regulation of the spinal cord (Attia and Engel 1983). The sympathetic nerves exit the spinal cord at T1–L3. Therefore, tetraplegics (>C7) with complete spinal cord injury lose all sympathetic innervation, which leads to the greatest alterations in thermoregulation. The heart is innervated by T1–T5, so injuries above T6 result in an impaired ability to increase heart rate and actively increase contractility. All increases in heart rate in individuals with complete lesions above T1 are the result of vagal withdrawal. Lesions above T5 result in a loss of innervation of the splanchnic region (T5–L2), thereby impairing the ability to effectively redistribute blood flow. In addition, loss of innervation to the kidneys and adrenal glands (T4–T11) can affect hormonal control of the circulation during exercise and passive heat stress (Minson et al. 1999). The skin of the face and neck is innervated by T1–T4. Thus, despite normal sensory function of these regions, tetraplegics may have little or no control of sympathetically mediated vasodilation of the face. The skin of the upper extremity is innervated by T5–T7 segments, the trunk by T4–T12, and the lower extremity by T10–L3 (Minson and Brunt 2016; Normell 1974). Figure 33.2 shows the distribution of the thermoreceptors and sweat glands and the thermoregulation reflex arc, which consisted of an afferent input of the thermoreceptors in the skin, muscle, and abdomen and an efferent output to the sweat glands.

As shown in Fig. 33.3, the core temperature decreases due to the inability to constrict cutane-

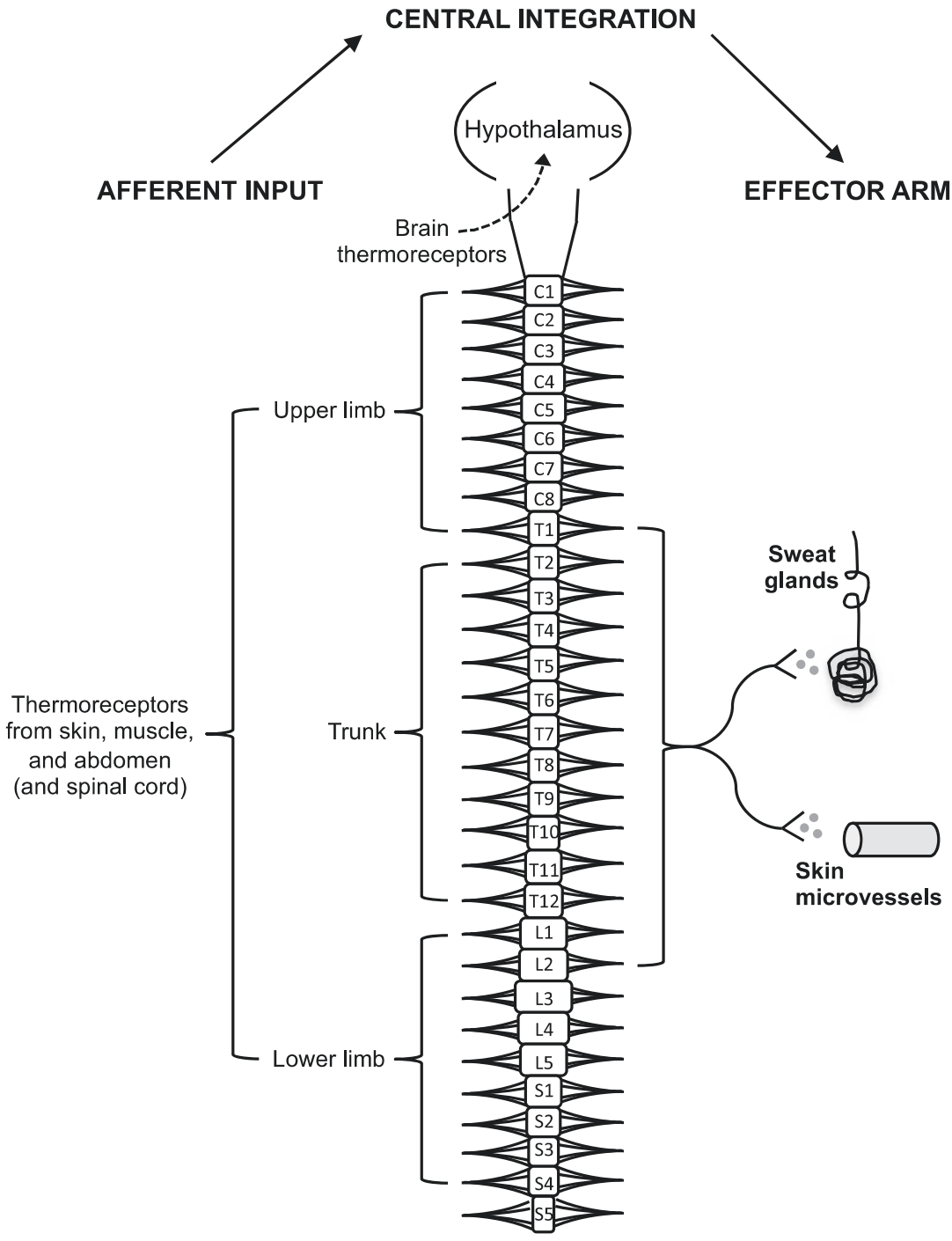

Fig. 33.2 Distribution of the thermoreceptors and sweat glands and the thermoregulatory reflex arc consisted of the thermoreceptors and sweat glands. From Minson and Brunt (2016), with permission

ous blood vessels or activate shivering when exposed to cold ambient conditions. In contrast, due to an impaired ability to sweat and increase skin blood flow under conditions of increased heat, core temperature rises at a much faster rate in people with spinal cord injuries compared to

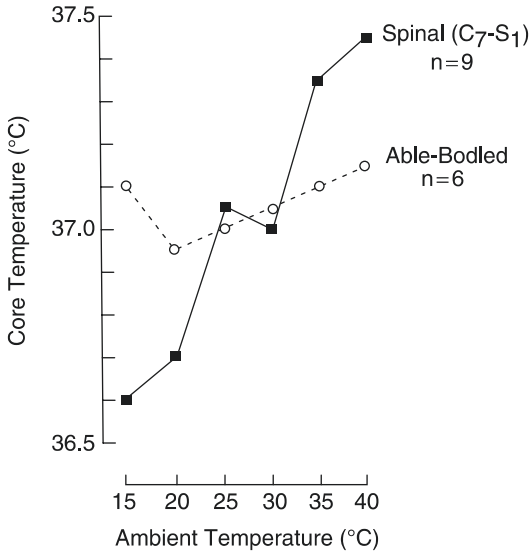

Fig. 33.3 Individuals with intact nervous systems are able to maintain core temperature across a wide range of ambient temperatures. However, body temperature in spinal cord injured individuals can vary greatly with changes in ambient temperature. Data from Attia and Engel (1983) redrawn by Sawka et al. (1989). From Minson and Brunt (2016), with permission

their able-bodied individuals (Minson and Brunt 2016). Disruption of the afferent pathways, including the spinothalamic tract, to the thermoregulatory center of the hypothalamus in people with spinal cord injuries decreases their ability to regulate body temperature. Individuals with complete spinal cord injuries above the T6 level usually have difficulty maintaining a normal core temperature with respect to changes in ambient temperature and are referred to as "partially poikilothermic" (Menard and Hahn 1991; Schmidt and Chan 1992). The hypothalamic efferent response is also affected by loss of sympathetic connections, resulting in impaired vasomotor control, impaired sweating below the level of injury, and loss of shivering (Biering-Sørensen et al. 2017; Karlsson et al. 2012). These poikilothermic effects are exacerbated by exercise, as the cardiovascular system cannot meet the demands for blood flow to maintain both exercise and thermoregulation. During exercise, the increased metabolic rate challenges the autonomic and cardiovascular systems to increase skin blood flow to divert warm blood to the skin surface for the heat dissipation (Minson and Brunt 2016).

People with spinal cord injuries may be susceptible to hypothermia or hyperthermia due to significant disturbances in the mechanisms of normal body temperature regulation, but hypothermia is more common (Khan et al. 2007). Patients with cervical cord lesions are at the greatest risk of maintaining their core temperature. Spinal cord injuries below the cervical level are at a much lower risk because they have more active voluntary muscles and maintain normal sympathetic activity which leads to sweating and vasomotor activity below the level of lesion. Shivering can occur only above the neurological level of injury, and thermoregulatory sympathetically mediated changes in vasomotor tone, metabolism, and sweating will theoretically be absent throughout the body (sympathetic outflow occurs at T1−L2). Therefore, thermoregulation after a cervical spinal cord injury depends on behavioral modification of the environment, local vasomotor reflexes, basal metabolic rate, and shivering above the level of the injury (Schmidt and Chan 1992). People with complete tetraplegia are particularly prone to hyperthermia, which is defined as rectal temperature above 101 °F (38.4 °C) due to impaired thermoregulation, and hypothermia defined as rectal temperature below 95 °F (35 °C). Since they often cannot control their body temperature in a narrow range, they often show poikilothermic, so that the body temperature can vary greatly depending on the ambient temperature. Sweat glands below the lesion are less sensitive to cholinergic activation, regardless of central or exogenous stimulation. However, glands above the level of the lesion can be more productive when individuals are exposed to physical exercise and physiologic stress (Yaggie et al. 2002). The mechanisms of thermoregulation in normal persons and persons with spinal cord injuries are summarized in Table 33.2.

During the acute phase of spinal cord injury or spinal shock, patients may be more severely poikilothermic and may not be able to regulate their body temperature because of severe vasodilatation and heat loss due to loss of sympathetic stimulation of the blood vessels and unopposed vagal

Table 33.2 Mechanisms affecting thermoregulation in normal persons and persons with spinal cord injuries

Mechanisms	Thermoregulatory reflexes		
	Normal persons	Persons with tetraplegia	Persons with paraplegia
To increase body temperature			
Vasoconstriction	First-line mechanism	Local reflexes only	Above LOI + local reflexes
Environmental modification	First-line mechanism	Heat-seeking behavior	Heat-seeking behavior
Shivering	Most potent	Above LOI	Above LOI
Metabolism	Less potent CT increases (immediately) + thyroid activity increases (weeks)	Shivering above LOI + thyroid activity increases (weeks)	Shivering above LOI + thyroid activity increases (weeks) + CT increases (sympathetic center)
To decrease body temperature			
Vasoconstriction	First-line mechanism	Local reflexes only	Above LOI + local reflexes
Environmental modification	First-line mechanism	Cold-seeking behavior	Cold-seeking behavior
Sweating	Most potent	Local or spinal reflexes	Above LOI + reflexes below LOI
Metabolism	Less potent CT decrease (immediately) + thyroid activity decreases (weeks)	Thyroid activity decreases (weeks)	Thyroid activity decreases (weeks) + CT decreases (sympathetic center)

CT chemical thermogenesis, *LOI* level of injury. From Schmidt and Chan (1992) with permission

activity. As a hypothermic condition, it is usually considered that the core body temperature is below 35 °C. After transection of the spinal cord, thermoregulatory sweating appears to be abolished in regions where the integrity of sympathetic connections with the thermoregulatory centers in the brain is not preserved. The core temperature of patients with cervical cord lesion by exposure to heat rapidly increases. Patients with T9 lesion might maintain a constant body temperature in hot air (35–37 °C) due to evaporation of sweat from normally innervated areas. Patients with T4 lesion gave an intermediate response (Guttmann et al. 1958).

The higher and more complete the spinal cord injury, the more abnormal the temperature regulation. The higher the injury, the larger the body surface area impaired, and the greater the temperature control dysfunction. People with complete tetraplegia may have normal body temperature from 1 °F to 2 °F (0.5–1 °C) lower than in neurologically intact individuals. Therefore, even patients with a low-grade fever may have significant infections. On the other hand, high body temperatures can be due to a higher ambient temperature or excessive warming by blankets. Abnormal thermoregulation may cause a rise in body temperature, but the cause of infection for a sustained or significant increase in temperature should be considered. Drugs that have autonomic activity, such as nifedipine and bethanechol, may cause hypothermic episodes (Menard and Hahn 1991). Anticholinergics can inhibit sweat production, which can be dangerous for someone exercising in the heat who already has impaired sweating capacities (Minson and Brunt 2016).

33.3 Assessment of Thermoregulatory Function

An international collaboration between the American Spinal Injury Association (ASIA) and the International Spinal Cord Society (ISCoS) was initiated to develop international standards for the documentation of the remaining autonomic functions after spinal cord injury (Alexander et al. 2009), which to be the first edition of the International Standards to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) in 2012 (ASIA 2012; Krassioukov et al. 2012). A second edition, designed to more

effectively determine the level and severity of autonomic nervous system injury after spinal cord injury and to measure changes over time and changes in response to therapeutic interventions, was published in 2021 (Wecht et al. 2021). In the second edition, the assessment points related to thermoregulation are core body temperature, with core temperature changing outside the normal range from exposure to hot or cold environmental temperature: hypothermia (≤35 °C), hyperthermia (≥38.0 °C), subnormal (35.1–36.3 °C), elevated (37.7–37.9 °C), or normal (36.4–37.6 °C). The environmental conditions for the thermoregulation assessment were conditional: 20–25 °C (68–77 °F); 30–50% relative humidity; wearing single-layer, indoor garments; after 10 min of rest; no liquid intake for at least 10 min prior to oral temperature measurement; no acute illness or infection. Also see Chap. 21.

33.4 Management of Poikilothermia

After an acute spinal cord injury, prehospital and emergency medical treatment requires special attention to body temperature as these individuals may be poikilothermic. Sometimes, poikilothermic hyperthermia or hypothermia is considered to be a serious pathological condition (Colachis and Otis 1995). In acute spinal cord injury in cold environments, measures to prevent hypothermia, such as the use of Mylar or blankets, are required. Drug commonly prescribed for people with spinal cord injuries, sedatives and opioids, may further reduce the impaired ability to conserve heat, while anticholinergics, serotonergics, and antihistamines may reduce heat dissipation (Handrakis et al. 2017).

People with spinal cord injuries, especially tetraplegia, should be careful to avoid excessive temperatures because they may not be able to get water without help. They can be in urgent situation if they are dehydrated and hypernatremia occurs. When the temperature is above 90 °F (32 °C), they should stay in the air-conditioned environment, remain hydrated by drinking water, wear light clothing, limit time and intensity of outdoor activity, and stay in shady and cooler areas. Strenuous exercise in hot and humid weather should be avoided (Price 2006).

References

Alexander MS, Biering-Sorensen F, Bodner D, et al. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord. 2009;47:36–43.

American Spinal Injury Association (ASIA). International standards to document remaining autonomic function after spinal cord injury. 1st ed. Atlanta, GA: American Spinal Injury Association; 2012.

Attia M, Engel P. Thermoregulatory set point in patients with spinal cord injuries (spinal man). Paraplegia. 1983;21:233–48.

Biering-Sørensen F, Alexander MS, van Asbeck FWA, et al. Version 1.1 of the international spinal cord injury skin and thermoregulation function basic data set. Spinal Cord. 2017;55:566–9.

Colachis SC 3rd, Otis SM. Occurrence of fever associated with thermoregulatory dysfunction after acute traumatic spinal cord injury. Am J Phys Med Rehabil. 1995;74:114–9.

Coon EA, Cheshire WP Jr. Sweating Disorders. Continuum (Minneap Minn). 2020;26:116–37.

Downey JA, Chiodi HP, Darling RC. Central temperature regulation in the spinal man. J Appl Physiol. 1967;22:91–4.

Guttmann L, Silver J, Wyndham CH. Thermoregulation in spinal man. J Physiol. 1958;142:406–19.

Handrakis JP, Trbovich M, Hagen EM, et al. Thermodysregulation in persons with spinal cord injury: case series on use of the autonomic standards. Spinal Cord Ser Cases. 2017;3:17086.

Karlsson AK, Krassioukov A, Alexander MS, et al. International spinal cord injury skin and thermoregulation function basic data set. Spinal Cord. 2012;50:512–6.

Kellogg DL, Pergola PE, Piest KL, et al. (1995) cutaneous active vasodilation in humans is mediated by cholinergic nerve cotransmission. Circ Res. 1995;77:1222–8.

Khan S, Plummer M, Martinez-Arizala A, et al. Hypothermia in patients with chronic spinal cord injury. J Spinal Cord Med. 2007;30:27–30.

Krassioukov A, Biering-Sørensen F, Donovan W, et al. International standards to document remaining autonomic function after spinal cord injury. J Spinal Cord Med. 2012;35:201–10.

Menard MR, Hahn G. Acute and chronic hypothermia in a man with spinal cord injury: environmental

and pharmacologic causes. Arch Phys Med Rehabil. 1991;72:421–4.
Minson CT, Brunt VE. Chapter 7 Thermoregulatory considerations for the performance of exercise in SCI. In: Taylor JA, editor. The physiology of exercise in spinal cord injury. New York: Springer; 2016.
Minson CT, Wladkowski SL, Pawelczyk JA, et al. Age, splanchnic vasoconstriction, and heat stress during tilting. Am J Phys. 1999;276(1 Pt 2):R203–12.
Mitchell D, Laburn HP. Pathophysiology of temperature regulation. Physiologist. 1985;28:507–17.
Normell LA. Distribution of impaired cutaneous vasomotor and sudomotor function in paraplegic man. Scand J Clin Lab Invest Suppl. 1974;138:25–41.
Pallubinsky H, Schellen L, van Marken Lichtenbelt WD. Exploring the human thermoneutral zone - a dynamic approach. J Therm Biol. 2019;79:199–208.
Phillips WT, Kiratli BJ, Sarkarati M, et al. Effect of spinal cord injury on the heart and cardiovascular fitness. Curr Probl Cardiol. 1998;23:641–716.
Price MJ. Thermoregulation during exercise in individuals with spinal cord injuries. Sports Med. 2006;36:863–79.
Price MJ, Trbovich M. Thermoregulation following spinal cord injury. Handb Clin Neurol. 2018;157:799–820.
Sawka MN, Latzka WA, Pandolf KB. Temperature regulation during upper body exercise: able-bodied and spinal cord injured. Med Sci Sports Exerc. 1989;21(5 Suppl):S132–S40.
Schmidt KD, Chan CW. Thermoregulation and fever in normal persons and in those with spinal cord injuries. Mayo Clin Proc. 1992;67:469–75.
Sessler DI. Thermoregulatory defense mechanisms. Crit Care Med. 2009;37(7 Suppl):S203–10.
Struhal W, Lahrmann H, Fanciulli A, et al., editors. Bedside approach to autonomic disorders. A clinical tutor. Cham: Springer; 2017.
Tan CL, Knight ZA. Regulation of body temperature by the nervous system. Neuron. 2018;98:31–48.
Wecht JM, La Fountaine MF, Handrakis JP, et al. Autonomic nervous system dysfunction following spinal cord injury: cardiovascular, cerebrovascular, and thermoregulatory effects. Curr Phy Med Rehabil Rep. 2015;3:197–205.
Wecht JM, Krassioukov AV, Alexander M, et al. International standards to document autonomic function following SCI (ISAFSCI): second edition. Top Spinal Cord Inj Rehabil. 2021;27:23–49.
Yaggie JA, Niemi TJ, Buono MJ. Adaptive sweat gland response after spinal cord injury. Arch Phys Med Rehabil. 2002;83:802–5.

Recommended Additional Reading

Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.
Green D, Olson DA, editors. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.
Guttmann L. Spinal cord injuries. Comprehensive management and research. Oxford: Blackwell Scientific Publications; 1976.
Illis LS, editor. Spinal cord dysfunction: assessment. Oxford: Oxford University Press; 1988.
Noback CR, Strominger NL, Demarest RJ, et al. The human nervous system: structure and function. 6th ed. Totowa, NJ: Humana Press; 2005.
Robertson D, Bigaaioni I, Burnstock G, et al. Primer on the autonomic nervous system. 3rd ed. London: Elsevier; 2011.
Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, third series, vol. 109. London: Elsevier; 2012.
Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury, Progress in brain research, vol. 152. New York: Elsevier; 2006.

Spasticity and Contractures in Spinal Cord Injuries

34

Spasticity can cause serious problems in the activity and participation of people with spinal cord injuries. It can also be a significant challenge for rehabilitation. However, current management approaches, including new drugs and technologies, can provide significant benefits for people with spinal cord injuries. This chapter aims to provide an overview of spasticity in spinal cord injuries, including definition, pathophysiology, and management.

Spasticity is usually defined as a velocity-dependent increase in the tonic stretch reflex (muscle tone) with exaggerated tendon jerks, clonus, and spasms, resulting from the hyperexcitability of the stretch reflex (Lance 1980). Initially, spasticity was defined on the basis of a strict and narrow physiological change. Lance's definition of spasticity has been widely accepted and used. More recently, spasticity has been defined as "a disorder of sensorimotor control, resulting from an upper motor neuron lesion, presenting as an intermittent or sustained involuntary activation of muscles" (Pandyan et al. 2005). This broad definition recognizes other symptoms of upper motor neuron syndrome that are part of the patient's experience: spasms (flexor, extensor, adductor), hyperreflexia, hypertonia, clonus, dyssynergia (inappropriate co-contraction of antagonistic muscle groups), and abnormal reflexes (Babinski, Hoffman, crossed adductor) (Cabahug et al. 2020). The original definition of spasticity by Lance (Lance 1980), *a motor disorder characterized by a velocity dependent increase in the tonic stretch reflex (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neuron syndrome,* could not describe the clinical relevance of upper motor neuron lesion collectively. Spasticity, which indicates an abnormal stretch reflex behavior, is a disabling component of upper motor neuron lesion including spinal cord injury. The upper motor neuron system consists of all the pathways above the anterior horn cell, including the spinal cord, brain stem, and brain. Spasticity includes a wide range of abnormal motor behavior due to upper motor neuron lesion. This causes increased muscle tone, increased muscle reactivity, reduced precision of voluntary muscle control, and the emergence of involuntary motor output. All of these effects can show time-dependent differences in static vs. dynamic conditions, flexor vs. extensor movements, and many other permutations. Clinically, spasticity can be easily recognized, but can be difficult to quantify and treat. The pathophysiology of spasticity is complex and controversial. There are many subtle considerations in the management of spasticity, and sometimes the clinician has to negotiate with the patient when adjusting the spasticity.

Spasticity is clinically apparent as spinal shock resolved. Spasticity is characterized by a velocity-dependent resistance to passive joint movement. The classic clinical definition of

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spasticity is velocity-dependent hypertonia that faster passive muscle stretch results in a stronger antagonistic contraction associated with greater and more synchronous activation of Ia afferents due to disruption of descending fibers, regardless of whether their origin is the cortical, bulbar, or spinal cord. The clinical "clasp-knife" phenomenon refers to a joint resistance that becomes stiffer at the beginning of its passive range of motion and then "gives way" over the rest of the range of motion. The clasp-knife phenomenon appears to be due to an exaggerated withdrawal reflex and the excitation-decay patterns of segmental interneurons (Cleland and Rymer 1990). Other clinical findings of spasticity include hyperactive muscle stretch reflex and clonus. Many persons with spinal cord injury also experience flexor and cutaneomotor spasms. It is important to differentiate spasticity from rigidity because both are more resistant to passive movement. Rigidity is a velocity-independent, bidirectional phenomenon associated with tremor, bradykinesia, or other extrapyramidal signs.

Spasticity is a dynamic entity. It changes over time and can be affected by other conditions unrelated to the original damage to the cord (Cabahug et al. 2020). The prevalence of spasticity depends on the level of injury, the severity of injury, injury pattern, time since injury, and other factors. The severity of spasticity does not linearly correlate with the severity of spinal cord injury (Adams and Hicks 2005). For example, a person with mild upper cervical central cord injury may have more severe spasticity in the upper extremities than the lower extremities, while in a person with the same central cord injury, slightly caudal lesion of the central cord syndrome may have decreased tone in the upper extremities relative to the lower extremities. More severe spasticity in a moderate degree of injury is likely to occur rather than in mild or very severe injury (Adams et al. 2007).

34.1 Pathophysiology

The underlying mechanism of spasticity is complex and not fully understood. Because spasticity results from lesions in the pyramidal and extrapyramidal pathways, its pathophysiology varies depending on the site of the lesion but commonly develops in the antigravity muscles (Burke 1988). For instance, excessive muscle tone in the upper extremity flexor muscles is prominent in spasticity following stroke, with relatively lesser involvement of muscle spasms. On the other hand, excessive muscle spasms in the lower extremity extensor muscles are prominent following spinal cord injury. It is also believed that the mechanisms underlying spasticity in stroke and spinal cord injury are different (Elbasiouny et al. 2010).

It is believed that the main mechanism of spasticity in spinal cord injury is the loss of descending inhibitory signals as a result of spinal cord injury. The loss of descending inhibition leads to hyperactivity of segmental reflexes. However, it is also thought that denervation hypersensitivity at the receptors over time reduces the activation threshold for the motor unit and increased the response to stimuli. Abnormal branching and communication of undamaged spinal interneurons may also be caused (Elbasiouny et al. 2010).

Hyperexcitability of spinal reflexes forms the basis of most of the "positive" clinical signs of the upper motor neuron syndrome, which have in common excessive muscle activity. These spinal reflexes can be divided into two groups: proprioceptive reflexes and nociceptive/cutaneous reflexes (Table 34.1). Proprioceptive reflexes include stretch reflexes (tonic and phasic) and the positive supporting reaction. Nociceptive/cutaneous reflexes include flexor and extensor reflexes including the Babinski sign. The clasp-knife phenomenon combines features of both groups, at least in the lower extremities. The stretch of muscle spindles causes a discharge of their sensory afferents, which synapse directly with and excite the motor neurons in the spinal cord innervating the stretched muscle. This stretch reflex arc is the basis of the deep tendon reflex, which is called the phasic stretch reflex because of the very short stretch time. Reflex muscle contractions caused by prolonged stretches of the muscle, such as during clinical testing of muscle tone, are known as tonic stretch reflexes (Barnes and Johnson 2008).

Table 34.1 Pathophysiological mechanism and clinical features of upper motor neuron syndrome

A. Afferent-disinhibited spinal reflexes	1. Proprioceptive (stretch) reflexes	• Spasticity (tonic) • Tendon hyperreflexia and clonus (phasic) • Clasp-knife reaction • Positive support reaction (?)
	2. Cutaneous and nociceptive reflexes	
	a. Flexor withdrawal reflexes	• Flexor spasms • Clasp-knife reaction (with tonic stretch reflex) • Babinski sign
	b. Extensor reflexes	• Extensor spasms • Positive supporting reaction
B. Efferent-tonic supraspinal drive (?)	• Spastic dystonia (?) • Associated reactions/synkinesia (?) • Co-contraction (?)	

Adapted from Barnes and Johnson (2008)

Table 34.2 The response of muscle spindle to muscle movement

	Muscle spindle	Golgi tendon organ
Passive stretching	+	+
Active contraction	–	+

Table 34.3 Components of muscle stretch reflex

Component	Reflex	Activation
Phasic component	• Tendon jerk reflex • Clonus • Short-acting • Monosynaptic	By limb movement and muscle length change
Tonic component	• Postural reflex • Long acting • Polysynaptic	By muscle stretch

Table 34.4 Fibers and characteristics of muscle spindle

Fibers	Innervations	Reactions
Intrafusal fibers (muscle spindle)	• Gamma-motor neurons • Afferent group Ia and II	• Activated by passive stretch (lengthening) • Not activated by active contraction (shortening)
Extrafusal fibers (Golgi tendon organ)	• Alpha-motor neurons • Afferent group II	• Activated by muscle stretch (lengthening) • Activated by active contraction (shortening) • Ceiling effect on muscle contraction

The clinical signs of hyperexcitability of phasic stretch reflexes include hyperactive deep tendon reflex and clonus. The spindle activity of these other muscles could contribute to the tendon reflex. Clonus is the result of the effects of Ia afferent synaptic input from the primary ending of the muscle spindle on hyperexcitable motor neurons (Barnes and Johnson 2008) (Table 34.2). The clasp-knife reflex involves the central actions of unmyelinated and small myelinated high-threshold mechanoreceptors that inhibit reflex activity in extensor muscles. These reflexes are released with spinal cord lesions that affect descending reticulospinal pathways, transversing the dorsolateral funiculi of the spinal cord (Rymer et al. 1979). The hyperactive stretch reflex is caused by increased excitability of the motor neuronal pool or by enhanced stretch-evoked synaptic excitation of motor neurons. Increased motor neuronal excitability may be the result of increased excitatory synaptic interneurons or descending pathways. In addition, reduced inhibitory synaptic input by Renshaw cell recurrent inhibition, Ia inhibitory interneurons, or Ib afferent fibers can also increase the excitability of the motor neuronal pool (Katz and Rymer 1989). Tonic stretch reflex is mediated by the excitatory central actions of spindle receptors (primary and secondary ending) (Table 34.3). These central excitatory effects are countered by inhibitory central actions of the Golgi tendon organ afferent through inhibitory (Ib) interneurons (Birch 2013; Woolacott and Burne 2006) (Table 34.4, Fig. 34.1). When muscle tone is clinically tested by passive movement of a joint with the muscles relaxed, the examiner will feel resistance to the movement, which is a tonic component of muscle stretch reflexes. Clinically, tonic stretch reflexes

are observed that slow movements often do not show hypertonia, but faster movements lead to an increase in resistance depending on the speed of the passive movements.

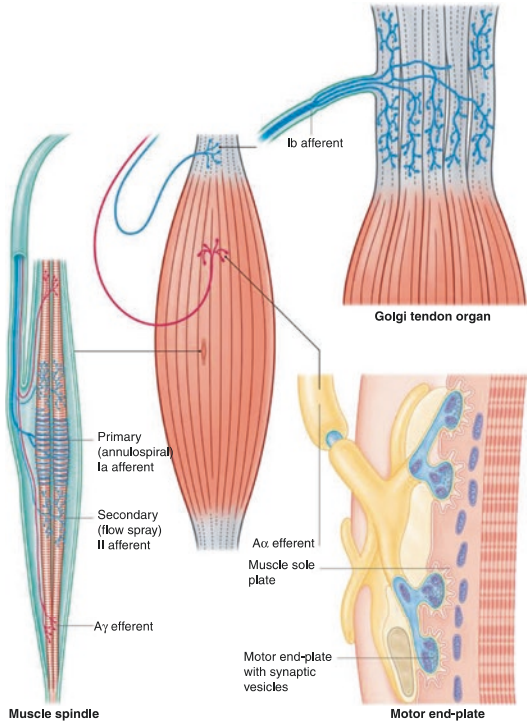

Fig. 34.1 The afferent and efferent innervation of skeletal muscle. From Birch (2013), with permission

34.1.1 Evolution of Reflexes and Spasticity Following Spinal Cord Injury

Spasticity takes time to develop after spinal cord injury. Immediately after spinal cord injury, spinal motor neurons may be in a period of shock clinically manifested by the flaccid tone and unobtainable deep tendon reflexes caudal to the level of injury. Polysynaptic or oligosynaptic cutaneous reflexes such as the bulbocavernosus and the cremasteric reflexes may persist for the period of spinal shock except in the severe cases (Ditunno et al. 2004; Hiersemenzel et al. 2000; Ko et al. 1999). The early presence of cutaneous reflexes that do not depend on muscle spindles further implicates spindle and gamma-motor neuron suppression as key mechanism of absent deep tendon reflex during spinal shock (Ditunno et al. 2004) (Table 34.5).

As spinal shock begins to resolve, the traditional dogma of reflexes returning in a caudorostral direction has not been identified in a study (Ko et al. 1999). Polysynaptic cutaneous reflexes such as the delayed plantar response (S1S2) and the cremasteric reflex (L2) may be present before the bulbocavernosus reflex (S2-S5) (Ditunno et al. 2004; Ko et al. 1999). When the reflexes return, they are almost brisker than before the

Table 34.5 Recovery of reflexes: four phases of spinal shock

	0–1 day	1–3 days	1–4 weeks	1–12 months
DPR	+ + +	+ + +	+ /0	+ /0
BC reflex	+ /0	+ +	+ +	+ +
AW reflex	+ /0	+ +	+ +	+ +
CM reflex	+ /0	+ +	+ +	+ +
Babinski sign	0	+	+ +	+ +
Flexor withdrawal reflex	0	+ /0	+ +	+ + +
DTRs	0	+ /0	+ +	+ + +
Tibial H-reflex	0	+ +	+	+ + +
Extensor spasm	0	0	0	+ + +
Interlimb reflexes	0	0	0	+ + +
Reflex neurogenic bladder	0	0	0	+ + +
Autonomic hyper-reflexia	0	0	0	+ + +

DPR, delayed plantar reflex; BC, bulbocavernosus; AW, anal wink; CM, cremasteric; 0, absent; +, weak response; ++, moderate response; +++, brisker response. From Ditunno et al. 2004, with permission

injury, which may be due to a combination of loss of descending inhibitory influences and afferent plasticity such as sprouting (Little et al. 1999; Ditunno et al. 2004).

34.1.2 Upper Motor Neuron Syndrome and Function

Clinical examination of spasticity shows a resistance to passive stretch that is velocity dependent. Weakness, hyperactive muscle stretch reflexes, and abnormal primitive reflexes such as Babinski sign and ankle clonus, which are part of the upper motor neuron syndrome, are common (Dietz and Sinkjaer 2012). The upper motor neuron syndrome includes both positive and negative findings of the pyramidal and extrapyramidal lesion. Positive manifestations that are signs or symptoms of new or obvious or abnormal behaviors by increased levels of involuntary motor activity include spasticity, clonus, hyperreflexia, athetosis, primitive reflexes, rigidity, and dystonia. Negative findings, which are symptoms or signs caused by weakness or reduction or poor performance by a reduction in voluntary motor activity, include weakness, paralysis, decreased dexterity, and fatigue. These negative symptoms or phenomena of upper motor neuron syndrome are actually associated with more disability than the positive symptoms. The positive symptoms can also be disabling, but they are nevertheless somewhat more compliant with active intervention (Barnes and Johnson 2008). The goal of the management of upper motor neuron lesions is to improve performance deficits (negative symptoms) by reducing the number of abnormal behaviors (positive symptoms) (Table 34.6).

Table 34.6 Clinical features of movement dysfunction in the upper motoneuron syndrome

Type	Neurological tonicity	Clinical signs
Positive symptoms	Spasticity	Increased muscle tone Exaggerated tendon reflexes (phasic stretch reflex) Stretch reflex spread to extensors Repetitive stretch reflex discharges: clonus Babinski sign
	Released flexor reflexes	Mass synergy patterns
	Extensor spasms	Mass synergy patterns
	Dyssynergic patterns	Co-contraction during movement
Negative symptoms	Loss of finger dexterity	
	Weakness	Inadequate force generation Slow movement Fatigue
	Loss of selective control of muscles and limb segments	Loss of dexterity
Rheologic changes in spastic muscle	Stiffness Contracture Fibrosis Atrophy	

All symptoms of the upper motor neuron syndrome do not require treatment. Sometimes, spasticity and spasms can be beneficial. Spasticity may have beneficial effects on weight bearing and transfer activity due to spastic extensor muscle tone in the legs. Spastic muscle activity can reduce the rate of osteoporosis in large leg bones. The problematic symptoms include painful large muscle spasms, co-contracting agonist-antagonist muscles that impede effective movements, and stiffness that compromises comfort in a chair or bed (Adams et al. 2007; Westerkam et al. 2011). Detrusor-external urethral sphincter dyssynergia is a case of spastic co-contraction because the external urethral sphincter contracts inappropriately while the detrusor muscle attempts to expel urine from the full bladder. Triggers such as certain movements, medications such as antidepressants, time of day, infection, pressure injuries, weather patterns, and others can exacerbate the symptoms of spasticity (Fleuren et al. 2009). If shortened muscle fibers are not treated or undertreated for long periods of time, it becomes more difficult to stretch shortened muscle fibers and to alter connective tissue in their tendons and joints, resulting in contractures or fixed immobility of

muscles and joints. Spasticity affects sitting stability and sleep. It interferes with the individual's daily activities and prevents caregivers from optimally supporting dressing, personal hygiene, and grooming. Complications of severe and chronic spasticity include joint contractures, joint subluxation, and pressure injuries.

34.1.2.1 Flexor and Extensor Spasms

Severe muscle spasms are common in the upper motor neuron lesion. These can be either flexor or extensor patterns. Extensor spasms are probably more common than flexor spasms in incomplete spinal cord injuries, but the specific associated pathology has not been known. The most common of flexor spasm is flexion of the hip, knee, and ankle. The flexor and extensor spasm can also sometimes occur spontaneously or in response to stimulation, even milder. If the spasms suddenly get worsen, it is worth it due to aggravating factors such as bladder distention of fecal impaction with constipation, urinary tract infection, pressure injuries, irritation of a catheter, an ill-fitting orthosis, or tight catheter leg bag. Extensor spasms are common in extension of the hip and knee with plantar flexion and ankle inversion. Sometimes a spasm can be useful from a functional point of view, such as standing using a strong extensor leg spasm or putting on pants using an extensor spasm. The spasms either extensor or flexor can be painful.

34.1.2.2 Dexterity Loss

Weakness, a negative symptom associated with spasticity, inevitably affects dexterity. As a result, it exacerbates difficulties in self-care, including catheterization and personal hygiene care, feeding, and writing. All of these issues can lead to a loss of independence, which can lead to increased dependency on caregivers.

34.1.2.3 Pain

Spasticity itself can be painful. If the patient is more painful due to extreme flexor or extensor spasms, it may simply require an analgesic before management to improve function. Stimulation problems that worsen flexor or extensor spasms, such as pressure injuries or ingrown toenails, should be prevented or treated. Problems associated with spasticity and flexor or extensor spasms can lead to musculoskeletal complications.

34.2 Assessment

Assessment should include assessment of severity and location of spasticity, identification of triggering or causative factors that may cause or exacerbate spasticity, and effects on function, comfort, and sleep. Any noxious stimulus can aggravate spasticity. The causes include urinary tract infections, bladder stones, bowel impaction, hemorrhoids, ingrown toenails, pressure injuries, fractures, menstruation, posttraumatic syringomyelia, or intra-abdominal pathology. A number of tools and scales have been used to assess spasticity in the clinical and research fields (Table 34.7). Nothing has been proven to be opti-

Table 34.7 Assessment tools for spasticity

Category	Assessment tool
Clinical assessments of tone	• Ashworth and modified Ashworth scales • Pendulum test • Resistance to passive movement • Tardieu
Clinical assessments of spastic reflexes	• Spinal Cord Assessment Tool for Spastic reflexes (SCATS) Clonus Scale • Deep tendon reflexes and cutaneous reflexes
Patient-reported symptom assessment	• Penn Spasm Frequency Scale • Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET) • Patient-Reported Impact of Spasticity Measure (PRISM)
Electrophysiological tests	• Reflex testing • H reflex, H/M ratio • Multichannel electromyography

mal because of the complexity, variability, and dynamic nature of spasticity. There is a need to develop consensus tools to quantify various areas of spasticity objectively.

The Ashworth and Modified Ashworth Scales are the most commonly used assessment tools based on the results of the clinical examination (Ashworth 1964). The Spasm Frequency Score is based on the report of a person who has an abnormal muscle tone. Researchers can use electrophysiological examination, such as parameters of F-wave and H reflex measurement parameters, to quantify spasticity. However, changes in electrophysiological measurements may not correlate with clinical or functional improvements. Some studies have also used the pendulum test. This test involves placing the patient in a supine position with the legs hanging over the edge of the plinth. The leg is allowed to fall, and the knee movement is assessed using an electrogoniometer (Kheder and Nair 2012).

Penn Spasm Frequency Score, Spinal Cord Assessment Tool for Spastic Reflexes (SCATS) Clonus Scale, Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET), and the Patient-Reported Impact of Spasticity Measure (PRISM) have been developed and used. SCATS can be used for evaluation of the extensor spasm and flexor spasm scale (Priebe et al. 1996; Rekand 2010).

34.2.1 Clinical Scales to Quantify Spasticity

34.2.1.1 Modified Ashworth Scale

The Ashworth scale has been developed originally for the assessment of patients with multiple sclerosis (Ashworth 1964). Modified Ashworth Scale (MAS) is the most commonly used spasticity assessment tool. While a subject is supine, the examiner will subjectively assess the tone of each joint through the range of motion by determining the score with 5 (original, unmodified; Ashworth Scale) or 6-point (modified) scales between 0 and 4 (Bohannon and Smith 1987; Haas et al. 1996). In MAS, 1+ was created between 1 and 2. If the muscle to be examined is the flexor of the joint, the patient is placed in the maximal flexion position, and the examiner moves the joint to the maximal extension of the joint. The Ashworth Scale or Modified Ashworth Scale is a subjective assessment and examines only the resistance of a single joint during passive ROM at a specific time. It does not examine the effect of muscle chain interactions, frequency of spasm, possible triggers of spasticity, or impact of spasticity on function. Modified Ashworth Scale is easy and does not require equipment. The velocity-dependent response of the muscles to passive stretching is rated on a 6-point nominal scale (Table 34.8).

Table 34.8 Ashworth scale and modified Ashworth scale

Score	Ashworth scale (Ashworth 1964)	Modified Ashworth scale (Bohannon and Smith 1987)
0	No increase in muscle tone	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch when the limb was moved in flexion and extension	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM when the affected part(s) is moved in flexion or extension
1+		Slight increase in muscle tone, manifested by a catch followed by minimal resistance throughout the remainder (<50%) of the ROM
2	More marked increase in muscle tone through most of the range of motion, but affected limb is easily moved	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone; passive movement difficult	Considerable increase in muscle tone, passive movement difficult
4	Limb rigid in flexion or extension	Affected part(s) rigid in flexion or extension, contracted

34.2.1.2 Penn Spasm Frequency Score (Table 34.9)

Spasms are measured by the number of spontaneous flexors and extensor muscle spasm over a 1 h period.

- **0 =** No spasms
- **1 =** Spasms induced only by stimulation; mild spasms induced by stimulation; no spontaneous spasms
- **2 =** Spasm occurring less than once per hour; infrequent spontaneous spasms
- **3 =** Spasms occurring between 1 and 9 times per hour
- **4 =** Spasms occurring 10 or more times per hour; continuous contraction

34.2.1.3 Spasm Frequency Scale

Spasms are measured by the number of spasms in the last 24 h. Spasms are defined as follows: (1) Spasm is a jumping or twitching of the muscle or limb without control; (2) a spasm can be a "shooting" of the body part into a position without control; and (3) a rapid series of "spasms" without significant pausing/resting is defined as one spasm.

- **0 =** No spasms
- **1 =** One spasm or fewer per day
- **2 =** Between one and five spasms per day
- **3 =** Between five and nine spasms per day
- **4 =** Ten or more spasms per day.

34.2.1.4 Tardieu Scale

The Tardieu Scale requires both longer test time for both patients and clinicians and more clinician expertise and has similar drawbacks that affect interrater reliability (Tardieu et al. 1954). Measurement of spasticity is performed with the patient lying supine, head midline, and at three different velocities: V1, speed lower than limb falling under gravity; V2, speed equivalent to limb falling under gravity; and V3, speed faster than limb falling under gravity.

0 = No resistance throughout the course of passive movement
1 = Slight resistance throughout the course of passive movement with no clear catch
2 = Clear catch interrupting the passive movement, followed by the release
3 = Fatigable clonus (lasting <10 s when maintaining the pressure)
4 = Infatigable clonus (lasting >10 s when maintaining the pressure)
5 = Joint is immovable.

34.2.1.5 Spinal Cord Assessment Tool for Spasticity (SCATS)

SCATS (Table 34.10) is a more comprehensive assessment and a more objective scoring system than MAS. It is a response to rapid dorsiflexion of the ankle and toe and leg flexor responses to a standardized noxious stimulus to the sole of the foot, and leg extensor response to the simultaneous extension of the hip and knee (Benz et al. 2005).

Table 34.10 Spinal Cord Assessment Tool for Spastic reflexes (SCATS)

Clonus of ankle plantar flexors with rapid passive dorsiflexion of foot	
0	No reaction
1	Mild: clonus <3 s
2	Moderate: clonus lasts between 3 and 10 s
3	Severe: clonus >10 s

Table 34.9 Penn spasm frequency scale and the Spasm frequency score

Penn spasm frequency scale	Score	Spasm frequency score
No spasms	0	No spasms
Mild spasms at stimulation	1	One or fewer spasms per day
Irregular strong spasms less than 1 time/h	2	1–5 spasms per day
Spasms more often than 1 times/hour (1–9 times/h)	3	5–9 spasms per day
Spasms more than 10 times/h	4	≥10 spasms per day, or continuous contractions

34.2.1.6 Patient-Reported Assessments

It is important that objective or quantitative assessment tools for spasticity correlated with patient's perceptions. The Penn Spasm Frequency Scale (PSFS) and Patient-Reported Impact of Spasticity Measure (PRISM) are self-assessments of the actual impact of spasticity on individual's daily life. The Penn Spasm Frequency Scale is completed by a self-assessment questionnaire reporting the spasm frequency: 0 = no spasms; 1 = spasms induced only by stimulation; 2 = infrequent spontaneous spasms occurring less than once per hour; 3 = spontaneous spasms occurring more than once per hour; 4 = spontaneous spasms occurring more than ten times per hour, and intensity, 1 = mild; 2 = moderate; 3 = severe (Priebe et al. 1996). The Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET) uses a 7-point Likert scale for each of 34 questions regarding the positive or negative effects of various elements of spasticity in patients with spinal cord injuries (Adams et al. 2007).

34.2.1.7 Pendulum Test

Pendulum test measures the static tone in the knee joint in a subject sitting after the release of the leg from an extended position (Wartenberg 1951).

34.2.1.8 Electrophysiological Evaluation

Electrophysiological evaluation measures the threshold of activation for motor unit activity using surface EMG and H reflex and the H/M ratio. The H/M ratio is increased in individuals with spasticity, and it has been demonstrated that it correlated with the Ashworth Scale.

34.3 Treatment

Spasticity can be disabling. It can affect the ability to perform activities of daily living, such as catheterization, bowel care, dressing, positioning, transfers, mobility, and participation in rehabilitation therapies. It can increase the caregiver burden. Spasticity can be associated with pain, fatigue, poor sleep, impaired sexual function, negative self-image, and decreased quality of life. Severe hip flexor and adductor spasms can interfere with catheterization or perineal hygiene, while extensor spasms can interfere with the bowel regimen (Cabahug et al. 2020). It is not necessary to treat all spasticities. It has been reported that spasticity is helpful in 23–40% of patients with spinal cord injuries. Some people can cause spasticity for their own benefit, for example, to assist with transfers and bed positioning. People with incomplete spinal cord injury may need lower extremity extensor spasticity to contribute to the stability of the knee during standing and walking. It is known to maintain the mass of bones (Lofvenmark et al. 2009) and muscles, which reduces the risk of fracture and protects muscle atrophy, and to prevent deep vein thrombosis, depending on the severity of spasticity. The lipid profile and glucose metabolism can be improved (Jung et al. 2017). Additionally, a change in the severity of spasticity can be a warning sign of pathology or new injury below the level of injury. Therefore, prior to the treatment of spasticity, treatment goals and targets and individualized approaches are required. The negative and positive effects of spasticity in people with spinal cord Injuries are listed in Table 34.11.

If spasticity is considered for treatments, the clinician should consider the effects of the activities of daily living and life of the patient with spinal cord injury, as well as the presence or severity of the symptoms. Treatment decisions should be based on factors such as interference of spasticity with function, pain associated with spasms or tone, interference with sleep, and the risk of causing complications associated with spasticity. Identification and management of

Table 34.11 Effects of spasticity

Negative effects	Positive effects
Catheterization	Transfer
Perineal hygiene	Standing
Bowel care	Walking
Sexual function	Bed positioning
Self-image	Bone mass
Sleep	Muscle mass
Pain	DVT risk
Fatigue	Edema

other underlying pathophysiological processes are important. Increased spasticity may be secondary to urinary tract infections, bladder calculi, ingrown toenails, hemorrhoids, constipation, or fecal impaction. Urethral catheters, fractures, menstruation, deep venous thrombosis, pressure injuries, heterotopic ossification, SSRI, cholecystitis, appendicitis, or other abdominal process can exacerbate spasticity.

Spasticity treatment includes physical, medical, and surgical procedures. The common approach to spasticity is stepwise. It begins with positioning, stretching, and orthoses and identifies and eliminates noxious stimuli. Oral medications are added and titrated for optimal management. Compared to physical and other non-pharmacological approaches, pharmacotherapy is much easier to standardize in terms of dose, scheduling, and administration. Drugs also have disadvantages in terms of side effects and drug interactions. Chemodenervation is considered, especially if the goal is to treat localized spasticity. If the oral medications are not effective or are not well tolerated, intrathecal baclofen is considered.

34.3.1 Positioning

Tone may be affected by the positions of the head and body. Tonic neck and vestibular reflexes may be useful for modulating and controlling spasticity. For example, some people with spinal cord injuries have decreased tone in the partially recumbent position. Proper lumbar support in wheelchairs and avoiding sacral sitting in wheelchairs can reduce spasticity. Casting or splinting an extremity can also reduce spasticity.

34.3.2 Physical Therapy

A stretching program can reduce the tone. It must be integrated into the daily living of the individual. When stretching the muscles, sustained stretch at the end-of-range of motion is important to reduce the tone. Heating modalities, cryotherapy, and electrical stimulation can reduce spasticity for hours after use. Heat decreases muscle spasms and tone and increases the pain threshold.

Continuous cold application over a muscle group for 20 min can reduce spasticity. Alternatively, rapid cooling or electrical stimulation of the antagonist of the spastic muscle group may cause reciprocal inhibition to reduce muscle tone. However, patients with spinal cord injuries do not have a sensation below the neurological level of injury and should be prescribed with caution. Prolonged stretch can decrease the sensitivity of the muscle spindle and Ia and group II afferent input, thus decreasing excitation of motor neurons. Other emerging therapies include neuromodulation by epidural or transcutaneous spinal cord stimulation. The application of transcutaneous spinal cord stimulation at higher frequencies (50 Hz) has been shown to temporarily improve spasticity in spinal cord injuries (Hofstoetter et al. 2014). Epidural spinal cord stimulation at frequencies of 50 Hz or higher can improve spasticity (Minassian et al. 2012).

34.3.3 Orthoses

Tone-reducing orthotics such as ankle-foot orthoses (AFOs) can improve the effectiveness of muscle stretch in reducing spasticity. Serial casting has been used as a key component in the treatment of joint contracture. The cast can be bivalved for skin inspection. Prolonged stretch or chemodenervation is often performed before casting to improve stretching.

34.3.4 Medications

Oral medications are usually first-line treatment for spasticity. Appropriate patient selection is important, as initiation of a medication to a generally decreased tone may actually be detrimental to the performance of certain activities of daily living. Almost all antispastic medications can cause side effects and can limit the use of medications. Drug selection is considered according to age, cognition, and medical comorbidities. It is

usually recommended to use only one of these substances, at least initially. There are patients who cope best with modest doses of two drugs with different targets (e.g., baclofen and tizanidine), so that combination therapy may be necessary (Dietz and Young 2003). Best antispastic effects are reported for baclofen, tizanidine, and benzodiazepines (e.g., diazepam and clonazepam). Baclofen is the first-line choice, and diazepam is used if necessary, as a rule of choice for the treatment of spinal cord injured patients. After that, it is recommended to select dantrolene and tizanidine in order. Almost all antispastic drugs can cause adverse effects, often drowsiness and nausea. The dosage is adjusted based on the effect seen with increasing doses, such as somnolence, respiratory depression, hypotonia, and confusion (McClugage and Bauer 2021). The appropriate dose and adverse effects of commonly used antispasticity drugs are summarized in Table 34.12, and the pediatric doses of these drugs are summarized in Table 34.13. The presumed actions of the antispastic drugs are illustrated in Fig. 34.2.

Table 34.12 Commonly used antispasticity medication

Medications	Actions	Dose, maximum	Side effects
Baclofen	Binds to GABA receptors in spinal cord	• Initial 5 mg tid • 40–80 mg in divided dose (up to 150–240 mg/d)	• Sedation, dizziness, withdrawal syndrome, weakness • Avoid abrupt discontinuation
Baclofen (intrathecal)		500–1000 μg	
Tizanidine	Central alpha2-adrenergic receptor agonist	• Initial 2 mg daily • 36 mg in divided dose	Sedation, weakness, dizziness, elevating liver enzymes
Dantrolene	Reduces the release of calcium into the sarcoplasmic reticulum	• Initial 25 mg daily x 7 d • 400 mg in divided dose	Muscle weakness, sedation, hepatotoxicity
Diazepam	Facilitates the postsynaptic action to GABA	• Initial 2 mg tid • 60 mg in divided dose	Sedation, dizziness, cognitive impairment, dependence, withdrawal syndrome
Clonidine	Central acting alpha2-adrenergic agonist	• Initial 0.05 mg bid to 0.1 mg bid • 0.4 mg in divided dose	Hypotension, bradycardia, dizziness, constipation
Gabapentin	Blocks voltage-dependent calcium channels	3600 mg in divided dose	Sedation, dizziness

Table 34.13 Children doses of antispasticity medications

Medications	Dose
Baclofen (0.125–1 mg/kg/d)	• 1–7 years.: 2.5–10 mg qid (10–40 mg/d) • 8–12 years: 5 mg tid-15 mg qid (15–60 mg/d) • 12–16 years: 5–20 mg qid (20–80 mg/d)
Diazepam (0.12–0.8 mg/kg/d)	• 0.5–10 mg tid
Dantrolene sodium (3–12 mg/kg/d)	• >5 years: commence at 0.5 mg/kg bid for 7 days, then 0.5 mg/kg tid for 7 days, then 1 mg/kg tid for 7 d, then 2 mg/kg tid to a maximum of 3 mg/kg qid or 400 mg/d • Discontinue promptly if liver enzymes are elevated
Tizanidine	• <10 years: commence 1 mg orally at bedtime initially, increasing to 0.3–0.5 mg/kg in 4 divided doses • ≥10 years: commence 2 mg orally at bedtime initially, increased according to response, to a maximum of 24 mg/d in 3 to 4 divided doses
Clonidine	• 0.025–0.1 mg in 2 or 3 divided doses
Gabapentin	• Blocks voltage-dependent calcium channels

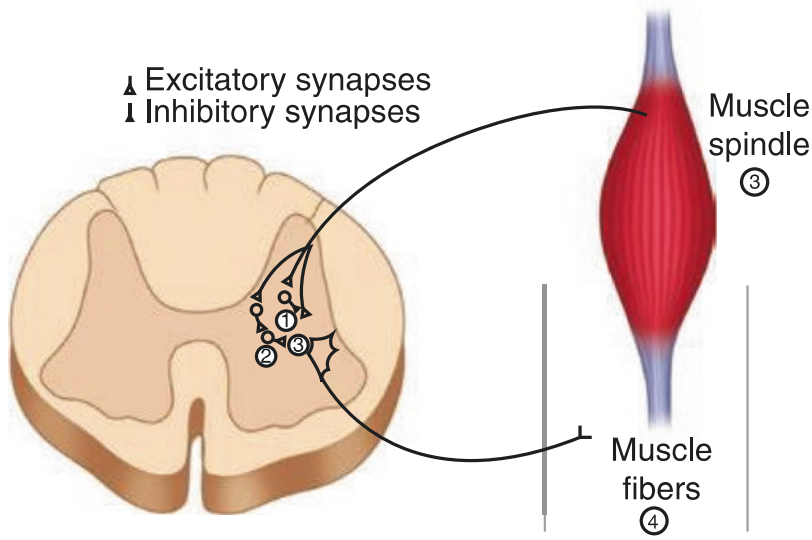

Fig. 34.2 Presumed site of action of drugs with antispastic effects: (1) diazepam/clonazepam facilitate GABA-A-mediated presynaptic inhibition; (2) baclofen inhibits activity of polysynaptic reflexes by GABA-B receptor activation; (3) tizanidine acts on alpha2-adrenergic receptors; (4) dantrolene reduces release of calcium ions from the sarcoplasmic reticulum. Adapted from Dietz and Young (2003)

Table 34.14 Clinical features of baclofen toxicity and baclofen withdrawal

Effect system	Baclofen toxicity	Baclofen withdrawal
Systemic effects	Hypothermia, death	Hyperthermia, pruritus, multisystem failure, death
Cardiovascular effects	Bradycardia, tachycardia, hypotension, hypertension, conduction abnormalities, prolonged QTc interval	Bradycardia, tachycardia, hypotension, hypertension, autonomic dysreflexia, acute reversible cardiomyopathy, cardiac arrest
Respiratory effects	Respiratory failure	Respiratory failure
Musculoskeletal effects	Hypotonia	Hypertonia, rhabdomyolysis
Gastrointestinal effects	Nausea, vomiting	Nausea, vomiting, diarrhea
Neurological effects	Somnolence, confusion, memory impairment, lethargy, hyporeflexia, seizures, encephalopathy, coma	Headache, hyperreflexia, tremor, paresthesia, delirium, altered mental status, seizures
Psychiatric	Agitation, hallucination, catatonia, mania	Anxiety, hallucinations, delusion, paranoia

34.3.4.1 Baclofen

Baclofen is the most commonly used primary agent in the spasticity of spinal cord injuries. Baclofen acts as a γ-aminobutyric acid (GABA)-B agonist at the spinal level presynaptically and less postsynaptically. Monosynaptic stretch reflexes are more effectively depressed than polysynaptic reflexes, but flexor spasms are particularly reduced (Dietz and Sinkjaer 2012). It is often used as the first-line drug in the management of spasticity of spinal cord injury. Dosages of 15–80 mg per day are administered in divided doses, but some patients require more doses. Some patients tolerated higher doses up to 120 mg/d. It has a short half-life of 3.5 h and may require frequent dosing to maintain a therapeutic effect throughout the day and night. It can have anxiolytic and analgesic effects. Side effects include sedation, fatigue, weakness, nausea, dizziness, paresthesias, and hallucinations (Table 34.14). Progressive tapering discontinuation is necessary to prevent sudden withdrawal symptoms, including seizures, visual disturbances, and hallucinations. Since baclofen is excreted by the kidneys, adjustments may be necessary for patients with renal dysfunction (Kita and Goodkin 2000).

34.3.4.2 Benzodiazepine

Benzodiazepines include diazepam and clonazepam. These drugs do not bind directly to GABA receptors, but they act through the GABA system. Benzodiazepines amplify the inhibitory action of GABA-A at a presynaptic and postsynaptic level. Increasing presynaptic inhibition in patients with spinal cord injuries is believed to reduce the release of excitatory transmitters from afferent fibers, thereby reducing the increase in the spinal stretch and flexor reflexes (Davidoff 1985; Dietz and Sinkjaer 2012). The use of this type of drug is limited by known side effects such as sedation, depression, cognitive impairment, and tolerance. Serious side effects such as the development of tolerance, dependency, and drowsiness are reported for diazepam. Doses of diazepam start at 2 mg/d, with a maximum of 60 mg/d (Strommen 2013).

34.3.4.3 Dantrolene

Dantrolene acts directly on muscle fibers to decrease calcium-dependent excitation-contraction coupling by preventing the release of calcium ions from the sarcoplasmic reticulum along muscle fibers. This drug is nonselective and can lead to the weakening of normal and spastic muscles, which can be important for people with marginal strength. Dantrolene affects fast twitch muscles more than slow twitch and fortunately has little effect on cardiac or smooth muscle. It can lead to hepatotoxicity (<1%) and sometimes fulminant hepatic failure, and baseline and periodic liver function tests are therefore necessary. If an abnormality in liver function tests is indicated, dantrolene should be discontinued. The dosage starts at 25–50 mg/d, with a maximum recommended dose of 400 mg/d in divided doses.

34.3.4.4 Tizanidine and Clonidine

Alpha-2 agonists (tizanidine and clonidine) bind to presynaptic α2-receptors on interneurons in the dorsal horn of the spinal cord and depress polysynaptic reflexes by decreasing the release of excitatory amino acids such as glutamate and aspartate and facilitating the action of glycine that is an inhibitory amino acid neurotransmitter. Clonidine and presumably tizanidine produce marked inhibition of spinal reflex responses in α-motor neurons to group II activity (Schomburg and Steffens 1988). Tizanidine can inhibit spinal polysynaptic pathways by facilitating the release of glycine. Tizanidine has a shorter half-life and a much lower rate of hypotension than clonidine. Tizanidine also results in non-opiate analgesia by action on α2-receptors in the spinal dorsal horn, which inhibit release of substance P. This would diminish flexor reflex afferent-mediated actions. The dose may be increased to 8 mg tid or qid starting with 2–4 mg before bedtime. Patients taking antihypertension medications should be cautious about lowering blood pressure. In particular, drug interactions between ciprofloxacin, fluvoxamine, and oral contraceptive drug with tizanidine may increase plasma levels and should be used with caution. By decreasing tizanidine, reduce to 4 mg/week. Hallucinations were reported at a lower rate during the first week of treatment. It can cause elevated liver enzymes in 5% of cases, and liver function tests are routinely recommended at baseline and periodically at 1, 3, and 6 months.

Clonidine reduces the sympathetic outflow from the brain and brainstem and suppresses afferent input to the spastic reflex arc in the substantia gelatinosa of the dorsal horn. Clonidine can be administered orally, transdermally, and intrathecally. The transdermal patch has two advantages designed to deliver the specific dose over 7 d and has fewer side effects than the oral form. Known side effects include sedation, hypotension, and dry mouth. To minimize side effects, it should be initiated at a low dose and carefully titrated. A dosage of 0.1–0.4 mg/d is administered orally or a transdermal patch is more convenient to use.

34.3.4.5 Gabapentin

Gabapentin, a GABA-related drug, is effective particularly for the treatment of painful muscle spasms. Gabapentin is structurally related to neurotransmitter GABA but does not interact with GABA receptors (Cutter et al. 2000). The activity may involve voltage-gated calcium channels, but the exact mechanism of action to decrease spas-

ticity is unknown. It is excreted exclusively by the kidneys. Blood levels and liver enzyme monitoring are not required.

34.3.4.6 Cannabis

Some patients report significant benefits on the spasticity of marijuana, namely, cannabis and cannabidiol (CBD). Delta-9-tetrahydroccabinol (THC) is the main active ingredient. Pure THC is now available as dronabinol (Marinol) or as synthetic cannabinoid, nabilone (Cesamet). There are many medicinal cannabis CBD products with or without THC on the market. There have been anecdotal reports of muscle-relaxant effects of smoking marijuana for spasticity in people with spinal cord injuries (Joseph and Schulze 2021; Whiting et al. 2015). The mechanism of action of the cannabinoids is not fully understood, but it is known that they interact with the cannabinoid receptors CB-1 and CB-2. CB-1 is the primary target in spasticity therapy and is located in the central nervous system, while CB-2 is more broadly distributed, including the immune system (Chiurchiù et al. 2018).

34.3.5 Chemoneurolysis

Chemoneurolysis is usually used in individuals with focal spasticity or in those who want to assess the functional gain of future surgical treatments prior to the surgical procedure (Elbasiouny et al. 2010). Chemoneurolysis can be done with a variety of agents, such as motor point blocks with phenol or alcohol and botulinum toxin injection (Table 34.15). Nerve blocks involve injecting

Table 34.15 Local treatment or chemoneurolysis for spasticity

	Maximum dose or concentration	Main risks	Indications	Technique
Local anesthetics	• Lidocaine (0.5–2%): <4.5 mg/kg • Bupivacaine (0.25–0.75%): <3 mg/kg • Etidocaine (1–1.5%):<6 mg/kg	• CNS and cardiovascular toxicity • Hypersensitivity	• Efficacy test before long-term block • Muscle relaxation before casting • Analgesic before IM injection	• Stimulation • Motor point • Resuscitation equipment available
Ethyl alcohol (>10%)	• 10–50%	• Pain at injection (IM++) • Chronic dysesthesia and pain (perineural++) • Vascular complications • Permanent peripheral nerve palsy	• Proximal and large muscles • Sensory integrity not a primary concern • Hygiene and comfort purposes • Combination with botulinum toxin	• Stimulation • Motor point • Intramuscular "wash"?
Phenol (>3%)	• <1 g (10 ml of 5% phenol)	• Pain at injection (IM++) • Chronic dysesthesia and pain (perineural++) • Vascular complications • Permanent peripheral nerve palsy	• Proximal and large muscles • Sensory integrity not a primary concern • Hygiene and comfort purposes • Combination with botulinum toxin	• Stimulation • Motor point?
Botulinum toxin	• ≤400 U within 3 mon for Botox®	• No major risk	• Muscles accessible for IM injection • Sensory integrity indispensable • Purposes of active function • Combination with neurolytic agents	• Stimulation • Endplate targeting? • Dilution 100, 50, or 20 U/mL

drugs close to a nerve that cause temporary or permanent dysfunction. Temporary nerve block can be done with lidocaine or bupivacaine. This allows clinicians to evaluate the potential benefits of a nerve block and facilitate the use of other interventions such as serial casting or dynamic splinting. For more sustainable use, chemical neurolysis agents such as phenol and ethanol can be used (Lui et al. 2015). Phenol (2–6% solution) injections of peripheral nerves or muscles are effective in reducing spasticity and usually last 3–6 months. Phenol was effectively used to manage spasticity with good target blocks, but phenol solutions could not be manufactured commercially.

Nerve blocks in sensorimotor nerves can lead to unwanted dysesthesias or anesthesia. However, if a person with spinal cord injury is insensate at the site of the nerve block, potential sensory side effects are less of a concern for sensory complications. A motor branch block is a type of chemical neurolysis with a lower risk of sensory complications that is blocked at the most distal motor branches of a peripheral nerve. Phenol blocks cause fibrosis of the nerves and make future nerve blocks more difficult on the same site.

Localization of the nerve for a nerve block is important for a successful nerve block. The closer the medication is delivered to the nerve, the less medication and less side effects. A Teflon-coated needle connected to the electrical stimulator is attached to a syringe. As the needle approaches the nerve, muscle contraction will occur. The closer the needle is to the nerve, the less current will be required. Ultrasonographic guide localization can be an alternative. The effects of chemical neurolysis duration vary from 3 to 9 months. In some individuals, the effects last for years. If the nerve block is used as part of rehabilitation treatment programs by adding a stretching exercise, the effects can be further extended.

34.3.6 Botulinum Toxin

Botulinum serotype A preparations should be stored in a freezer and reconstituted with normal saline. Botulinum serotype B agents need not to be reconstituted. It is injected directly into the muscle. This effect is dose dependent and dependent on the muscle volume and severity of symptoms. The initial effect does not appear for several days, but it can last for 3–6 months. Some clinicians use EMG signals to help locate muscles. Subsequent injections may be less effective due to antibody-mediated resistance to the botulinum toxin. The most common side effects are excessive weakening of the injected muscle and sometimes spread to nontarget muscles.

34.3.7 Intrathecal Baclofen

Intrathecal administration of drugs such as baclofen is optional for patients who have failed oral therapy with antispasticity medication or who cannot tolerate side effects. The treatment includes the use of an implanted device to deliver the medication continuously into the intrathecal space to bypass the blood–brain barrier. It is generally desirable for people with diffuse symptoms of spasticity and is more effective in treating spasticity of the lower extremities than the trunk and upper extremities (Francisco 2004). Oral baclofen has a very low penetration rate of the blood–brain barrier and therefore has a high dose to reduce the desired spasticity. Intrathecal baclofen (ITB) can have a much more effectiveness on spasticity reduction effect with less than 1/1000 of the oral doses. In general, a test dose of 50 μg is injected into the subarachnoid space, and if there is a reduction of 2 or more points in MAS or Penn Spasm Frequency Scale, the patient is designated ITB candidate.

Screening includes objective and subjective monitoring for the effect of baclofen injection into the cerebrospinal fluid through a lumbar puncture. Fifty μg of baclofen is administered. The onset of effect is within 45–60 min. The maximum effect usually appears after about 4 h and disappears after 8 h (Penn et al. 1989). If the lower doses are ineffective and there are no significant side effects, a 100 μg dose can be tried. If effective, a permanent catheter is implanted. After the catheter is tunneled subcutaneously, the

pump is implanted subcutaneously in the anterior abdominal wall and inserted into the spinal canal at the L1 vertebral level and inserted into the subarachnoid space to the desired level. Pump management involves refilling at scheduled time intervals. For refills, the pump reservoir accesses through the central access port, removes any remaining medication in the reservoir, and then injects the new medication into the reservoir. Pump programming updates information on reservoir volume, drug concentration, dosing method, and alarm dates.

Complications include catheter disconnection, kinking, or blockage, pump failure, infection, and baclofen overdosage. Early signs of underdosage include increased spasticity, pruritis, hypotension, and paresthesias. Sudden withdrawal can lead to fever or hyperthermia, changes in mental status, exaggerated spasticity, muscle rigidity, itching, fever, tachycardia, hypotension or hypertension, multi-organ failure, rhabdomyolysis, or DIC. Immediate attention is needed, if it is not treated promptly, as it can lead to rhabdomyolysis, multiple organ system failure, and death. Autonomic dysreflexia can occur when the intrathecal baclofen stops abruptly. If baclofen cannot be restored intrathecally or cannot be prescribed immediately, high oral baclofen may be administered, but improvement may take several hours with oral treatment. Intravenous benzodiazepines were also administered. In case of severe hyperthermia, dantrolene administration is indicated. Overdose of ITB is usually due to miscalculation during dosing adjustments or concentration changes. Symptoms of intrathecal baclofen overdose include drowsiness, lightheadedness, dizziness, and drowsiness. Respiratory depression, seizures, progressive hypotonia, and impaired consciousness may occur. Initial management includes maintenance of airway, respiration, and circulation. Secondary measures include reducing or temporarily interrupting intrathecal administration by reprogramming pump. Optional measures for ITB overdose include cerebrospinal fluid drainage through the catheter access port (CAP) aspiration or lumbar puncture, and administration of an "antidote." Although there are no true antidotes, physostigmine and flumazenil have been reported to reduce central side effects, such as somnolence and respiratory depression. Physostigmine is the most commonly used agent, but can produce side effects such as bradycardia, seizures, increased respiratory secretions, bladder contraction, and autonomic dysreflexia.

34.3.8 Surgical Procedures

Surgical procedures are commonly used when none of the above techniques can treat spasticity. They include motor nerve ablation and/or selective dorsal rhizotomy of sensory spinal roots to interrupt the sensory input. Ablation of motor nerves is effective when spasticity is focal in muscles innervated by the same nerve trunk and is usually selective in suppressing the spasticity without causing excessive muscle weakening (Elbasiouny et al. 2010).

34.4 Contractures

Contractures are defined as a fixed loss of passive joint range of motion caused by the pathology of surrounding soft tissues, including connective tissue, tendons, ligaments, joint capsules, or cartilage. Restriction in range of motion is not always simply due to an increase of tone and spasticity in the affected muscles. It is likely that such contractures and soft tissue changes are caused by the muscle being maintained in a shortened position. Contracture and spasticity can coexist in upper motor neuron lesions. Movement decreases as the tone increases. The result can have deleterious consequences. Contractures can be classified as arthrogenic, soft tissue, or myogenic. Arthrogenic contractures are caused by pathology, which involves the intrinsic joint components. Arthrogenic contractures typically cause a range of motion restrictions in multiple directions. Soft tissue contractures result in the shortening of tendons, ligaments, and skin. These contractures generally restrict the movement in one direction. Myogenic contractures can be divided into

intrinsic and extrinsic lesions. Intrinsic muscle contracture is secondary to a primary disorder of muscle fibers, such as muscular dystrophy. Most patients with spinal cord injuries have extrinsic muscle contractures because the muscles are placed in a shortened position for periods of time. The muscle is histologically normal. Factors that can lead to extrinsic contractures include spasticity, immobility, improper positioning, and pain. Heterotopic ossification can also cause extrinsic myogenic contractures.

34.4.1 Common Sites of Contractures

In the lower extremities, ankle plantar flexion, hip flexion, and knee flexion contractures are common. Depending on the level of injury, elbow flexion and supination contractures in the upper extremities are possible. Some patients also may cause shoulder adduction and internal rotation contractures. Muscles across multiple joints such as the biceps, hamstrings, tensor fascia lata, and gastrocnemius are vulnerable to contracture formation.

34.4.2 Beneficial Contractures

Some contractures can improve functional status and thus should be encouraged to develop. For example, patients with C6 tetraplegics have intact wrist extension, which allows the utilization of the tenodesis effect in which active movement of one joint results in the passive movement of other joint. In C6 tetraplegia, the active extension of the wrist causes passive flexion of the MCP, PIP, and DIP joints. Shortening of the paralyzed flexor digitorum profundus and superficialis promotes this passive flexion and increases functional independence. To achieve this tenodesis effect, the MCP, PIP, and DIP joints should be allowed to contract in slight flexion at 20 degrees. A wrist-driven orthosis will further promote tenodesis. A biceps flexion contracture may also be useful. When an individual is weak in biceps strength, a slight elbow flexion contracture can improve the muscle's mechanical advantage.

34.4.3 Prevention of Disadvantageous Contractures

Contracture can be prevented by early mobilization, range of motion exercises, proper positioning, and orthotic devices. It is possible, but not absolutely proven, that maintaining a joint with full range of movement can prevent the long-term development of soft tissue contractures. The frequency of the stretching, either active or passive, necessary to prevent contractures is unknown. However, it is important to ensure proper posture in bed and seating posture so that the muscles are stretched as fully as possible at least every day. The recommendation is that muscles be put through a full stretch for 2 h in every 24 h (Barnes and Johnson 2008). The patients must leave the bed as soon as possible. Educating patients and caregivers is essential, emphasizing the importance of home stretching programs. Improper bed positioning can affect the contractures. The supine position promotes hip flexion and ankle plantar flexion contractures. Another bed position to avoid is to encourage extreme adduction and internal rotation of the shoulder. Patients should be advised to lie prone in bed to avoid hip flexion contractures. The shoulder should be placed in the bed as abduction and external rotation.

Splinting is an effective adjunctive treatment for contracture management. However, it does not replace comprehensive rehabilitation treatment. Orthotics can be prescribed to maintain the position of the hands, elbows, knees, and ankles. The comfort of the patient is essential for a successful splinting program. Skin irritation and pain can cause discomfort. After initial fabrication of the orthosis, the patient should be monitored every 30 min for skin problems. If a pressure zone is not detected, a 2-h wearing schedule begins. If the skin tolerance allows, patient can increase the wearing schedule through the night.

Appropriate wheelchair seating and positioning are also important to prevent contractures. The placement of armrest and lapboards on the wheelchair can prevent contractures and sublux-

ation of the shoulder. By positioning the armrest forward, the extension of the elbow is promoted. The pelvis needs to be tilted slightly forward (anterior tilt), which may lead to normal lordosis in the lumbar spine and kyphosis in the thoracic spine. Leg straps can be used to prevent the abduction of the lower extremities while sitting in the wheelchair. Changing the position of the ankle, foot, knee, and hip can be achieved by adjusting the footrest height.

34.4.4 Treatment of Contractures

Physical management includes therapeutic heat, i.e., ultrasound, before stretching program. In areas with sensory impairment, care must be taken when treating heat. It is important to have sustained stretching at the end of the range of motion. Regional osteoporosis can lead to bone fragility, and vigorous stretching may lead to a fracture. Serial casting or dynamic splinting may be an adjunct treatment to a stretching program. If there are pain or pressure injuries, serial casting should be stopped. Dynamic splinting uses splints with movable parts to accommodate contractile forces. In refractory cases, orthopedic surgical procedures can be considered.

References

Adams MM, Hicks AL. Spasticity after spinal cord injury. Spinal Cord. 2005;43:577–86.

Adams MM, Ginis KAM, Hicks AL. The spinal cord injury spasticity evaluation tool: development and evaluation. Arch Phys Med Rehabil. 2007;88:1185–92.

Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. Practitioner. 1964;192:540–2.

Barnes MP, Johnson GR. Upper motor neurone syndrome and spasticity. Clinical management and neurophysiology. 2nd ed. Cambridge: Cambridge University Press; 2008.

Benz EN, Hornby TG, Bode RK, et al. A physiologically based clinical measure for spastic reflexes in spinal cord injury. Arch Phys Med Rehabil. 2005;86:52–9.

Birch R. Peripheral nerve injuries: a clinical guide. London: Springer; 2013.

Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther. 1987;67:206–7.

Burke D. Spasticity as an adaptation to pyramidal tract injury. Adv Neurol. 1988;47:401–23.

Cabahug P, Pickard C, Edmiston T, et al. A primary care provider's guide to spasticity management in spinal cord injury. Top Spinal Cord Inj Rehabil. 2020;26:157–65.

Chiurchiù V, van der Stelt M, Centonze D, et al. The endocannabinoid system and its therapeutic exploitation in multiple sclerosis: clues for other neuroinflammatory diseases. Prog Neurobiol. 2018;160:82–100.

Cleland CL, Rymer WJ. Neural mechanisms underlying the clasp-knife reflex in the cat. I. Characteristics of the reflex. J Neurophysiol. 1990;64:1303–18.

Cutter NC, Scott DD, Johnson JC, et al. Gabapentin effect on spasticity in multiple sclerosis: a placebo-controlled, randomized trial. Arch Phys Med Rehabil. 2000;81:164–9.

Davidoff RA. Antispasticity drugs: mechanisms of action. Ann Neurol. 1985;17:107–16.

Dietz V, Sinkjaer T. Spasticity. Handb Clin Neurol. 2012;109:197–211.

Dietz V, Young R. The syndromes of spastic paresis. In: Brandt T, Caplan L, Dichgans L, et al., editors. Neurological disorders. Course and treatment. Amsterdam: Academic Press; 2003.

Ditunno JF, Little IW, Tessler A, et al. Spinal shock revisited: a four-phase model. Spinal Cord. 2004;42:383–95.

Elbasiouny SM, Moroz D, Bakr MM, et al. Management of spasticity after spinal cord injury: current techniques and future directions. Neurorehabil Neural Repair. 2010;24:23–33.

Fleuren JF, Voerman GE, Snoek GJ, et al. Perception of lower limb spasticity in patients with spinal cord injury. Spinal Cord. 2009;47:396–400.

Francisco GE. The role of intrathecal baclofen therapy in the upper motor neuron syndrome. Eur Med Phys. 2004;40:131–43.

Haas BM, Bergstrom E, Jamous A, et al. The interrater reliability of the original and of the modified Ashworth scale for the assessment of spasticity in patients with spinal cord injury. Spinal Cord. 1996;34:560–4.

Hiersemenzel LP, Curt A, Dietz V. From spinal shock to spasticity: neuronal adaptations to a spinal cord injury. Neurology. 2000;54:1574–82.

Hofstoetter US, McKay WB, Tansey KE, et al. Modification of spasticity by transcutaneous spinal cord stimulation in individuals with incomplete spinal cord injury. J Spinal Cord Med. 2014;37:202–11.

Joseph D, Schulze J. Cannabinoid activity-is there a causal connection to spasmolysis in clinical studies? Biomol Ther. 2021;11:826.

Jung IY, Kim HR, Chun SM, et al. Severe spasticity in lower extremities is associated with reduced adiposity and lower fasting plasma glucose level in persons with spinal cord injury. Spinal Cord. 2017;55:378–82.

Katz RT, Rymer WZ. Spastic hypertonia: mechanisms and measurement. Arch Phys Med Rehabil. 1989;70:144–55.

Kheder A, Nair KP. Spasticity: pathophysiology, evaluation and management. Pract Neurol. 2012;12:289–98.
Kita M, Goodkin DE. Drugs used to treat spasticity. Drugs. 2000;59:487–95.
Ko HY, Ditunno JF, Graziani V, et al. The pattern of reflex recovery during spinal shock. Spinal Cord. 1999;37:402–9.
Lance JW. Pathophysiology of spasticity and clinical experience with Baclofen. In: Lance JW, Feldman RG, Young RR, et al., editors. Spasticity: disordered motor control. Chicago, IL: Year Book; 1980. p. 185–204.
Little JW, Ditunno JF Jr, Stiens SA, et al. Incomplete spinal cord: neuronal mechanisms of motor recovery and hyperreflexia. Arch Phys Med Rehabil. 1999;80:587–99.
Lofvenmark I, Werhagen L, Norrbrink C. Spasticity and bone density after a spinal cord injury. J Rehabil Med. 2009;41:1080–4.
Lui J, Sarai M, Mills PB. Chemodenervation for treatment of limb spasticity following spinal cord injury: a systematic review. Spinal Cord. 2015;53:252–64.
McClugage SG 3rd, Bauer DF. Review of tone management for the primary care provider. Pediatr Clin N Am. 2021;68:929–44.
Minassian K, Hofstoetter U, Tansey K, et al. Neuromodulation of lower limb motor control in restorative neurology. Clin Neurol Neurosurg. 2012;114:489–97.
Pandyan AD, Gregoric M, Barnes MP, et al. Spasticity: clinical perceptions, neurological realities and meaningful measurement. Disabil Rehabil. 2005;27:2–6.
Penn RD, Savoy SM, Corcos D, et al. Intrathecal baclofen for severe spinal spasticity. N Engl J Med. 1989;320:1517–21.
Priebe MM, Sherwood AM, Thornby JI, et al. Clinical assessment of spasticity in spinal cord injury: a multidimensional problem. Arch Phys Med Rehabil. 1996;77:713–6.
Rekand T. Clinical assessment and management of spasticity: a review. Acta Neurol Scand Suppl. 2010;190:62–6.
Rymer WZ, Houk JC, Crago PE. Mechanisms of the clasp-knife reflex studied in an animal model. Exp Brain Res. 1979;37:93–113.
Schomburg ED, Steffens H. The effect of DOPA and clonidine on reflex pathways from group II muscle afferents to alpha-motoneurones in the cat. Exp Brain Res. 1988;71:442–6.
Strommen JA. Management of spasticity from spinal cord dysfunction. Neurol Clin. 2013;31:269–86.
Tardieu G, Shentoub S, Delarue R. Research on a technic for measurement of spasticity. Rev Neurol (Paris). 1954;91:143–4.
Wartenberg R. Pendulousness of the legs as a diagnostic test. Neurology. 1951;1:18–24.
Westerkam D, Saunders LL, Krause JS. Association of spasticity and life satisfaction after spinal cord injury. Spinal Cord. 2011;49:990–4.
Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. JAMA. 2015;313:2456–73.
Woolacott AJ, Burne JA. The tonic stretch reflex and spastic hypertonia after spinal cord injury. Exp Brain Res. 2006;174:386–96.

Recommended Additional Reading

Barnes MP, Johnson GR. Upper motor neurone syndrome and spasticity: clinical management and neurophysiology. 2nd ed. Cambridge: Cambridge University Press; 2008.
Brashear A. Spasticity: diagnosis and management. 2nd ed. New York: Demos Medical; 2015.
Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.
Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation. Philadelphia, PA: Elsevier; 2014.
Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Gelber DA, Jeffery DR, editors. Clinical evaluation and management of spasticity. New York: Springer Science; 2002.
Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia, PA: Elsevier; 2016.
Pandyan AD, Hermens HJ, Conway BA. Neurological rehabilitation: spasticity and contractures in clinical practice and research. In: Scherer MJ, Muller D, editors. Rehabilitation science in practice series. Boca Raton, FL: CPC Press; 2018.
Vanderah T, Gould DJ. Nolte's the human brain. Philadelphia, PA: Elsevier; 2016.
Vogel LC, Zebracki K, Betz RR, Mulcahey MJ, editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.

Neurogenic Heterotopic Ossification in Spinal Cord Injuries

35

Heterotopic ossification is defined as the formation of extraosseous mature lamellar bone in the extraskeletal soft tissues surrounding peripheral joints, where bone does not usually exist (Keschner and Paksima 2007; Pittenger 1991). Heterotopic ossification is a biological process of new bone formation in nonosseous tissues. The term "heterotopic ossification" is preferred over terms such as ectopic ossification, paraosteoarthropathy, myositis ossificans, neurogenic osteoma, or haterotopic calcification when discussing the formation of new bone near joints as a result of spinal cord injury. When associated with CNS injury, it is referred to as neurogenic heterotopic ossification (Botte et al. 1997). Microscopically, the bones are formed through a true "ossific" process that evolves into new bone formation and not soft tissue calcification. Spinal cord injuries are associated with a variety of complications in the acute, subacute, and chronic phases. Heterotopic ossification is one of these complications and a potential cause of increased morbidity due to complications resulting from immobilization (van Kuijk et al. 2002). Heterotopic ossification was first identified by Reidel, a German physician, in 1883. First described as "paraosteo-arthropathy" by French neurologists Dejerne and Ceillier in 1918, based on the observation of a soldier with spinal cord injury during World War I (Dejerne and Ceillier 1918).

Heterotopic ossification is seen in many conditions including spinal cord injury, traumatic brain injury, stroke, burns, ambulations, and even drug abuse. Patients with spinal cord injuries are predisposed to the formation of extraosseous bone formation or heterotopic ossification below the level of injury (Cipriano et al. 2009a). Heterotopic ossification after spinal cord injuries can lead to loss of joint mobility, loss of function, peripheral nerve entrapment, and pressure injuries. The upper and lower extremities can be affected, but the most commonly affected joints are the hip. The most common location in patients with spinal cord injury is inferomedial or anteromedial to the hip, which appears to be related to adductor spasticity of the hip, followed by the knee, elbow, and shoulder, and rarely occurs in the small joints of the hand and foot. In the case of brain injury, heterotopic ossification occurs in a different way from spinal cord injury (Edwards and Clasper 2015; Garland 1988; Gennarelli 1988; Moreta and Mozos 2014). The next most common area in patients with traumatic brain injuries is the shoulders and elbows, where knees are rarely affected. Knee involvement is common after spinal cord injury, but uncommon in patients with brain damage. When it occurs in a knee, it usually occurs in the medial aspect (Aubut et al. 2011). If the ossified tissue around the hip extends from the symphysis pubis to the medial or anteromedial femoral shaft, the femoral neurovascular bundle that is located anteriorly (Fig. 35.1). Other locations around the hip are the posterior and anterior aspect of the joint, below the anterior superior iliac spine

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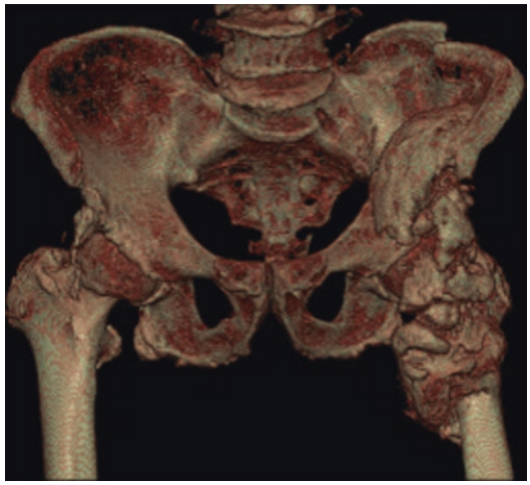

Fig. 35.1 Heterotopic ossification originating from the medial side of the left hip. It encircles the hip and extends to the iliac crest

(Garland 1988). When the posterior aspect is involved, the sciatic nerve can be affected. When the ossification occurs anteriorly, it can involve the femoral neurovascular structure.

The incidence of heterotopic ossification after major neurological injury is not known accurately, but the incidence after spinal cord injury varies from 10% to 53%, according to the report (Brady et al. 2018; Rawat et al. 2019; Reznik et al. 2014). The incidence of progression to bony ankylosis in patients with spinal cord injuries is less than 5% (Dai 1998; Lal et al. 1989; Wittenberg et al. 1992). Loss of joint mobility due to heterotopic ossification can impair mobility, positioning, hygiene, and activities of daily living. Heterotopic ossification can also lead to breakdown of overlying skin and increased spasticity. Autonomic dysreflexia can occur in people with spinal cord injury above T6. In rare instances, nerve compression or vascular occlusion may occur. Risk factors for heterotopic ossification following spinal cord injury include complete injury, male, older age, deep vein thrombosis, spasticity, prolonged immobility, thoracic level injury, pneumonia, pelvic trauma, and pressure injury (Citak et al. 2012; Suero et al. 2018; Yolcu et al. 2020). Other factors such as nicotine use, tracheostomy, and urinary tract infection are implicated (Citak et al. 2012).

35.1 Pathogenesis

Although underlying pathogenesis of heterotopic ossification following spinal cord injury is still relatively unknown, there are a few hypotheses regarding bone morphogenic protein expression and alkaline phosphatase activity that results in ectopic bone formation in soft tissues, most frequently muscle tissue (Yolcu et al. 2020). It has been suggested believed that a combination of proprioceptive dysfunction related to disruption of the central nervous system, local inflammatory changes due to trauma, spasticity, immobilization related hypercalcemia, and humoral factors can lead to the migration of mesenchymal osteoprogenitor cells into the joint space or soft tissue (van Kuijk et al. 2002) (Fig. 35.2). An inflammatory process leads to increased blood flow in the soft tissue. Alkaline phosphatase acts to suppress inhibitors of bone formation is known to be elevated in vascular smooth muscle tissue in the presence of inflammatory cytokines and macrophages (Yoon et al. 2018). Acute rehabilitation, transfer activities, and repeated microtrauma can lead to an accumulation of mechanical stress that predisposes to the formation of heterotopic ossification.

Heterotopic ossification is derived from dormant osteoprogenitor stem cells within the soft tissues. The stem cells are stimulated to differentiate into osteoblasts that begin osteoid formation and eventually develop into mature heterotopic bone (Da Paz et al. 2007; Pape et al. 2004). There is evidence that heterotopic ossification is the result of rapid metaplastic osteogenesis and some chondrogenesis, resulting in the formation of lamellar corticospingiosal bone (Rossier et al. 1973). What triggers cellular metaplasia and why it does not appear similar in all cases remains unanswered. Abnormalities in sympathetic nerve activity may promote heterotopic ossification by increasing local vascularity and blood perfusion around the joints. The influence of an association between human leukocyte antigens (HLA) and heterotopic ossification is not clear. Some authors suggest a high prevalence of HLA-B18 and HLA-B27 in patient with heterotopic ossification, but these findings should be confirmed (Minare 1984).

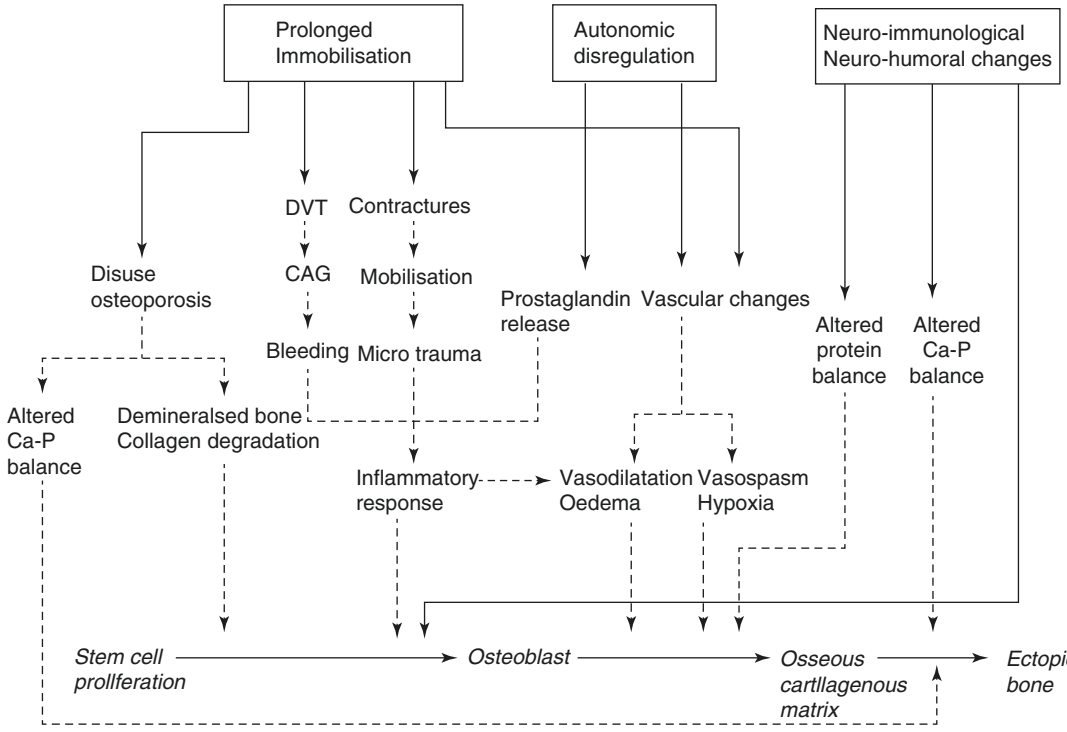

Fig. 35.2 Schematic representation of the possible pathogenesis of heterotopic ossification in spinal cord injuries. *OAC* oral anticoagulant; *DVT* deep vein thrombosis. Adapted from van Kuijk et al. (2002)

Bone formation in heterotopic ossification occurs primarily in the connective tissue between muscle planes rather than the muscle itself. Lamellar bone formation begins at the periphery and progresses centrally, and it is surrounded by compressed muscle fibers and connective tissue (Banovac and Gonzalez 1997). Histologically, the maturation schedule is as follows: in the first week after injury, spindle cells proliferate; in the second week, the primitive osteoid has formed, and primitive cartilage is deposited; in weeks 2 to 5, trabecular bones are formed; at week 6, there are immature undifferentiated tissues that are surrounded centrally by mature lamellar bone. Heterotopic bone formation peaks 4 to 12 weeks after spinal cord injury. The bone matrix is precipitated and mineralized, and this sequence achieves a steady-state maturation after 6 to 18 months. The histology of heterotopic ossification is similar to that of normal mature bone with well-developed cortical and trabecular structures. The bones have a high metabolic rate which is more than three times that of normal bone (McIntyre et al. 2014).

35.2 Clinical Features

Heterotopic ossification most commonly occurs between 3 and 12 weeks after spinal cord injury and is associated with warmth, swelling, erythema and soft tissue breakdown, which makes it difficult to diagnosis as these symptoms share similarities with other inflammatory conditions including sepsis, cellulitis, deep vein thrombosis, and osteomyelitis (Brady et al. 2018). The highest-risk period for the occurrence of heterotopic ossification after spinal cord injury is 5 months (Wittenberg et al. 1992). It takes 12 to 24 months to progress to mature bones. About 90% of neurogenic heterotopic ossification occur around the hip (Citak et al. 2012), but heterotopic

ossification may occur any part of the body (Hernandez et al. 1978). Heterotopic ossification of the hip can lead to serious complications, including loss of joint mobility and function, peripheral nerve entrapment, and pressure injuries (Suero et al. 2018). According to the evolution pattern of heterotopic ossification, type I (class I) occurs over a period of 6 months, and type II (class II) is a heterotopic ossification with evolution over a prolonged period and unremitting course. Type II tends to have a worse prognosis and progresses to ankylosis (Garland and Orwin 1989).

The patient who develops heterotopic ossification will progress from the initial symptoms of swelling to develop a palpable mass as well as induration and stiffness (Bossche and Vanderstraeten 2005). Clinical presentations ossification within soft tissues may lead to erythema, pain, swelling, decreased joint range of motion, increased spasticity, and mild fevers. Long-term complications of heterotopic ossification include difficulty in sitting secondary to reduced joint range of motion, chronic pain, pressure injuries, deep vein thrombosis, and increased spasticity and, in severe cases, compression of the adjacent neurovascular structures resulting in swelling of the distal extremities and nerve entrapment. The clinical picture depends on the stages of the disorder. Clinically, four stages have been described: acute, subacute, chronic immature, and chronic mature (Table 35.1).

The differential diagnosis for these clinical presentations includes deep vein thrombosis, cellulitis, lower extremity fracture, septic arthritis, abscess, hematoma, and tumor (Table 35.2). The most common sites for heterotopic ossification in spinal cord injury are the hips and knees. In the hip, the lesion is usually anterior to the hip joint. In the knee, the lesion is usually the distal anteromedial knee. Heterotopic ossification in people with spinal cord injuries rarely affects the shoulders or elbows. The extent of tissue involvement by heterotopic ossification varies. A large amount of ossification can cause serious functional limitation or ankylosis of the joint, while a small amount of bone around the joint will not cause joint dysfunction.

35.3 Diagnosis

The diagnosis of heterotopic ossification begins with physical examination. Unfortunately, it often presents with a similar picture to septic arthritis and deep vein thrombosis with warmth, erythema, swelling, and limited range of motion. The mean time from injury to diagnosis of heterotopic ossification is 2 months, but may range from 2 weeks to 1 year (Cipriano et al. 2009a). Laboratory tests for heterotopic ossification are sensitive but not specific. Serum alkaline phosphatase is a nonspecific marker, but it is the earliest laboratory finding of heterotopic ossification and often precedes radiographic presentation within 2–3 weeks of the onset of heterotopic ossification. Persistent elevation of serum alkaline phosphatase and phosphorus levels reflects osteoblastic activity (Kim et al. 1990). Alkaline phosphatase is a glycosylated protein, or glycoprotein, which is produced by bone, renal, hepatic, intestinal, and placenta cells. In bone, alkaline phosphatase is located mainly in the plasma membrane of osteoblasts (Zychowicz 2013). Alkaline phosphatase is also limited due to elevated in, for example, skeletal injuries, surgery, and abdominal problems. In addition, alkaline phosphatase levels do not correlate with degree of bone activity or maturation of heterotopic ossification and therefore cannot be used to assess maturity of the ectopic bone or predict recurrence. Higher levels of serum alkaline phosphatase continue for an average 5 months. Alkaline phosphatase is an easy screening tool to detect early heterotopic ossification and begin with treatment. Normalization of serum alkaline phosphatase levels does not correlate with maturation of heterotopic ossification, nor does the peak alkaline phosphatase level correlate with peak osteogenic activity (van Kuijk et al. 2002).

Nonspecific markers of inflammation, such as C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR), may be useful in following disease activity, with normalization of the CRP correlating with resolution of the inflammatory phase of heterotopic ossification. Urinary excretion of hydroxyproline and collagen metabolites correlates with alkaline phosphatase levels

Table 35.1 Stages of heterotopic ossification

Stage	Duration	Signs	Alkaline phosphatase	ESR	Radiologic grade	Bone scan
Acute	2 weeks	Inflammation	↑	↑	Negative	± Activity
Subacute	2–8 weeks	• ↓Inflammation • ↓ROM	↑	↑	Grade I	Increasing
Chronic active immature	6–8 months	• ↓ROM • Irregular palpable bone masses	↑	↑	Grade II	Decreasing
Chronic mature	8–18 months	• ↓ROM • Ankylosis • Hard bone masses	↓ Normal	Normal	Grade III	Almost normal scan

Adapted from Green (1996)

Table 35.2 Differential diagnosis of heterotopic ossification

Sign/symptom	Heterotopic ossification	DVT	Infection	Hematoma	Tumor
Swelling	+	+	+	+	+, progressive
Pain	+	+	+	+	+
Alkaline phosphatase	↑	–	–	–	↑
Radiography	New bone formation with demarcation from cortex, no cortex destruction	–	–	–	Periosteal reaction, cortex destruction
Bone scan	+	–	–	–	+
Doppler flow studies	–	+	–	–	–
Response to antibiotics	No change	No change	resolves	No change	No change

and can also be used as indirect markers for the presence of heterotopic ossification. Creatinine kinase may increase due to damage to surrounding muscles during ossification formation of heterotopic ossification (Sherman et al. 2003; Singh et al. 2003). The 24-h urinary excretion of prostaglandin E2 increases until the maturation of the heterotopic ossification and is proposed as a not commonly used but useful marker (Schurch et al. 1997).

Bone scans or scintigraphy is considered the most sensitive method for early detection of heterotopic ossification, and detection is possible after 2 weeks of symptom onset (Shehab et al. 2002). Three-phase bone scans are a common confirmation study. Bone scintigraphy using 99mTc-methylene disphosphonate provides imaging in three phases: phase I (dynamic blood flow study), phase II (static study for blood pool), and phase III (static bone phase). The first phase of the three-phase bone scan is the period immediately following the intravenous injection of the radionuclides and detects areas of increased blood blow, which is an early indicator of the inflammation process (the dynamic blood flow phase). The second phase (the static blood pool phase) identifies areas of increased blood pooling several minutes after the injection. The third phase (the static bone phase) determines the degree of osseous uptake of the labeled radionuclides several hours after the injection (van Kuijk et al. 2002). Bone scans normalize as the heterotopic ossification matures usually within 6–18 months after the first clinical signs (Orzel and Rudd 1985). Compared to plain X-ray, bone scan is a more sensitive diagnostic test for early heterotopic ossification, but X-ray is more specific. A disadvantage of the three-phase bone scan is its low specificity, which leads to potential difficulties in discriminating heterotopic ossification from other inflammatory, traumatic, or degenerative processes of the bone, e.g., fracture, bone tumor, metastasis, or osteomyelitis, all of which show increased osteoblastic activity and thereby increased uptake of osteotropic radionuclides (van Kuijk et al. 2002).

The first two phases are most sensitive for early detection of heterotopic ossification at 2 or 3 weeks. Evidence of heterotopic ossification can be seen as early as 2–3 weeks after onset of the lesion in the first two phases of the bone scan showing hyperemia and blood pooling. In phase III, this test occurs approximately 1 week later. The activity level on the delayed bone scans usually peaked at 2 months and decreased gradually. Scintigraphy activity returns to normal after about 12 months but can be maintained even when the ossification matures (Shehab et al. 2002; Svircev and Wallbom 2008). The period between a positive phase I and II scan with a negative phase III scan may vary from 2 to 4 weeks before plain radiographic appearance of heterotopic ossification. Bone scans are the best method in monitoring the maturation of heterotopic ossification, and sequential decrease or steady-state uptake is a reliable indicator of maturity.

Standard X-rays are not sensitive for early diagnosis of heterotopic ossification (Orzel and Rudd 1985). Plain radiographs are a simple method for detecting heterotopic ossification, but it may take up to 6 weeks for ossification to be obvious. Anteroposterior and lateral radiographs provide sufficient information to establish the relationship between the heterotopic ossification and the joints, but additional radiological techniques (CT scan, MRI) should be performed to obtain detailed information about the anatomy and joint status. A typical radiographic appearance of ectopic bone is a circumferential ossification with a lucent center (Shehab et al. 2002). Figure 35.3 shows the developmental sequence of abnormalities of serum alkaline phosphatase, radionuclide bone images, and radiography in relation to clinical symptoms of heterotopic ossification.

Ultrasonography can be positive early with finding of an echogenic peripheral zone and echolucent center and has the advantage of relatively inexpensive examination without the need for radiation (Cassar-Pullicino et al. 1993). MRI with increased T2 signal intensity in muscles and subcutaneous tissue can help to diagnose heterotopic ossification. MRI suggests changes compatible with ectopic bone formation, especially after 2 days of clinical presentation in the knee. CT scan can be used to determine the bone

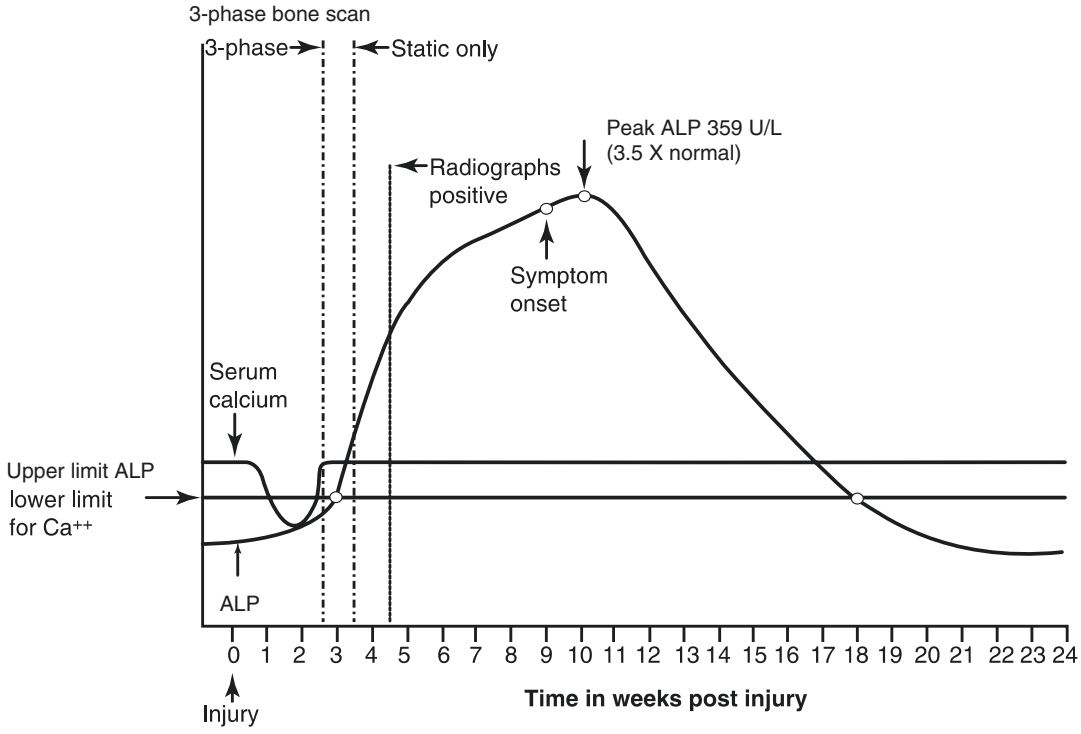

Fig. 35.3 The developmental sequence of abnormalities of serum alkaline phosphatase, radionuclide bone images, and radiography in relation to clinical symptoms of heterotopic ossification. *ALP* alkaline phosphatase. From Orzel and Rudd (1985), with permission

volume to plan surgical resection, but it is rarely used to make an early diagnosis. Combined with 2D and 3D reconstruction, CT scans provide good differentiation and extent of the ectopic bone and its relationship with the joint and surrounding neurovascular structures. If surgical treatment is required, thorough blood vessel evaluation is required. Therefore, MRI with contrast or spiral CT should be one of the requirements of preoperative evaluation for surgical resection of heterotopic ossification.

35.4 Classifications of Heterotopic Ossification

Several classifications for heterotopic ossification are based primarily on radiographic findings. Garland (Garland and Orwin 1989) proposed five groups of radiographic classification for preoperative grading based on the extent of bone formation in soft tissue: 1, minimal; 2, mild; 3, moderate; 4, severe; and 5, ankylosis. Based on radiographic findings and clinical course, Garland proposed 2 classes of heterotopic ossification. Class I patients have elevated serum alkaline phosphatase for 5-6 months with heterotopic ossification and a radiographic progression of heterotopic ossification. Class II is characterized by a persistent bone scan activity and a radiographic course of heterotopic ossification. Patients in class II eventually need surgery. This classification can be used for any location of heterotopic ossification (Garland and Orwin 1989).

The Brooker classification for heterotopic ossification of the hip is the most commonly used to describe the pattern and extent of ossification in total hip arthroplasty on the supine anteroposterior plain X-ray of the hip (Ampadiotaki et al. 2021; Brooker et al. 1973; Hug et al. 2015). This classification is also used for heterotopic ossification resulting from neurogenic cause including

spinal cord injuries. It is a relatively simple and valid measurement. The extent of ectopic bone correlates well with the degree of functional impairment. There are four types according to this classification (Fig. 35.4):

- Class 1: Bone islands within the soft tissues about the hip
- Class 2: Bone spurs from the pelvis or proximal end of the femur, leaving at least 1 cm between opposing bone surfaces
- Class 3: Bone spurs from the pelvis or proximal end of the femur, reducing the space between opposing bone surfaces to less than 1 cm
- Class 4: Apparent bone ankylosis of the hip.

A more comprehensive classification was established in order to classify heterotopic ossification considering ossification in the region of surgical approach (Schmidt and Hackenbroch 1996) (Table 35.3). Mavrogenis et al. (Mavrogenis et al. 2012) proposed four types of neurogenic heterotopic ossification based on the anatomical localization of the heterotopic ossification as shown on axial CT scans of the hip and proximal femur, clinical ankyloses of the hip joint, and the etiology of the neurogenic injury. There are two subtypes (a and b) according to the etiology of neurological injury, spinal cord injury (a) and brain injury (b): type 1, at the anterior hip; type 2, at the posterior hip; type 3, at the anterior and medial hip; and type 4, around the hip (circumferential). The authors suggested that this classification permits an estimation of the prognosis regarding blood loss, transfusion requirements, and recurrence of the neurogenic heterotopic ossification and provides a better evaluation of the prognosis after surgical excision than the Brooker classification (Mavrogenis et al. 2012).

35.5 Prophylaxis

Prophylactic heterotopic ossification treatment with medications for all spinal cord injuries is probably not guaranteed. Maintaining joint motion by treating spasticity and gentle physical therapy is the goal of early treatment. If there is suspicion of heterotopic ossification, treatment should begin with medical treatment, and then once the ectopic bone is established, carefully consider symptomatic surgical resection, not radical.

Prevention should begin with early joint mobilization. When gentle passive movements of the large peripheral joints are started and maintained from the day of the injury, the joint capsules will be kept as flexible as possible, the muscles will not be so easily shorten, and contractures will not occur as quickly, thus preventing heterotopic ossification (van Kuijk et al. 2002). If early ossifications are suspected, passive ROM exercise should be given. If the patient is conscious, physical therapy should involve an assisted range of motion exercises with gentle stretch and end resistance training (Stover et al. 1975). It is important to achieve a good range of motion without causing pain. Avoid aggressive exercise as they increase the risk of more bone formation. Medical treatment aims to prevent the formation of heterotopic ossification and to prevent recurrence when surgical resection is required. Early prevention is considered as the development of heterotopic ossification may occur within 1–2 months after the injury. There is no consensus on which medications to use and when to start treatment (Genet et al. 2009).

Prophylaxis of heterotopic ossification in spinal cord injury using disodium etidronate and slow-release indomethacin has been studied, with less heterotopic ossification formation and less functional deficits than placebo. Indomethacin is known to be useful in the prevention of heterotopic ossification after total hip replacement. This medication, given in 3–6 weeks at a dose of 75 mg/day within 2 months after injury, can reduce the incidence of heterotopic ossification by two–three times. The selective COX-2 inhibitor, celecoxib, can be used to prevent heterotopic ossification after spinal cord injury, and the risk of developing ectopic bone is 2.5 times lower. Celecoxib can be an attractive choice because of its low gastrointestinal side effects. In conclusion, indomethacin remains the gold standard for pharmacological prevention of heterotopic

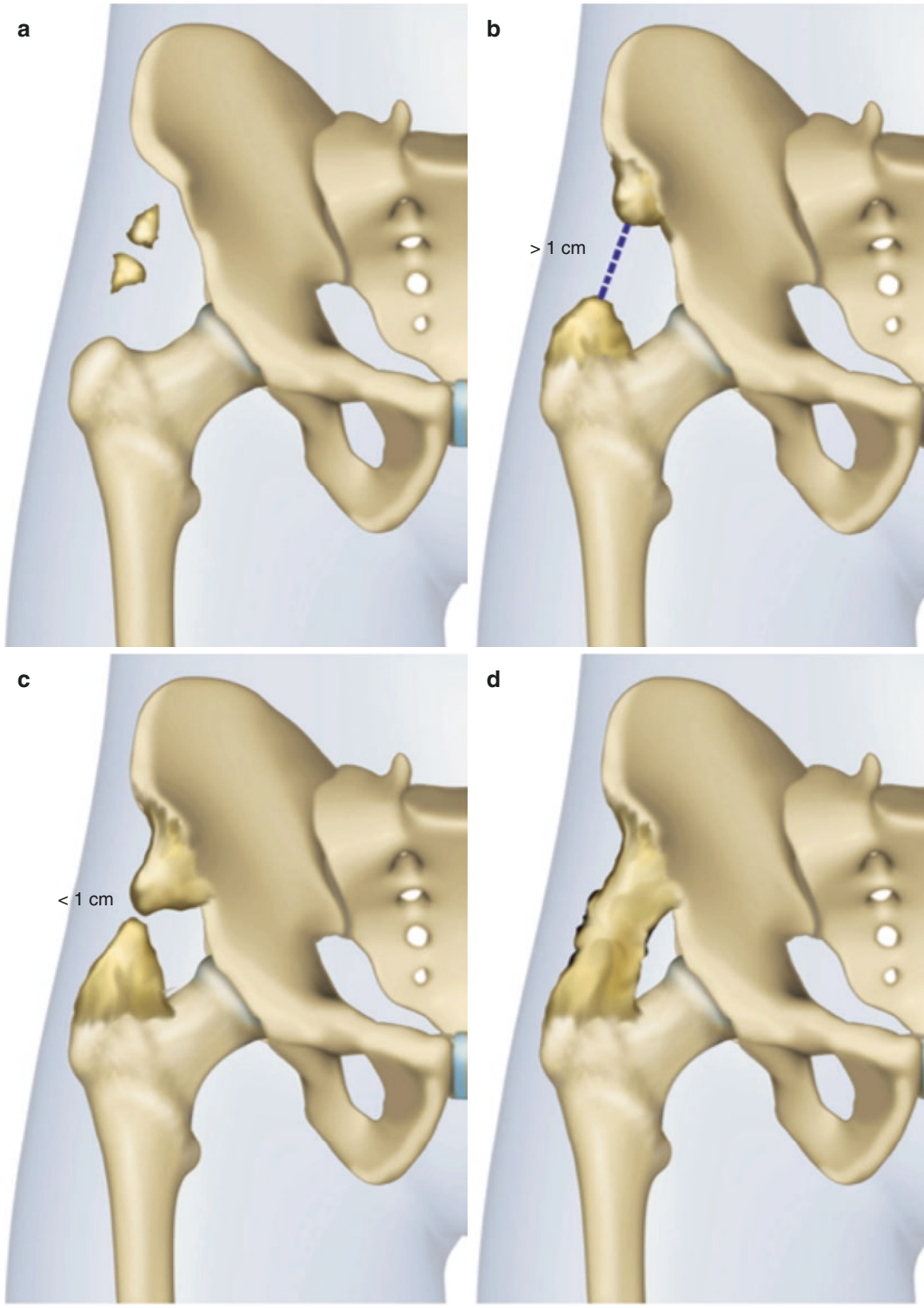

Fig. 35.4 Brooker classification of heterotopic ossification around the hip: (**a**) Class 1 is described as islands of bone within the soft tissues about the hip; (**b**) Class 2 includes bone spurs originating from the pelvis or proximal end of the femur, leaving at least 1 cm between opposing bone surfaces; (**c**) Class 3 consists of bone spurs originating from the pelvis or proximal end of the femur, reducing the space between opposing bone surfaces to less than 1 cm; and (**d**) Class 4 shows apparent bone ankylosis of the hip. From Hug et al. (2015), with permission

Table 35.3 Schmidt and Hackenbroch classification of heterotopic ossification

Score	Specification
0	No heterotopic ossifications on AP and lateral view of the hip
Region	
I	Heterotopic ossifications strictly below the tip of the greater trochanter
II	Heterotopic ossifications below and above the tip of the greater trochanter
III	Heterotopic ossifications strictly above the tip of the greater trochanter
Grade	
A	Single or multiple heterotopic ossifications smaller than 10 mm maximal extent without contact to pelvis or femur
B	Heterotopic ossifications larger than 10 mm without contact to the pelvis but possibly to the femur. No bridging from caudal to proximal from the greater trochanter
C	Heterotopic ossifications with bridging from the femur to the proximal part of the greater trochanter with no evidence of ankylosis
D	Ankylosis by means of firm bridging from the femur to the pelvis

ossification. This is a simple and inexpensive option. Celecoxib is a reasonable option for patients without cardiovascular diseases because it shows good results with few gastrointestinal effects. Indomethacin is now the gold standard pharmacological prevention of heterotopic ossification. The optimal time to start treatment is within 2 months of the injury and should be done for 4–6 weeks. The standard dosing is 75 mg long-acting indomethacin daily, or 25 mg standard-release indomethacin three times daily (Banovac et al. 2001).

Bisphosphonates have also been used to prevent heterotopic ossification. Disodium etidronate is a well-studied bisphosphonate and appears to be effective in early ossifications (Banovac 2000) and later phases of the disease. This drug inhibits precipitation of calcium phosphate and blocks the aggregation and mineralization of hydroxyapatite crystals. Bisphosphonates can also have long-term effects on prevention after treatment. Some researchers do not recommend the routine use of bisphosphonates because additional fractures are often associated with neurological damage, and the use of bisphosphonates may interfere with fracture healing (Sullivan et al. 2013).

35.6 Management

Management decisions of heterotopic ossification should be individualized. In some individuals, heterotopic ossification is not functionally important and does not require intervention. Others suffer from multiple lesions that seriously affect functioning. Patients with minimal lesions may not need treatment. Treatment options include range of motion exercise with gentle stretching, bisphosphonates, nonsteroid anti-inflammatory drugs (NSAIDs) in the absence of contraindications, possible radiation therapy, and surgical resection. The goal of physical therapy is to maintain functional range of motion. Due to the possibility of pathologic fractures, forceful manipulations are generally not recommended in patients with spinal cord injuries. There is some debate as whether ROM exercise affects the formation or deterioration of heterotopic ossification in the ROM limitations. In animal model studies, new bone formation can occur with aggressive ROM exercise, stretching, and forceful manipulation (Michelsson and Rauschning 1983; Snoecx et al. 1995). NSAIDs act by inhibiting the osteogenic differentiation of progenitor cells (Ranganathan et al. 2015). One of the proposed mechanisms of heterotopic ossification development is overproduction of prostaglandin E2, and NSAIDs also act as cyclooxygenase inhibitors leading to blockage of prostaglandin production (Kozak et al. 2006).

Once heterotopic ossification is diagnosed, aggressive ROM exercises, which can lead to additional tissue microtrauma that may increase the formation of heterotopic ossification, are not recommended (Crauford et al. 1986). Careful and gentle mobilization of the affected joints does not cause further loss of ROM and promotes heterotopic ossification (Banovac et al. 2004). After a period of acute inflammation, a ROM that maintains a gentle and constant pressure to slowly increase or maintain the range may be achieved. Low-load prolonged stretching at end range can increase the ROM without tissue damage, with the goal of maintaining the ROM within a functional range. More frequent but shorter duration of ROM exercise can be helpful (Snoecx et al. 1995).

Bisphosphonate treatment has been shown to reduce the rate of new bone formation in patients with heterotopic ossification. The commonly used bisphosphonate, etidronate, inhibits the formation of bone mineral, however organic matrix deposition is unaffected and bone formation usually recurs if treatment continues for <6 months following injury (Vanden Bossche and Vanderstraeten 2005). However, this does not affect already deposited bone. Disodium etidronate is a structural analog of inorganic phosphate and inhibits ossification by blocking the formation of hydroxyapatite crystals. This drug blocks the later stage of bone formation, the mineralization stage, preventing the conversion of amorphous calcium phosphate to hydroxyapatite. Oral doses of 20 mg/kg/day etidronate should be administered once or twice for 6 months, with a 10 mg/kg/day for an additional 3 months (Garland et al. 1983). The most common side effects of etidronate are gastrointestinal symptoms, including nausea and vomiting, which occur in 10–20% of patients. There is a possibility that heterotopic ossification will resume after the drug has been discontinued. Etidronate cannot prevent the radiologic progression of lesions even at the beginning of disease progression.

Low dose radiotherapy has also been used to prevent the formation and/or recurrence of heterotopic ossification following surgical excision. Radiation therapy appears to be effective in preventing the differentiation of mesenchymal cells into osteoblasts that can initiate bone formation. Various doses of radiation therapy for patients with early heterotopic ossification have been described. A single or fraction dose of 600–750 rads (6–7.5 Gy) is appropriate. Long-term risks were not studied (Sautter-Gihl et al. 2000). Typical dose of radiation therapy used for total hip arthroplasty has not been effective in preventing recurrence of neurogenic heterotopic ossification in high-risk patients (Cipriano et al. 2009b).

Surgical resection is required for patients who have severe ROM limitations that cause significant functional limitations in mobility or ADLs or that cause medical complications such as severe pressure injuries. Surgical indications for the removal of heterotopic ossification of the shoulder or elbow are aimed at improving daily activities such as feeding, hygiene, dressing, and clinical evidence of progressive ulnar nerve compression (McAuliffe and Wolfson 1997). Most clinicians are advised to wait 12–18 months for the ectopic bone to mature on a bone scan (McAuliffe and Wolfson 1997). These recommendations are based primarily on the usual time to radiological maturation that is observed with spinal cord injury and, in the case of traumatic brain injury, the added time for motor recovery to occur. The purpose of waiting until maturity is to minimize the rate of recurrence after resection (Sullivan et al. 2013). In one study, a higher rate of recurrence when the heterotopic ossification is excised in an earlier phase is not confirmed (Genet et al. 2009). In addition, delaying the operation too much will cause ankylosis and profound osteoporosis and intraarticular joint destructions. Patients considered for surgery should also perform an appropriate assessment of cognitive and physical functions.

In general, the surgical goal is to remove enough bone to improve and preserve the joints, and the ectopic bone is not eradicated. Surgery should be planned if heterotopic ossification is at a quiescent state with normal alkaline phosphatase levels, mature radiographic appearance, and baseline bone scan. Wedge resection is the most commonly used procedure. After resection, it is beneficial to start gentle ROM exercise at 72 h postoperatively and wait 1–2 weeks until soft tissue swelling subsides until active physical therapy begins. Postoperative treatment includes 6 weeks of NSAIDs and/or etidronate (20 mg/kg/day) for 3–12 months and/or radiation therapy (McIntyre et al. 2014; van Kuijk et al. 2000). Recurrence of heterotopic ossification after resection is common; the measure of success of the surgery is a functional improvement such as wheelchair sitting, grooming, hygiene, feeding, and mobility.

References

Ampadiotaki MM, Evangelopoulos DS, Pallis D, et al. New strategies in neurogenic heterotopic ossification. Cureus. 2021;13:e14709.

Aubut JA, Mehta S, Cullen N, et al. A comparison of heterotopic ossification treatment within the traumatic brain and spinal cord injured population: an evidence based systematic review. NeuroRehabil. 2011;28:151–60.

Banovac K. The effect of etidronate on late development of heterotopic ossification after spinal cord injury. J Spinal Cord Med. 2000;23:40–4.

Banovac K, Gonzalez P. Evaluation and management of heterotopic ossification in patients with spinal cord injury. Spinal Cord. 1997;35:158–62.

Banovac K, Sherman AL, Estores IM, et al. Prevention and treatment of heterotopic ossification after spinal cord injury. J Spinal Cord Med. 2004;27:376–82.

Banovac K, Williams JM, Patrick LD, et al. Prevention of heterotopic ossification after spinal cord injury with indomethacin. Spinal Cord. 2001;39:370–4.

Vanden Bossche L, Vanderstraeten G. Heterotopic ossification: a review. J Rehabil Med. 2005;37:129–36.

Botte MJ, Keenan MA, Abrams RA, et al. Heterotopic ossification in neuromuscular disorders. Orthopedics. 1997;20:335–41; quiz 342-3.

Brady RD, Shultz SR, McDonald SJ, et al. Neurological heterotopic ossification: current understanding and future directions. Bone. 2018;109:35–42.

Brooker AF, Bowerman JW, Robinson RA, et al. Ectopic ossification following total hip replacement. Incidence and a method of classification. J Bone Joint Surg Am. 1973;55:1629–32.

Cassar-Pullicino V, McClelland M, et al. Sonographic diagnosis of heterotopic bone formation in spinal cord patients. Paraplegia. 1993;31:40–50.

Cipriano CA, Pill SG, Keenan MA. Heterotopic ossification following traumatic brain injury and spinal cord injury. J Am Acad Orthop Surg. 2009a;17:689–97.

Cipriano C, Pill SG, Rosenstock J, et al. Radiation therapy for preventing recurrence of neurogenic heterotopic ossification. Orthopedics. 2009b;32:orthosupersite.com/view.asp?rID=42854. https://doi.org/10.3928/01477447-20090728-33. PMID: 19750999.

Citak M, Suero EM, Backhaus M, et al. Risk factors for heterotopic ossification in patients with spinal cord injury: a case-control study of 264 patients. Spine. 2012;37:1953–7.

Crauford C, Varghese G, Mani MM, et al. Heterotopic ossification: are range of motion exercises contraindicated? J Burn Care Rehabil. 1986;7:323–7.

Da Paz AC, Artal FJC, Kalil RK. The function of proprioceptors in bone organization: a possible explanation for neurogenic heterotopic ossification in patients with neurological damage. Med Hypoth. 2007;68:67–73.

Dai L. Heterotopic ossification of the hip after spinal cord injury. Chin Med J (Engl). 1998;111:1099–101.

Dejerne A, Ceillier A. Para-osteo-arthropathies des paraplegiques par lesion medullaire; etude clinique et radiographique. Ann Med. 1918;5:497.

Edwards DS, Clasper JC. Heterotopic ossification: a systematic review. J R Army Med Corps. 2015;161:315–21.

Garland DE. Clinical observations on fractures and heterotypic ossification in spinal cord injury and traumatic brain injury patient. Clin Orthop Relat Res. 1988;233:86–101.

Garland DE, Alday B, Venos KG, et al. Diphosphonate treatment for heterotopic ossification in spinal cord injury patients. Clin Orthop Relat Res. 1983;176:197–200.

Garland DE, Orwin JF. Resection of heterotopic ossification in patients with spinal-cord injuries. Clin Ortho Relat Res. 1989;242:169–76.

Genet F, Marmorat JL, Lautridou C, et al. Impact of late surgical intervention on heterotopic ossification of the hip after traumatic neurological injury. J Bone Joint Surg Br. 2009;91-B:1493–8.

Gennarelli TA. Heterotopic ossification. Brain Inj. 1988;2:175–8.

Green D, editor. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.

Hernandez AM, Forner JV, de la Fuente T, et al. The para-articular ossifications in our paraplegics and tetraplegics: a survey of 704 patients. Paraplegia. 1978;16:272–5.

Hug KT, Alton TB, Gee AO. Classifications in brief: Brooker classification of heterotopic ossification after total hip arthroplasty. Clin Orthop Relat Res. 2015;473:2154–7.

Keschner MT, Paksima N. The stiff elbow. Bull NYU Hosp Jt Dis. 2007;65:24–8.

Kim SW, Charter RA, Chai CJ, et al. Serum alkaline phosphatase and inorganic phosphorus values in spinal cord injury patients with heterotopic ossification. Paraplegia. 1990;28:441–7.

Kozak KR, Milne GL, Morrow JD, et al. Hypertrophic osteoarthropathy pathogenesis: a case highlighting the potential role for cyclooxygenase-2-derived prostaglandin E2. Nat Clin Pract Rheumatol. 2006;2:452–6.

Lal S, Hamilton BB, Heinemann A, et al. Risk factors for heterotopic ossification in spinal cord injury. Arch Phys Med Rehabil. 1989;70:387–90.

Mavrogenis AF, Guerra G, Staals EL, et al. A classification method for neurogenic heterotopic ossification of the hip. J Orthopaed Traumatol. 2012;13:69–78.

McAuliffe JA, Wolfson AF. Early excision of heterotopic ossification about the elbow followed by radiation therapy. J Bone Joint Surg Am. 1997;79A:749–55.

McIntyre A, Thompson S, Mehta S, et al. Heterotopic ossification following spinal cord injury. In: Eng JJ, Teasell RW, Miller WC, et al., editors. Spinal cord injury rehabilitation evidence (SCIRE), Version 5.0; 2014. p. 1–19.

Michelsson JE, Rauschning W. Pathogenesis of experimental heterotopic bone formation following

temporary forcible exercising of immobilized limbs. Clin Orthop Relat Res. 1983;176:265–72.
Minare P. Neurologic injuries, paraosteoarthropathies and human leukocyte antigens. Arch Phys Med Rehabil. 1984;65:5531.
Moreta J, Mozos JLM. Heterotopic ossification after traumatic brain injury. In: Sadaka F, editor. Traumatic brain injury. London: IntechOpen; 2014. https://doi.org/10.5772/57343. Available from: https://www.intechopen.com/books/traumatic-brain-injury/heterotopic-ossification-after-traumatic-brain-injury.
Orzel JA, Rudd TG. Heterotopic bone formation: clinical, laboratory, and imaging correlation. J Nucl Med. 1985;26:125–32.
Pape HC, Marsh S, Morley JR, et al. Current concepts in the development of heterotopic ossification. J Bone Joint Surg Br. 2004;86B:783–7.
Pittenger DE. Heterotopic ossification. Orthop Rev. 1991;20:33–9.
Ranganathan K, Loder S, Agarwal S, et al. Heterotopic ossification: basic-science principles and clinical correlates. J Bone Joint Surg Am. 2015;97:1101–11.
Rawat N, Chugh S, Zachariah K, et al. Incidence and characteristics of heterotopic ossification after spinal cord injury: a single institution study in India. Spinal Cord Ser Cases. 2019;5:72.
Reznik JE, Biros E, Marshall R, et al. Prevalence and risk-factors of neurogenic heterotopic ossification in traumatic spinal cord and traumatic brain injured patients admitted to specialised units in Australia. J Musculoskelet Neuronal Interact. 2014;14:19–28.
Rossier AB, Bussat P, Infante F, et al. Current facts of paraosteo-arthropathy (POA). Paraplegia. 1973;11:38–78.
Sautter-Gihl ML, Liebermeister E, Nanassy A. Radiotherapy as a local treatment option for heterotopic ossifications in patients with spinal cord injury. Spinal Cord. 2000;38:33–6.
Schmidt J, Hackenbroch MH. A new classification for heterotopic ossifications in total hip arthroplasty considering the surgical approach. Arch Orthop Trauma Surg. 1996;115:339–43.
Schurch B, Capaul M, Vallotton MB, et al. Prostaglandin E2 measurements: their value in the early diagnosis of heterotopic ossification in spinal cord injury patients. Arch Phys Med Rehabil. 1997;78:687–91.
Shehab D, Elgazzar AH, Collier BD. Heterotopic ossification. J Nucl Med. 2002;43:346–53.
Sherman AL, Williams J, Patrick L, et al. The value of serum creatine kinase in early diagnosis of heterotopic ossification. J Spinal Cord Med. 2003;26:227–31.
Singh RS, Craig MC, Katholi CR, et al. Predictive value of creatine phosphokinase and alkaline phosphatase in identification of heterotopic ossification in patients after spinal cord injury. Arch Phys Med Rehabil. 2003;84:1584–8.
Snoecx M, Demuynck M, Vanlacre M. Association between muscle trauma and heterotopic ossification in spinal-cord injured patients-reflections on their causal relationship and the diagnostic-value of ultrasonography. Paraplegia. 1995;33:464–8.
Stover SL, Hataway CJ, Zeiger HE. Heterotopic ossification in spinal cord injured patients. Arch Phys Med Rehabil. 1975;56:199–204.
Suero EM, Meindl R, Schildhauer TA, et al. Clinical prediction rule for heterotopic ossification of the hip in patients with spinal cord injury. Spine (Phila Pa 1976). 2018;43:1572–8.
Sullivan MP, Torres SJ, Mehta S. Heterotopic ossification after central nervous system trauma: a current review. Bone Joint Res. 2013;2:51–7.
Svircev JN, Wallbom AS. False-negative triple-phase bone scans in spinal cord injury to detect clinically suspect heterotopic ossification: a case series. J Spinal Cord Med. 2008;31:194–6.
van Kuijk AA, Geurts AC, van Kuppevelt HJ. Neurogenic heterotopic ossification in spinal cord injury. Spinal Cord. 2002;40:313–26.
van Kuijk AA, van Kuppevelt HJM, van der Schaaf DB. Osteogenesis after treatment for heterotopic ossification in spinal cord injury with the combination of surgery, irradiation, and an NSAID. Spinal Cord. 2000;38:319–24.
Wittenberg RH, Peschke U, Bötel U. Heterotopic ossification after spinal cord injury: epidemiology and risk factors. J Bone Joint Surg Br. 1992;74-B:215–8.
Yolcu YU, Wahood W, Goyal A, et al. Pharmacologic prophylaxis for heterotopic ossification following spinal cord injury: a systematic review and metaanalysi. Clin Neurol Neurosurg. 2020;193:105737.
Yoon BH, Park IK, Sung YB. Ankylosing neurogenic myositis ossificans of the Hip: a case series and review of literature. Hip Pelvis. 2018;30:86–91.
Zychowicz ME. Pathophysiology of heterotopic ossification. Orthop Nurs. 2013;32:173–7; quiz 178-9

Recommended Additional Reading

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.
Guttmann L. Spinal cord injuries. Comprehensive management and research. Oxford: Blackwell Scientific Publications; 1976.
Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.

Pain Taxonomy and Management in Spinal Cord Injuries

36

Pain is a common complication and one of the most difficult complications of spinal cord injury and has serious consequences for patients. Pain has long-term negative effects on the quality of life of patients (Kennedy et al. 2006; Finnerup et al. 2008). Chronic spinal cord injury-related pain also is related to functional disability. It can significantly impair sleep, mood, and mental health. Neuropathic pain accounts for a significant percentage of all pain symptoms in patients with spinal cord injuries and is often complex (Hatch et al. 2018). The onset of pain usually occurs less than 1 year after spinal cord injury. Statistics in large-sample studies showed that approximately 65–85% of all patients with spinal cord injuries experience pain and that about a third of these patients will experience severe/excruciating pain (Siddall et al. 2003). Pain often increases over time, and more than 50% of patients with spinal cord injuries develop chronic pain as the disease progresses. Chronic pain has also been significantly associated with depression, chronic fatigue, and a decreased quality of life (Hatch et al. 2018). Pain is ranked as one of the top 5 most common perceived problems after spinal cord injury in a large study examining patient's perception of the main consequences of spinal cord injuries and associated with patients' perception of their cognitive, physical, and emotional functionality after spinal cord injury (Widerström-Noga et al. 1999). Identifying pain subtypes is a critical step in determining appropriate treatment (Hatch et al. 2018). Musculoskeletal pain is common in the acute phase of spinal cord injuries, and musculoskeletal, neuropathic, and visceral pains are the most common types of pain in the chronic phase. Musculoskeletal pain in patients with spinal cord injury is observed in approximately 60% and neuropathic pain in 50–60% after 3 to 5 years of spinal cord injury (Siddall et al. 2003; van Gorp et al. 2015). Patients with cauda equina lesions are more likely to complain of severe pain than paraplegic patients with thoracic cord injury or tetraplegic patients.

Injury or damage to peripheral tissues induces activation of free nerve endings, leading to the perception of neurogenic pain. In contrast, neuropathic pain is perceived due to abnormal functioning within nerve cells at a certain level of the neuraxis. In neuropathic pain, differentiation may be established between abnormal peripheral function, e.g., neuralgia after peripheral nerve injury of postherpetic neuralgia, where abnormal firing may occur in dorsal root ganglion cells, and central neuropathic pain, in which the pain generator is considered to be within the brain and spinal cord. A central phenomenon in neuropathic pain is ectopic and inappropriate generation of nociceptive information in the central mechanism of pain perception, although the underlying pathophysiology remains unclear (Mehta et al. 2013).

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Peripheral nociceptors associated with free nerve endings are activated by peripheral tissue injury, and impulses are transmitted to the spinal cord by the C-fibers and A-δ fibers. After synapse in the dorsal horn, the impulses are transmitted rostrally through the collateral spinothalamic tract to the brainstem and brain. Hyperalgesia, which lowers the threshold for pain and increases pain for suprathreshold stimuli, occurs after most peripheral nerve injury (LaMotte et al. 1991). Secondary hyperalgesia occurs in the area surrounding the original insult and has been shown to be due to a central effect in which increasingly secure synaptic connections develop between those nociceptive pathways and pathways that previously may not have been involved in the perception of pain (LaMotte et al. 1991). This secondary hyperalgesia results in a small area around the tissue damage, and stroking in this area can cause a painful perception. This phenomenon, also known as allodynia, generally suggests synaptic contacts between low-threshold peripheral mechanical receptors, which are usually associated with touch perception, and nociceptive pathways. Table 36.1 lists the pain terms sampled from the 2011 version of IASP pain terminology.

Table 36.1 Pain definition from the 2011 version of IASP pain terminology

Pain	Definition
Pain	An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage
Allodynia	Pain due to a stimulus that does not normally provoke pain
Analgesia	Absence of pain in response to stimulation which would normally be painful
Causalgia	A syndrome of sustained burning pain, allodynia, and hyperpathia after a traumatic nerve lesion, often combined with vasomotor and sudomotor dysfunction and later trophic changes
Central pain	Pain initiated or caused by a primary lesion or dysfunction in the central nervous system
Dysesthesia	An unpleasant abnormal sensation, whether spontaneous or evoked. Special cases of dysesthesia include hyperalgesia and allodynia
Hyperalgesia	Increased pain from a stimulus that normally provokes pain
Hyperesthesia	Increased sensitivity to stimulation, excluding the special senses
Hyperpathia	A painful syndrome characterized by an abnormally painful reaction to stimulus, especially a repetitive stimulus, as well as an increased threshold
Hypoalgesia	Diminished pain in response to a normally painful stimulus
Hypoesthesia	Decreased sensitivity to stimulation, excluding the special senses
Neuropathic pain	Pain caused by a lesion or disease of the somatosensory nervous system
Nociceptive pain	Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors
Paresthesia	An abnormal sensation, whether spontaneous or evoked

IASP International Association of Study of Pain

36.1 Pathophysiology

Although pathophysiology of neuropathic pain is not fully understood, it probably includes both central and peripheral mechanisms. Pathophysiology of pain varies according to the type. After spinal cord injury, nociceptive musculoskeletal pain is caused by activation of sensory nociceptive receptors in musculoskeletal tissues. This is mainly the result of overuse injuries due to repetitive upper extremity forces during activities such as wheelchair propulsion, overhead reaching, and transfers (Finnerup and Baastrup 2012). Mechanisms may include cortical reorganization, neuronal hypersensitivity due to changes in receptors and ion channels, abnormal sprouting and connections, ectopic impulse generation, loss of inhibitory interneurons, and altered function of descending inhibitory and facilitatory pathways. In addition to pathophysiological mechanisms, psychosocial mechanisms are an important factor in the generation and maintenance of pain (Finnerup et al. 2001).

36.2 Pain Terminology and Classification of Spinal Cord Injury

Pain has different qualities or descriptors. The word "aching" is generally used to describe musculoskeletal pain, while "burning" is typically associated with neuropathic pain. In patients with spinal cord injuries, there is often an overlap of pain types and subtypes. Numerous classification and assessment tools have been developed, including questionnaires, physical examinations, or instrument-based tools that allow a more sophisticated and accurate evaluation of the various types of pain. The first important distinction to understand is the difference between nociceptive and neuropathic pain. Nociceptive pain is defined as pain caused by the activation of the nerve endings, or nociceptors in peripheral tissues including muscle, tendon, bones, ligaments, and skin. Nociceptive pain can be further subdivided into musculoskeletal pain and visceral pain. In contrast, neuropathic pain arises as direct result of a lesion or disease that affects the somatosensory system. In other words, neuropathic pain is caused by nerve injury (Hatch et al. 2018).

Pain after spinal cord injury can have many causes and is often multifactorial. Various classifications have been used for spinal cord injury pain (Table 36.2). The classification of pain associated with spinal cord injury has been reviewed by Siddall et al. (1997) (Table 36.3). They suggested the following terms based on the system involved: musculoskeletal, visceral, neuropathic, and other types. They subdivided this in two ways: first, by the site of presumed origin of pain, neuropathic at the level of the injury, and below the level, and second, by probable cause, either radicular or central. Thus, pain should be at the level of the injury caused by damage to the nerve root and with increased pain on movement would be "neuropathic at-level radicular pain." Pain below the level would be "neuropathic below-level central pain" (Cardenas and Felix 2009; Siddall et al. 1997).

The Cardenas classification scheme published in 2002 is initially divided into two main pain categories (neurologic and musculoskeletal) and characteristics and location in terms of the level of injury and in terms of activity, position, and light touch (Cardenas et al. 2002) (Table 36.4). The International Association of Study of Pain (IASP) has established a standardized classification scheme for pain associated with spinal cord injuries. The scheme was based on Siddall's classification. The Siddall classification consisted of four main categories: musculoskeletal, visceral, neuropathic, and other (Siddall et al. 1997). There are only two main categories of pain in the IASP taxonomy: nociceptive and neuropathic (Table 36.5). The Bryce-Ragnarsson classification system classifies pain first by regional location and then by type. It is similar to the IASP classification, but reverses Tiers I and II (Bryce et al. 2006; Bryce and Ragnarsson 2000; Hatch et al. 2018) (Table 36.6).

A currently accepted classification based on expert consensus is the International Spinal Cord Injury Pain (ISCIP) Classification. The ISCIP scheme was a link between the IASP and Bryce-Ragnarsson classification, but with important changes (Bryce et al. 2012b; Hatch et al. 2018). The ISCIP Classification is based on three tiers: pain type, pain subtype, and pain source or pathology, respectively (Bryce et al. 2012a, b). The first tier (Tier 1) classifies pain into nociceptive, neuropathic, other, and unknown pain. Other pains are pain that cannot be categorized as nociceptive or neuropathic, e.g., irritable bowel syndrome or fibromyalgia. Unknown pain can neither be assigned to any of the above categories nor can it be associated with a specific pain syndrome. The second tier (Tier 2) subdivides neuropathic pain into spinal cord injury-related pain (at level or below level) and other neuropathic pain. The third tier (Tier 3) is used to specify the possible underlying causes or pathology of all subtypes of pain (Bryce et al. 2012a, b) (Table 36.7).

36.2.1 Nociceptive Pain

Painful stimuli for tissues, such as mechanical, thermal, or pathological processes, activate nociceptors and cause nociceptive pain. Nociceptive

Table 36.2 Various classification schemes for pain in spinal cord injuries prior to the early 1990s

	Musculoskeletal	Visceral	Neuropathic at-level	Neuropathic below-level	Others
Riddoch, 1938			Local or segmental	Remote	
Davis, 1947		Visceral	Root	Diffuse, burning	
Pallock, 1951		Visceral	Root	Below lesion	
Kaplan, 1962	Musculoskeletal	Visceral	Root	Phantom	Psychic, sympathetic
Michaelis, 1970	At level		At level	Below level	Headache
Burke, 1973		Visceral	Root	Central	
Davis, 1975	Trauma site		Radicular	Below level	
Burke and Woodward, 1976	Early, chronic spinal	Visceral	Early "burning," root, end-zone	Diffuse "burning"	Headache
Bedbrook, 1981			Neurologic	Central	Psychologic
Donovan, 1982	Mechanical	Visceral	Segmental	Central dysesthetic	Psychogenic
Tunks, 1986	Musculoskeletal		Radicular, border reaction	Central	Syringomyelia
Davidoff, 1987				Dysesthetic	
Britell, 1991	Mechanical		Radicular	Dysesthetic	
Bonica, 1991	Musculoskeletal	Visceral	Root	Central	RSD, mononeuropathy
Nashold, 1991		Visceral	Radicular, segmental	Phantom	Syringomyelia

Table 36.3 The Siddall classification of pain following spinal cord injury

Axis 1 (System)	Axis 2 (Site)	Axis 3 (Source)
Musculoskeletal		
Visceral		
Neuropathic	At level	Radicular
	Below level	Central
Other	e.g., syringomyelia, CRPS, overuse syndromes, headache associated with AD, compressive mononeuropathies	

Adapted from Siddall et al. (1997)

Table 36.4 The Cardenas classification of chronic pain associated with spinal cord injury

Pain category (major)	Pain category (specific)	Location
Neurologic	SCI pain	Below injury in area without normal sensation
	Transitional zone pain	At level of injury, bilateral
	Radicular pain	At any dermatomal level, usually unilateral, usually radiates
	Visceral pain	In abdomen
Musculoskeletal	Mechanical spine pain	In back or neck, often bilateral
	Overuse pain	Often above injury in areas of normal sensation, in an incomplete injury can be below

Adapted from Cardenas et al. (2002)

pain is the most common type of pain in spinal cord injury. It is necessary that the patient has at least some preserved sensation in which the pain is. The patient should also be able to pinpoint the pain in a particular area or region (Hatch et al. 2018). It is possible to differentiate the pain types by determining pain quality/characteristics, distribution, clinical course, and response to any therapeutic approach. Nociceptive pain may be well responded to a variety of therapeutic strategies including surgical/interventional, pharmacological, and physical therapies. Nociceptive pain can be classified into three different subtypes by its etiology: musculoskeletal pain, visceral pain, and other nociceptive pain.

Musculoskeletal pain is a major cause of nociceptive pain in chronic spinal cord injuries. This type of pain has several causes: overuse of joints, ligaments, and tendons, decreased functional use of joints, fracture, heterotopic ossification, and spasticity. Visceral pain is also a common cause of nociceptive pain in the late chronic spinal cord injury and typically occurs in the chest or in abdominal/pelvic structures (Bryce et al. 2012c). Although evidence-based insights in the underlying mechanisms of abdominal pain are still lacking, the preexisting problem such as constipation is a major cause (Faaborg et al. 2013). Other nociceptive visceral pain can be caused by cholecystitis, gall bladder stones, biliary stone, appendicitis, pyelonephritis, or bowel obstruction. Individuals with paraplegia may describe visceral pain as "cramping," "dull pressing," or "causing nausea" similar to those of nondisabled individuals. Patients with tetraplegia and visceral pain, however, may have symptoms that are not easy to complain. Unless there is clear evidence that visceral involvement causes visceral pain through invasive or noninvasive diagnostic procedures, there could be another type of pain, such as neuropathic pain (Bryce et al. 2014).

Other nociceptive pain is pain that cannot be attributed to the musculoskeletal or visceral pain categories. They may be related or unrelated to spinal cord injury but must fulfill the criteria for nociceptive pain (Bryce et al. 2012c; Bryce et al. 2014). During ISCIP development, clinicians reported they were very confident in their judgements, but they found that certain subtypes of pain were more difficult to classify than others (Hatch et al. 2018). It includes pain due to pressure injuries or headaches as a consequence of autonomic dysreflexia.

Table 36.5 IASP pain taxonomy of pain following spinal cord injury

Broad type (Tier 1)	Broad system (Tier 2)	Specific structures/pathology (Tier 3)
Nociceptive	Musculoskeletal	Bone, joint, muscle trauma or inflammation, mechanical instability, muscle spasm, secondary overuse syndromes
	Visceral	Renal calculus, bowel, sphincter dysfunction, etc. Dysreflexic headache
Neuropathic	Above level	Compressive mononeuropathies, CRPS
	At level	Nerve root compression including cauda equina, syringomyelia, spinal cord trauma/ischemia (transitional zone, etc.) Dual-level cord and root trauma (double-lesion syndrome)
	Below level	Spinal cord trauma/ischemia

IASP International Association of Study of Pain Adapted from Siddall et al. (2003)

Table 36.6 Bryce-Ragnarsson SCI pain taxonomy

Location		Type	Etiologic subtype
Above level	Nociceptive	1	Mechanical/musculoskeletal
		2	Autonomic dysreflexia headache
		3	Other
	Neuropathic	4	Compressive neuropathy
		5	Other
At level	Nociceptive	6	Mechanical/musculoskeletal
		7	Visceral
	Neuropathic	8	Central
		9	Radicular
		10	Compressive neuropathy
		11	CRPS
Below level	Nociceptive	12	Mechanical/musculoskeletal
		13	Visceral
	Neuropathic	14	Central
		15	Other

Adapted from Bryce and Ragnarsson (2000)

36.2.2 Neuropathic Pain

Neuropathic pain describes a syndrome of various sensory symptoms and signs, although it is not a term applied to a single underlying mechanism or disease. Neuropathic pain is generally defined as pain caused by a lesion or disease of the somatosensory nervous system (Jensen et al. 2007). Neuropathic pain is subdivided into peripheral and central neuropathic pain, depending on whether the lesion or disease is in the peripheral (nerve root or nerve) or central (brain or spinal cord) nervous system.

After spinal cord injury, patients may experience central neuropathic pain due to the spinal cord lesions or peripheral neuropathic pain caused by lesions or compression of the nerve roots, including cauda equina. Neuropathic pain after spinal cord injury is classified as *at-level* and *below-level* neuropathic pain because it is difficult to distinguish between peripheral and central pain in some cases (Bryce et al. 2012a). Patients with spinal cord injuries may have *other* neuropathic pain other than spinal cord injury, such as carpal tunnel syndrome associated with wheelchair use and intercostal nerve injury resulted from thoracotomy. Other neuropathic pain can be located *at*, *above*, or *below* the level of injury.

At-level neuropathic pain is located anywhere within the dermatome of the neurological level of injury and/or three of the dermatomes below the

Table 36.7 The International Spinal Cord Injury Pain (ISCIP) Classification: Tier 1, pain type; Tier 2, pain subtype; Tier 3, source of pain

Tier 1 (Pain type)	Tier 2 (Pain subtype)	Tier 3 (Source of pain)
Nociceptive pain	Musculoskeletal pain	e.g., Articular trouble/joint pain, fracture associated pain, spasm-related muscle pain, back pain/lumbago
	Visceral pain	e.g., Angina pectoris, constipation/ileus, cystitis/pyelonephritis, UTI, ureteral calculus
	Other nociceptive pain	e.g., Pressure sore-related pain, general wound pain, headache due to migraine or autonomic dysreflexia, migraine
Neuropathic pain	SCI-related pain	
	At-level SCI pain	e.g., Spinal cord compression, nerve root compression, cauda equina compression
	Below-level SCI pain	e.g., Spinal cord ischemia, spinal cord compression
	Other neuropathic pain	
		e.g., Brachial plexus injury, entrapment syndromes (i.e., carpal tunnel syndrome, ulnar nerve entrapment), generalized nerve damages (i.e., metabolic nerve damage, inflammatory polyneuropathies)
Other pain		e.g., Fibromyalgia, CRPS type I, interstitial cystitis, irritable bowel syndrome
Unknown pain	Pain that can neither be assigned to any of the above-listed categories nor be related to a specific pain syndrome	

level (Bryce et al. 2012a). Pain caused by damage to the cauda equina is always classified as at-level pain even if extends more than three dermatomes below the neurological level of injury. *Below-level neuropathic pain* is located in more than three dermatomes below the neurological level of injury but may extend to the at-level area.

People who suffer from neuropathic pain often describe the pain as tingling, burning, electric shock-like, cold, pricking, pins and needles, squeezing, sharp, itchy, and/or shooting. In addition, patients describe it as spontaneous and evoked (Hatch et al. 2018). Allodynia, mostly to touch or cold stimuli and hyperalgesia to pinprick or thermal stimuli, may be present. Neuropathic pain after spinal cord injury may occur immediately at the time of injury but may also occur with delayed onset up to several months. At-level neuropathic pain often occurs earlier than below-level pain (Siddall et al. 2003). Neuropathic pain can be reduced or relieved in the first year but often becomes chronic, and patients who experience neuropathic pain at 6 months are likely to experience neuropathic pain with the same intensity 5 years after spinal cord injury (Siddall and Middleton 2006).

36.3 Diagnosis and Screening of Pain

Neurological examination based on the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) is essential for the diagnosis of neuropathic pain. Given the variety of their manifestations and the possible overlap in their symptoms, it is difficult to diagnose pain associated with spinal cord injury. Significant impairment of sensory function below the level of lesion makes interpretation of the symptoms difficult. Assessing the history of a patient with pain requires an accurate assessment of all aspects of the symptoms, including course, effect, and multidimensional aspects of pain. The pain distribution should be reflected in body diagrams. Pain intensity can be assessed using a categorical scale such as mild, moderate, or severe. Other one-dimensional scales, such as the visual analog scale (VAS), are commonly used.

The character and quality of pain, its onset and its course over time, exacerbating and relieving factors or situations, and associated symptoms should be included in the assessment. The effect

of pain on daily life was related to the effects on quality of life, function, sleep, mood, and impact on social relationships. The International Spinal Cord Injury Core Data Set was developed to enable physicians to standardize the collection of relevant pain data. The data sets include classification, location, temporal aspects, intensity, impact, and treatment of pain (Widerström-Noga et al. 2016).

Reliable and valid differentiation and classification of pain types are required. Positive diagnostic criteria and a grading system of definite, probable, and possible presence of neuropathic pain have been reported. Four criteria must be met to ensure the presence of neuropathic pain: (1) a history of a relevant nervous system lesion, (2) at least one test confirming such a lesion, (3) pain in the area of the body consistent with the location of the lesion, and (4) negative (e.g., hypoesthesia) and/or positive (e.g., allodynia) sensory perception in the painful area (Treede et al. 2008). Dynamic mechanical allodynia can be assessed by gently brushing the skin with a small brush or cotton.

It can be assumed that psychological factors such as mood, thoughts, and social interactions have a bidirectional relationship with all types of pain, with these factors playing a particularly important role in the development of chronic pain and pain-related functional disability (Ullrich 2007). In addition, emotional disorders, level of independence from caregivers, level of social support, and a lack of efficient coping strategies are important in this regard and would be associated with greater severity of pain. Catastrophizing refers to exaggerated negative expectations or interpretations of an experience, such as pain. The extent of the catastrophe ("I can't stand this pain! It will never get better!") is believed to be related to the impact of pain on outcomes such as functioning and well-being. Catastrophizing in people with spinal cord injuries is thought to be a potent predictor of pain-related functional disability (Ullrich 2007).

Screening tools for neuropathic pain differ the complex classification. The Neuropathic Pain Scale (NPS) was developed to measure various neuropathic pain qualities or descriptors such as intense, sharp, hot, dull, cold, sensitive, and itchy (Galer and Jensen 1997). In the UK, the Leeds Assessment of Neuropathic Signs and Symptoms (LANSS) was developed to differentiate neuropathic pain from nociceptive pain. Various sensory pain descriptors and an examination of sensory dysfunction examination at the bedside were used (Hatch et al. 2018). The latest screening tool to differentiate neuropathic pain from non-neuropathic pain in the spinal cord injury population is the Spinal Cord Injury Pain Instrument (SCIPI) (Bryce et al. 2014). Figure 36.1 shows various pain assessment tools specified for spinal cord injuries or general neuropathic pain.

36.4 Psychological Problems Related to Pain in Spinal Cord Injuries

Pain in people with spinal cord injuries is associated with several psychosocial issues, including depression, anxiety, anger, fatigue, sleep disturbance, familial/social difficulties, and general psychosocial impairment. People with spinal cord injuries are at increased risk for depression, anxiety, and posttraumatic stress disorder. Pain and depression develop over time in spinal cord injuries, so pain appears to be an important determinant of depression (Cairns et al. 1996). While pain persists and is often resistant to conventional medical treatments, it inevitably affects several aspects of a person's life that in turn contribute to the pain experience. In the biomedical model, psychological (e.g., depression and anxiety) and social (e.g., unemployment and family problems) factors are viewed as reactions to disease/illness and are therefore considered as of secondary importance. The biopsychosocial model recognizes that all biological, psychological, and social factors interact to contribute to the experience and response to pain. Therefore, the large variability in pain expression in people with similar physical pathology may be explained by the complex interactions of biological, psychological, and social/cultural factors (Wegener and Haythornthwaite 2001).

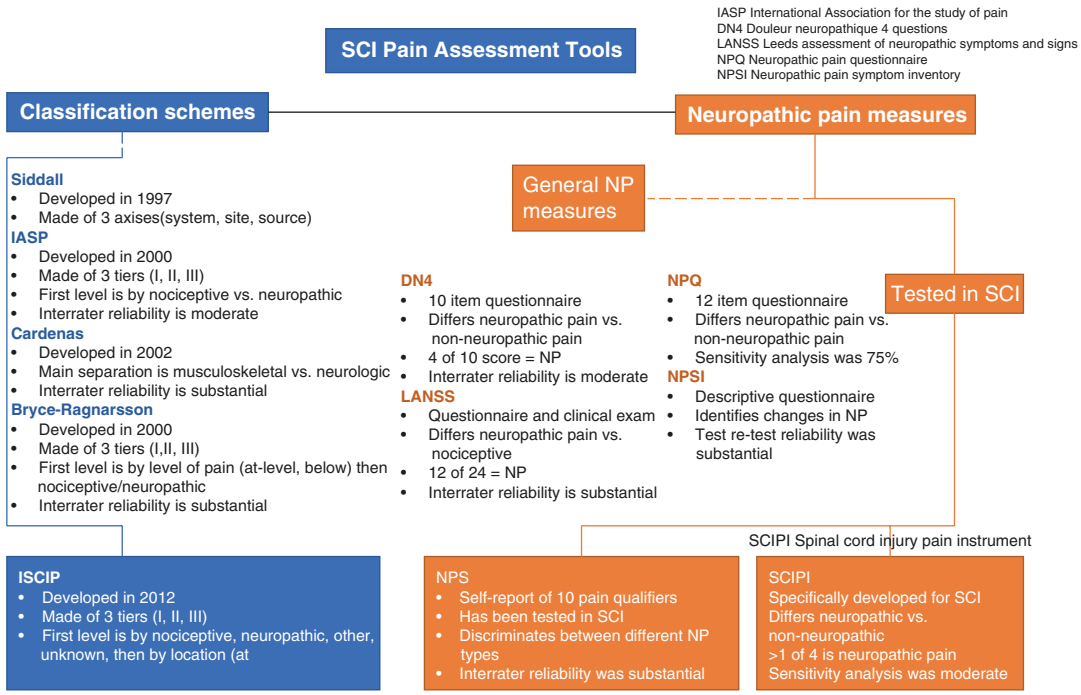

Fig. 36.1 Classification systems and assessment tools of pain following spinal cord injury. Adapted from Hatch et al. (2018)

A comprehensive assessment of biological, psychological, and social factors is necessary for treatment planning. Due to the relatively higher incidence of cognitive impairments in people with spinal cord injuries, their cognitive abilities should be assessed to determine whether there are impairments requiring modification of assessment or treatment procedures (Davidoff et al. 1992). Given the higher risk of depression compared to other comorbidities, a screening scale such as the Beck Depression Inventory may be useful in determining whether a more in-depth assessment of depression is needed. Substance abuse is a common comorbidity in recently injured people with spinal cord injuries (Heinemann et al. 1990). Cognitive behavioral therapy (CBT) is based on basic and clinical studies of the nature of humans and the determinants of human experience and behavior. In practice, CBT uses a structured psychotherapeutic approach to develop the beliefs, attitudes, thoughts, and skills of patients to modify various components of the pain experience. There is evidence that CBT techniques can be used by people with spinal cord injuries. CBT has been used to reduce symptom of depression in people newly injured with spinal cord injuries (Craig et al. 1997). Cognitive pain management strategies, such as education, distraction, problem solving, coping self-statements, and cognitive restructuring, are unlikely to require significant modification. However, relaxation-based approaches such as deep breathing, progressive muscle relaxation, guided imagery can be helpful (Wegener and Haythornthwaite 2001).

36.5 Treatment

There is a wide range of approaches to managing pain in patients with spinal cord injuries, ranging from physical therapy and pharmacotherapy to instrument-based approaches. The first important step is the diagnosis of pain type in patients with spinal cord injuries. During the treatment of pain, the level and character of the pain and side effects

should be carefully monitored. If the pain has become chronic and is associated with a disability, a multidisciplinary approach is preferred, and it is important to evaluate and treat the associated depression, sleep disturbance, and psychological distress.

Treatment of nociceptive pain should focus primarily on the elimination of the underlying causes such as fracture treatment, wound care, or reduced stress on overused joints. Current therapeutic strategies are mainly represented by temporary pharmacological treatment such as nonsteroidal anti-inflammatory drugs and non-opioid pain drugs. In case of neuropathic pain, the underlying causes must be treated, but usually only symptomatic treatment is possible. It is important to exclude other causes of pain, such as musculoskeletal pain, and to consider factors that may aggravate neuropathic pain, such as pressure injuries, spasticity, or urinary tract infection. It is also important to evaluate the effects of pain on daily life, sleep and mood, psychological factors, and risk of suicidal ideation.

The Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain updated the evidence-based treatment recommendations for neuropathic pain (Finnerup et al. 2015). Based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system, pregabalin, gabapentin, serotonin-noradrenaline reuptake inhibitor (SNRI) antidepressants duloxetine and venlafaxine, and tricyclic antidepressants (TCAs) are strongly recommended for use in neuropathic pain as first-line medications. The CanPain SCI practice guidelines recommended pregabalin, gabapentin, and amitriptyline as first-line drugs (Guy et al. 2016) (Table 36.8). Opioids and a combination of selected first-line agents are weak recommendations, while weak recommendations against the use of cannabinoids and valproate and strong recommendations against the use of levetiracetam and mexiletine. There are no studies of the efficacy of NASID and paracetamol in neuropathic pain. Therefore, NeuPSIG recommends pregabalin, gabapentin, SNRIs, and TCAs as first-line drugs, tramadol, lidocaine patches, and high concentration capsaicin patches as second-line drugs, and strong opioids (particularly oxycodone and morphine) and botulinum toxin A as third-line treatments for neuropathic pain. A combination of pregabalin/gabapentin and duloxetine/TCAs can be considered as an alternative to increasing doses in patients who do not respond to moderate dose monotherapy (Finnerup 2013; Finnerup et al. 2015).

Patients with spinal cord injuries may be particularly sensitive to CNS-related side effects, including dizziness and somnolence, which may be due to their frequent use of antispastic drugs. The most common side effects of pregabalin and gabapentin are somnolence and dizziness, which are particularly troublesome in spinal cord injury (Cardenas et al. 2013). Pregabalin has a black box warning for the rare but serious side effect of suicidal ideation in a very small percentage of patients. Other side effects include peripheral edema, nausea, and weight gain. Gabapentin is given three times daily with a slowly increasing dosage, starting with 200 mg the first day and increased by 300 mg every 1–7 days. The final dose is between 1800 and 3600 mg. Pregabalin is given twice daily and slowly titrated from 75 or 150 mg daily to 600 mg daily (Teasell et al. 2010). In spinal cord injury individuals with renal insufficiency, lower doses are used. The dosage must be adjusted once creatinine clearance falls below 60 ml/min (Table 36.9).

Antidepressants are comparatively weak evidence, but they are also used to treat neuropathic pain. These include TCAs (amitriptyline, imipramine, and nortriptyline) and SNRIs (venlafaxine and duloxetine), while the effect of SSRIs is even less certain (Finnerup et al. 2015). Side effects of TCA include dry mouth, somnolence, constipation, urinary retention, orthostatic hypotension, and sweating. TCA is contraindicated in patients with epilepsy, heart failure, and cardiac conduction blocks, and an EKG is required prior to initiation of treatment. TCA should be titrated slowly starting at 10 or 25 mg daily up to 150–225 mg daily. Nortriptyline may be chosen for

Table 36.8 Recommended medications based on CanPain SCI practice guidelines

Treatment	Dosage	Comments (maximum dose, side effects)
First-line treatments		
Pregabalin	• 25–150 mg/d • Dose increase to 300 mg BID within 1 week based on tolerability • Increased effectiveness and reduced side effects with smaller dose, recommending 50 mg TID	• Maximum dose 600 mg/d • May be contraindicated in patients with heart conditions, renal insufficiency • Effect may be seen as quickly as 1 week • FDA approved for treatment of SCI neuropathic pain • Somnolence, peripheral edema, dry mouth, dizziness, fatigue, blurred vision
Gabapentin	• 100–300 mg/d • Increase dose by 100–300 mg/d every week	• Maximum dose 3600 mg/d • Consider renal function when choosing dose • Somnolence, dizziness, peripheral edema, dry mouth, weight gain, diarrhea, constipation, asthenia, loss of balance or coordination
Amitriptyline	• Initially 10–25 mg/d bedtime • Increase dose as tolerated up to 150 mg/d	• Maximum dose 150 mg/d • Orthostatic hypotension, dry mouth, diarrhea, constipation, angioedema, blurred vision, nausea • May be contraindicated in patients with ischemic cardiac disease: Screening ECG is recommended for patients >40 years • May be most effective in patients with comorbid depression symptoms
Second-line treatments		
Tramadol	• 50–100 mg every 4–6 h	• Maximum dose 400 mg/d • Side effects may be intolerable • Not suggested as a long-term treatment strategy • Somnolence, dry mouth, constipation, sweating, dizziness, nausea
Lamotrigine	• Initially 25 mg QD	• Maximum dose 400 mg/d
Third-line treatments		
Transcranial direct current stimulation (tDCS)		
Fourth-line treatments		
TENS		
Opioid analgesics (morphine, oxycodone, fentanyl, hydromorphone)	• Constipation, sedation, dry mouth, nausea, vomiting, drug tolerance, hyperalgesia, endocrinopathy, misuse, physical dependence, fatal overdose • Principles initiating opioid: Start at the lowest dose; avoid in patients with active substance abuse; caution if therapy lasts >3–6 months; avoid driving until no sedation from opioids is established; restrict dose to less than 50 mg morphine equivalents for patients starting opioid therapy; restrict dose less than 90 mg morphine equivalents for patients on long-term opioid therapy; caution withdrawal syndrome within 2–4 weeks while tapering.	

Table 36.9 Pharmacologic management for neuropathic pain in spinal cord injuries

Medication	Usual dose range (per day)	Side effects	Special considerations
Anticonvulsants			
Gabapentin	400–3600 mg	Somnolence, dizziness, peripheral edema, dry mouth, weight gain, diarrhea, constipation, asthenia	• Consider renal function when choosing dose
Pregabalin	150–600 mg	Somnolence, dizziness, peripheral edema, dry mouth, constipation,	• May be contraindicated in patients with heart conditions, renal insufficiency • Effect may be seen as quickly as 1 week • FDA approved for treatment of SCI neuropathic pain
Carbamazepine	600–1200 mg	Leukopenia, thrombocytopenia	• Needs serial CBC, LFT, and drug level
Clonazepam	1–6 mg		• Associated with withdrawal syndrome
Antidepressants			
Amitriptyline	125–150 mg	Orthostatic hypotension, dry mouth, constipation	• May be contraindicated in patients with ischemic cardiac disease: Screening ECG is recommended for patients >40 years • May be most effective in patients with comorbid depression symptoms
Venlafaxine	150–250 mg	Sedation, dizziness, headache, nausea	• Should monitor changes in blood pressure during treatment • May be contraindicated in patients with cardiac disease • Should use slow tapering to avoid possible withdrawal syndrome
Duloxetine	60–120 mg	Somnolence, dizziness, headache, nausea, vomiting	• Use cautiously in patients with seizures or a bleeding tendency • Should monitor blood pressure during treatment
Opioids			
Tramadol	100–400 mg	Somnolence, dry mouth, constipation, sweating, dizziness, nausea	• Side effects may be intolerable • Not suggested as a long-term treatment strategy

patients with severe anticholinergic side effects such as dry mouth and tachycardia due to amitriptyline. It is important to recognize the side effects, such as serotonin syndrome, that can occur when the codeine analog tramadol and other antidepressants such as SSRIs and SNRIs are combined. Serotonin syndrome is characterized by flu-like symptoms, rapid heart rate, high blood pressure, nausea/vomiting, and severe sweating and can lead to agitation, confusion, hallucination, and muscle rigidity. High fever, irregular heart rate, seizures, and unconsciousness are eventually symptoms in severe cases of serotonin syndrome.

Second-line agents include opioids, and tramadol, which have low-affinity binding to the mu opioid receptors and inhibit reuptake of serotonin and norepinephrine (Barrera-Chacon et al. 2011). Major side effects of opioids include constipation, nausea, and sedation. Another important concern is abuse, misuse, or addiction. Risk factors include previous substance abuse and family history of substance abuse. In addition, endocrine abnormalities may occur in patients taking long-term opioids, including decreased testosterone, progesterone, estradiol, and reduced cortisol response to stress (Hatch et al. 2018). Opioid is recommended for short-term use because the side effects mentioned above and risk of abuse or addiction are high. Opioids may produce hypotension as a result of sympatholysis, vagally mediated bradycardia, and histamine release (Cardenas and Felix 2009). Tramadol is the only medication recommended for the oral use of opioid medications for neuropathic pain in patients with spinal cord injuries. Tramadol is recommended as a second-line option for neuropathic pain in patients with spinal cord injuries who have not responded to gabapentin, pregabalin, or other TCAs. Tramadol, however, lowers the seizure threshold and can contribute to the development of serotonin syndrome when combined with SSRIs, SNRIs, or TCAs. Therefore, special caution should be taken when considering use in patients with depression. Elderly patients and patients with renal or hepatic impairment should also be treated with reduced doses (Hatch et al. 2018). Oxycodone is not recommended because it causes severe constipation in patients with spinal cord injuries (Barrera-Chacon et al. 2011). An agreement on opioid drugs should be considered. Cannabinoids have mixed efficacy in clinical trials. A recently published report described that cannabis is used to reduce pain after spinal cord injuries and enable increased community participation (Bourke et al. 2019). Intrathecal treatment with clonidine and morphine or with neurotoxins such as ziconotide can be used for severe refractory neuropathic pain.

Cognitive behavioral therapy and neurostimulation therapies such as transcranial direct current stimulation and repetitive transcranial magnetic stimulation or invasive procedures have been shown in RCTs, without convincing evidence.

References

Barrera-Chacon JM, Mendez-Suarez JL, Jauregui-Abrisqueta ML, et al. Oxycodone improves pain control and quality of life in anticonvulsant-pretreated spinal cord-injured patients with neuropathic pain. Spinal Cord. 2011;49:36–42.

Bourke JA, Catherwood VJ, Nunnerley JL, et al. Using cannabis for pain management after spinal cord injury: a qualitative study. Spinal Cord Ser Cases. 2019;5:82.

Bryce TN, Ragnarsson KT. Pain after spinal cord injury. Phys Med Rehabil Clin N Am. 2000;11:157–68.

Bryce TN, Dijkers MP, Ragnarsson KT. Reliability of the Bryce/Ragnarsson spinal cord injury pain taxonomy. J Spinal Cord Med. 2006;29:118–32.

Bryce TN, Biering-Sorensen F, Finnerup NB, et al. International spinal cord injury pain (ISCIP) classification: part 2. Initial validation using vignettes. Spinal Cord. 2012a;50:404–12.

Bryce TN, Biering-Sorensen F, Finnerup NB, et al. International spinal cord injury pain classification: part I. background and description. March 6–7, 2009. Spinal Cord. 2012b;50:413–7.

Bryce TN, Ivan E, Dijkers M. Proposed international spinal cord injury pain (ISCIP) classification: preliminary validation data. Top Spinal Cord Inj Rehabil. 2012c;18:143–5.

Bryce TN, Richards JS, Bombardier CH, et al. Screening for neuropathic pain after spinal cord injury with the spinal cord injury pain instrument (SCIPI): a preliminary validation study. Spinal Cord. 2014;52:407–12.

Cairns DM, Adkins RH, Scott MD. Pain and depression in acute traumatic spinal cord injury: origins of chronic problematic pain? Arch Phys Med Rehabil. 1996;77:329–35.

Cardenas DD, Felix ER. Pain after spinal cord injury: a review of classification, treatment approaches, and treatment assessment. PM R. 2009;1:1077–90.
Cardenas DD, Turner JA, Warms CA, et al. Classification of chronic pain associated with spinal cord injuries. Arch Phys Med Rehabil. 2002;83:1708–14.
Cardenas DD, Nieshoff EC, Suda K, et al. A randomized trial of pregabalin in patients with neuropathic pain due to spinal cord injury. Neurology. 2013;80:533–9.
Craig AR, Hancock K, Dickson H, et al. Long-term psychological outcomes in spinal cord injured persons: results of a controlled trial using cognitive behavior therapy. Arch Phys Med Rehabil. 1997;78:33–8.
Davidoff GN, Roth EJ, Richards JS. Cognitive deficits in spinal cord injury: epidemiology and outcome. Arch Phys Med Rehabil. 1992;73:275–84.
Faaborg PM, Finnerup NB, Christensen P, et al. Abdominal pain: a comparison between neurogenic bowel dysfunction and chronic idiopathic constipation. Gastroenterol Res Pract. 2013;2013:365037.
Finnerup NB. Pain in patients with spinal cord injury. Pain. 2013;154:S71–6.
Finnerup NB, Baastrup C. Spinal cord injury pain: mechanisms and management. Curr Pain Headache Rep. 2012;16:207–16.
Finnerup NB, Johannesen IL, Sindrup SH, et al. Pain and dysesthesia in patients with spinal cord injury: a postal survey. Spinal Cord. 2001;39:256–62.
Finnerup NB, Faaborg P, Krogh K, et al. Abdominal pain in long-term spinal cord injury. Spinal Cord. 2008;46:198–203.
Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015;14:162–73.
Galer BS, Jensen MP. Development and preliminary validation of a pain measure specific to neuropathic pain: the neuropathic pain scale. Neurology. 1997;48:332–8.
Guy SD, Mehta S, Casalino A, et al. The CanPain SCI clinical practice guidelines for rehabilitation management of neuropathic pain after spinal cord: recommendations for treatment. Spinal Cord. 2016;54(Suppl 1):S14–23.
Hatch MN, Cushing TR, Carlson GD, et al. Neuropathic pain and SCI: identification and treatment strategies in the 21st century. J Neurol Sci. 2018;15(384):75–83.
Heinemann AW, Mammoth BD, Schnoll S. Substance use by persons with recent spinal cord injuries. Rehabil Psychol. 1990;35:217–28.
Jensen M, Stoelb B, Molton I. Measuring pain in persons with spinal cord injury. Top Spinal Cord Inj Rehabil. 2007;13:20–34.
Kennedy P, Lude P, Taylor N. Quality of life, social participation, appraisals and coping post spinal cord injury: a review of four community samples. Spinal Cord. 2006;44:95–105.
LaMotte RH, Shain CN, Simone DA, et al. Neurogenic hyperalgia: psychophysical studies of underlying mechanism. J Neurophysiol. 1991;66:190–211.
Mehta S, Orenczuk K, McIntyre A, et al. Neuropathic pain post spinal cord injury part 1: systematic review of physical and behavioral treatment. Top Spinal Cord Inj Rehabil. 2013;19:61–77.
Siddall PJ, Middleton JW. A proposed algorithm for the management of pain following spinal cord injury. Spinal Cord. 2006;44:67–77.
Siddall PJ, Taylor DA, Cousins MJ. Classification of pain following spinal cord injury. Spinal Cord. 1997;35:69–75.
Siddall PJ, McClelland JM, Butkowski SB, et al. A longitudinal study of the prevalence and characteristics of pain in the first 5 years following spinal cord injury. Pain. 2003;103:249–57.
Teasell RW, Mehta S, Aubut JA, et al. A systematic review of pharmacologic treatments of pain after spinal cord injury. Arch Phys Med Rehabil. 2010;91:816–31.
Treede RD, Jensen TS, Campbell JN, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology. 2008;70:1630–5.
Ullrich PM. Pain following spinal cord injury. Phys Med Rehabil Clin N Am. 2007;18:217–33.
van Gorp S, Kessels AG, Joosten EA, et al. Pain prevalence and its determinants after spinal cord injury: a systematic review. Eur J Pain. 2015;19:5–14.
Wegener ST, Haythornthwaite JA. Psychological and behavioral issues in the treatment of pain after spinal cord injury. Top Spinal Cord Injury Rehabil. 2001;7:73–83.
Widerström-Noga E, Biering-Sørensen F, Bryce TN, et al. The international spinal cord injury pain extended data set (version 1.0). Spinal Cord. 2016;54:1036–46.
Widerström-Noga EG, Felipe-Cuervo E, Broton JG, et al. Perceived difficulty in dealing with consequences of spinal cord injury. Arch Phys Med Rehabil. 1999;80:580–6.

Recommended Additional Reading

Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. Wolters Kluwer: New Delhi; 2015.
Kennedy P, editor. The Oxford handbook of rehabilitation psychology. Oxford: Oxford University Press; 2012.
McMahon SB, Koltzenburg M, Tracey I, et al., editors. Wall and Melzack's textbook of pain. 6th ed. Philadelphia: Elsevier; 2013.
Verhaagen J, McDonald JW III. Spinal cord injury. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 109. London: Elsevier; 2012.

Spinal Cord Injuries/Diseases in Children

37

Compared to adults, spine and spinal cord injuries are rare in children, particularly in young children, due to both anatomical differences and the causes of the injury. The main mechanisms of traumatic spinal cord injuries are motor vehicular accidents (41.9%), falls (23.0%), violence (16.8%), and sports (10.0%), which affect children under 15 less often: vehicular accidents (36.7%), sports (24.1%), violence (23.4%), and falls (8.0%). The most common age at spinal cord injury is 19 years of age. Almost a quarter (23.7%) of all spinal cord injuries occur between the ages of 17 and 22 years, nearly half (47.0%) of all spinal cord injuries occurred between the ages of 16 and 30, and 12.2% of all injuries occur aged 60 or older. The cumulative incidence of spinal cord injuries under 10 years of age 0 was 0.57% and under 18 years of age is 12.78%. There is a consistent trend toward older age at time of injury. The mean injury age has increased from 28.7 years in 1972–1979 to 43.2 years in 2015–2020 (NSCISC 2021).

Several anatomical differences affect the pediatric spine. The head of a young child is relatively larger relative to body mass than that of adults and heavy on the cervical spine. The neck muscles are still underdeveloped, which means that the fulcrum of movement is higher in the spine. At birth, the spine is fully developed with bone, cartilage, and fair ligamentous stability. By the age of 8, the ligaments are fully developed. There is no wedging of the vertebral bodies. The cervical musculature, which is very important for the cervical spine of the adult, is still poorly developed in infants. The occiput to the C2 complex is stable with firm ligamentous fixation and anatomically stable occiput-C1 joints, including the tectorial membrane and posterior atlanto-occipital membrane posteriorly, the atlanto-occipital joint capsules laterally and the anterior atlanto-occipital membrane anteriorly (Pang and Wilberger 1980). The alar ligaments also provide support. Hypermobility is found in the upper cervical spinal below C2. The pseudosubluxation is a combination of a close proximity to the stable occiput-C2 complex and horizontally oriented facets in the midcervical spine. At the cervicothoracic junction, the facets become more vertical. The transition between the mobile cervical spine and the stable thoracic spine represents a high stress point and contributes to the explanation of the injury occurrence here (Bradford and Hensinger 1985). Therefore, children under the age of 9 have a higher percentage of upper cervical spine injuries than older children and adults. A young child's spine is also very flexible, with pliable bones and ligaments, so fractures of the spine are exceedingly rare. However, this increased mobility is not always a positive feature. The transfer of energy that distorts the spine may not compromise the structural integrity of the bones and ligaments of the spine, but it can still lead to significant spinal cord injury. This phenomenon of spinal cord injury without

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radiographic abnormalities (SCIWORA) is more common in children than adults.

37.1 Characteristics of the Spine and Spinal Cord in Children

The term "SCIWORA" is unique in the pediatric population. The mechanism is not known, but an increase elasticity of the spine in a child allows for sufficient displacement to cause spinal cord injury without fracture (Atesok et al. 2018). The term is relatively out of date because almost all injuries of spinal cord can be detected by MRI, but it is still clinically useful when referring to spinal cord injuries as evaluated by plain radiographs or CT (Hacein-Bey 2021). There seem to be two forms of SCIWORA. The infantile form is associated with severe injury of the cervical or thoracic spinal cord. These patients are unlikely to recover completely. Infants and children younger than 5 years are more likely to have fractures and mechanical disruption of spinal elements in the upper cervical spine between the occiput and C3. In older children and adolescents, SCIWORA is less likely to be seriously injured and is more likely to recover completely over time. The adolescent form, also known as "transient neurapraxia," is thought to be a spinal cord concussion or mild contusion, as opposed to the severe spinal cord injury associated with spinal mobility of the spine in young children.

37.1.1 Anatomy of the Immature Spine

There are significant anatomical differences between the spines of adult and children. These differences explain the characteristic patterns of spinal injuries seen in children. Loose ligaments and joint capsules, in combination with the predominantly cartilaginous nature of the infantile vertebrae, contribute to characteristic radiographic patterns that must be well understood when dealing with children with suspected spinal injuries. Appropriate assessment and treatment of children with spinal injuries require understanding of normal epiphyseal development, progressive ossification of the spine, and the limitations of physiological mobility in the pediatric spine (Carpenter 1961).

37.1.1.1 Epiphyseal Development

Epiphyseal plates in children are smooth, regular, and predictable in location. Although a complete understanding of the exact times of appearance and resolution of the epiphyseal plates in the spine is not necessary, some understanding of their typical appearance is important (Carpenter 1961; Wilberger 1986). The time line of the appearance and fusion of the ossification centers are shown in Figs. 37.1 and 37.2 (Meyers 2017; Wilberger 1986).

Atlas

At birth, the atlas or C1 has three ossification centers, one for the body and one for each of the neural arches. The neural arches characteristically form a complete ring by the age of 3 and fuse with the body of C1 by the seventh year (Fig. 37.3). These epiphyseal plates or synchondroses are especially visible in open-mouth views of the atlas (Carpenter 1961).

Axis

The axis or C2 has four ossification centers, one for each neural arch, one for the body of the C2, and one for the odontoid process. The odontoid is fully fused with the body and neural arches of C2 by about 3–6 years of age (Fig. 37.4). The dens is separated from the body of the axis by a broad cartilaginous band, which corresponds to the actuality of an intervertebral disc. This characteristic synchondrosis at the base of the dens is often confused with a fracture. It can be seen in all children at 3 years of age and approximately 50% of children 5 years of age. The cartilaginous odontoid tip is separated from the rest the dens by a V-shaped cartilaginous plate. At the age of 3–6 years, the ossification of the odontoid tip and fusion with the body of the odontoid occurs. The persistence of the unfused apical odontoid tip is known as an ossiculum terminale and has no pathological significance (Hensinger et al. 1978).

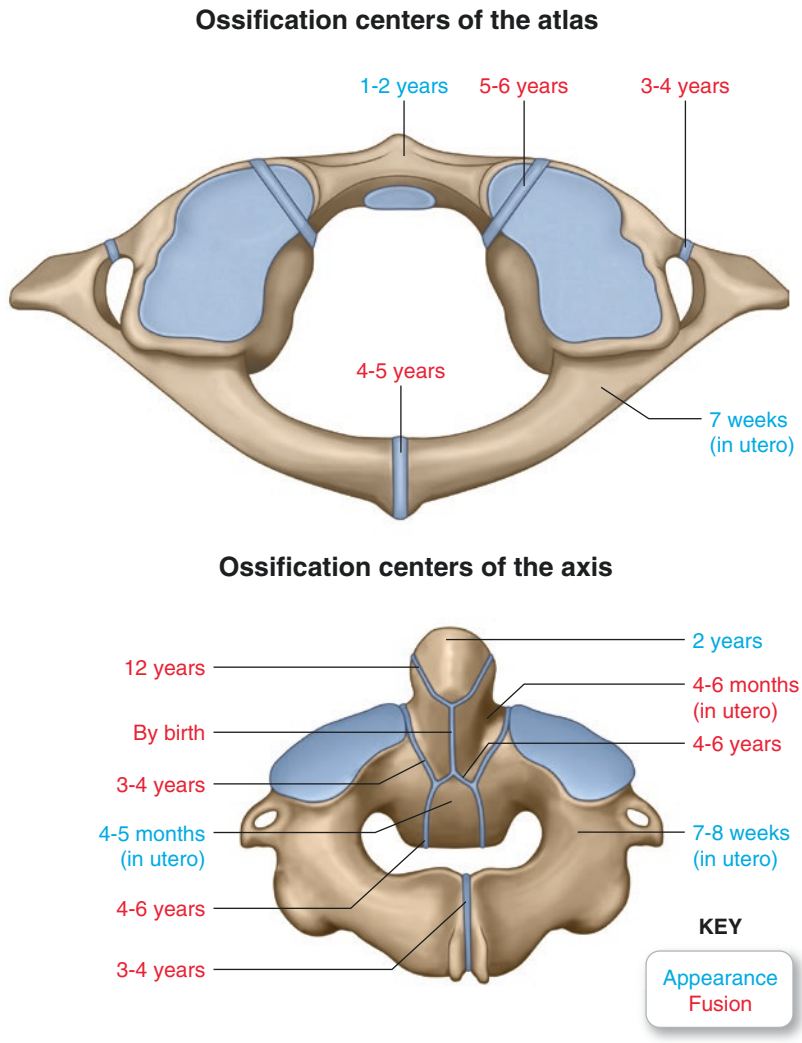

Fig. 37.1 Multiple ossification centers in C1 and C2 at birth. Adapted from Meyers (2017)

Os Odontoideum

Os odontoideum occurs when the odontoid is completely separated from the body of the axis by a varying width gap. Originally it was assumed that this was due to a failure of fusion of the odontoid with the axis. However, it has been suggested that os odontoideum occurs in traumatic lesions caused by an occult odontoid fracture at an early age. Recognition of this congenital abnormality is important because clinically significant C1–C2 subluxation with spinal cord compression may occur in the presence of an os odontoideum (Fielding et al. 1980; Hensinger et al. 1978) (Fig. 37.5). Patients with asymptomatic or myelopathic atlantoaxial instability secondary to os odontoideum are at risk for acute spinal cord injury after minor trauma. Fixation and fusion should be performed as a prophylactic treatment for patients at risk of developing myelopathy and to avoid the neurological deterioration associated with acute traumatic cervical cord injury (Zhang et al. 2010).

Lower Cervical, Thoracic, and Lumbar Spine

The C3 through C7, as well as thoracic and lumbar vertebrae, show a similar pattern of ossification. Ossification centers are formed in each of the two neural arches and in the vertebral body shortly after birth. Complete ossification with

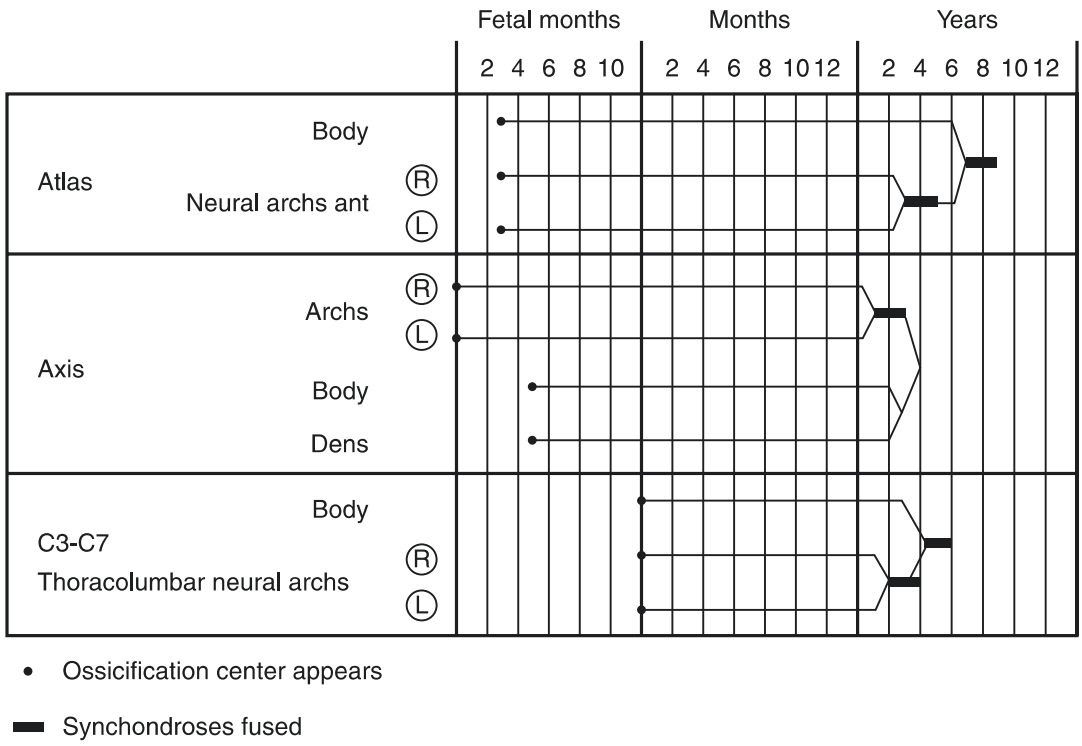

Fig. 37.2 A chart outlining the appearance of ossification centers and the time to fusion of synchondroses in the immature spine. The majority of epiphyseal plates are fused by age six. From Wilberger (ed) (1986), with permission

fusion of the neural arches to the vertebral body generally occurs at the age of 3–6 years (Fig. 37.6). Complete fusion of the posterior neural arches usually occurs by the age of 2-3 years and should not be confused with congenital anomalies such as spina bifida. At the age of 8, the cervical and the thoracic and lumbar spine generally reach the characteristics of the adult.

37.1.1.2 Joint and Ligamentous Development

The shape of the articulating surfaces of the joints and the elastic properties of the supporting ligaments are very different between the spines of adult and children. The elastic nature of these structures is much more prominent in children, which makes the pediatric spine highly mobile. In the pediatric spine, the ligamentous structures do not reach normal elastic properties and sometime allow abnormal mobility between the vertebral bodies with minor trauma. It was suggested that the ligamentous features of the adult should reach 8 years of age (Carpenter 1961). In the lower cervical spine, the orientation of the facet joints was changed from 55° to 70°, while in the upper cervical spine, initial angles were recorded at 30° and then gradually changed to 60–70° by 10 years of age. In addition to changing the orientation of the joints, the facets often do not ossify until about 7–10 years of age and cannot achieve significant stability until complete ossification.

37.1.2 Biomechanics of the Immature Spine

Biomechanics of the spine depends on two main factors: the geometry of the articulating joint or facets and the mechanical properties of the ligaments. The main differences between adult and pediatric biomechanics are the increased physiological mobility of the pediatric spine due to various factors such as ligamentous laxity, incomplete ossification and shallow angulation of the facet

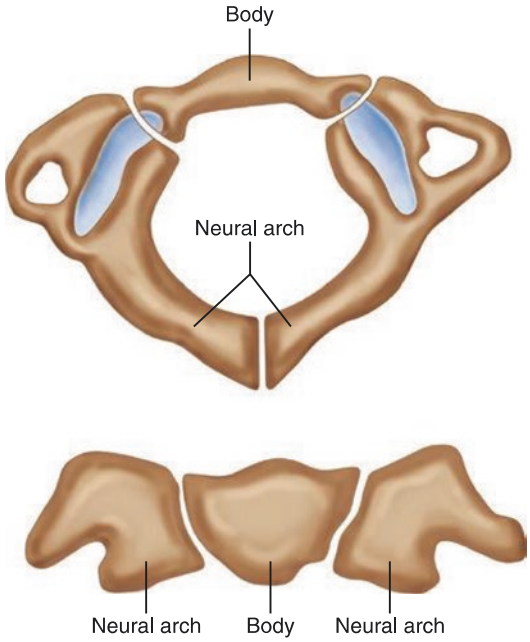

Fig. 37.3 At birth, the atlas (C1) has three ossification centers (one for the body and one for each of the neural arches). The neural arches characteristically close by the third year of life to form a complete ring and subsequently fuse with the body of C1 by the seventh age. These epiphyseal plates or synchondrosis can be readily seen on open mouth view of the atlas. From Wilberger (ed) (1986), with permission

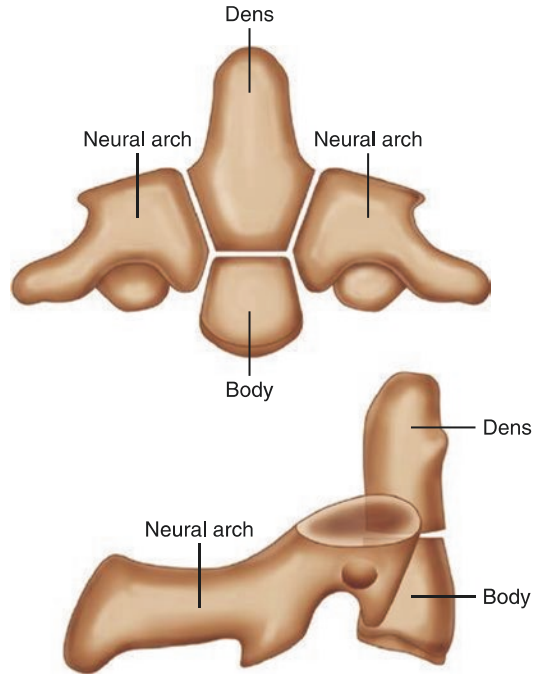

Fig. 37.4 Schematic anatomical representation of ossification centers and epiphyseal plates of the axis. From Wilberger (ed) (1986), with permission

joints, incompletely ossified and wedge-shaped vertebral bodies, and underdeveloped neck musculature (Roaf 1960). In children, the movements of the lower cervical spine are usually different from those of adults. With flexion and extension in adults, motion is greatest at the C5–C6 level. In children, the greatest motion occurs at the C2–C3, and the fulcrum of motion gradually shifts downward as aging occurs. Motion characteristics of adult spine are usually developed by 8–10 years of age (Penning 1978).

Since the infantile vertebral bodies are mostly cartilaginous, overall lengthening of the immature spine occurs easily with axial loading. Axial loading with distraction of the spine can lead to spine elongation of up to 2 in. As a result, the spinal cord must also accommodate, otherwise irreversible injury could result. With flexion and extension, spinal cord segments individually can change up to 25% to prevent severe traction injury to the nervous tissue (Hohl 1964). The overall anatomical characteristics of the immature spine predispose it to excessive mobility. For these reasons, children with significant spinal cord injuries may have no evidence of bony abnormalities on radiological examination (Cusick and Yoganandan 2002).

37.2 Traumatic Spinal Cord Injury in Children

37.2.1 Epidemiology

In the USA, approximately 3% of spinal cord injuries occur in children under 15 years of age (NSCISC 2021). At the age of 3, spinal cord injuries occur equally in males and females, with increasing preponderance in males as age increases. Children under 8–10 years are more likely to have paraplegia and complete injuries than adults. Infants and younger children aged 0–2 years have a higher rate of severe cervical

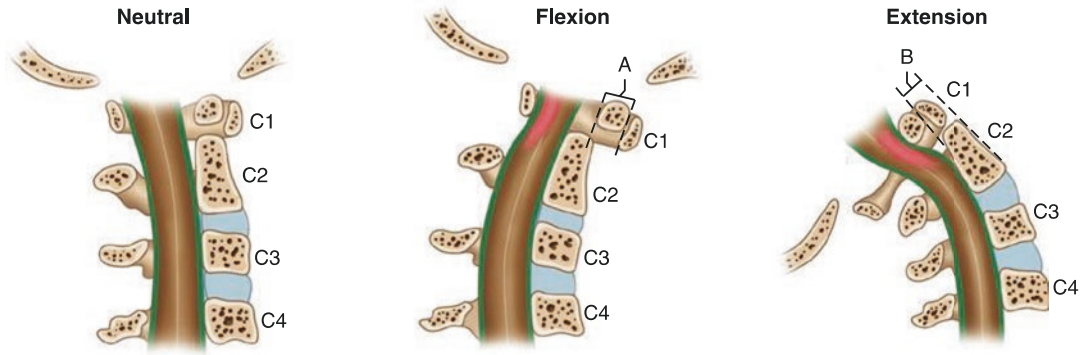

Fig. 37.5 Effect of postural effect of the os odontoideum on the spinal cord. Since the os odontoideum and C1 anterior parts of the C1 move as a mass, flexion and extension movements of the cervical spine lead to repeated compression injuries to the posterior aspect of the spinal cord and the anterior aspect of the spinal cord, respectively

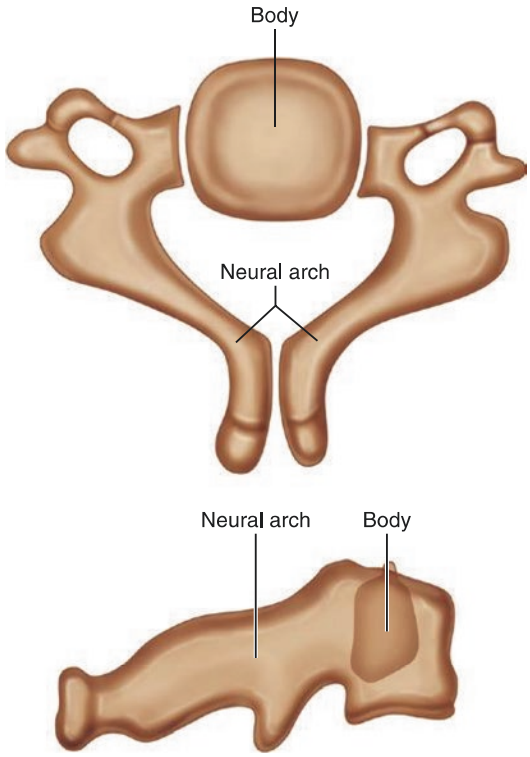

Fig. 37.6 Schematic anatomical representation of the ossification centers and epiphyseal plates of a lower cervical vertebra. The C3 through C7, as well as thoracic and lumbar vertebrae, show a similar pattern of ossification. From Wilberger (ed) (1986), with permission

injuries from C1 to C4. This can be related with disproportionately large heads and underdeveloped cervical muscles. Sixty to 80% of spine injuries in children occur in the cervical region, while in adults it is 30–40% of cervical spine injuries. The upper cervical spine is injured twice as often in the younger child; lower cervical injuries are equally common in younger and older children. Thoracolumbar injuries are more common in the older child (Basu 2012).

Spinal cord injuries in children have several unique causes, such as seat/lap belt injuries, birth injuries, and child abuse. Lap belt injuries (seat belt injuries) are more common in children between 40 and 60 pounds (18–27 kg). The lap belt can be used as a fulcrum during impact, which can cause flexion-distraction forces on the midlumbar spine. This is usually associated with inappropriate use of the booster seat (children safety seat) in a child who is too small to sit without it and an improperly adjusted seat belt. Spinal cord injury can be accompanied by abdominal contusions or intraabdominal bleeding. Vertebral injuries are most common between L2 and L4. Typical lesion is a transverse fracture through the vertebral body and posterior elements (Chance fracture). Twenty-five to thirty percent suffer from SCIWORA. Preventive measures include proper booster seats and seat belts for children aged 4–8 years and up to 4′9″ (144 cm) in height (Calhoun et al. 2013). Neonatal spinal cord injury due to birth trauma occurs in 1 per 60,000 births. Upper cervical injuries are caused by torsional injury during delivery, such as during difficult forceps delivery. Lower cervical and upper tho-

racic injuries occur during breech delivery. Neonatal lesions of the spinal cord can be associated with lesions such as brachial plexus and hypoxic brain injury (Calhoun et al. 2013). Spinal injuries related to non-accidental traumas caused by child abuse are usually the result of shaking of the infant or young child. There is a tendency to damage the vertebral body and anterior end plate, which is consistent with hyperflexion injuries (Bergstrom et al. 2003). Down syndrome with atlantoaxial instability, juvenile rheumatoid arthritis, and skeletal dysplasia are other conditions that accompany children with spinal cord injury (Bergstrom et al. 1999).

37.2.2 Pathophysiology

The anatomic differences from adults, along with the inherent elasticity of the pediatric spine, make pediatric spinal injuries a biomechanically separate entity. The cervical spine in children is much more flexible than the cervical spine in adults. Therefore, it is possible to injure the spinal cord without suffering an obvious damage to the bony spine, resulting in SCIWORA. Relative cephalocervical disproportion exists in young children. The average weight of a baby's head is 25% of body weight, compared to 10% in adults. This combines with poorly developed cervical musculature to mechanical disadvantage of the infants' cervical spine and explains the high incidence of high cervical lesions in infants (d'Amato 2005). Children have increased spinal elasticity, less flexible spinal cord, and vertebral anatomical differences, such as anterior wedge orientation of the vertebral bodies, horizontal orientation of the facets, and absence of uncinate processes on the cervical vertebral bodies, resulting in increased resistance of the ligamentous structures rather than the bones. This explains the high incidence of SCIWORA in children. SCIWORA reported more than 60% of spinal cord injuries in children younger than 5 years. SCIWORA usually occurs in the cervical cord, most commonly at C5–C8 levels. Delayed neurological abnormalities are more common in children, including children with SCIWORA. Possible factors may include occult injuries with repeated trauma, swelling of the cord, or posttraumatic radicular artery occlusion (Atesok et al. 2018).

37.2.3 Clinical Assessment

Clinical assessment of spinal injuries in children can be particularly challenging. Understanding the history of clinical lesions of the spinal or spinal cord injuries in children can be difficult. Neurological evaluation and classification of spinal cord injury should be made in accordance with the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), but the neurological exam is less reliable, difficult to interpret in children, and less useful in children under 4 years old. Some elements of the examination, such as anorectal examinations and pinprick testings, are often difficult to complete and interpret for children under 10 years of age. When assessing motor function, it is important to consider that normal motor strength of a young child is different from that of older adolescent or adults. Table 37.1 lists some causes of acute and chronic myelopathy in children. Also see *Chapter 11. Localization and Characterization of Spinal Cord Lesions.*

37.2.4 Imaging Studies

Multiple epiphyseal plates, the unique architecture of the immature vertebral bodies, incomplete vertebral ossification, and the characteristic hypermobility due to ligamentous laxity make radiological evaluation of the immature spine dangerous. Special considerations are needed when evaluating X-rays of the children's spine. Normal findings in children, such as anteriorly wedged vertebral body, absence of anterior ossification of the atlas, and atlanto-dental interval of 3–4.5 mm, may be considered pathological in adults, so that unused physicians may misinterpret plain radiographs of young children (Buhs et al. 2000; Dwek and Chung 2000; Gai 2004). The incidence of SCIWORA in children is high, but abnormalities can be observed in magnetic

Table 37.1 Causes of acute and chronic myelopathy in children

Categories	Diseases/conditions
Acute myelopathy	
Trauma	Accidental/nonaccidental injury, birth-related trauma, acute disc prolapse
Infection	Epidural abscess, epidural abscess, tuberculosis
Vascular	Thromboembolic events (pediatric intensive care unit) or hemorrhage (spinal epidural hematoma)
Neoplastic	Neuroblastoma, lymphoma, intrinsic spinal cord tumors
Demyelinating	Acute disseminated encephalomyelitis, neuromyelitis optica, multiple sclerosis
Toxins	Chemotherapeutic drugs
Chronic myelopathy	
Degenerative/metabolic	Bone pathology with compression, chronic disc prolapse, adrenomyeloneuropathy, sub-acute combined degeneration
Neoplastic	Neurofibromas
Genetic	Spinocerebellar ataxias, hereditary spastic paraplegia

resonance imaging if the plain radiographs are normal (Khanna and El-Khoury 2007).

37.2.4.1 Normal Pediatric Spine Radiographs

As in the assessment of cervical spine lesions in adults, the first principle of assessment of the cervical spine in children is to clearly visualize all seven cervical vertebrae. The four lines on the lateral view can be useful for evaluating the vertebral alignment and for detecting any spinal canal compromise: the anterior border of the vertebral bodies, the posterior border of the vertebral bodies, the anterior margins of the bases of the spinous processes, and the tips of the spinous processes (Kokoska et al. 2001). The alignment of the facet joints and the relationships of the spinous processes are better seen on anteroposterior views. Sometimes a swimmer's view is needed to visualize the C7–T1 level.

Sometimes, subtle bony damage on the cervical spine can cause significant soft tissue swelling. In children, retropharyngeal soft tissue is most commonly affected (Gai 2004). The space between the anterior edge of the upper cervical vertebrae and the pharyngeal air column must be no more than two-thirds thickness of the second cervical vertebra. Below the C3–C4 level, the prevertebral soft tissue must not exceed the width of the vertebral body.

The immature vertebral bodies are wedged anteriorly and do not have a normal adult configuration until 10 years old. This anterior wedging should not be misinterpreted as a compression fracture. The immature spinous process has a secondary ossification center that should not be mistaken for an avulsion fracture (Lustrin et al. 2003).

In adults, the C1-dens distance is typically less than 2 mm. However, in children, the anterior arch of C1 and the dens can be separated by up to 5 mm due to transverse detal ligament laxity in children. The lucent line at the base of the dens can last up to the age of 11 and should not be confused with fractures. Pseudosubluxation of up to 3–4 mm of C2 on C3 occurs in up to 40% of normal children under 8 years of age. Similar abnormalities can be observed up to 20% at the C3–C4 level (Hadley et al. 2002). The pediatric spine has reached adult characteristics by the age of 10 years, both anatomically and radiographically, and the radiographs of the spine must be interpreted according to the criteria of the adult (Pang and Wilberger 1982).

37.2.4.2 Spinal Cord Injury Without Radiographic Abnormality (SCIWORA)

In young children, radiological diagnosis may be complicated by the extreme elasticity of the cartilaginous spines and their supporting ligaments. This situation can explain the occurrence of severe spinal cord injury in the absence of any radiographic evidence of fracture or dislocation of the spine. The syndrome of spinal cord injury without radiographic abnormality (SCIWORA)

is estimated to affect up to two-thirds of children with severe spinal cord injuries under the age of 8. The mechanism of SCIWORA is not well understood and may be associated with severe hyperextension or flexion injuries with vascular involvement resulting in ischemic injury or infarction of the spinal cord (Szwedowski and Walecki 2014).

The occurrence of SCIWORA is seen in adults, but the most common type of neurological lesion is central cord syndrome resulting from hyperextension injury in patients with spondylosis of the cervical spine. However, in children, the neurological lesions associated with SCIWORA tend to be much more severe (Papavasiliou 1978). Neurological lesions in children under 8 are much worse than older children. In children younger than 8 years old, more complete cord transections and more severe incomplete lesions were found. If SCIWORA occurs in older children, the better the prognosis, the milder the lesion (Papavasiliou 1978).

It was also noted that a high proportion of children with SCIWORA would have a late onset of neurological symptoms. It has been reported that 52% of the children had delayed onset of paralysis (Pang and Wilberger 1980, 1982). The exact mechanism of this delayed onset of neurological deficits is unknown. This may be related to the well-known ligamentous laxity in children, which is further compromised that causes initial instability. Repeated movement for several hours may result in delayed cord injury. In addition, a vascular mechanism may result in delayed paralysis. Many of these children have recalled early symptoms, including paresthesia, numbness, or a subjective feeling of paralysis. These initial symptoms subsided and the delayed onset of neurological deficits occurred 2–24 h later (Pang and Wilberger 1982).

37.2.4.3 Concomitant Traumatic Brain Injury in Spinal Cord Injury

The presence of concomitant traumatic brain injury in people with spinal cord injuries presents an additional challenge such as the cognitive, psychological, behavioral complications, and additional physical dysfunction associated with traumatic brain injury impairing learning and executive functioning skills (Bowman and Macciocchi 2004; Watanabe et al. 1999). Traumatic brain injury in children adds complexity to rehabilitative efforts and lead to persistent learning and behavior disabilities. The diagnosis and classification of spinal cord injury are relatively straightforward and based on the International Standards of Neurological Classification of Spinal Cord Injury. On the other hand, the diagnosis and classification of severity of traumatic brain injury include a combination of loss of consciousness, duration of posttraumatic amnesia, Glasgow Coma Scale, and neuroimaging (Macciocchi et al. 2008). The diagnostic value of loss of consciousness is somewhat controversial in pediatric dual diagnosis, as the traumatic events that lead to the spinal cord injury can cause a loss of consciousness, irrespective of brain injury, especially in younger children under 5 years of age. Individuals with cervical cord injuries may prefer to associate with a brain injury. The prevalence of cervical injury is approximately one-third of school-aged children with spinal cord injuries (DeVivo and Vogel 2004).

Agitation is a common symptom after traumatic brain injury. It can manifest as physical or verbal aggression, explosive anger, restlessness, or inappropriate sexual behavior (Pangilinan et al. 2010). Before starting treatment, it is important to rule out organic causes of agitation such as seizures, hypoxia, electrolyte disorders, medications, or substance withdrawal. Modification to the patient's environment and behavior should be the first line of treatment for agitation; pharmacotherapy is indicated when such modifications alone are insufficient. Agitation control pharmacotherapy must be selected on the basis of the individual patient. Benzodiazepines, traditionally used to treat anxiety and agitation, are avoided after traumatic brain injury because they can cause sedation, memory loss, and potentially paradoxical increases in agitation. Atypical antipsychotic agents such as risperidone, quetiapine, clozapine, and olanzapine can be used for agitation management because they have fewer

cognitive side effects (Bowman and Macciocchi 2004, Hwang 2014; Pangilinan et al. 2010).

Both spinal cord injuries and traumatic brain injury can lead to autonomic abnormalities, that is, orthostatic hypotension and autonomic dysreflexia in spinal cord injuries and dysautonomia in traumatic brain injury. Dysautonomia, also known as paroxysmal sympathetic hyperactivity, is a consequence of acquired brain injury that manifests itself in temperature and hemodynamic homeostasis as well as dystonic muscle contractions (Kirk et al. 2012). Therapeutic options include symptomatic pharmacotherapy and environmental modification, such as maintaining a cooler room temperature or reducing external stimuli that can induce autonomic hyperactivity (Baguley et al. 2009). Pharmacologic management is to reduce sympathetic hyperactivity with beta-blockers or centrally acting alpha-agonists, to increase inhibitory neurotransmitter activity with GABAergic agents (gabapentin, baclofen, benzodiazepines), or to increase dopamine activity (chlorpromazine, bromocriptine). Beta-blockers should be used with caution in children with orthostatic hypotension. Beta-blockers can exacerbate hypotension (Hwang 2014).

37.2.5 Complications in Pediatric Spinal Cord Injury

Spinal cord injuries affect the body organs of both children and adults, including bladder and bowel dysfunction, autonomic dysfunction, cardiovascular problems, respiratory dysfunction, metabolic disorders, pressure injuries, and spasticity and contractures. Some complications are more common in children. Scoliosis, hip instability, and impaired growth of the paralyzed limb occur the age of 8–10 years before the development of skeletal maturation. Hypercalcemia in the first 3 months after spinal cord injury is particularly common in adolescent males due to high bone turnover. A latex allergy may occur and is likely due to frequent exposure to medical equipment or supplies containing latex. Young age at initial exposure and longer duration of exposure are risk factors. Young children and infants with tetraplegia and associated thermoregulation problems are particularly vulnerable to extreme environmental temperatures due to their relatively large surface area and poor communication and problem-solving abilities (Cirak et al. 2004).

37.2.6 Management

The basic principles of spinal cord injury management in children are similar to adults, but with some important differences.

37.2.6.1 Initial Management

Prehospital care focuses on resuscitation, airway, breathing, and circulation, assessment, immobilization, and safe and rapid transportation to the medical care facility. To stabilize the spine of children under the age of 8, child-specific spine boards with a cutout recess for the occiput should be used. Immobilization on a standard spine board can result in excessive neck flexion due to proportionately larger head size compared to the rest of the body. If a standard spine board is used, lift the torso 2–4 cm above the head with a mattress pad under the shoulder and chest to prevent excessive neck flexion.

37.2.6.2 Surgical Management

The main considerations for surgical treatment are decompression of the neural elements and stabilization of the spine to prevent further injury, as in adults. Some anatomical and developmental factors are important to consider when planning a surgery. Spinal fusion and related growth inhibition can have a significant impact on the development of the spine. It is therefore appropriate to limit the number of fusion levels. It is important to consider the effect of an isolated fusion on subsequent occurrence of excessive kyphosis. Some injuries that require surgical stabilization in adults may require nonsurgical management with immobilization in children, as the recovery capacity in children is relatively good.

Halo traction is also available for young children. The main concern is to prevent excessive pressure and skull erosion from the pins. Infants

and younger children use eight to ten pins instead of four in adults, and lower torque force is applied. A more commonly used option for stabilizing the spine is a custom-fabricated thermoplastic orthosis.

37.2.6.3 Psychosocial Considerations

The limited ability to adequately explore the environment due to impaired mobility following spinal cord injury can have significant psychosocial, educational, or vocational consequences. The influence of peers becomes particularly important during the school years. Adolescence can be particularly tumultuous. Anger or rebelliousness can become evident. Physical appearance and relationship problems may occur. Support groups and sexual counseling are important at this stage.

37.2.6.4 Rehabilitation Management

In addition to the rehabilitation principles applicable to adults with spinal cord injuries, the rehabilitation of children with spinal cord injuries has several unique aspects. The specific needs of the individual change from early childhood to adolescence and transition to adulthood. It is important to identify the children's special needs at different levels of development and to integrate development-based goals. As the size grows and changes as the child grows and changes, the need for equipment changes. The role of the family in spinal cord injury rehabilitation is very important and more important for children (Calhoun et al. 2013). Child rehabilitation usually integrates recreation activities and acts as an important component. Adaptive sports activities can be very useful (Cawley et al. 1997; Chen et al. 2008). An important part of rehabilitation is to send the child back to the most appropriate school setting. Treatment and support are provided at the school if necessary. Continuous communication with the school is very important, especially during the transition phase.

Bladder Care

Because bladder management is one of the determinants of long-term survival and social acceptance, it is an important priority in the medical management of children with spinal cord injury. Understanding the basic physiology of the bladder is a prerequisite for a rational approach to bladder management. The treatment for bladder management depends on the age, sex, size, and weight of the child and the type of the bladder.

Fluid intakes and outputs are crucial for establishing programs and schedules. For infants and young children, for whom the use of diapers is appropriate, adequate bladder emptying must be ensured. Infants with a flaccid bladder may perform effective emptying with Créde alone. However, if vesicoureteral reflux is suspected, Créde should never be used. Diapers are no longer appropriate when children reach school age and their continued use can affect their self-esteem and self-image.

Clean intermittent catheterization is an alternative and can be started at any age (Pekarovic et al. 1970). The goal of clean intermittent catheterization is not only to empty the bladder but also to prevent infection and retrain the bladder. The clean intermittent catheterization technique is relatively simple and can be taught to parents and patients. Children as young as 5 years of age can learn the technique of self-catheterization. Generally, a clean intermittent catheterization should be done every 4 h.

The Foley catheter should be removed as soon as possible and bladder retraining started. It is important to avoid repeated urinary tract infection and overdistention of the bladder to maintain normal bladder and renal function. During bladder retraining program, weekly urinalysis, regular urine cultures, and blood urea nitrogen and creatine levels should be monitored (Chang and Shortliffe 2006).

Characteristics of the Lower Urinary Tract in Children

During development, the muscle fibers of the external urethral sphincter appear at 20 weeks of gestation and then gradually form a circular ring that approaches from the posterior urethral portion. During the first year, the external urethral sphincter develops from the distal to the proximal part of the urethra to form a complete external urethral sphincter.

As the bladder capacity increases, the frequency of bladder emptying decreases relatively. In the prenatal period, urination occurs about 30 times in 24 h. However, the voiding frequency decreases rapidly within a few days after birth, and the voiding frequency increases again at 2–4 weeks after the first week. At age 12, an adult level of voiding frequency of 4–6 per day is achieved. At the age of 2–3 years, the voiding pattern of infant changes into the socially adaptable and voluntary urination pattern.

In general, the bladder capacity (mL) of the infants and children is estimated to be 38 + 2.5 × Age (mo) (Holmdahl's formula) and [Age (yr) + 2] × 30 (mL) (Koff's formula) for children above 5 years old, [2 + Age (yr) × 2] × 30 (ml) for children under 2 years old, and [2 + Age (yr)/2] × 30 (mL) (Keafer's formula) for above 2 years old. For children aged 5–15 years in Japan, the formula 25 × [Age (yr) + 2] (mL) applies.

The maximum detrusor pressure (Pdetmax) during voiding in children is higher than in adults. Male infants are higher than female infants (mean Pdetmax: 118 vs. 75 cmH_2O). The maximum detrusor pressure is 55–80 cmH_2O in boys and 30–65 cmH_2O in girls in children. The urethral resistance is higher in males as the urethra of the male is longer than that of the female, the urethral orifice is smaller, and the external urethral sphincter muscle is different in characteristics. During puberty, total cystometric bladder capacity, maximum detrusor pressure, and leak point pressure increase. This is because the prostate gland increases in puberty and the estrogen levels in women increases and the urethral pressure is increased. Therefore, urinary incontinence improves through puberty.

Initial Evaluation of the Neurogenic Bladder in Children

Neurological level of injury of the spinal cord, neurogenic bladder, and detrusor muscle and sphincter function are often inconsistent in children compared with adults. Therefore, appropriate treatment should be determined by the characteristics of the neurogenic bladder based on the neurological examinations and urodynamic studies. After spinal cord injury, a urodynamic study should be performed at 2–3 months and at 6–9 months after injury.

The urodynamic study evaluates cystometric bladder capacity, bladder filling pressure, leak point pressure, and the presence or absence of reflexic detrusor activity. The urodynamic study recommend that, unlike adults, the filling rate be slower than 10 mL/min (the International Children's Continence Society, ICCS). In general, the filling rate for urodynamic study in children is 1/10 of the predicted bladder capacity calculated by the formula. A higher filling rate is prone to errors that are too low for compliance.

Management of the Neurogenic Bladder in Children

The purpose of the treatment of pediatric neurogenic bladder is to prevent complications of the upper urinary tract and to prevent urinary incontinence. Management of neurogenic bladder in children should be done by early intermittent catheterization and anticholinergic medication. If a neurogenic bladder is recognized, immediate intermittent catheterization and administration of anticholinergic drugs should be performed to maintain the detrusor pressure at 30 cmH_2O or less regardless of the bladder capacity. When a neurogenic bladder is present, intermittent catheterization should be performed only if the bladder capacity is similar to the predicted bladder capacity or if the end-filling detrusor pressure is less than 30 cmH_2O.

Intermittent catheterization is initiated even before urodynamic study for myelomeningocele when a newborn is born, unless sufficient urination is achieved by spontaneous emptying or Créde method. For all children, intermittent catheterization can be easily adapted to intermittent catheterization by the family or themselves if it starts as soon as possible. Therefore, it is generally advisable to use intermittent catheterization at the age of 3 years and to be able to do it by themselves at the age of 5–6 years. Intermittent catheterization begins in infancy, when urination in infancy is not well performed by high-pressure

emptying, but is usually initiated at the age of 2–3 years and begins with intermittent catheterization at the time of general voiding training. The thickness of the catheter used for intermittent catheterization begins at 5F in infancy and gradually uses a thicker catheter. In general, 6–8F for preschool, 8–12F for school, and 12–16F for adolescence are used. The earlier the intermittent catheterization is performed, the lower the incidence of bladder augmentation surgery. The kidneys in the first year after birth are more susceptible to infection and pressure. Therefore, functional urinary tract obstruction and vesicoureteral reflux should be closely monitored.

The use of clean intermittent catheterization, self-catheterization, and anticholinergic drugs in children with detrusor overactivity is the absolute standard of care. If the detrusor filling pressure is greater than 40 cmH_2O or the voiding pressure is greater than 80–100 cmH_2O, intermittent catheterization and/or anticholinergic medication reduces the risk of urinary tract deterioration to 8–10%. Most children born with a neurogenic bladder have a normal upper urinary tract at birth, but if not managed properly, urinary tract infections and an increase in detrusor pressure will result in bladder wall deformation. Fifty-eight perent of the children suffer from upper urinary tract disorders before the age of 3 years. In addition, 71% of neonates with detrusor-sphincter dyssynergia have complications of the upper urinary tract within 3 years of age, but 17% without detrusor-sphincter dyssynergia.

Of the anticholinergic agents used in children, oxybutynin is the most commonly used and is known to be safe for long-term use in neonates and infants. Oxybutynin acts as an antagonist to the M3 receptor and has a variety of effects, including anticonvulsant, local anesthesia, and calcium channel blockade. It is usually administered at 0.3–0.6 mg/kg/day three divided doses. In addition, propiverine, ER oxybutynin, tolterodine (pediatric dose 0.25–1 mg, bid), solifenacin, etc. are used. However, the FDA-approved use of oxybutynin is the only one. Tolterodine is approved for use at age 12 and above. The use of ER oxybutynin is recommended because of the lower anticholinergic side effects than oxybutynin. Anticholinergic drugs should continue to be used as long as the bladder is overactive. If the response to the anticholinergic medication is not satisfactory, an intradetrusor injection of botulinum toxin is considered.

Bowel Care

Bowel control is an important issue for children with spinal cord injury. Fecal soiling is troublesome and socially unacceptable. Improper elimination of feces may result in nausea, vomiting, poor appetite, and increased incidence of urinary tract infection as a result of partial ureteral obstruction. Understanding the basic physiology of the bowel is a prerequisite for a rational approach to bowel management.

The purpose of bowel training is controlled the emptying of the large intestine. It is usually made up of a combination of dietary management, stool softeners, and some form of rectal stimulation. Dietary management includes regular eating habits and a well-balanced diet intake with the adequate amounts of fluid and fiber. Fiber can be increased by eating bran, fresh and dried fruits, fresh vegetables, whole grain products, and nuts. It may need to add a stool softener with or without a bowel stimulant. Mineral oil depletes the body of fat-soluble vitamins and their daily use is often forbidden as they lead to rectal seepage.

Common bowel regimens for a young child focus not only on a well-balanced diet, adequate fluids, use of manual stimulation, use of stool softness, and, where appropriate, suppositories but also on a regular toileting time. The child should be placed on the commode at the same time daily. The child needs to feel comfortable and relaxed. Physiologically the best time for the gastrocolic reflex is about 30 min after a main meal. Bowel programs should be initiated in children 2–4 years of age or earlier if they are experiencing diarrhea or constipation. Children who have proper hand function and who sit properly at the age of 5–6 years can become independent in self-catheterization and learn to insert a suppository for

bowel movements. Surgical options are sometimes considered for bladder or bowel care in children. The Mitrofanoff procedure creates a stoma on the abdominal wall through the umbilicus for catheterization of the bladder. Surgical procedures for the evacuation of bowel in children are the Malone procedure or antegrade continence enema, which creates a stoma, catheterizable appendicostomy, allowing for antegrade use of the enema for evacuation of bowel.

Hypercalcemia

Hypercalcemia and bone demineralization are common in rapidly growing children and adolescents, often due to spinal cord injury or other conditions that lead to immobilization. Hypercalcemia is probably secondary to an imbalance of osteoblastic and osteoclastic activity. The highest calcium levels were recorded between 1 and 12 weeks after injury and did not always correlate with the severity of the paralysis. These high levels were usually temporary and returned to normal within 3–4 months without specific treatment (Tori and Hill 1978). Hypercalcemia most commonly involves adolescent and young adult male, usually during the first 3 months after injury (Maynard 1986; Tori and Hill 1978). Hypercalcemia affects 10–23% of individuals with spinal cord injury (Maynard 1986). Serum calcium level is elevated above the age-adjusted normal range, which is 10.8 mg/dL in children and 102 mg/dL in adolescents. In addition, ionized calcium is elevated above its upper limit of 1.23 mol/L. Serum phosphorus is normal, and alkaline phosphatase is normal or slightly elevated. Parathyroid hormone is usually depressed because of hypercalcemia.

Clinically, hypercalcemia can occur with symptoms of abdominal pain and discomfort, anorexia, nausea, abdominal pain, dehydration, vomiting, malaise, headache, polydipsia, polyuria, or lethargy. Early mobilization and weight bearing on a tilt table contribute to the normalization of the high calcium level.

Management of hypercalcemia includes hydration, which requires intravenous normal saline, and furosemide, 0.5–2 mg/kg/day in divided doses every 6–12 h to facilitate renal excretion of calcium. Pamidronate is efficacious in the treatment of hypercalcemia (Lteif and Zimmerman 1998). It is administered intravenously at a dose of 1 mg/kg administered over 4 h. A single dose of pamidronate is usually effective in resolving the hypercalcemia.

Heterotopic Ossification

Heterotopic ossification, the abnormal deposition of bone in tissue, occurs in both neurologic and orthopedic disorders. The hips are the most common area of involvement, followed by the knees, elbows, and shoulders. Heterotopic ossification usually occurs 1–4 months after injury, but it takes 18–24 months for heterotopic bone to mature from the initial abnormal calcium deposition. Subtle signs may initially be thought to be a fracture or an abscess because of the inflammatory responses of increased redness, warmth, and swelling. To diagnose this early, a high index of suspicion is required, especially in children. Three-phase bone scans are often positive 4–6 weeks before ossification is demonstrated on X-ray films. Disodium etidronate is not recommended for growing children.

Scoliosis

The younger the child at the time of the injury, the greater the risk of deformity of spinal curvature. Children with lesion of T12 or lower are less likely to cause spinal curvature complications because the abdominal, back, and vertebral musculature are fully innervated.

As the scoliosis progresses, gravitational forces and the unequal muscle pull can cause the pelvis to deviate from its perpendicular position, resulting in pelvic obliquity. Functional implications of pelvic obliquity may include unequal ischial weight bearing in sitting, apparent leg length discrepancy, and disturbance in sitting balance. When the pelvis is pulled from its perpendicular position, the body weight concentrates on one ischium, predisposing this area to skin breakdown. If scoliosis progresses without intervention and the curvature exceeds 60°, cardiopulmonary function may be impaired.

Skin Care

Skin problems caused by prolonged pressure can cause serious complications for children with spinal cord injury. Prevention should be emphasized from the beginning as the best treatment of pressure injuries. Prevention is best achieved by frequent position changes, at least every 2 h in bed and often every 10–15 min during sitting, to avoid prolonged pressure, especially over bony prominences. The most common sites of pressure injuries are the sacral, ischial, malleolar, trochanteric, and coccygeal prominences. From the age of 5, children can learn the need and mechanics of skin monitoring. Moisture secondary to urinary incontinence can also cause skin breakdown. Frequent changes of diapers or clothing may be needed.

Spasticity

Spasticity is the hyperexcitability of stretch reflexes clinically manifested by hyperactive deep tendon reflexes, clonus, and a velocity-dependent resistance to movement. Spasticity is more severe if it is incomplete lesions than complete lesions. Spasticity may initially appear as flexor spasms. Ultimately, the extensor component predominates. Increased tone accompanied by spasticity can provide the support needed for activities of daily living or transfer activities but generally interferes with function and contributes to the development of contractures. Rapid increases in spasticity may result from irritant stimuli such as pressure injuries, tight clothing, ingrowing toenails, urinary tract infection, and heterotopic ossification.

The most commonly used medications for spasticity are baclofen, diazepam, and dantrolene sodium. Each of these drugs has advantages and disadvantages, and all have a very narrow margin between therapeutic effectiveness and unacceptable side effects when used with young children. Baclofen is not recommended for children under 12 years of age, but it may be the best choice for older patients because it acts primarily at the spinal cord level and is less likely to reduce voluntary motor control. Baclofen is the initial medication of choice and is initiated at 0.125 mg/kg two–three times a day. Doses are then increased every 3–5 days by increments of 0.125 mg/kg/dose with a maximum daily dose of 2 mg/kg/day.

Deep Vein Thrombosis

The development of deep vein thrombosis is relatively rare in children with spinal cord injuries (Vogel and Anderson 2003). In one series, no deep vein thrombosis was identified in children 5 years of age or younger and only 1.9% of those 6–12 years of age in comparison to 7.9–9.1% in adolescents (Vogel and Anderson 2003).

Prophylaxis of deep vein thrombosis includes anticoagulation and graduated elastic stocking for older children and adolescents. Elastic wraps should not be used because the unevenness of wrapping may cause venous obstruction, increasing the risk of deep vein thrombosis. Low molecular weight heparin is ideal for prophylactic anticoagulation because of the ease of administration and laboratory monitoring is generally not needed. The dose of low molecular heparin is 0.5 mg/kg administered subcutaneously every 12 h or 1 mg/kg every 24 h. The dose of low molecular weight heparin should be monitored with anti-factor Xa levels.

Treatment for deep vein thrombosis in children and adolescents with spinal cord injury is similar to that used in adults (Consortium for Spinal Cord Medicine, 1997). Individuals with deep vein thrombosis are anticoagulated with low molecular weight heparin (1 mg/kg every 12 h subcutaneously). Oral anticoagulation with warfarin sodium is initiated simultaneously to maintain a prothrombin time of 2–3 INR.

Autonomic Dysreflexia

The pathophysiology, clinical manifestation, and management of autonomic dysreflexia in children and adolescents with spinal cord injury are comparable to the adult spinal cord injury population (Hickey et al. 2004). The difference between the pediatric and adult spinal cord injury population include developmental variations of blood pressure, the need for different blood pressure cuff sizes and the communication ability of

children (Hickey et al. 2004). Systolic blood pressure elevation of 15 mmHg above baseline in children should be considered autonomic dysreflexia (Consortium for spinal cord medicine 2020).

Management of autonomic dysreflexia in children and adolescents should be conducted efficiently in a calm and reassuring atmosphere. For those not responsive to conservative measures, nitropaste should be applied or nifedipine (0.25 mg/kg) administered by chew and swallow for those who can follow directions or sublingually for younger children and infants. Patients with recurrent autonomic dysreflexia may be managed with prazosin, 25–150 μg/kg/24 h in divided doses every 6 h, or terazosin 1–5 mg daily.

37.2.7 Continuing Medical Care

It is important to integrate general pediatric and wellness care into management. In addition to the usual vaccination schedule, vaccination of pneumococcus and influenza is administered to reduce the risk of pulmonary infections. Nutrition is essential to avoid malnutrition and obesity. Prevention, rapid identification, and management of complications are important for continual management in many aspects look, like adults with spinal cord injuries. Transition to adulthood requires multidimensional planning and integration, including attention to independent living, employment, financial independence, social participation, and continuing healthcare for adult.

Latex allergies are likely frequent exposure to latex-containing medical equipment and supplies. The initial exposure and long-term exposure period are risk factors. Clinical signs include urticaria, angioedema, wheezing, and anaphylaxis. Intraoperative reactions, such as latex glove contact, may be missed due to skin coverage by surgical drapes and can lead to anaphylactic reaction, unexplained hypotension, and tachycardia. Rashes with latex balloons and allergy rashes for certain fruits can provide clues. Skin tests can help establish a diagnosis. Preventive measures include maintenance of a latex-free environment, medical alert confirmation, and preparing for auto-injectable epinephrine (EpiPen®) for emergency use.

Autonomic dysreflexia in children can occur in children with spinal cord injury above T6, as in adults with similar causes and pathophysiology. Young children cannot easily communicate headache and other autonomic dysreflexia-related symptoms. It is important to use an appropriate sized cuff to measure blood pressure in children, with a cuff width of 40% of arm circumference. If the cuff is too large, it tends to be underestimated, and if the cuff is too small, the blood pressure tends to be overestimated. It is important to recognize changes in the development of baseline blood pressure in children. Systolic blood pressure greater than 15–20 mmHg above the baseline in adolescents and greater than 15 mmHg in children can be a sign of autonomic dysreflexia.

Scoliosis is very common when spinal cord injury occurs prior to skeletal maturity, and many of them require surgical correction. Spine radiographs to monitor for scoliosis are recommended every 6 months before puberty and every year thereafter. Problems include pelvic obliquity and sitting posture with decreased function of the upper extremities, pressure injuries, cardiovascular dysfunction, gastrointestinal disorders, and pain (Driscoll and Skinner 2008). Prophylactic bracing using thoracolumbosacral orthosis (TLSO) may delay the need for surgery for curves less than 20°, but this may interfere with mobility and self-care. Surgical correction is indicated for curves more than 40° in children over 10 years. Younger children can be conservatively managed for curves up to 80° if they are flexible and decrease in TLSO, otherwise, surgery is indicated.

Hip instability, such as subluxation, dislocation, and contractures, is common with spinal cord injuries less than 8–10 years of age and requires surgical correction to improve function or if associated with complications such as pressure injuries, increased spasticity, and autonomic

dysreflexia. Preventive measures include soft tissue stretching, spasticity management, and prophylactic orthoses for abduction.

37.3 Nontraumatic Spinal Cord Injuries in Children

Most reports on the demographics, injury patterns, and functional outcomes in children and adolescents have focused on traumatic spinal cord injury, rather than nontraumatic etiology. The National SCI Statistical Center also did not reported data regarding nontraumatic spinal cord injuries. The pathogenesis of nontraumatic spinal cord injuries/lesions in children includes such entities as craniovertebral junction abnormalities, spinal stenosis, vascular ischemia, tumorous compression, and infectious and inflammatory disorders (Pruitt 2014) (Table 37.2).

Table 37.2 Causes of nontraumatic spinal cord injuries in infants and children. Adapted from Pruitt (2014)

Craniovertebral junction anomalies	• Down syndrome • Ehlers-Danlos syndrome • Skeletal dysplasia: Achondroplasia, mucopolysaccharidosis, spondyloepiphyseal dysplasia, Kniest dysplasia, chondrodysplasia punctata, metatropic dysplasia, metaphyseal chondrodysplasia, Larsen syndrome
Vertebral anomalies	• Os odontoideum • Klippel–Feil syndrome • Spinal stenosis
Vascular	• Arteriovenous malformation
Infection, inflammatory etiologies	• Juvenile rheumatoid arthritis • Inflammation after adenotonsillectomy • Spinal cord abscess • Transverse myelitis • Acute disseminated encephalomyelitis • Multiple sclerosis
Oncologic	• Intramedullary spinal cord tumors • Spinal cord compression: Extramedullary spinal cord tumors, metastasis • Radiation fibrosis syndrome

37.4 Congenital Abnormalities of the Spine and Spinal Cord

37.4.1 Spinal Dysraphism and Myelodysplasia: Open Neural Tube Defect

Many terms that describe these malformations are used interchangeably in the literature. Spinal dysraphism literally refers to an incomplete fusion process, but is used to describe these deformities, regardless of whether fusion abnormalities have occurred. The terms spina bifida aperta (open) and occulta (closed) were also used to describe midline development abnormalities. Spina bifida occulta, or occult dysraphism, is a form of minor vertebral anomalies, such as an absent spinous process with no neural malformation (Marson 1970). Congenital spinal cord abnormalities (myelodysplasia) and associated maldeveloped midline structures are the most common congenital anomalies of the central nervous system. These abnormalities can be classified as an open or closed, depending on whether there is an intact skin layer over malformation (Hoffman et al. 1976).

Open spinal cord anomalies are generally classified morphologically, but the forms are highly dependent on the stage of embryological development in which the malformation occurred. Open neural tube defects are presumably the result of a disorder of neurulation, and theories of embryogenesis are divided into two major groups: defects in closing the neural folds due to developmental arrest and overgrowth and reopening of the neural tube after normal closure by hydrodynamic force and neuroschisis. In myeloschisis, the neural tube of the site of the defect is completely opened without the surrounding meninges. Either the neural folds have not fused, or a newly formed neural tube has reopened on or before the 28th day. Most commonly, it occurs at the thoracolumbar junction, where the parts of the spinal cord formed by neurulation and canalization meet and are associated with spina bifida of the entire lumbar and sacral spine (Altman and

Bayer 2001). The exposed neural tissue is degenerated and usually has a complete neurological deficit below the level of lesion.

Regarding neural tube defects in the open cord neural tube defects, a number of spinal maldevelopment has been reported. Failure of normal neural tube development prevents formation of the posterior spinal elements, resulting in a widened spinal canal with the absence of the spinous processes and laminae and laterally displaced pedicle. The most common form of open neural tube defect, myelomeningocele, is a posterior midline cystic mass that is apparent at birth and contains cerebrospinal fluid, meninges, malformed spinal cord, and nerve roots. The roots are directed toward their normal dural exits and may terminate blindly in the lateral or dorsal encasement or overlying tissue. The neural malformation is covered by a gliotic membrane, which is commonly ruptured. In meningocele and myelomeningocele, the malformation occurs during or after neurulation more than 28 days after fertilization.

Meningocele is a skin- or membrane-covered cystic lesion that consists only meninges and, although it is continuous with the neural canal, contains only cerebrospinal fluid with no neural tissue. The dorsal half of one or more vertebrae is absent; the spinal cord runs through the ventral part of the dysraphic spinal canal. Meningoceles are about 10% of open spinal cord abnormalities and are sometimes associated with hydrocephalus or other central nervous system abnormalities. Although the prognosis for normal development is usually good, the meningocele may mask other occult myelodysplasia (Tryfonas 1973).

Most abnormalities that occur in open neural tube defects also affect the nervous system or the mesoderm related with it. Arnold-Chiari hindbrain anomalies are virtually always present and contribute to 90% incidence of hydrocephalus at or immediately after birth. Other brain development abnormalities include cerebral aqueduct stenosis, cerebellar dysgenesis, agenesis of the corpus callosum, midline lipoma, and microgyria. Besides open neural tube defects, there are other intraspinal lesions. Syringomyelia, split cord malformations, lipomas, epidermoid and dermoid cysts, and various tethering bands and adhesions may occur alone or in combination.

Classic delayed clinical symptoms are referred to as tethered cord syndrome. Originally, the term was referred to deterioration due to traction on a low-lying conus by a thickened filum terminale. About 3% of patients have late symptoms associated with a low-lying spinal cord caught by scar tissue at the site of the initial back repair. Other causes of a tethered cord include thickened filum terminale, arachnoid cysts, and dermoid and epidermoid tumors. Neurological deficits caused by a tethered cord may be caused by one or a combination of traction effects, compression, inflammation, or the effects of the primary neurological abnormalities. If the spinal cord fails to ascent normally, the cord is stretched and low lying, and the surface vessels seen to be stretched. Neurological dysfunction is believed to be due to repeated stretching and distortion with activity and growth, leading to eventually possible microvascular injury and chronic ischemia. Fixed neurological deficits can occur at birth as a result of the neural deformity itself. This neurological deficit is likely to deteriorate over time due to traction or compression.

37.4.1.1 Prenatal Diagnosis

Prenatal diagnosis of open neural tube defect is possible with alpha fetoprotein (AFP) measurements and ultrasonography. AFP is transferred from the cerebrospinal fluid to the amniotic fluid in the presence of an open neural tube defect and reaches its peak at about the 16 weeks of gestation. AFP can also be tested in maternal serum. Maternal serum AFP levels are reliable for screening, and mothers with positive screening tests should consider amniocentesis and serial ultrasound examinations.

37.4.1.2 Clinical Presentation

In addition to neurological and lesion evaluation, the initial evaluation of the neonates with open neural tube defects includes assessment of general well-being and search for other system anomalies. In 80% of patients, hydrocephalus occurs at birth or develops in the neonatal period

(McLone et al. 1985), and the head circumference should be measured. The rostral border of the lesion provides an approximation of the neurological level. In addition to location and size of the lesion, the size and shape of the skin defect and integrity of the sac will help to plan surgery (Adzick 2013). Overall, 45% of the lesions are at the level of the thoracolumbar junction, 20% are lumbar, 20% are at the level of the lumbosacral junction, and 10% are over the sacrum, with the remainder located at more rostral spines (Humphreys 1985).

The degree of malformation of the nervous system and neurological deficit is variable. Lower limb movements in response to pain that are associated with crying beyond the application of the stimulus are probably voluntary, while stereotyped movements that cease when stimulation stops and are not accompanied by crying are reflex responses. Motor loss may be of upper or lower motor neuron type. Mostly, it is a combination of both that produces a mixture of flaccid paralysis and involuntary reflexes. The absence of voluntary movement is usually symmetrical within one or two segments. Sensory loss is usually associated with the motor deficit within one or two segmental levels. The sensory level is usually slightly higher. More than 90% of patients with myelomeningocele have bladder dysfunction. Two-thirds of these patients have an upper motor neuron lesion, and the other one-third have lower motor neuron type neurological dysfunction. Bowel dysfunction is generally similar to bladder dysfunction.

Scoliosis is common in open tube lesions and may be classified as congenital or developmental. Congenital scoliosis occurs in 30% and is almost always progressive. The developmental scoliosis group usually has a straight spine at birth and spinal anomalies confined to the posterior spina bifida at the level of the lesion. Half of these patients develop a scoliosis between the ages of 5 and 10 years. Kyphosis may occur independently of scoliosis, which is the result of defective laminae, separated and everted pedicles, or maldevelopment of vertebral bodies, and most commonly occurs in the lumbar spine (Mulcahey et al. 2013).

37.4.1.3 Surgical Managements

The optimal time for surgical closure of the back lesion has been debated. Consensus prefers closure within 36–48 h as the placode is colonized by bacteria after this time and presents a significant risk of central nervous system infection. The goal of early surgery is to prevent infection and preserve existing neurological functions. If hydrocephalus is present at or before the myelomeningocele closure, a shunt may be performed before or simultaneously with back repair surgery.

37.4.2 Spinal Dysraphism and Myelodysplasia: Occult Neural Tube Defect

Tufts of hair, subcutaneous lipomas, hemangiomatous nevi, skin marks, and skin dimples may appear in the back with occult spinal malformation. Occult malformation of the spinal cord can be associated with fibrous bands, adhesion or attaching the cord, conus, filum terminale, or spinal roots to the dura. In some cases, the clinical syndrome of the tethered cord may be due to thickened filum terminale more than 2 mm in diameter. The syndrome of thickened filum terminale is believed to be due to failure of process of lengthening of neural tube and/or root elongation.

The lipomatous tissues within the intradural space may take the form of a lipoma of the spinal cord, a lipomyelomeningocele, or a filum terminale fibrolipoma, usually associated with a thickened filum terminale. Spinal cord lipomas are usually located in the thoracic region and appear in adulthood and are not uniformly considered to be myelodysplastic lesions. Lipomyelomeningoceles are located in the lumbosacral region in 90% of cases and are usually visible at birth in the form of a soft subcutaneous masses. The risk of neurological injury associated with surgery is low, less than 5% for permanent deterioration, with a strong approval of prophylactic surgery. The purpose of surgery is to relieve traction of the spinal cord and reduce compression caused by the lipoma. It is

not necessary to remove the entire lipoma. Decompression and untethering may lead to good clinical outcomes, and neurological function should not be risked for the removal of the total lipoma. Prevention of neurological deterioration was considered to be the main cause of the surgery; however, in several series, pain relief was achieved in almost all symptomatic patients and improvement in motor and bladder function in 30–50%.

There may be signs of upper and lower motor neuron lesions. Involvement of nerve roots or anterior horn cells in the conus medullaris by tethering lesion may result in lower motor neuron deficits and more proximal traction leading to upper motor neuron dysfunction. These numerous consequences are not only weakness but also spasticity and extensor plantar responses. Sensory loss is usually patchy or dispersed and nondermatomal in distribution. Neuromuscular symptoms may appear for the first time in periods of increased activity or rapid growth. Twelve percent of patients have scoliosis or other progressive curvature, possibly at the site of the primary spinal cord abnormality. The tethering effect of the lesion apparently affects at least some of pathogenesis of the curve, as untethering of the cord can improve or arrest the scoliosis in more than 50% of the patients (Hoffman et al. 1976; Keim and Greene 1973). In some patients, scoliosis should not improve with untethering of the cord due to hemivertebrae or other segmentation anomalies.

The caudal regression syndrome, also known sacral agenesis, refers to a failure of formation of the coccygeal, sacral, and sometimes lumbar vertebrae. This anomaly may be associated with malformation of the lower extremities, genitourinary system, and anorectal area. If upper sacral or lumbar segments are not involved, there is no neurological deficiency and no orthopedic abnormalities.

A congenital dermal sinus is an epithelium-lined tract that extends inward from the skin overlying the spine. These tracts may extend from the cervical to the sacral regions, and the depth varies from ending in the subcutaneous tissues to ending in the neural tissue. In the deeper lesions, there is the possibility of communication between the skin and the intradural space.

Anterior sacral meningocele is a herniation of the sacral meninges through a defect in the anterior sacrum. There are often abnormalities of the pelvic organs, but the spinal cord and cauda equina develop normally. The meningocele is located in the presacral, retroperitoneal space and contains cerebrospinal fluid. Neural elements are only rarely contained in the sac. Symptoms generally result from the mass effect of the sac on pelvic organs such as the rectum, bladder, uterus, and sacral nerve roots.

References

Adzick NS. Fetal surgery for spina bifida: past, present, future. Semin Pediatr Surg. 2013;22:10–7.

Altman J, Bayer SA. Development of the human spinal cord: an interpretation based on experimental studies in animals. 1st ed. New York: Oxford University Press; 2001.

Atesok K, Tanaka N, O'Brien A, et al. Posttraumatic spinal cord injury without radiographic abnormality. Adv Orthop. 2018;2018:7060654.

Baguley IJ, Nott MT, Slewa-Younan S, et al. Diagnosing dysautonomia after acute traumatic brain injury: evidence for overresponsiveness to afferent stimuli. Arch Phys Med Rehabil. 2009;90:580–6.

Basu S. Spinal injuries in children. Front Neurol. 2012;3:96.

Bergstrom EM, Short DJ, Frankel HL, et al. The effect of children spinal cord injury on skeletal development: a retrospective study. Spinal Cord. 1999;37:836–46.

Bergstrom EM, Henderson NJ, Short DJ, et al. The relation of thoracic and lumbar fracture configuration to the development of late deformity in childhood spinal cord injury. Spine. 2003;28:171–6.

Bowman BK, Macciocchi S. Dual diagnosis: diagnosis, management, and future trends. Top Spinal Cord Inj Rehabil. 2004;10:58–68.

Bradford DS, Hensinger RM. The pediatric spine. 1st ed. New York: Thieme Inc.; 1985.

Buhs C, Cullen M, Klein M, et al. The pediatric trauma C-spine: is the 'odontoid' view necessary? J Pediatr Surg. 2000;35:994–7.

Calhoun CL, Schottler J, Vogel LC. Recommendations for mobility in children with spinal cord injury. Top Spinal Cord Inj Rehabil. 2013;19:142–51.

Carpenter EB. Normal and abnormal growth of the spine. Clin Orthop. 1961;21:49–55.

Cawley MF, Yarkony GM, Bergman SB. Spinal cord injury rehabilitation. 5. Through the lifespan. Arch Phys Med Rehabil. 1997;78:S73–8.

Chang SL, Shortliffe LD. Pediatric urinary tract infections. Pediatr Clin N Am. 2006;53(379–400):vi.
Chen Y, Anderson CJ, Vogel LC, et al. Change in life satisfaction of adults with pediatric-onset spinal cord injury. Arch Phys Med Rehabil. 2008;89:2285–92.
Cirak B, Ziegfeld S, Knight VM, et al. Spinal injuries in children. J Pediatr Surg. 2004;39:607–12.
Consortium for Spinal Cord Medicine. Evaluation and management of autonomic dysreflexia and other autonomic dysfunctions: preventing the highs and lows. Management of blood pressure, sweating, and temperature dysfunction. Washington, DC: Paralyzed Veterans of America; 2020. https://pva.org/research-resources/publication/
Cusick JF, Yoganandan N. Biomechanics of the cervical spine 4: major injuries. Clin Biomech. 2002;17:1–20.
d'Amato C. Pediatric spinal trauma: injuries in very young children. Clin Orthop Relat Res. 2005;432:34–40.
DeVivo MJ, Vogel LC. Epidemiology of spinal cord injury in children and adolescents. J Spinal Cord Med. 2004;27(Suppl 1):S4–10.
Driscoll SW, Skinner J. Musculoskeletal complications of neuromuscular disease in children. Phys Med Rehabil Clin N Am. 2008;19:163–94.
Dwek JR, Chung CB. Radiography of cervical spine injury in children: are flexion-extension radiographs useful for acute trauma? AJR. 2000;174:1617–9.
Fielding JW, Hensinger RN, Hawkins RJ. Os odontoideum. J Bone Joint Surg Am. 1980;62:376–83.
Gai LY. Significance of prevertebral soft tissue measurement in cervical spine injuries. Eur J Radiol. 2004;51:73–6.
Hacein-Bey L. SCIWORA no more? The case for targeted cervical spine MRI in blunt trauma. J Neuroradiol. 2021;48:139–40.
Hadley MN, Walters BC, Grabb PA, et al. Management of pediatric cervical spine and spinal cord injuries. Neurosurgery. 2002;50:S85–599.
Hensinger RN, Fielding JW, Hawkins RJ. Congenital anomalies of the odontoid process. Orthop Clin North Am. 1978;9:901–12.
Hickey KJ, Vogel LC, Willis KM, et al. Prevalence and etiology of autonomic dysreflexia in chil- dren with spinal cord injuries. J Spinal Cord Med. 2004;27:S54–60.
Hoffman HJ, Hendrick EB, Humphreys RP. The tethered spinal cord: its protean manifestations, diagnosis and surgical correction. Childs Brain. 1976;2:145–55.
Hohl M. Normal motions in the upper portion of the cervical spine. J Bone Joint Surg Am. 1964;46:1777–9.
Humphreys RP. Spinal dysraphism. In: Wilkins RH, Rengachary SS, editors. Neurosurgery. New York: McGraw-Hill; 1985. p. 2041–58.
Hwang M. Dual diagnosis: concomitant traumatic brain injury in spinal cord injury. In: Vogel LC, Zebracki K, Betz RR, et al., editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.
Keim HA, Greene AF. Diastematomyelia and scoliosis. J Bone Joint Surg Am. 1973;55A:1423–35.
Khanna G, El-Khoury Y. Imaging of cervical spine injuries of childhood. Skelet Radiol. 2007;36:477–94.
Kirk KA, Shoykhet M, Jeong JH, et al. Dysautonomia after pediatric brain injury. Dev Med Child Neurol. 2012;54:759–64.
Kokoska ER, Keller MS, Rallo MC, et al. Characteristics of pediatric cervical spine injuries. J Pediatr Surg. 2001;36:100–5.
Lteif AN, Zimmerman D. Bisphosphonates for treatment of childhood hypercalcemia. Pediatrics. 1998;102:990–3.
Lustrin ES, Karakas SP, Ortiz AO, et al. Pediatric cervical spine: normal anatomy, variants, and trauma. RSNA. 2003;23:539–60.
Macciocchi S, Seel RT, Thompson N, et al. Spinal cord injury and co-occurring traumatic brain injury: assessment and incidence. Arch Phys Med Rehabil. 2008;89:1350–7.
Marson AJ. Spina bifida: the significance of the level and extent of the defect to the morphogenesis. Dev Med Cild Neurol. 1970;12:129–44.
Maynard FM. Immobilization hypercalcemia following spinal cord injury. Arch Phys Med Rehabil. 1986;67:41–4.
McLone DG, Dias L, Kaplan WE, et al. Concepts in the management of spina bifida. Concepts Pediatr Neurosurg. 1985;5:97–106.
Meyers SP. Differential diagnosis in neuroimaging: spine. New York: Thieme; 2017.
Mulcahey MJ, Gaughan JP, Betz RR, et al. Neuromuscular scoliosis in children with spinal cord injury. Top Spinal Cord Inj Rehabil. 2013;19:96–103.
National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham: University of Alabama at Birmingham; 2021. https://www.nscisc.uab.edu Last access: November 2021
Pang D, Wilberger JE Jr. Traumatic atlanto-occipital dislocation with survival: case report and review. Neurosurgery. 1980;7:503–8.
Pang D, Wilberger JE Jr. Spinal cord injury without radiographic abnormalities in children. J Neurosurg. 1982;57:114–29.
Pangilinan PH, Giacoletti-Argento A, Shellhaas R, et al. Neuropharmacology in pediatric brain injury: a review. PM R. 2010;2:1127–40.
Papavasiliou V. Traumatic subluxation of the cervical spine during childhood. Orthop Clin North Am. 1978;9:945–54.
Pekarovic E, Robinson A, Zachary RB, et al. Indications for manual expression of the neurogenic bladder in children. Br J Urol. 1970;42:191–6.
Penning L. Normal movements of the cervical spine. AJR Am J Roentgenol. 1978;130:317–226.
Pruitt DW. Non-traumatic pediatric spinal cord injury. In: Vogel LC, Zebracki K, Betz RR, et al., editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.

Roaf R. Vertebral growth and its mechanical control. J Bone Joint Surg Br. 1960;42-B:40–59.
Szwedowski D, Walecki J. Spinal cord injury without radiographic abnormality (SCIWORA)-clinical and radiological aspects. Pol J Radiol. 2014;79:461–4.
Tori JA, Hill LL. Hypercalcemia in children with spinal cord injury. Arch Phys Med Rehabil. 1978;59:443–6.
Tryfonas G. Three spina bifida defects in one child. J Pediatr Surg. 1973;8:75–6.
Vogel LC, Anderson CJ. Spinal cord injuries in children and adolescents: a review. J Spinal Cord Med. 2003;26:193–203.
Watanabe TK, Zafonte RD, Lairson EJ. Traumatic brain injury associated with acute spinal cord injury: risk factors, evaluation, and outcomes. Top Spinal Cord Injury Rehabil. 1999;5:83–90.
Wilberger JE, editor. Spinal cord injuries in children. New York: Futura Publishing Company; 1986.
Zhang Z, Zhou Y, Wang J, et al. Acute traumatic cervical cord injury in patients with os odontoideum. J Clin Neurosci. 2010;17:1289–93.

Recommended Additional Reading

Afifi AK, Bergman RA. Functional neuroanatomy: text and atlas. 2nd ed. New York: Lange Medical Books/McGraw-Hill; 2005.
Crossman A, Neary D. Neuroanatomy: an illustrated colour test. 5th ed. Philadelphia, PA: Elsevier; 2015.
Felten DL, O'Banion MK, Maida MS. Netter's atlas of neuroscience. 3rd ed. London: Elsevier; 2016.
Patestas MA, Gartner LP. A text book of neuroanatomy. Oxford: Blackwell Publishing; 2006.
Preston RA. Acid-base, fluids and electrolytes: made ridiculously simple. 2nd ed. Miami: MedMaster, Inc.; 2011.
Vogel LC, Zebracki K, Betz RR, et al., editors. Spinal cord injury in the child and young adult. London: Mac Keith Press; 2014.
Windle WF. The spinal cord and its reaction to traumatic injury. In: Bousquet WF, Palmer RF, editors. Modern pharmacology-toxicology: a series of monographs and textbooks. New York: Marcel Dekker, Inc.; 1980.

Aging and Spinal Cord Injuries in the Elderly

38

The average age at traumatic spinal cord injury in the USA increased from 28.3 to 37.1 years between 1970 and 2005 (DeVivo 2012; DeVivo and Chen 2011). The mean age between 2015 and 2020 is 43.2 years (NSCISC 2021). The percentage of new injuries that are at least 60 years old will continue to increase by 2% over the next decade and lesser amounts thereafter (Chen et al. 2013, 2015; DeVivo 2012). The life expectancy of people with traumatic spinal cord injury has steadily increased over the last 70 years (Middleton et al. 2012). However, the mortality rate in the spinal cord injury population is higher than in the general population.

Although advances in medical treatment have increased survival rate following spinal cord injury, overall life expectancy is still lower compared to the general population, particularly in those with tetraplegia and ventilator dependency (DeVivo 2012; Shavelle et al. 2015a). Although the mortality rate in the first posttraumatic year has been steadily decreasing since the 1970s, the annual mortality rate after the first posttraumatic year has not changed since the first year after the injury since the early 1980s. Therefore, although the life expectancy of the general population is generally increasing, the life expectancy of those with spinal cord injuries who survived the first year after injury has remained relatively constant, and the differences in life expectancy between those with spinal cord injuries and the general population of comparable age, sex, and race are increasing (Shavelle et al. 2015a, b). The development of medical care and rehabilitation management is expected to increase the life expectancy of the population with spinal cord injuries, but according to the US data, the life expectancy of patients with spinal cord injuries has not increased further in the past 30 years since the early 1980s. Thus, it is estimated that as the age of the general population increases, the average life expectancy difference between spinal cord injury patients and the general population increases relatively.

The incidence of spinal cord injury in the elderly is increasing. On the other hand, the incidence of spinal cord injuries decreases in younger years, while the incidence of spinal cord injury increases in the elderly due to biomechanical or anatomical degeneration in various parts of the body and degenerative changes in the spine and aging increases the risk of falls due to physiological degeneration, sarcopenia, and frailty. Aging of individuals with spinal cord injuries, along with the general population, causes a variety of changes in the properties of many of the body organ systems. Various factors may contribute to the proposed changes with aging of persons with spinal cord injuries. For example, after spinal cord injuries, lack of mobility, muscle activity, and weight-bearing lead to changes in body composition with decreased muscle mass and increased adipose tissue, decreased bone mineral density, and increase in cardiovascular risk

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factors. Overuse of the upper extremities can accelerate the problems of the musculoskeletal system (Furlan et al. 2009). In addition, the aging of spinal cord injury patients in childhood or young adults is a major concern (Capoor and Stein 2005). Therefore, this chapter describes the characteristics of spinal cord injuries in the elderly and the aging of spinal cord injuries in children or young adults.

38.1 Aging of Spinal Cord Injury

Optimal care for the elderly population requires understanding of the rehabilitation and medical problems. Patients with chronic spinal cord injury experience the same medical problems as able-bodied people. The clinical symptoms of these medical conditions may be atypical due to the complex physiological changes associated with spinal cord injury (Charlifue et al. 2010; Groah et al. 2012).

38.1.1 Respiratory Problems in Elderly Spinal Cord Injury

The effects of aging should be understood before considering the effects of chronic spinal cord injury on pulmonary function. Vital capacity is usually maximum at about 20 years old and gradually decreases by 1% per year. Vital capacity decreases with age, but total lung capacity does not decrease. As the vital capacity decreases, the residual volume of the lung increases. Loss of vital capacity can be caused by a lack of deep breathing activities, and the elderly can often be more sedentary. Patients whose vital capacities and tidal volumes reductions initially and who do not take intermittent deep breaths can rapidly cause small airways and alveolar collapse (Capoor and Stein 2005). Pulmonary infections and mucus plugging lead to a rapid decline in the vital capacity. With concomitant deterioration in lung capacity, microatelectasis can lead to uneven ventilation, especially in the dependent portion of the lung. Impaired cough due to age-related changes in lung mechanics and decreased intercostal and abdominal muscle strength can affect secretion clearance and may prolong the course of respiratory infections. (Capoor and Stein 2005; Charlifue et al. 2010).

As the aging progresses, respiratory failure may occur in tetraplegics who have been using mechanical ventilation because of decrease in compliance of the chest wall and lung, number of alveoli, and volume of spirometry, obesity, progression of scoliosis or kyphosis of the vertebrae, and posttraumatic syringomyelia. The condition may worsen, causing respiratory failure.

Respiratory disease is the leading cause of death in long-term spinal cord injury patients. Tetraplegics and high-level paraplegics change the mechanisms of cough due to paralysis of the abdominal and intercostal muscles, leading to a high risk of pneumonia. Treatment of patients with spinal cord injuries with acute respiratory infections includes the standard approach for people with respiratory disease. Loosening of secretions should be attempted with warm mist via tracheostomy mask or half face mask. Nebulizer treatment with albuterol may be necessary. With these standard approaches, people with chronic spinal cord injury require aggressive respiratory physical therapy (Capoor and Stein 2005; Charlifue et al. 2010). If ventilation appears to be a necessary intervention, noninvasive positive pressure ventilation should be considered.

As the risk of pneumonia increases in the elderly, pneumococcal vaccination and annual influenza vaccination should be performed.

38.1.2 Cardiovascular Disorders in Elderly Spinal Cord Injury

The life expectancy of people with spinal cord injuries has increased, and mortality from coronary artery disease has increased. Risk factors include elevated total serum cholesterol, increased low-density lipoprotein and decreased high-density lipoprotein, diabetes, obesity, smoking, hypertension, immobility, and family history of heart disease. It has also been shown that fibrinogen levels, homocystinemia, and uric acid play an important role in the development of

coronary artery disease (Capoor and Stein 2005; Charlifue et al. 2010). People with spinal cord injuries may have an increased risk for coronary artery disease due to relative inactivity, insulin resistance or decreased levels of high-density lipoprotein. Various changes in blood pressure due to autonomic instability following spinal cord injury can lead to intimal damage.

In tetraplegia and high-level paraplegia above T5, perception of pain is impaired due to disruption of afferent spinal pathways from the heart and coronary vessels. Cardiac ischemia and myocardial infarction may present unusual pain referral patterns, symptoms of autonomic dysreflexia, or other atypical signs such as changes in spasticity. Silent ischemia and infarction are also possible. In patients with spinal cord injuries, it is difficult to distinguish between dependent edema and congestive heart failure, and it is difficult to distinguish between bronchiectasis and congestive heart failure when there is abnormal auscultation indicative of bronchiectasis (Capoor and Stein 2005; Charlifue et al. 2010).

Screening for heart disease begins with thorough clinical assessment and identification of risk factors. Evaluation of ischemic heart disease may include arm ergometry exercise test in paraplegics or low-level tetraplegics. Persantine thallium or MIBI studies may be useful in high tetraplegics (Stiens et al. 1995). In patients with spinal cord injuries, echocardiography may show symmetrical atrophy of heart muscle due to lack of cardiac load from immobility, severe orthostatic hypotension, and reduced venous return. These abnormalities are different from the concentric cardiac hypertrophy seen in people with hypertension (Capoor and Stein 2005; Charlifue et al. 2010).

Methods for reducing the risk of cardiovascular disease in patients with spinal cord injuries require generalized management, such as limiting the intake of saturated fat and cholesterol and taking medication to control weight, quit smoking, and fat metabolism.

In addition, patients with spinal cord injuries cannot be diagnosed with peripheral arterial disease because they cannot feel intermittent claudication pain related to gait. Therefore, it is common to diagnose late onset of ischemic symptoms of the lower extremities.

38.1.3 Genitourinary System in Elderly Spinal Cord Injury

In the general population, bladder capacity and bladder compliance decrease, and there is an increase in uninhibitory detrusor contraction, increased residual urine, and decreased renal function. In the elderly, there is a great risk of urinary tract infection due to decreased immune function, menopause, and prostate disease. In patients with spinal cord injuries, the long-term increase in lower urinary tract pressure and the effects of detrusor hypertrophy are cumulative, leading to complications in the upper urinary tract. In addition to the development of neurogenic bladder management in patients with spinal cord injuries, the mortality rate from urinary tract infection has been reduced to 4–5%, but urinary tract infection is still the leading cause of readmission of spinal cord injured patients (Stern 2006).

Benign prostatic hyperplasia is a high incidence in old age, and it can affect the assessment and treatment of urinary disorders associated with spinal cord injury. Because of the high risk of bladder cancer in patients with long-term urethral or suprapubic catheter, periodic screening is necessary. The incidence of bladder cancer in patients with urethral catheter is four times that in patients without urethral catheter. Recurrent urinary tract infections, urinary stone, and smoking are also affecting the incidence of bladder cancer. Urine cytology and biochemical markers for screening for bladder cancer in neurogenic bladder are recommended. Screening by cystoscopy is recommended because urinary tract infections and hematuria increase the false-positive rate, and the reliability is low. On the other hand, the incidence of urethral adhesions and epididymitis increases in patients with long-term intermittent catheterizations.

Recurrent urinary tract infections are likely to cause chronic prostatitis and suggest that the incidence of prostate cancer in patients with

chronic spinal cord injury is high. In practice, however, the incidence of prostate cancer in spinal cord injured patients is not significantly higher than that in the general population. However, when prostate cancer is diagnosed, progression and progression stages of prostate cancer tend to be high in spinal cord injuries. Thus, screening for advanced adenocarcinoma as in the general population is recommended (Capoor and Stein 2005; Charlifue et al. 2010).

In elderly patients with spinal cord injuries, changes in dexterity and mobility of the hand, cognitive dysfunction associated with stroke, and arthritis complicate the previously performed intermittent catheterizations.

38.1.4 Gastrointestinal System in Elderly Spinal Cord Injury

Constipation is a problem in all patients with spinal cord injuries, regardless of age, and constipation is more frequent when age and duration of injury are increased. According to one study, 42% of patients with spinal cord injury 20 years later suffer from constipation, 27% by fecal incontinence, and 35% from general gastrointestinal pain. Although transanal irrigation may be a significant aid to defecation, colostomy may be helpful in improving the quality of life of elderly patients with spinal cord injuries who cannot find a satisfactory method.

Decreasing gastrointestinal motility with aging may aggravate constipation. The additional loss of dexterity and mobility as a result of aging can compromise the ability to perform proper digital stimulation, necessitating a modification of the previously established bowel care program. Bleeding from local anorectal problems or trauma, which may occur in patients with spinal cord injuries, may indicate stool examination for colon cancer screening. It is recommended for people older than 50, as the general population. Colonoscopy for cancer screening requires a special bowel preparation to enable proper visualization. People with tetraplegia develop more common dental diseases, as regular dental hygiene is difficult to perform.

Assessment of acute abdominal pathology in patients with spinal cord injury with potentially impaired sensory function can be very difficult. Typical clinical features of the acute abdomen such as fever, guarding, and rebound may not be present. Pain may be atypical in quality and location. Increased spasticity and a general discomfort may be the only signs of acute abdomen requiring surgical emergencies. Diagnostic options include cholecystitis, appendicitis, pancreatitis, gastric and duodenal ulcers, abdominal malignancies, and volvulus are some of the diagnostic possibilities. Urological causes such as nephrolithiasis, epididymitis, and testicular torsion should also be considered. Gynecological pathology in women, such as ectopic pregnancy, ruptured ovarian cysts, or pelvic inflammatory diseases, can cause acute abdomen (Charlifue et al. 2010).

An endoscopic examination is recommended because the stool occult blood test may not be suitable as a screening test as the hemorrhoid or rectal escape and other distal rectal lesions are common. Bleeding from local lesions and rectal injuries may also affect colorectal cancer screening. These patients require detailed bowel preparation for effective colonoscopy for colorectal cancer screening. However, there is little evidence that the risk of colorectal cancer increases in patients with spinal cord injuries. Hemorrhoids and rectal bleeding are very common complications in patients with chronic spinal cord injuries. Surgical treatments such as ligation or hemorrhoidectomy are also performed in elderly spinal cord injured patients.

38.1.5 Osteoporosis

Osteoporosis is a group of disorders affecting the bones, characterized by a decrease in osteoblastic formation compared to osteoclastic resorption. After acute spinal cord injury, patients have a regional osteoporosis syndrome. Within the first few months, 20–50% of bone mass in lower extremities is lost. Bone mobilization can occur as early as the first 2 weeks after the injury (Capoor and Stein 2005; Charlifue et al. 2010).

The maximum bone mobilization is approximately in the 16th week after the injury. Calcium mobilization gradually decreases and plateauing between 5 to 24 months after injury. Hypercalciuria and hydroxyprolinuria are observed in most patients.

Osteoporosis is defined as bone density that is less than or equal to 2.5 standard deviation of the mean on bone densitometry assessment. Laboratory evaluation of osteoporosis should include measurement of serum calcium, phosphorus, PTH, and serum alkaline phosphatase. Serum calcium, phosphorus, alkaline phosphatase, and PTH levels should be normal in individuals with osteoporosis. People with spinal cord injury should be screened for hyperthyroidism (TSH, T4 levels) every year because it is a treatable cause of osteoporosis.

Some male patients with acute cervical lesions may develop clinically significant hypercalcemia with osteoporosis. Symptoms of hypercalcemia include nausea, vomiting, malaise, anorexia, headache, gastric distention, abdominal pain, fecal impaction, and depression. In cases of severe hypercalcemia, seizure, cardiac arrhythmia, and death are possible. Treatment of hypercalcemia begins with hydration with normal saline solution followed by diuresis with furosemide. Treatment bisphosphonates may be required in refractory cases. Femur fractures are common osteoporotic fracture in patients with long-term spinal cord injuries. People with long-term spinal cord injuries need a bone densitometry screening. In some patients, administration of bisphosphonate and vitamin D should be considered (Frontera and Mollett 2017).

38.1.6 Syringomyelia

Symptoms of posttraumatic syringomyelia vary considerably, as are other forms of syringomyelia. The most common initial symptoms are pain and numbness followed by muscle weakness a few years later. Dysautonomic features such as new onset orthostatic hypotension or autonomic dysreflexia can also be identified. If the syrinx extends into the upper cervical segments, trigeminal nerve symptoms and Horner's sign may occur. If the lesion involves the brainstem, symptoms include hiccups, nystagmus, recurrent laryngeal nerve palsy, hypoglossal nerve palsy, or death. Coughing, sneezing, or body movements can worsen all symptoms of syringomyelia (Frontera and Mollett 2017).

38.1.7 Psychosocial Issues in Elderly Spinal Cord Injury

As the aging progresses, it is necessary to make psychological efforts to adapt to and prepare for future care plans and negative thoughts and feelings about death. Aging and the loss of spouses deteriorate independence and reduce opportunities for social participation (Charlifue et al. 2004; Groah et al. 2002). The quality of life of patients with spinal cord injuries was not deteriorated due to the aging of the patients, and the frequency of depression peaked at the age of 25–45 years of age, and thereafter the depression tended to decrease depression for 20 years. It is important to recognize that factors that cause depression in patients with spinal cord injury are likely to be triggered by functional deterioration due to deterioration of other underlying diseases and when appropriate measures are not taken (Capoor and Stein 2005; Charlifue et al. 2010; Whiteneck et al. 1992).

38.1.8 Functional Ability

Functional deterioration to the extent of 70 years of age in the general population occurs at 49 years in patients with tetraplegia and at 55 years in patients with paraplegia (Whiteneck et al. 1992).

38.2 Spinal Cord Injury in the Elderly

Survival after spinal cord injury is affected by the neurological level of injury, degree of spinal cord injury, age at injury, and duration after injury. In addition, the higher the damage site, the complete

the injury, and the higher the age at the time of injury, the higher the mortality rate (Fassett et al. 2007). After spinal cord injury, health and functional levels are maintained for a considerable period of time, but deterioration of physical function by natural aging occurs. Recently, the age at the time of the spinal cord injury tends to increase gradually, so that they are influenced earlier by the effect of aging (Bracken et al. 1981). According to an annual report by the National Spinal Cord Injury Statistical Center (NSCISC) of the USA in 2014, new spinal cord injuries occur in all age groups but account for 24.3% between 17 and 22 years, and older people over 60 years accounted for 10.7%. The average age of the spinal cord injuries in the 1970s (1973–1979) was 28.7 years, 38.0 years in 2000, and 43.2 years in the period 2015–2020 (NSCISC 2021). This trend shows that the aging of the spinal cord injury is pronounced.

Vertebral fractures and spinal cord injuries in the elderly are severe in neurological impairments and have a high mortality rate (Smith et al. 2010). Spinal cord injuries occur more frequently in physically active age groups such as adolescents and early adults. Older people over the age of 65, however, are the second most common age group. Elderly people with problems such as vision and balance abnormalities, postural hypotension, diabetes mellitus, Parkinson's disease, and osteoarthritis have a higher risk of fall, resulting in an increased incidence of spinal cord injury in the elderly. According to the 2014 NSCISC data, the highest frequency of spinal cord injury is 19 years old, and almost half (48.9%) occur in the age group between 16 and 30 years old. In a 1981 report, only 20% of all traumatic spinal cord injuries were older than 65 years, but the rate of increase in the elderly population suggests that the rate of spinal cord injury has increased considerably. Spinal cord injuries over the age of 45 years are reported to be related to falls in 77%. In addition, 53% of patients with spinal cord injuries older than 50 years reported that alcohol was affected by falls. According to US data in 2007, it is reported that the spinal cord injury due to falls is as high as 74% in the elderly over 70 years of age. The hospital mortality rate for patients with spinal cord injuries over 70 years is 46% and the mortality rate within 1 year after injury is 66%. If the patient is 65 years of age or older, the mortality rate during the initial hospital treatment is increased five times (Jabbour et al. 2008).

The survival rate at 7 years after spinal cord injury is 86.7% in people before age 50, but only 22.7% in people over 50 years old. In underlying diseases such as respiratory diseases or Parkinson's disease, mortality and life expectancy reduce rapidly. In practice, for example, in patients with C5–C8 spinal cord injuries at the age of 20 years, life expectancy is reduced by 32.7%. However, if they are injured at age 60, life expectancy will decrease by 56.1% and 69.4% if they are injured at the age of 75. Life expectancy after spinal cord injuries has been gradually increased, but has not increased further in the past 30 years (Shavelle et al. 2015a).

38.2.1 Characteristics of Spinal Cord Injury in the Elderly

The formation of osteophytes, reduction in disc height, and thickening of the ligamentum flavum promote the degenerative changes of the spine and develop into spinal stenosis and compress the spinal cord. Therefore, as the spinal stenosis progresses, the protective mechanism of the spinal cord by cerebrospinal fluid is eliminated, and the spinal cord may be damaged even without fracture or ligament injury (Breig and el-Nadi 1966; Breig et al. 1966).

In adults, spinal cord injury without radiographic abnormality (SCIWORA) is common, with neurological impairment due to spinal cord injury without any radiographic findings or CT findings suggestive of a spinal fracture (Como et al. 2012). The term SCIWORA is generally recognized as a term used in children. However, the term SCIWORA in adults is inadequate due to frequent degenerative changes and spinal stenosis in adults and the elderly. The term spinal cord injury without radiologic evidence of trauma (SCIWORET) or spinal cord injury without computed tomography evidence of trauma

(SCIWOCTET) is recommended (Como et al. 2012). Of the spinal cord injury patients, 8.2% are classified as SCIWOCTET (Kasimatis et al. 2008).

In 26% of elderly people aged 65 years or older with no symptoms, spinal stenosis is found by MRI. Ninety percent of males aged 50 years or older and 60 years or older have degenerative changes in the cervical spines. As the degenerative changes in the vertebrae progress, the range of motion of the vertebrae decreases, especially in C4–C5 and C5–C6, and the flexibility loss and leverage effect on external impact are prone to spinal fracture or spinal cord injury. Degenerative cervical myelopathy of the elderly is often caused by hyperextension injury of the cervical spine during fall. Central cord syndrome that the upper extremity is more severely impaired than the lower extremity occurs (Henderson et al. 2005).

Patients with spinal cord injury older than 65 years should be tested for cognitive function. Cognitive dysfunction, which is common in older patients with spinal cord injuries, is more likely to be depression than delirium or dementia. Therefore, history and screening for depression are required. In addition, the prevalence of delirium is high due to initial medical problems such as brain damage, use of opioid analgesics, electrolyte abnormality, hypoglycemia, and drug interactions (Furlan et al. 2009). Therefore, early detection of delirium symptoms and proper treatment are very important. Anticholinergic drugs such as tricyclic antidepressants and diphenhydramine, oxybutynin, and baclofen are also drugs that induce delirium. Although the cause has been identified and the treatment has been performed, if the delirium persists, a small amount of haloperidol may be used. Haloperidol for delirium should be given 0.5 mg once at night or twice daily in the morning and evening. In severe cases, 0.5–2.5 mg is injected intramuscularly or intravenously. Lorazepam 0.5–1.0 mg can be administered orally. The purpose of haloperidol administration is to stabilize the patient without affecting the level of consciousness level. Thus, if an intramuscular or intravenous injection is given, the patient should be monitored every 30 min and, if necessary, an additional double initial dose should be administered. In addition to delirium and depression, a history of dementia is required. In elderly patients with spinal cord injury who are suspected of delirium, depression, or dementia, they should be screened for common blood test, urinalysis, electrolyte test, thyroid test, liver function test, serum levels of ammonia, vitamin B12 and folate, ESR and CRP, blood glucose, and brain MRI or CT. In some cases, neuropsychological tests, syphilis tests, and EEG tests are added.

Spinal cord injuries and spinal fractures of the elderly are mainly degenerative cervical myelopathy, central spinal cord syndrome, extension-traction injury of the cervical spine, and odontoid fracture.

38.2.1.1 Degenerative Cervical Myelopathy

Spondylotic changes in the cervical spine are a natural phenomenon of aging. Cervical myelopathy due to degeneration of the cervical spine is a common cause of neurologic impairment in adults, particularly in the elderly. Ninety percent of older people over the age of 65 have spondylotic changes, but most of them have no symptoms, and 5–10% have symptoms of myelopathy. Cervical spondylosis, or cervical osteoarthritis, is an umbrella term for various osteoarthritic changes that occur in the cervical spine. Cervical spondylotic myelopathy is defined as a myelopathy due to compression of the spinal cord by cervical spondylotic pathogeneses and is a common cause of spinal dysfunction usually seen in the elderly (Baron and Yong 2007). Cervical spondylosis is a condition in which deformities of the spine appear mainly due to the aging process. Cervical spondylosis itself can be associated with cervical pain, but it is neurologically asymptomatic. It is only when these structural changes compress the spinal cord that cervical spondylosis can cause myelopathy (Yamaguchi et al. 2018). The pathophysiology of cervical spondylotic myelopathy is multifactorial. Two major factors are static and dynamic damage to the spinal cord (Fig. 38.1). The static factor is persistent compression of the spinal cord by osteoarthritic changes. When mechanical stresses exceed the

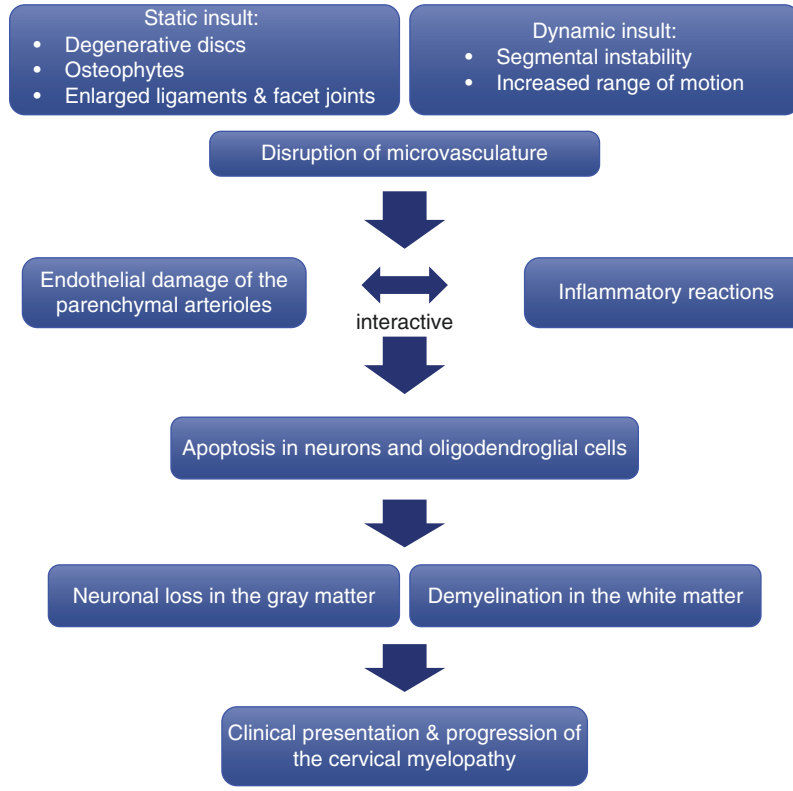

Fig. 38.1 The cascade of pathobiology of cervical spondylotic myelopathy. From Yamaguchi et al. (2018) with permission

effect of stabilization by spondylotic changes, the associated spinal segment becomes unstable and hypermobile. Increased range of motion acts as a dynamic factor in the deterioration of myelopathy (Yamaguchi et al. 2018).

Pathogeneses of degenerative cervical myelopathy can be classified according to the following conditions: cervical spondylotic myelopathy, nonosteoarthritic degeneration, and predisposing factors, such as congenital anomalies (congenital canal stenosis, Down syndrome, and Klippel-Feil syndrome) (Yamaguchi et al. 2018). Degenerative cervical myelopathy has been proposed as an umbrella term to cover various myelopathic pathophysiologies caused by degeneration of the cervical spine rather than spondylotic myelopathy (Nouri et al. 2015) (Table 38.1). Risk factors for degenerative cervical myelopathy include cigarette smoking, repetitive injuries due to heavy occupation, cerebral palsy, and Down syndrome.

Degenerative changes in the spine due to aging can cause abnormalities in the spinal cord.

Table 38.1 The concept of degenerative cervical myelopathy, compromising various degenerative pathologies

Degenerative cervical myelopathy	
Cervical spondylotic myelopathy	Non-spondylotic myelopathy
• Osteophytes • Disc diseases • Deformity of vertebral body • Facet joint arthritic changes • Hypermobility • Spondylolisthesis • Others	• Ligamentous pathologies Ossification of posterior longitudinal ligament Ossification of ligamentum flavum • Congenital/inherited factors • Occupational/behavioral factors • Systemic factors • Sports related factors

Adapted from Yamaguchi et al. (2018), with permission

In particular, degenerative cervical myelopathy can occur in patients older than 55 years of age and accounts for approximately 25% of patients admitted with spastic tetraplegia. Degenerative cervical myelopathy can occur as a result of aging of the spine and intervertebral disc

(Henderson et al. 2005). The spinal cord may be compressed anteriorly by the ossification of posterior longitudinal ligament and compressed backward by hypertrophic calcification of the ligamentum flavum. In addition, facet joints and uncovertebral joint hypertrophy can cause spinal cord compression. Swallowing disorders can be caused by diffuse idiopathic skeletal hyperostosis (DISH), which is caused by the formation of osteophytes in the anterior part of the cervical spine and hypertrophic anterior longitudinal ligament.

Degenerative cervical myelopathy is more common in congenital spinal stenosis with a sagittal diameter of less than 13 mm. In normal adults, the sagittal diameter of the spinal cord in the cervical region is 10 mm. If the sagittal diameter of the spinal canal is less than 12 mm, the incidence of myelopathy is high. If more than 16 mm, the risk is low. In addition, flexion and extension movements of the spinal cord in the narrow spinal canal play an important role in myelopathy. The spinal cord is pinched by osteophytes in the anterior portion of the spinal canal or by thickening of the ligamentum flavum in the posterior part of the spinal canal (Shedid and Benzel 2007; Tavee and Levin 2015).

Clinical Presentation of Degenerative Cervical Myelopathy

Progressive deterioration of gait disturbance is the most common initial symptom in patients with degenerative cervical myelopathy. Muscle strength is initially preserved, but patients complain of abnormal balance, vague sensory abnormalities, and stiffness. The sensory abnormality in the hand causes a pronounced dexterity disorder. Bladder dysfunction, such as urinary incontinence, is not a common symptom at an early stage (Sweeney 1995). Symptoms of myelopathy depend on the anatomical structure involved, and there are symptoms of upper motor neuron lesions that include spastic gait, ankle clonus, Hoffman's sign, and signs of the posterior column injury such as proprioceptive sense abnormality. Abrupt hyperextension of the cervical spines in patients with asymptomatic spondylotic stenosis can cause central cord syndrome due to folding protrusion of the ligamentum flavum (Klineberg 2010).

Current clinical practice guidelines give recommendations based on the clinical assessment according to the modified Japanese Orthopaedic Association (mJOA) scale. Although there is moderate evidence to make a strong recommendation for surgical intervention in severe (mJOA $\leq$11) and moderate (mJOA 12–14) cases of degenerative cervical myelopathy, there is little evidence to make management conclusions of mild (mJOA 15–17) degenerative cervical myelopathy or nonmyelopathic patients with evidence of cord compression (Moghaddamjou et al. 2020).

Prognosis of Degenerative Cervical Myelopathy

The natural course of degenerative cervical myelopathy is very diverse (Karadimas et al. 2013). With severe compression without surgery, necrosis of the spinal cord and cavity formation within the gray matter may aggravate the neurological symptoms (Nikolaidis et al. 2010). Postoperative prognosis for degenerative cervical myelopathy is affected by the duration of the disease and the severity of the symptoms. MRI findings are not an absolute clinical predictor, but high-intensity signals at T2WIs and low-intensity signals at T1WI at the compression site appear to have poor prognosis. However, changes in signal intensity at T2WI due to edema are more likely to recover.

38.2.1.2 Cervical Central Cord Syndrome

Acute traumatic central cord syndrome due to cervical spondylosis is the most common symptom of incomplete spinal cord injury in the elderly. Fracture may be not visible in the initial radiography, so the mechanism of injury may be overlooked, and the initial evaluation may not accurately diagnose it. In patients older than 50 years, 76% of central cord syndromes are caused by hyperextension injury in the presence of a degenerative spine. Hyperextension is thought to cause the ligamentum flavum to buckle, resulting in sudden impingement of the

spinal cord in the anteroposterior plane (Badhiwala et al. 2020; Schneider et al. 1954; Schneider et al. 1958) (Fig. 38.2). Early treatment of the elderly should focus on reducing the risk of surgical treatment. Basically, surgical treatment increases the possibility of recovery and prevents further neurological deterioration. Although there is controversy about the timing of surgery, early surgery is known to be safe and beneficial for neurological recovery.

38.2.1.3 Extension-Distraction Injury

As the aging process causes the disc protrusion and disc height to decrease, the vertebrae lose their flexibility and the range of motion of the vertebrae is limited. If people hit the face or forehead with a fall, the cervical spine is damaged by hyperextension and distraction (Weingarden and Graham 1989). In this case, an "open book" fracture occurs in which the anterior column of the vertebral body or the intervertebral disc cracks due to a hyperextension load of the anterior column of the vertebrae. On initial radiography, slight damage may not be visible and easy to overlook. On plain radiograms and CT, there may be swelling of the soft tissue in the anterior vertebrae or widening of the intervertebral discs. The MRI can better confirm the damage to the anterior longitudinal ligament or other ligaments. Fracture in this case requires surgery. Extension-distraction injuries are also common in patients with ankylosing spondylitis.

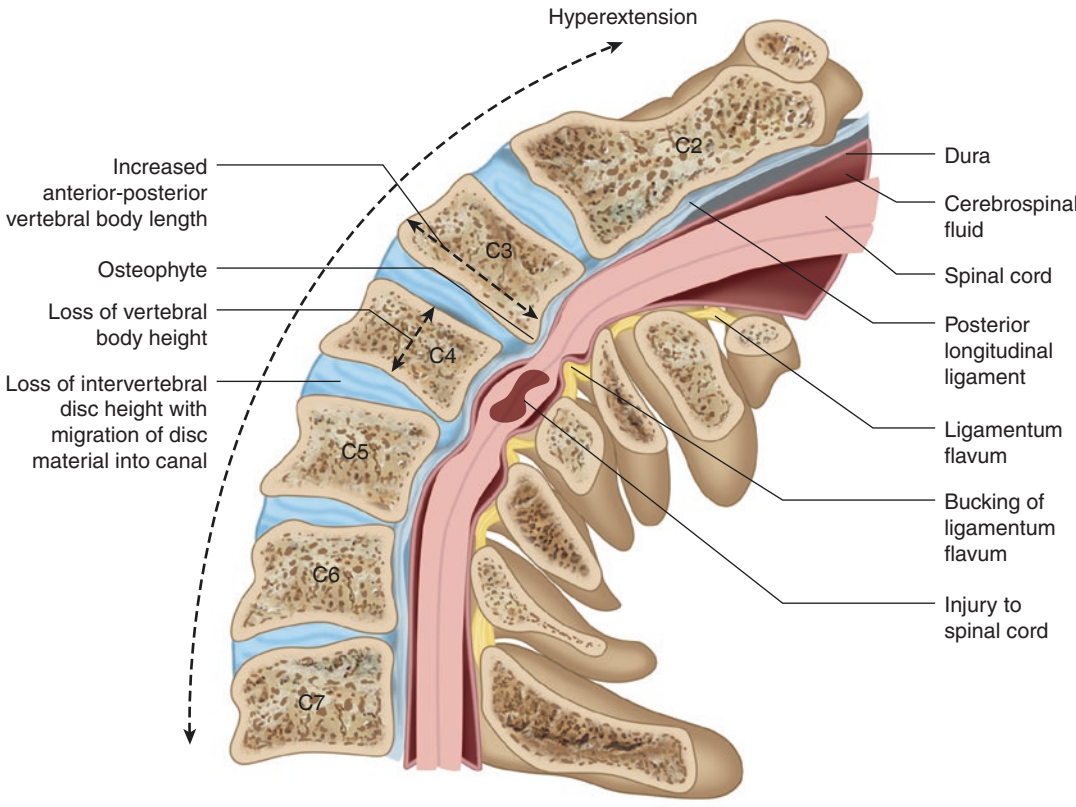

Fig. 38.2 Etiology of traumatic central cod syndrome. Central cord syndromes can be caused by hyperextension injuries in the presence of a degenerative spine. Adapted from Badhiwala et al. (2020)

38.2.1.4 Odontoid Fracture

Type 2 odontoid fracture is also common in the elderly. The odontoid process, which is pushed back by the fracture, compresses the spinal cord, leading to spinal cord injury. However, since the spinal canal is large at this site, less than 6% of the cases cause neurological damage due to spinal cord injury. If the treatment is not appropriate, the fracture site migrates to cause further neurological deterioration, pain, and sudden death. Treatment with halo fixation may be done in adults. In the elderly, surgical fixation is recommended as halo fixation is not easy and the incidence of pseudoarthrosis is high.

38.2.1.5 Syringomyelia

Syrinx formation in the spinal cord occurs mainly in the cervical spinal cord, and it can extend to the brainstem and the conus medullaris. Congenital syringomyelia is caused by Chiari deformity or tethered cord, but acquired syringomyelia may be caused by trauma to the spinal cord, which may interfere with the flow of the cerebrospinal fluid.

References

Badhiwala JH, Ahuja CS, Akbar MA, et al. Degenerative cervical myelopathy - update and future directions. Nat Rev Neurol. 2020;16:108–24.

Baron EM, Young WF. Cervical spondylotic myelopathy: a brief review of its pathophysiology, clinical course, and diagnosis. Neurosurgery. 2007;60(1 Supp1 1): S35–41.

Bracken MB, Freeman DH Jr, Hellenbrand K. Incidence of acute traumatic hospitalized spinal cord injury in the United States, 1970-1977. Am J Epidemiol. 1981;113:615–22.

Breig A, el-Nadi AF. Biomechanics of the cervical spinal cord. Relief of contact pressure on and overstretching of the spinal cord. Acta Radiol Diagn (Stockh). 1966;4:602–24.

Breig A, Turnbull I, Hassler O. Effects of mechanical stresses on the spinal cord in cervical spondylosis. A study on fresh cadaver material. J Neurosurg. 1966;25:45–56.

Capoor J, Stein AB. Aging with spinal cord injury. Phys Med Rehabil Clin N Am. 2005;16:129–61.

Charlifue S, Lammertse DP, Adkins RH. Aging with spinal cord injury: changes in selected health indices and life satisfaction. Arch Phys Med Rehabil. 2004;85:1848–53.

Charlifue S, Jha A, Lammertse D. Aging with spinal cord injury. Phys Med Rehabil Clin N Am. 2010;21:383–402.

Chen Y, Tang Y, Vogel LC, et al. Causes of spinal cord injury. Top Spinal Cord Inj Rehabil. 2013;19:1–8.

Chen Y, Tang Y, Allen V, et al. Aging and Spinal Cord Injury: External Causes of Injury and Implications for Prevention. Top Spinal Cord Inj Rehabil. 2015;21:218–26.

Como JJ, Samia H, Nemunaitis GA, et al. The misapplication of the term spinal cord injury without radiographic abnormality (SCIWORA) in adults. Acute Care Surg. 2012;73:1261–6.

DeVivo MJ. Epidemiology of traumatic spinal cord injury: trends and future implications. Spinal Cord. 2012;50:365–72.

DeVivo MJ, Chen Y. Trends in new injuries, prevalent cases and aging with spinal cord injury. Arch Phys Med Rehabil. 2011;92:332–8.

Fassett DR, Harrop JS, Maltenfort M, et al. Mortality rates in geriatric patients with spinal cord injuries. J Neurosurg Spine. 2007;7:277–81.

Frontera JE, Mollett P. Aging with spinal cord injury: an update. Phys Med Rehabil Clin N Am. 2017;28:821–8.

Furlan JC, Kattail D, Fehlings MG. The impact of comorbidities on age-related differences in mortality after acute traumatic spinal cord injury. J Neurotrauma. 2009;26:1361–7.

Groah SL, Stiens SA, Gittler MS, et al. Spinal cord injury medicine. 5. Preserving wellness and independence of the aging patient with spinal cord injury: a primary care approach for the rehabilitation medicine specialist. Arch Phys Med Rehabil 2002;83(3 suppl 1):S82–9, S90–8.

Groah SL, Charlifue S, Tate D, et al. Spinal cord injury and aging: challenges and recommendations for future research. Am J Phys Med Rehabil. 2012;91:80–93.

Henderson FC, Geddes JF, Vaccaro AR, et al. Stretch-associated injury in cervical spondylotic myelopathy: new concept and review. Neurosurgery. 2005;56:1101–13.

Jabbour P, Fehlings M, Vaccaro AR, et al. Traumatic spine injuries in the geriatric population. Neurosurg Focus. 2008;25:E16.

Karadimas SK, Erwin WM, Ely CG, et al. Pathophysiology and natural history of cervical spondylotic myelopathy. Spine (Phila Pa 1976). 2013;38:S21–36.

Kasimatis GB, Panagiotopoulos E, Megas P, et al. The adult spinal cord injury without radiographic abnormalities syndrome: magnetic resonance imaging and clinical findings in adults with spinal cord injuries having normal radiographs and computed tomography studies. J Trauma. 2008;65:86–93.

Klineberg E. Cervical spondylotic myelopathy: a review of the evidence. Orthop Clin North Am. 2010;41:193–202.

Middleton JW, Dayton A, Walsh J, et al. Life expectancy after spinal cord injury: a 50-year study. Spinal Cord. 2012;50:803–11.

Moghaddamjou A, Badhiwala JH, Fehlings MG. Degenerative cervical myelopathy: changing frontiers. World Neurosurg. 2020;135:377–8.

National Spinal Cord Injury Statistical Center (NSCISC). The 2020 annual statistical report for the spinal cord model systems. Birmingham: University of Alabama at Birmingham; 2021. https://www.nscisc.uab.edu Last accessed September 2021

Nikolaidis I, Fouyas IP, Sandercock PA, et al. Surgery for cervical radiculopathy or myelopathy. Cochrane Database Syst Rev 2010;2010:CD001466.

Nouri A, Tetreault L, Singh A, et al. Degenerative cervical myelopathy: epidemiology, genetics, and pathogenesis. Spine (Phila Pa 1976). 2015;40:E675–93.

Schneider RC, Cherry G, Pantek H. The syndrome of acute central cervical spinal cord injury; with special reference to the mechanisms involved in hyperextension injuries of cervical spine. J Neurosurg. 1954;11:546–77.

Schneider RC, Thompson JM, Bebin J. The syndrome of acute central cervical spinal cord injury. J Neurol Neurosurg Psychiatry. 1958;21:216.

Shavelle RM, DeVivo MJ, Brooks JC, et al. Improvements in long-term survival after spinal cord injury? Arch J Phys Med Rehabil. 2015a;96:645–51.

Shavelle RM, Paculdo DR, Tran LM, et al. Mobility, continence, and life expectancy in persons with ASIA impairment scale grade D spinal cord injuries. Am J Phys Med Rehabil. 2015b;94:180–91.

Shedid D, Benzel EC. Cervical spondylosis anatomy: pathophysiology and biomechanics. Neurosurgery. 2007;60:S7–13.

Smith S, Purzner T, Fehlings M. The epidemiology of geriatric spinal cord injury. Top Spinal Cord Inj Rehabil. 2010;15:54–64.

Stern M. Neurogenic bowel and bladder in an old adult. Clin Geriatr Med 2006;22:311–30; ix.

Stiens SA, Johnson MC, Lyman PJ. Cardiac rehabilitation in patients with spinal cord injuries. In: Halar EH, editor. Physical medicine and rehabilitation clinic of North America: cardiac rehabilitation: part II, vol. 6; 1995. p. 263–96.

Sweeney PJ. Clinical evaluation of cervical radiculopathy and myelopathy. Neuroimaging Clin N Am. 1995;5:321–7.

Tavee JO, Levin KH. Myelopathy due to degenerative and structural spine diseases. Continuum (Minneap Minn). 2015;21:52–66.

Weingarden SI, Graham PM. Falls resulting in spinal cord injury: patterns and outcomes in an older population. Paraplegia. 1989;27:423–7.

Whiteneck GG, Charlifue SW, Frankel HL, et al. Mortality, morbidity, and psychosocial outcomes of persons spinal cord injured more than 20 years ago. Paraplegia. 1992;30:617–30.

Yamaguchi S, Mitsuhara T, Abiko M, et al. Epidemiology and overview of the clinical spectrum of degenerative cervical myelopathy. Neurosurg Clin N Am. 2018;29:1–12.

Recommended Additional Reading

Benzel EC. Biomechanics of spine stabilization. 3rd ed. New York: Thieme; 2015.

Byrne TN, Benzel EC, Waxman SG. Diseases of the spine and spinal cord. Oxford: Oxford University Press; 2000.

Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.

Durrant DH, True JM. Myelopathy, radiculopathy, and peripheral entrapment syndromes. Boca Raton, FL: CRC Press; 2002.

Flint G, Rusbridge C, editors. Syringomyelia, a disorder of CSF circulation. London: Springer; 2014.

Gatchel RJ, Schultz IZ, Ray CT, editors. Handbook of rehabilitation of older adults. Cham: Springer; 2018.

Green D, editor. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.

Passias PG. Cervical myelopathy. Philadelphia, PA: Jaypee Brothers Medical Publishers (P) Ltd; 2016.

Steinmetz MP, Benzel EC. Benzel's spine surgery. Technique, complication avoidance, and management. 4th ed. Philadelphia: Elsevier; 2017.

Vodusek DB, Boller F. Neurology of sexual and bladder disorders. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 130. London: Elsevier; 2015.

Weaver LC, Polosa C, editors. Autonomic dysfunction after spinal cord injury. Progress in brain research, vol. 152. New York: Elsevier; 2006.

39 Dual Diagnosis of Traumatic Brain Injury with Spinal Cord Injury

Almost half of patients with spinal cord injuries experience significant associated injuries, many of which are life threatening (Saboe et al. 1991). Most often they are injured in the head, chest, and long bones. Ten percent have three or more such injuries. The reported incidence of concomitant brain and spinal cord injuries varies from 25% to more than 60%, depending on the criteria used, especially when the injury mechanism is a motor vehicle collision or a fall (Inoue et al. 2013; Macciocchi et al. 2008; Sommer and Witkiewicz 2004). Viewed in isolation, either spinal cord injury or traumatic brain injury can be a significantly disabling event with significant mortality and morbidity. When a person sustains a concurrent spinal cord injury and traumatic brain injury, also known as a dual diagnosis, the prognosis, recovery, treatment, and rehabilitation understandably become more complicated (Bowman and Macciocchi 2004).

Cervical spinal cord injury, complete spinal cord injury and trauma associated with alcohol intoxication are factors that increase the risk of a concomitant traumatic brain injury (Macciocchi et al. 2008). The highest rate of traumatic brain injury occurs in patients with spinal cord injury with C1–C4 levels of injury (Macciocchi et al. 2008). Traumatic spinal cord injuries with accompanying traumatic brain injuries have a significant impact on the rehabilitation outcome of a spinal cord injury (Macciocchi et al. 2004). Traumatic spinal cord injury will likely suppress the awareness of concomitant brain injury unless the patient is unconscious on admission (Hagen et al. 2010). Clinical signs and symptoms of brain injury may also have another source. Cervical spine injuries can also cause vertebral artery occlusion and cause similar symptoms. With sufficient collateral vascular supply, unilateral vertebral artery occlusion may not lead to any neurologic deficits. However, it has been reported that bilateral vertebral artery occlusion in cervical spine injuries results in significant disability and even death (Golinvaux et al. 2015; Strickland et al. 2019; Veras et al. 2000).

There should be increased suspicion for concomitant traumatic brain injury when examining the epidemiology of spinal cord injury caused by high-velocity impact and rapid deceleration events such as motor vehicle accidents. Concurrent traumatic brain injury is evidenced by a history of loss of consciousness; impaired Glasgow Coma Scale that assesses eye opening, verbal response, and best motor response (Table 39.1); and/or imaging abnormalities. The duration of loss of consciousness and duration of posttraumatic amnesia are key features in assessing concomitant brain injury. The presence and duration of posttraumatic amnesia are associated with functional outcome after traumatic brain injury and can be assessed by tests such as the Galveston Orientation and Amnesia Test (GOAT) (Fig. 39.1).

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Table 39.1 Glasgow Coma Scale

Scale value	Best motor response	Verbal response	Eye opening response
6	Obeys commands for movement	–	–
5	Purposeful movement to stimulus	Oriented	–
4	Withdraws from painful stimulus	Confused conversation, but able to answer questions	Eyes open spontaneously
3	Abnormal flexion of arm(s) Decorticate posture	Inappropriate response, word discernible States recognizable words or phrases	Eyes open to verbal command, speech, or shout
2	Extension response Decerebrate posture	Incomprehensible sounds or speech	Eyes open to painful stimulus (not applied to face)
1	No motor response	No verbal response	Remain closed, no eye opening

Minor brain injury = 13–15; moderate brain injury = 9–12; severe brain injury = 3–8

Question	Error score	Notes
What is your name?	/2	Must give both first name and surname
When were you born?	/4	Must give day, month, and year.
Where do you live?	/4	Town is sufficient
Where are you now? (a) City	/5	Must give actual town
(b) Building	/5	Usually in hospital or rehab center Actual name necessary
When were you admitted to this hospital?	/5	Date.
How did you get here?	/5	Mode of transport.
What is the first event you can remember after the injury?	/5	Any plausible event is sufficient (record answer)
Can you give some detail?	/5	Must give relevant detail.
Can you describe the last event you can recall before the accident?	/5	Any plausible event is sufficient (record answer)
What time is it now?	/5	1 for each half-hour error, etc.
What day of the week is it?	/3	1 for each day error, etc.
What day of the month is it? (i.e. the date)	/5	1 for each day error, etc.
What is the month?	/15	5 for each month error, etc.
What is the year?	/30	10 for each year error.
Total Error:		
100 - total error		Can be a negative number.

76-100 = Normal
66-75 = Borderline
< 66 = Impaired

Fig. 39.1 Galveston Orientation and Amnesia Test (GOAT)

Concurrent spinal cord and traumatic brain injuries result in a diagnostic and management dilemma. The detection and treatment of life-threatening intracranial lesions and intracranial pressure increases are priority over the treatment of spinal cord injury. The presence of both head injury and spinal cord injury requires the clinician to decide which injury is more life- and neurologically threatening in order to make a decision as to which injury should be treated first. Physical, cognitive, and/or emotional impairments due to a traumatic brain injury present significant challenges in the rehabilitation of spinal cord injured patients. Prompt diagnosis of a concomitant traumatic brain injury in patients with spinal cord injury is important in planning appropriate rehabilitation interventions for the prevention and early treatment of possible related medical complications and in maximizing functional recovery. A diagnosis of traumatic brain injury, especially mild and moderate brain injury, may be missed during the acute care hospitalization of patients with spinal cord injury, if there is a need for sedation, intubation, and/or the presence of acute trauma-related life-threatening issues. Awareness of the potential for associated brain injury in traumatic spinal cord injury as well as vigilance for related symptoms, signs, and/or complications is important to improve both clinical and functional outcomes (Kushner 2015; Kushner and Alvarez 2014).

39.1 Associated Problems with Concurrent Brain Injury in Patients with Spinal Cord Injury

In addition to motor and sensory impairments, cognitive impairments may include deficits of attention, information processing speed, problem-solving, learning, memory, and communication. Emotional issues may include apathy, emotional lability, agitation, aggression, disinhibition, impaired task initiation, anxiety, and depression (Kushner and Alvarez 2014). Mild traumatic brain injury occurs most commonly in patients with spinal cord injury accompanied by brain injury, occurring in approximately 64–73% of cases, but moderate traumatic brain injury occurs in 10–23% and severe brain injury in 17–23% of cases (Macciocchi et al. 2008). Traumatic spinal cord injury may suppress the awareness of associated brain injury unless the patient is unconscious on admission (Hagen et al. 2010).

Rehabilitation strategies and expected outcomes for patients with a spinal cord injury can be complicated by a dual diagnosis of traumatic brain injury. Traumatic brain injuries lead to more subtle consequences such as learning difficulties. Traumatic spinal cord injuries with concomitant brain injuries have a significant impact on the rehabilitation outcome of a spinal cord injury (Macciocchi et al. 2004). The presence of traumatic brain injury can significantly impair the new learning and follow-up required during rehabilitation and reduce tolerance. Tasks need to be simplified for practice or divided into small components to avoid multitasking. Altered attention and memory may affect compliance and may require reminders, repetition, and/or written backup. Excessive stimulation should be avoided, and patients often perform best in a quiet and nondistracting environment. This may be obvious in some cases in terms of impaired memory, judgment, impulse control, and reasoning, but it can be much more subtle and difficult to detect in others. Concurrent traumatic brain injury can extend the time required to learn new tasks and affect other aspects of rehabilitation, such as social and familial adjustment. In the more severe cases, where cognitive and behavioral deficits persist, return to school and work as well as successful social integration can be compromised.

Those with more severe traumatic brain injury can develop posttraumatic complications such as hydrocephalus and/or seizures. Cerebrally mediated autonomic dysfunction (also known as autonomic storming or dysautonomia) may occur in the early recovery phase of those with severe traumatic brain injury or brainstem injury, and paroxysmal tachycardia, hypertension, tachypnea, sweating, fever, and rigidity occur. Although paroxysmal increase in blood pressure and sweating that occur with dysautonomia overlap with signs of autonomic dysreflexia associ-

ated with spinal cord injury, the other characteristic clinical features help differentiate the two conditions.

39.2 Classification of Brain Injury Severity

Severity of traumatic brain injury is classified as mild, moderate, or severe based on criteria such as initial Glasgow Coma Scale, duration of posttraumatic amnesia, duration of loss of consciousness, and neuroimaging findings consistent with intracranial trauma, such as concussion, axonal shear injury, hemorrhage, and encephalomalacia (Kushner 2015; Kushner and Alvarez 2014; Macciocchi et al. 2008). Standard classification of severity of traumatic brain injury based on these four diagnostic criteria is shown in Table 39.2.

39.3 Evaluation of Traumatic Brain Injury

It is important that patients with spinal cord injury associated with traumatic brain injury should be treated appropriately with the relevant physical, cognitive, and behavioral symptoms and performed specialized rehabilitation accordingly. There are also complications that threaten the various potentially life-threatening and/or quality of life of traumatic brain injury that may be missed if a dual diagnosis is not made (Kushner and Alvarez 2014). Brain injuries, especially concussive mild traumatic brain injury, may not become evident until a patient with spinal cord injury is transferred to an inpatient rehabilitation unit with symptoms such as headaches, dizziness, sleep disturbance, balance and coordination defect, emotional lability, depression and anxiety, impaired visual function and communication, and behavior and executive dysfunction (Inoue et al. 2013; Macciocchi et al. 2008; Sommer and Witkiewicz 2004).

The assessment should begin with the review of acute care records looking for documents with loss of consciousness, Glasgow Coma Scale scores, posttraumatic amnesia duration, confusion, behavioral issues, seizures, and/or abnormal results of any brain imaging studies, with particular attention to review paramedic reports, emergency care note, intensive care unit note, nursing note, etc. (Macciocchi et al. 2008). Once a patient attains a score above 75 on the GOAT, he or she is considered to have emerged from the period of posttraumatic amnesia. Executive functions may also be impaired in patients with traumatic brain injury. Executive functions are the processes of the brain responsible for higher order complex activities such as planning, judgment, and decision-making. These processes depend on working memory, prospective memory, strategic planning, cognitive flexibility, abstract reasoning, and self-monitoring to function properly. The frontal lobe is believed to be responsible for executive function, in conjunction with broad cortical and subcortical circuits.

Neuropsychological tests incorporating a battery of tests performed by a qualified mental health practitioner are indicated for patients with cognitive or learning disabilities or suspected or diagnosed traumatic brain injury. Motor impairment due to a spinal cord injury cannot complete a test involving writing or drawing, so it is necessary to adjust the test accordingly.

Table 39.2 Classification of traumatic brain injury severity

TBI severity	None	Mild	Moderate	Severe
Initial GSC score	15	13–15	9–12	3–8
Initial LOC duration	No	<30 min	>30 min	>30 min
PTA duration	No	<24 h	<1 week	>1 week
Neuroimaging findings	No	Yes	Yes	Yes

39.4 Brain Injury-Related Complications and Their Management

Potential complications of moderate to severe brain injury may include physical, cognitive and behavioral, and metabolic complications. Potential complications of concomitant moderate to severe traumatic brain injury with spinal cord injury are listed in Table 39.3.

39.4.1 Dysphagia

Another complication that often occurs with moderate to severe traumatic brain injury and spinal cord injury is dysphagia due to mechanical, obstructive, or neurologic problems. Dysphagia is likely to be more severe in patients with traumatic brain injury with tracheostomy, a history of ventilation of more than 2 weeks, a Rancho Los Amigos level 6 or less, a midline shift or brainstem lesions, and/or intracranial pathology requiring emergency surgery (Mackay et al. 1999a, b). The likelihood of dysphagia increases in patients with spinal cord injury of upper cervical spine trauma, older age, tracheostomy, ventilation, and cervical surgery, which may include anterior and/or posterior instrumentation or occipitocervical fusion (Kirshblum et al. 1999; Tian and Yu 2017). Modified barium swallowing studies are the diagnostic tests that can be performed to identify and confirm swallowing disorders. Although there are many treatment options for mechanical, obstructive, and neurologic causes of dysphagia, cognitive and behavioral impairments are a particular challenge to the treatment.

Table 39.3 Potential complications of concomitant moderate to severe traumatic brain injury with spinal cord injury

Potential complications in moderate to severe traumatic brain injury with spinal cord injury	
• Seizure/epilepsy • Dysphagia • Communication impairments • Apraxia/cognitive-motor disorders • Agitation/aggression • Impaired arousal/apathy • Depression/anxiety • Impaired cognition and perception	• Aspiration pneumonia • Neuroendocrine dysfunction excess ADH/hyponatremia low ADH/hypernatremia-DI • Spasticity • Heterotopic ossification • Obstructive hydrocephalus • Paroxysmal sympathetic hyperactivity

39.4.2 Cognitive Problems

A wide range of cognitive impairments can be observed after a traumatic brain injury. Information processing and attention, general intellectual functioning, memory, spatial cognition, and executive functions are among the important cognitive domains affected by traumatic brain injuries. Patients with traumatic brain injury are at risk for psychological problems that may include adjustment disorders and neuropsychiatric and cognitive problems, such as depression, anxiety, agitation, aggression, impulsive behavior, memory impairment, attention deficit disorder and impaired concentration, and sleep disorders (Chew and Zafonte 2009; Neurobehavioral Guidelines Working Group et al. 2006). The Rancho Los Amigos Scale, also known as the Ranchos Scale describes the cognitive and behavioral patterns found in brain injury patients as they recover from injury (Table 39.4). The scale was developed based on assumption that observation of the type, nature, and quality of the patient's behavioral responses can be used to estimate the cognitive level at which the patient is functioning (Flannery 1993). Cognitive and neuropsychiatric problems are likely in patients with lesions involving the frontal and/or temporal lobes, amygdala, and limbic system.

The pharmacologic management of impaired concentration, attention, and speed of information processing is controversial, but there is some consensus on the usefulness of methylphenidate. The pharmacologic management of agitation, aggression, and restlessness in traumatic brain injury remains controversial, but it is generally acceptable that beta-blocker medication may be helpful (Chew and Zafonte 2009; Neurobehavioral Guidelines Working Group et al. 2006). Traumatic

Table 39.4 Rancho Los Amigos Level of cognitive functioning scale

Level	Description	Assistance needed
I	No response • No response to external stimuli	Total assistance
II	Generalized response • Responds inconsistently and non-purposefully to external stimuli • Responses are often the same regardless of the stimulus	Total assistance
III	Localized response • Responds inconsistently and specifically to external stimuli • Responses are directly related to the stimulus, for example, patient withdraws or vocalizes to painful stimuli • Responds more to familiar people (friends and family) versus strangers	Total assistance
IV	Confused/agitated • The individual is in a hyperactive state with bizarre and non-purposeful behavior • Demonstrates agitated behavior that originates more from internal confusion than the external environment • Absent short-term memory	Maximal assistance
V	Confused, inappropriate non-agitated • Shows increase in consistency with following and responding to simple commands • Behavior and verbalization is often inappropriate, and individual appears confused and often confabulates • Different from level IV in that individual does not demonstrate agitation to internal stimuli. However, they can show agitation to unpleasant external stimuli	Maximal assistance
VI	Confused, appropriate • Able to follow simple commands consistently • Able to retain learning for familiar tasks they performed pre-injury (brushing teeth, washing face) however unable to retain learning for new tasks • Responses may be incorrect secondary to memory impairments but appropriate to the situation	Moderate assistance
VII	Automatic, appropriate • Oriented in familiar settings • Daily routine automatically with minimal to absent confusion • Demonstrates carry over for new tasks and learning in addition to familiar tasks • Beginning to show interest in social and recreational activities in structured settings	Minimal assistance for daily living skills
VIII	Purposeful, appropriate • Consistently oriented to person, place and time • Independently carries out familiar tasks in a non-distracting environment • Beginning to show awareness of specific impairments and how they interfere with tasks, however, requires standing by assistance to compensate • Often depressed, irritable and with low frustration threshold	Stand by assistance
IX	Purposeful, appropriate • Able to shift between different tasks and complete them independently • Aware of and acknowledges impairments when they interfere with tasks and able to use compensatory strategies to cope • Continues to demonstrate depression and low frustration threshold	Stand by assistance on request
X	Purposeful, appropriate • Able to multitask in many different environments with extra time or devices to assist • Independently anticipates obstacles that may occur as a result of impairments and take corrective actions • Demonstrate intermittent periods of depression and low frustration threshold when under stress • Able to appropriately interact with others in social situations	Modified independent

Table 39.5 Medication for mood disorders and agitation/aggression

Medication	Purpose	Side effects
Anticonvulsants (carbamazepine, valproate, etc)	Agitation, seizure prophylaxis	Sedation, thrombocytopenia, hepatotoxicity
Benzodiazepines (lorazepam, diazepam, clonazepam)	Acute agitation, anxiety	Sedation, cognitive impairment, weakness
Methylphenidate	Cognition, concentration, attention, memory, agitation	Tachycardia, hypertension, headache, rash
Amantadine	Cognition, concentration, attention, agitation	Decreased seizure threshold
Beta-blocker (propranolol, pindolol)	Agitation, anxiety	Orthostatic hypotension, bradycardia
Tricyclic antidepressants (amitriptyline, nortriptyline, doxepin, imipramine)	Depression, agitation	Tachycardia, decreased seizure threshold, dizziness, drowsiness
SSRI	Depression, agitation	Suicidal ideation, increased spasticity

brain injury can also cause fatigue and depression. Sleep disturbances are also common and can make the symptoms worse. Trazodone, 25–50 mg at night, may help with sleep disturbance. Benzodiazepines can worsen cognitive function and should be avoided in these patients. Options for pharmacologic management of neurobehavioral and cognitive disorders after traumatic brain injury are summarized in Table 39.5. If delirium is not controlled, haloperidol should be administered at a dose of 0.5 mg twice daily in the evening or in the morning and evening. In severe cases, 0.5–2.5 mg of haloperidol is injected intramuscularly or intravenously. Lorazepam 0.5–1.0 mg may be administered orally. If acute agitation is present, haloperidol 1–2 mg is administered intramuscularly or intravenously, 0.5–1.0 mg bid or qid orally or intramuscularly until controlled. Since haloperiodol administration aimed at stabilizing the patient's level of consciousness, an intramuscular or intravenous injection allows the patient to be observed every 30 minutes and to inject twice as much of the initial dose as needed.

39.4.3 Metabolic Disorders

Metabolic problems, including disorders of serum sodium regulation and/or neuroendocrine dysfunction, may occur in patients with traumatic brain injury, especially if a lesion involves the hypothalamic–pituitary brain pathway. Hyponatremia may occur in syndrome of inappropriate antidiuretic hormone secretion (SIADH) or cerebral salt-wasting syndrome (Harrigan 2001; Lohani and Devkota 2011; Moro et al. 2007). In SIADH, there is normovolemic to hypervolemic hyponatremia resulted from dilution of serum sodium concentration due to renal water retention and sodium excretion by excessive release of antidiuretic hormone by hypothalamus (Moro et al. 2007). SIADH is treated with sodium supplementation, fluid restriction, and sometimes mineralocorticoids. In cerebral salt-wasting syndrome, hypovolemic hyponatremia due to excessive renal excretion of both water and sodium leads to dehydration caused by disruption of hypothalamic–pituitary pathways stimulating adrenal release of cortisol. Cerebral salt-wasting syndrome is treated with sodium supplementation, hydration, and mineralocorticoids. Severe hyponatremia without treatment may result in encephalopathy and seizures (Table 39.6). When traumatic brain injury results in inadequate or absent secretion of antidiuretic hormone, diabetes insipidus rarely occurs, causing dehydration with hypernatremia by excessive renal loss of free water. It can be treated with antidiuretic hormone, also known as vasopressin (Harrigan 2001; Lohani and Devkota 2011; Moro et al. 2007).

Table 39.6 Common electrolyte abnormalities associated with traumatic brain injury

Electrolyte abnormality	Causes	Clinical features	Management
Hyponatremia		Mental changes, seizure, or hyperreflexia in severe hyponatremia caused by all etiologies: And plus the following symptoms	
	SIADH	Clinically euvolemic, high urine osmolarity and urine sodium	Fluid restriction, demeclocycline
	Cerebral salt-wasting syndrome	Hypovolemia, high urine osmolarity and urine sodium	Sodium and fluid replacement
	Psychogenic polydipsia	Polydipsia, polyuria	Fluid restriction, clozapine
Hypernatremia	DI, diuretics, dehydration	Lethargy, weakness, mental status changes, thirst, polyuria for central DI	Fluid replacement, desmopressin (DDAVP)
Hyperkalemia	Hypoaldosteronism, hemolyzed blood specimen, renal dysfunction	Muscle weakness, cardiac conduction block, peaked T waves on ECG	Correct underlying disorder, kayexalate, diuretics
Hypokalemia	Diuretics, hypomagnesemia, excess catecholamines	Lethargy, weakness, hyporeflexia, arrhythmia	Correct underlying disorder, potassium replacement

References

Bowman BK, Macciocchi S. Dual diagnosis: diagnosis, management, and future trends. Top Spinal Cord Injury Rehabil. 2004;10:58–68.

Chew E, Zafonte RD. Pharmacological management of neurobehavioral disorders following traumatic brain injury–a state-of-the-art review. J Rehabil Res Dev. 2009;46:851–79.

Flannery J. Psychometric properties of a cognitive functioning scale for patients with traumatic brain injury. West J Nurs Res 1993;15:465–77; discussion 477–82.

Golinvaux NS, Basques BA, Bohl DD, Laurans MS, Grauer JN. Bilateral vertebral artery injury in a patient with upper cervical spine fractures leading to fatal vertebrobasilar infarction: a case report. Orthop Surg. 2015;7:281–5.

Hagen EM, Eide GE, Rekand T, et al. Traumatic spinal cord injury and concomitant brain injury: a cohort study. Acta Neurol Scand Suppl. 2010;190:51–7.

Harrigan MR. Cerebral salt wasting syndrome. Crit Care Clin. 2001;17:125–38.

Inoue T, Lin A, Ma X, et al. Combined SCI and TBI: recovery of forelimb function after unilateral cervical spinal cord injury (SCI) is retarded by contralateral traumatic brain injury (TBI), and ipsilateral TBI balances the effects of SCI on paw placement. Exp Neurol. 2013;248:136–47.

Kirshblum S, Johnston MV, Brown J, et al. Predictors of dysphagia after spinal cord injury. Arch Phys Med Rehabil. 1999;80:1101–5.

Kushner DS. Strategies to avoid a missed diagnosis of co-occurring concussion in post-acute patients having a spinal cord injury. Neural Regen Res. 2015;10:859–61.

Kushner DS, Alvarez G. Dual diagnosis: traumatic brain injury with spinal cord injury. Phys Med Rehabil Clin N Am. 2014;25:681–96.

Lohani S, Devkota UP. Hyponatremia in patients with traumatic brain injury: etiology, incidence, and severity correlation. World Neurosurg. 2011;76:355–60.

Macciocchi S, Seel RT, Thompson N, et al. Spinal cord injury and cooccurring traumatic brain injury: assessment and incidence. Arch Phys Med Rehabil. 2008;89:1350–7.

Macciocchi SN, Bowman B, Coker J, Apple D, Leslie D. Effect of co-morbid traumatic brain injury on functional outcome of persons with spinal cord injuries. Am J Phys Med Rehabil. 2004;83:22–6.

Mackay LE, Morgan AS, Bernstein BA. Swallowing disorders in severe brain injury: risk factors affecting return to oral intake. Arch Phys Med Rehabil. 1999a;80:365–71.

Mackay LE, Morgan AS, Bernstein BA. Factors affecting oral feeding with severe traumatic brain injury. J Head Trauma Rehabil. 1999b;14:435–47.

Moro N, Katayama Y, Igarashi T, et al. Hyponatremia in patients with traumatic brain injury: incidence, mechanism, and response to sodium supplementation or

retention therapy with hydrocortisone. Surg Neurol. 2007;68:387–93.
Neurobehavioral Guidelines Working Group, Warden DL, Gordon B, et al. Guidelines for the pharmacologic treatment of neurobehavioral sequelae of traumatic brain injury. J Neurotrauma. 2006;23:1468–501.
Saboe LA, Reid DL, Davis LA, et al. Spinal trauma and associated injuries. J Trauma. 1991;31:43–8.
Sommer JL, Witkiewicz PM. The therapeutic challenges of dual diagnosis: TBI/SCI. Brain Inj. 2004;18:1297–308.
Strickland B, Lewis CS, Pham MH. Bilateral vertebral artery occlusion after cervical spine fracture dislocation. World Neurosurg. 2019;124:304–9.
Tian W, Yu J. The role of C2-C7 angle in the development of dysphagia after anterior and posterior cervical spine surgery. Clin Spine Surg. 2017;30:E1306–14.
Veras LM, Pedraza-Gutiérrez S, Castellanos J, Capellades J, Casamitjana J, Rovira-Cañellas A. Vertebral artery occlusion after acute cervical spine trauma. Spine (Phila Pa 1976). 2000;25:1171–7.

Recommended Additional Reading

Ashley MJ, Hovda DA. Traumatic brain injury. Rehabilitation, treatment, and cases management. New York: CRC Press; 2018.
Campbell WW. DeJong's the neurologic examination. 7th ed. New York: Wolters Kluwer Lippincott Williams & Wilkins; 1992.
Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation. Physical medicine and rehabilitation clinics of North America. Philadelphia, PA: Elsevier; 2014.
Mtuid E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. 7th ed. Philadelphia, PA: Elsevier; 2016.
Tsao JW, editor. Traumatic brain injury. A clinician's guide to diagnosis, management, and rehabilitation. New York: Springer; 2012.

Sleep Disorder in Spinal Cord Injuries

40

Sleep disorders occur more frequently in people with spinal cord injuries than in the general population and likely contribute to reduced societal participation and quality of life (Sankari et al. 2019a). Primary sleep disorders such as sleep-disordered breathing (SDB), especially in people with high thoracic and cervical lesions (Sankari et al. 2019b), sleep-related movement disorders while awake and asleep (Peters et al. 2018), and insomnia disorders are common after spinal cord injuries (Sankari et al. 2019a). In addition, various factors can negatively affect sleep after spinal cord injury, including pain, insomnia, and/or the circadian rhythm sleep–wake disorders (Giannoccaro et al. 2013; Norrbrink Budh et al. 2005). Subsequently, people with spinal cord injuries report daytime symptoms such as fatigue, excessive daytime sleepiness (Sankari and Badr 2016; Stepanski et al. 1984), difficult concentration, and impaired quality of life. Fatigue and excessive daytime sleepiness can be associated with pain (Biering-Sørensen and Biering-Sørensen 2001; Norrbrink Budh et al. 2005), spasticity (Terson de Paleville et al. 2011), depression (Elliott and Frank 1996), side effects of medications, postural discomfort (Hammell et al. 2009), and autonomic dysfunction (Krassioukov 2009) in people with spinal cord injuries (Sankari et al. 2019a).

Respiratory problems are the leading cause of morbidity and mortality in people with spinal cord injuries and are exacerbated by the physiology of sleep and especially rapid eye movement (REM) sleep (Castriotta and Murthy 2009; Giannoccaro et al. 2013). The most important forms of SDB in people with spinal cord injuries are sleep-related hypoventilation and obstructive sleep apnea, but there are also a number of non-respiratory sleep problems that are common, such as insomnia, restless legs syndrome, circadian rhythm disorders, and sleep-related limb movements during sleep (Giannoccaro et al. 2013; Peters et al. 2018). In the general population, sleep disorders are known to cause a variety of problems, including hypertension, dyslipidemia, cardiac arrhythmias, and neurocognitive impairment (Punjabi 2008). In patients with spinal cord injuries, SDB also leads to neurocognitive impairment that impairs rehabilitation (Castriotta et al. 2012; Redline and Strohl 1998).

40.1 Sleep Physiology

40.1.1 Normal Sleep Stages

Human sleep can be defined as an altered state in which the conscious awareness of the external world is impaired with different controls, rhythms, emotions, and dreams. It is a transient natural, periodic, physiologic phenomenon that is reversible and thus different from irreversible coma and death (Chokroverty 2017b). The sleep–wake cycle actually consists of three distinct

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stages: wakefulness, non-REM (NREM) sleep, and REM sleep.

Full wakefulness is characterized by mixed frequencies, low amplitude EEG activity, often associated with high chin muscle tone, eye blinks and rapid eye movements, and continuous postural muscle tone in the EMG. Sleepiness begins at sleep onset before reaching stage 1 NREM sleep (N1 sleep) with heaviness and drooping of the eyelids, clouding of the sensorium, and inability to see, hear, or perceive things in a rational or logical manner (Chokroverty 2017b). If the patient immediately falls asleep with their eyes closed, wakefulness is characterized by a sinusoidal activity of 8–13 Hz called alpha sleep. Alpha sleep is best recorded in the occipital region and is attenuated by opening the eyes (Badr 2012).

Nonrapid eye movement (NREM) sleep makes up most of sleep and is characterized by the predominance of homeostatic mechanisms for breathing, cardiovascular and gastrointestinal function, and normal thermoregulation. NREM sleep is divided into three stages. N1 sleep is a period of transition in which the person still usually has some awareness of the environment. Slow eye movements are commonly seen during N1 sleep. N1 sleep occupies 3–8% of sleep time. N1 sleep is characterized by a slowing of the background wake EEG frequencies with a predominance of low amplitude activity at 4–7 Hz (often referred to as theta activity). N2 sleep is a period when the person is generally no longer aware of the environment. N2 sleep begins after approximately 10–12 min of N1 sleep (Chokroverty 2017b). N2 sleep comprises 45–55% of sleep time. N2 sleep is characterized by the appearance of sleep spindles and K complexes superimposed on the background of theta activity. Sleep spindles are 12–14 Hz rhythmic sinusoidal waves that are usually best recorded on central EEG leads. K complexes are diphasic waves with a sharp negative component followed by a slow positive component. After about 30–60 mins of N2 sleep, stage 3 (N3) sleep begins. N3 sleep, commonly referred to as slow wave sleep, is assessed when slow wave activity (particularly in a delta frequency range, 0.5–4 Hz) is recorded over >20% of an epoch. Slow waves are defined as having low frequency (generally 0.5–2 Hz) and large amplitude (>75 mV) (Badr 2012).

Rapid eye movement (REM or Stage R) sleep accounts for 20–25% of total sleep time. ERM sleep is characterized by moderate rapid EEG activity that paradoxically occurs during behavioral sleep with the complete absence of postural muscle tone in the EMG, or muscle atonia, as well as variations and instability in cardiopulmonary function and instability of body temperature control. In addition, Stage R is characterized by the presence of REMs, dreaming, decreased chin muscle tone, relative atonia of all muscle groups except the diaphragm, and erections in men. Stage R is a unique time of the night dreaming during Stage R sleep. REM sleep can be subdivided into two stages: tonic and phasic. Tonic stage persists throughout the REM sleep, whereas the phasic stage is discontinuous and superimposed on the tonic stage (Chokroverty 2017a). Stage R is characterized by low amplitude, mixed frequency EEG, similar to that in Stage N1 sleep (Badr 2012).

The behavioral characteristics of each sleep stage are listed in Table 40.1. Table 40.2 lists the physiologic criteria for wakefulness and sleep.

40.1.2 Normal Sleep Cycle

The normal sleep cycle in a young adult (generally considered the standard) begins with transitioning from wakefulness to Stage N1 sleep and then a rapid transition to Stage N2 and N3 sleep. The first occurrence of Stage R sleep is generally around 90 min and individuals then cycle between NREM and REM sleep every 90 to110 min throughout the night. During a normal sleep period in adults, 4–6 such cycles are noted. In general, N3 sleep (slow wave sleep) predominates in the first third of the night, whereas Stage R predominates in the last third of the night (Badr 2012; Chokroverty 2017b; Ohayon et al. 2004; Redline et al. 2004). The sleep time of each sleep state is shown in Table 40.3. Overall sleep architecture is dependent upon the stage of develop-

Table 40.1 Behavioral characteristics of each sleep stage

Behavior	Awake	NREM sleep	REM sleep
Posture	Erect, sitting, or recumbent	Recumbent	Recumbent
Mobility	Normal	Slightly reduced or immobile; posture shifts	Moderately reduced or immobile; myoclonic jerks
Response to stimulation	Normal	Mildly to moderately reduced	Moderately reduced to no response
Level of alertness	Alert	Unconscious but reversible	Unconscious but reversible
Eyelids	Open	Closed	Closed
Eye movements	Waking eye movements	Slow rolling eye movements	Rapid eye movements

NREM nonrapid eye movement, *RMG* rapid eye movement. From Chokroverty (2017a), with permission

Table 40.2 Physiologic criteria for wakefulness and sleep

Measurement	Awake	NREM sleep	REM sleep
Electroencephalography	Alpha waves; desynchronized	Synchronized	Theta or saw tooth waves; desynchronized
Electromyography	Normal	Mildly reduced	Moderately to severely reduced or absent
Electrooculography	Waking eye movements	Slow rolling eye movement	Rapid eye movement

NREM nonrapid eye movement, *RMG* rapid eye movement. From Chokroverty (2017a), with permission

Table 40.3 Sleep time of each sleep stage

Sleep stage	Sleep time (%)
NREM sleep	75–80
N1	3–8
N2	45–55
N3	15–23
REM sleep	20–25

NREM nonrapid eye movement, *RMG* rapid eye movement. From Chokroverty (2017a), with permission

ment and aging. The evolution with age of the different sleep stages as a percentage of sleep time across the age span is shown in (Fig. 40.1). For instance, infants generally spend up to 50% of the night in Stage R sleep and often have a cycle of REM sleep prior to NREM sleep (Ohayon et al. 2004). In addition, the duration of the NREM–REM cycle is 60 min through most of childhood. Over the span of time between young adulthood to elderly, there are changes in most sleep stages, including decreased total sleep time and sleep efficiency, increased percentage of Stages N1 and N2, and decreased percentage of Stages N3 and R (Ohayon et al. 2004; Redline et al. 2004).

40.1.3 Effects of Sleep on Central Neural Centers

The suprachiasmatic nucleus regulates the sleep–wake cycle. The circadian clock functions in a cycle that lasts a little longer than 24 h. The suprachiasmatic nucleus is primarily "set" by visual cues of light and darkness that anchor to the 24-hour day (Perez and Salas 2020). The neurons distributed through the core of the brainstem in the mesencephalic, pontine, and medullary reticular formation are essential for maintaining a state of wakefulness with cortical activation and postural muscle tone, as well as behavioral arousal and responsiveness. Specific neural systems, which are located in specific areas of the brain and contain specific neurotransmitters, generate and maintain the states of wakefulness, NREM sleep, and REM sleep (Sowho et al. 2014).

Multiple neural networks between the brainstem and cortex (ascending arousal system) are important for both arousal and wakefulness (España and Scammell 2011; Saper et al. 2005).

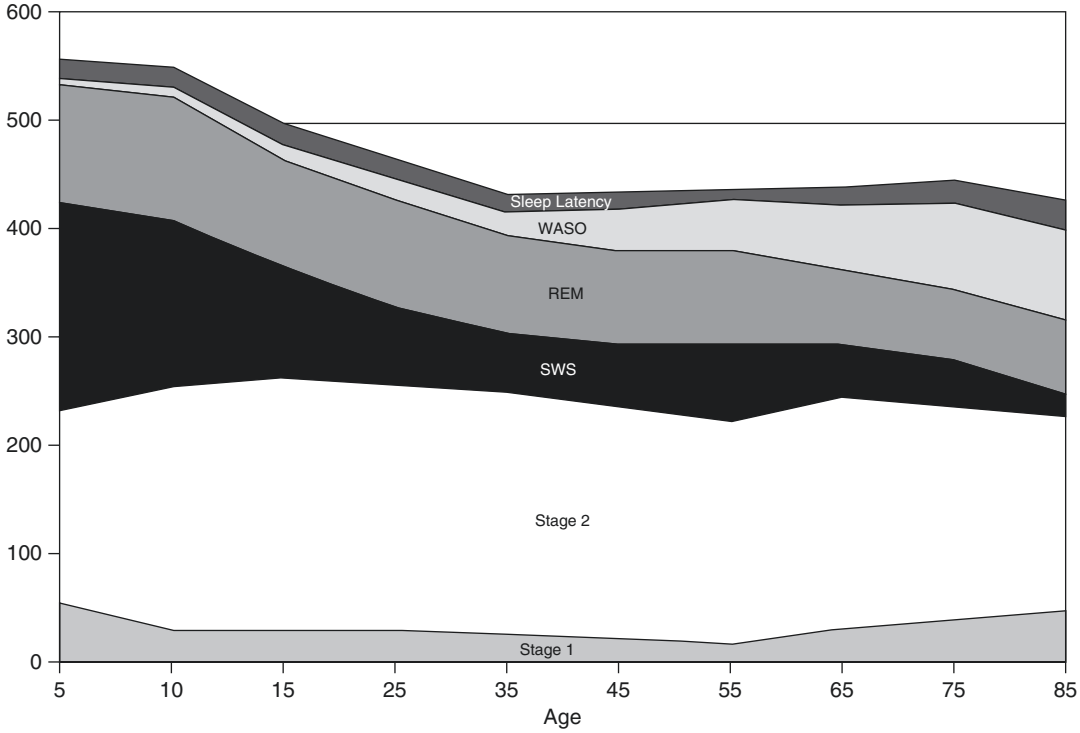

Fig. 40.1 The evolution with age of the different sleep stages. Age-related trends for Stage 1 (N1) sleep, Stage 2 (N2) sleep, SWS (slow wave sleep, N3), REM (rapid eye movement) sleep, WASO (wake after sleep onset), and sleep latency in minutes. From Ohayon et al. (2004), with permission

These systems include serotonergic neurons (dorsal raphe nucleus), noradrenergic neurons (locus coeruleus), histaminergic neurons (tuberomammillary nucleus), dopaminergic neurons (ventral periaqueductal gray), cholinergic neurons (basal forebrain), and orexin (perifornical region of the hypothalamus) (Sowho et al. 2014). These systems influence respiration through projections onto the medulla, pons, and spinal cord. NREM sleep is a dynamic process generated by activity from the ventrolateral preoptic area, the hypothalamus, and basal forebrain (Horner 2011). REM sleep is characterized by a decrease in serotonin and noradrenergic neuron activity, which leads to a loss of inhibition to the pedunculopontine tegmental and laterodorsal tegmental nuclei (Horner 2011; Saper et al. 2005). This leads to acetylcholine release in the pontine reticular formation, which promotes REM sleep (Sowho et al. 2014). Neurotransmitters, neuropeptides, immunomodulators, and hormones generated and maintained by specific neural networks during wakefulness, NREM sleep, and REM sleep are summarized in Table 40.4. Other chemicals like enkephalins, growth hormone, prolactin, and vasoactive intestinal peptide also regulate sleep and wakefulness.

40.1.4 Breathing Effect During Sleep

The respiratory system is a complex interaction between the central nervous system, respiratory motor neurons, and respiratory muscles. The primary purpose of the ventilatory control system is to regulate the exchange of respiratory and blood gases, particularly arterial CO_2 ($PaCO_2$), within a relatively narrow range (Table 40.5). Several processes are responsible for regulating ventilation during wakefulness and include metabolic control, behavioral control, and the wakefulness stimulus (Wellman and White 2011). During wakefulness, the volitional and metabolic pathways are active to determine the minute ventila-

Table 40.4 Central nervous system centers and neurotransmitters associated with states of wakefulness and sleep

State	CNS centers	Neurotransmitters
Wakefulness	Dorsal raphe nucleus	Serotonin
	Locus coeruleus	Norepinephrine
	Tuberomammillary nucleus	Histamine
	Ventral periaqueductal gray	Dopamine
	Basal forebrain	Acetylcholine
	Hypothalamus–perifornical region	Orexin
Non-rapid eye movement	Ventrolateral preoptic area	γ-Aminobutyric acid
	Hypothalamus	Galanin
	Basal forebrain	
Rapid eye movement	Pedunculopontine tegmentum	Serotonin
	Laterodorsal tegmentum	Norepinephrine
	Pontine reticular formation	Acetylcholine
	Medullary reticular formation relay neurons	Glycine

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Table 40.5 Normative arterial blood gas values

Blood gas analyte	Normal ranges	Value meaning and interpretation
Arterial carbon dioxide partial pressure ($Paco_2$)	35–45 mm hg	An indicator of metabolic production of CO_2. Hypercapnia refers to an elevated $Paco_2$ owing to hypoventilation. Hypocapnia refers to a reduced $Paco_2$ owing to hyperventilation
Arterial oxygen partial pressure (Pao_2)	75–100 mm hg	Intermittent or sustained reductions in Pao_2 indicate poor oxygenation or hypoxemia
pH	7.34–7.44	Hydrogen ion concentration [H^+]. increased levels result in alkalemia (pH > 7.45). Decreased levels result in acidemia (pH < 7.35)
H^+	35–45 nmol/L	$H^+ > 45$: Acidemic or $H^+ < 35$: alkalemic
HCO_3^-	22–26 mEq/L	Bicarbonate ion (HCO_3^-) is a blood CO_2-buffering electrolyte. Low HCO_3^- results in metabolic acidosis. High HCO_3^- results in metabolic alkalosis

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tion required to maintain eucapnia. With the onset of sleep, behavioral control and wakefulness stimuli decrease and metabolic control becomes the primary stimulus for ventilation (Sowho et al. 2014). The onset of sleep leads to a significant reduction of compensatory mechanisms that can promote hypoventilation and the development of sleep-related breathing disorders. Ventilatory motor output during sleep decreases from its normal levels in wakefulness, which leads to decreased tidal volume and minute ventilation. The decrease in ventilation is accompanied by a decrease in the upper airway dilator muscle activity, resulting in decreased upper airways caliber and increased airflow resistance. These biological changes may explain the increase in PaCO2 and decrease in PaO2 during sleep, despite the decrease in overall metabolic rate during sleep. In contrast to NREM sleep, REM sleep is characterized by variability in ventilation. Because of this variability, it has been shown that the minute ventilation in REM sleep is the same, increased, or decreased compared to NREM sleep (Badr 2012).

Chemosensitivity is influenced by changes in neural activity during sleep. Thus, hypoxic and hypercapnic chemoresponsiveness contributes to maintaining ventilation during sleep. Conversely, hypocapnia is a potent inhibitor of ventilation during NREM sleep and a key mechanism of central apnea (Badr 2012; Skatrud and Dempsey 1983). The sleep state in human adults is characterized by a reduced ventilatory response to hypercapnia compared to wakefulness. While the sensitivity to $PaCO_2$ does not seem to differ within NREM sleep stages, the ventilatory response to hypercapnia (hypercapnic ventilatory response, HCVR) is further depressed during REM stage compared

to NREM sleep (Berthon-Jones and Sullivan 1984). Similarly, hypoxic ventilatory response (HOVR) is also diminished during NREM sleep compared to wakefulness, with a further decrease in REM sleep (Hedemark and Kronenberg 1982). The etiology of the decline of chemoreceptor responsiveness with NREM sleep remains controversial (Sowho et al. 2014). Reduced $PaCO_2$ is a powerful inhibitor of ventilation during sleep. Therefore, central apnea develops when $PaCO_2$ is reduced below a highly reproducible hypocapnic apneic threshold, which is unmasked by NREM sleep (Skatrud and Dempsey 1983). Hypocapnia is probably the most important inhibiting factor during NREM sleep. Hypocapnia, secondary to hyperventilation, is key to the genesis of central sleep apnea in congestive heart failure, and idiopathic central sleep apnea, and can also be relevant for the pathogenesis of obstructive sleep apnea (Badr 2012). Hypoxia is considered a poor arousal stimulus in humans, both in NREM and REM sleep. Individuals can remain asleep even with oxygen saturation as low as 70% during REM and NREM sleep (Berthon-Jones and Sullivan 1984).

40.1.5 Sleep Effect on Upper Airway

The upper airway extends from the external entrance of the nares and the oral cavity to the glottis at the entrance of the larynx (Ayappa and Rapoport 2003). The muscles of the upper airway consist of 24 pairs of striated muscles that extend from the nares to the larynx (Horner 1996). There are at least ten muscles that are classified as pharyngeal dilators. The upper airway is traditionally divided into 4 anatomic regions (Fig. 40.2): (1) nasopharynx (from the posterior nasal choanae to the caudal margin of the hard palate), (2) velopharynx (from the cranial to caudal margin of the soft palate), (3) oropharynx (from the tip of the

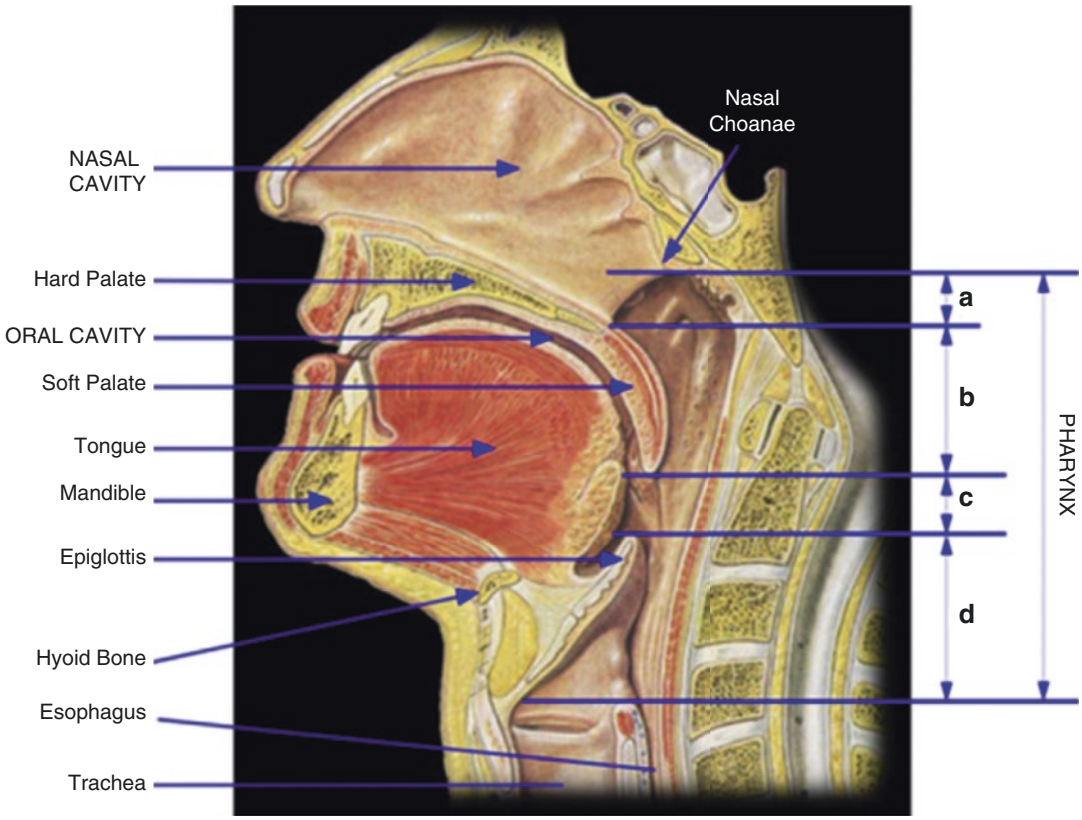

Fig. 40.2 Upper airway anatomy and 4 anatomical regions: (**a**) Nasopharynx, (**b**) velopharynx, (**c**) oropharynx, and (**d**) hypopharynx. From Sowho et al. (2014), with permission

soft palate to the tip of the epiglottis), and (4) hypopharynx (from the cranial margin of the epiglottis to the glottis) (Sowho et al. 2014). Except for the dorsal support provided by the posterior vertebral column, the upper airway has no bony or cartilaginous support, making it highly deformable and prone to collapse during sleep, which can lead to a sleep-disordered breathing. The most deformable region of the upper airway and therefore at risk of collapse is the velopharynx, followed by the oropharynx (Isono et al. 1985, 1996; Oliven et al. 2010; Sowho et al. 2014).

The consequences of loss of wakefulness at the onset of sleep are decreased activity of upper airway dilators, decreased upper airway lumen size, increased upper airway resistance, loss of load compensation, and increased pharyngeal compliance and collapsibility. Ultimately, these changes lead to reduced tidal volume and hypoventilation. During NREM sleep, the available evidence suggests a reduction in either the tonic or phasic activity for a variety of upper airway muscles (Horner 1996), including the levator palatini, tensor palatini, palatoglossus, and geniohyoid. The effect of REM sleep on upper airway muscle activity is more apparent, with strong evidence that activity of phasic upper airway dilating muscles, such as the genioglossus, is significantly attenuated during REM sleep, particularly during periods of phasic REMs (Badr 2012; Wiegand et al. 1985).

40.2 Sleep Disorders in Spinal Cord Injuries

40.2.1 Changes in Respiratory Physiology During Sleep

Hypoventilation and resulting hypoxia occur normally during sleep, particularly in REM sleep. Spinal cord injuries result in a number of pathophysiological changes causing impaired ventilation that deteriorates during sleep, in part due to a normally lower hypoxic and hypercapnic ventilatory drive during sleep. During non-REM (NREM) sleep, the minute ventilation in healthy adults is reduced by 0.4 to 1.5 L/min with a mean reduction in tidal volume by 132 mL (Bulow 1963; Douglas et al. 1982a; Sowho et al. 2014), which leads to an increase in PCO2 by 3 to 7 torr (Douglas et al. 1982a). In REM sleep, hypercapnic respiratory drive is reduced by 70% compared with waking state, so that hypoventilation related to REM sleep can often occur in predisposed individuals (Douglas et al. 1982b). The hypoxic ventilatory drive is also reduced by 40% in NREM sleep compared to waking state and by a further 50% during REM sleep (Douglas et al. 1982b). In phasic REM sleep, alveolar ventilation is reduced by 10–25% compared to waking state (Douglas et al. 1982b). Thus, in patients with spinal cord injuries, ventilatory impairment can be expected to worsen during sleep, especially during REM sleep (Castriotta et al. 2012).

40.2.2 Sleep-Disordered Breathing in Spinal Cord Injuries

Sleep-related breathing disorders are divided into four sections: obstructive sleep apneas, central sleep apnea syndromes, sleep-related hypoventilation disorders, and sleep-related hypoxemia disorder (Sateia 2014). The *International Classification of Sleep Disorders, Third Edition* (ICSD-3), emphasizes that obstructive respiratory disturbance includes not only obstructive apnea and hypopnea but also respiratory effort-related arousal (Sateia 2014). Sleep-disordered breathing (SDB) is very common after spinal cord injury. These include the increased frequency of obstructive sleep apnea (Giannoccaro et al. 2013), increased hypoventilation at sleep onset (Bascom et al. 2015), nocturnal hypoventilation due to reduced ventilatory drive during sleep and/or respiratory muscle paralysis, central sleep apnea, and a narrow CO2 reserve, a marker of increased susceptibility to central sleep apnea in cervical spinal cord injuries (Sankari et al. 2014, 2019a). The CO2 reserve is the measure of the magnitude of hypocapnia that is required to induce central apnea. Zolpidem does not affect breathing in terms of occlusion pressure, ventilation, PCO2, SaO2, ventilatory response to CO2,

or respiratory disturbance index. Therefore, it is unlikely that zolpidem affected the CO2 reserve or the apnea threshold. Drugs such as opioids, muscle relaxants, or nicotine use can affect breathing in patients with spinal cord injuries during sleep. Opioids in particular can affect breathing patterns and precipitate central sleep apnea (Sankari et al. 2014). The prevalence of obstructive sleep apnea in chronic tetraplegia ranges from 56% to 74% (Leduc et al. 2007; Sankari et al. 2014) which is higher than in people over the age of 40 without disability (up to 50% in men and 23% in women) (Heinzer et al. 2015). Obesity, cardiovascular morbidity, and diabetes are common in spinal cord injuries, increasing the possibility that unrecognized SDB may contribute to these comorbidities (Bauman et al. 2016).

Sleep-disordered breathing seems to develop quickly after the onset of spinal cord injury (Berlowitz et al. 2005). Chronically, SDB in people with spinal cord injuries has a prevalence of 40–91% (Sankari et al. 2014). Several mechanisms predispose to the development of SDB in spinal cord injuries. These include increased upper airway collapsibility, a reduced dilator muscle responsiveness/effectiveness, a reduced arousal threshold, and an unstable ventilatory control system (Sankari et al. 2014, 2019a). The increased collapsibility of the upper airway can be related to a variety of anatomical and physiological factors such as obesity, age, BMI, neck circumferences, medications including sedatives, muscle relaxants, spasticity medication, and narcotics (Sankari et al. 2019a). The severity of SDB is classified by the apnea-hypopnea index (AHI), which is the number of episodes of cessation of breathing (apnea) and reductions in airflow (hypopnea) associated with desaturation of 3 or 4% or arousal per hour of sleep (Sankari et al. 2019a). Conventionally, a value of less than 5 events/h is usually considered within normal limits, between 5 and 15 events/h mild, 15 and 30 events/h moderate, and at least 30 events/h severe (Ayas et al. 2016). In a recent meta-analysis, the reported SDB prevalence rates in people with tetraplegia were between 46 and 97%. The prevalence of at least mild (AHI $\geq$ 5) was 83%, moderate (AHI $\geq$ 15) 59%, and severe (AHI $\geq$ 30) SDB 36% (Graco et al. 2021).

People with chronic spinal cord injury and SDB suffer from reduced cognitive function associated with nocturnal arterial hypoxemia and sleep fragmentation due to sleep apnea, which can be observed early after injury. Nocturnal hypoxia affects daytime cognitive function in people with chronic spinal cord injury and SDB, especially attention, concentration, memory, and learning skills (Sajkov et al. 1998). People with SDB often report poor sleep quality and daytime sleepiness. A person with acute tetraplegia and undiagnosed or untreated SDB is less able to participate in rehabilitation due to sleepiness and fatigue (Sankari et al. 2019a). Treatment with continuous positive airway pressure (CPAP) significantly improves daytime sleepiness in the general population with SDB (Patel et al. 2003). Untreated SDB is strongly associated with the incidence of cardiovascular and cerebrovascular disease including hypertension, strokes, and myocardial infarction (Ayas et al. 2016). Given the high rates of cardiovascular disease in people with spinal cord injuries, the associations between SDB and cardiovascular risks in spinal cord injuries need to be further investigated (Sankari and Badr 2016).

40.2.3 Effects of Circadian Rhythm Sleep–Wake Disorders

Unlike cortisol and thyroid-stimulating hormone (TSH), which have a circadian rhythm, melatonin is believed to be influenced by the suprachiasmatic nuclei primarily via an efferent neural pathway through the brain and spinal cord, with innervation of the pineal gland by the superior cervical ganglia (Zeitzer et al. 2000). Melatonin has been used as a marker of the central circadian pacemaker in humans. Melatonin, the main brain-derived hormone governing circadian variations, is highly associated with daylight patterns (Kostovski et al. 2018). A complete cervical spinal cord injury, which cuts the suprachiasmatic nuclei to superior cervical ganglion pathway, is

associated with an almost complete abolition of circadian melatonin rhythm and a significantly reduced circulating level (Kostovski et al. 2018; Zeitzer et al. 2000). This means that the circadian rhythm of melatonin is disrupted in tetraplegia (Sankari et al. 2019a). The normal circadian rhythm is that light striking the retina during the daytime stimulates afferent pathways through the suprachiasmatic nuclei which in turn pass to the superior cervical ganglion and onward to the pineal gland to inhibit melatonin production, and darkness removes this inhibition and melatonin production ensues (Sankari et al. 2019a). Melatonin levels range from ~10 pg/mL at the end of the light period up to 200 pg/mL near the midpoint of the dark period in healthy adults, whereas in tetraplegic subjects the corresponding values are closer to 2 and 15 pg/mL (Kostovski et al. 2018).

Other endocrine rhythms that are similarly changed by circadian influences, such as cortisol and TSH, are not markedly affected by cervical spinal cord injury, but the temperature is affected (Sankari et al. 2019a; Thijssen et al. 2011). For reference, the circadian rhythm of cortisol and TSH is as follows. Cortisol, which is controlled by neurohumoral signaling in the hypothalamus–pituitary–adrenal axis, is a pulsatile hormone secreted with daily rhythmicity, so that its lowest level occurs a few hours before bedtime, and it reaches its peak just after wake time. Similarly, TSH is controlled by neurohumoral signaling in the hypothalamus–pituitary–thyroid axis so that it is secreted with a daily sinusoidal pattern that begins a few hours before bedtime (Czeisler and Klerman 1999). Peak levels of TSH can be seen with sleep deprivation, but are suppressed by sleep (Zeitzer et al. 2000).

40.2.4 Sleep-Related Movement Disorders

Sleep-related movement disorders are conditions that are characterized by simple, usually stereotyped movements occurring during sleep that disturb sleep. Sleep-related movement disorders in the ICSD-3 include restless legs syndrome, periodic limb movement disorder, sleep-related leg cramps, sleep-related bruxism, sleep-related rhythmic movement disorder, benign sleep myoclonus of infancy, propriospinal myoclonus at sleep onset, sleep-related movement disorder due to a medical disorder, sleep-related movement disorder due to a medication or substance, and sleep-related movement disorder, unspecified (Sateia 2014).

Periodic leg movements and restless legs syndrome can lead to significant disturbance in sleep quality and are typically associated with excessive daytime sleepiness (Dickel et al. 1994; Peters et al. 2018; Sankari et al. 2019a). Periodic limb movement is diagnosed when the frequency of limb movements in adults is 15/h. The periodic limb movements must be accompanied by sleep disturbance or other functional impairments in order to make diagnosis (Sateia 2014). The prevalence of periodic leg movement disorder appears to be significantly increased in people with spinal cord injuries. The prevalence in people with a lesion above T10 has been reported to be approximately 50–100% (Dickel et al. 1994; Sankari et al. 2019a). Periodic leg movements are characterized by periodic episodes of repetitive, nonepileptiform movement of the legs, and highly stereotyped limb movements, typically extension of the great toe and ankle, often accompanied by knee and hip flexion. Periodic leg movements are often preceded by sensorimotor symptoms that occur in the evening and before sleep, or when lying down, known as restless legs syndrome (Levy et al. 2018). Mechanism of periodic leg movement is not well understood, but it is likely that dopaminergic descending pathways are involved (Clemens et al. 2006). Some studies have hypothesized that periodic leg movements in people with spinal cord injuries originate within the spinal cord, in a central pattern generator. Periodic leg movements in people with spinal cord injuries, particularly during REM sleep, could be related to the disruption of REM sleep-related inhibitory spinal pathways, which cause the disconnection or disinhibition of a spinal generator or pacemaker similar to subconscious gait integration (Dickel et al. 1994).

Restless legs syndrome (Willis-Ekbom disease) is characterized by uncomfortable leg sensations, usually prior to sleep onset (Dickel et al. 1994; Peters et al. 2018). The diagnosis of restless legs syndrome in adults involves abnormal uncomfortable and unpleasant limb sensations (paresthesia) that can decrease with motor activity, worsen at rest, and occur primarily or worsen during the evening or night, and the condition is not better explained by another sleep disorder, medical or neurological disorder (Clemens et al. 2006). This movement disorder is very common in the elderly. The peak prevalence is between 60 and 69 years for women and between 50 and 59 years for men (Bliwise and Scullin 2017). Up to 80% of restless legs syndrome patients also suffer from periodic leg movement syndrome, defined as five or more periodic leg movement events per hour of sleep (Ferri et al. 2015). Both phenomena are alleviated by dopaminergic agents, dopamine D2-like receptor agonists, particularly the non-ergot-derived, D3 receptor-preferring agents (Clemens et al. 2006).

40.2.5 Insomnia

Before 2014, insomnia was divided into primary insomnia and secondary (i.e., comorbid) insomnia disorder. Primary insomnia was previously further divided into psychophysiologic, idiopathic, and paradoxical (sleep-state misperception) insomnia disorders. The ICSD-3 abandoned the classification of insomnia into subtypes and consolidated all insomnia diagnoses (i.e., primary and comorbid) under a single, chronic insomnia disorder (Sateia 2014). The ICSD-3 also eliminated the severity criteria. The insomnia diagnoses for ICSD-3 are chronic insomnia disorder, short-term insomnia disorder, and other insomnia disorders.

Chronic insomnia includes the difficulty initiating sleep or maintenance difficulty, despite having adequate opportunity and circumstances to sleep, along with a report of experiencing daytime consequences (Perez and Salas 2020; Sateia 2014). The ICSD-3 duration criterion for chronic insomnia disorder is 3 months, and frequency criterion (at least 3 times per week) has been added. Insomnia is highly prevalent in the general population, with estimates between 15 and 30%, and women are 1.4 times more like to have insomnia than men. Insomnia symptoms in people with spinal cord injuries were reported to be 57% (Shafazand et al. 2019).

40.3 Evaluation of Sleep Disorders in Spinal Cord Injuries

Due to the high prevalence of sleep disorders associated with spinal cord injuries, sleep-related complaints need to be further evaluated so that appropriate treatment can be initiated. Common symptoms are daytime fatigue/sleepiness, poor sleep quality, nocturnal awakenings, and apneas. These symptoms are nonspecific and further investigation is usually required to identify the correct diagnosis. The gold standard for diagnosing SDB and periodic leg movement is nighttime polysomnography in the sleep laboratory. The polysomnography records the following signals: (1) 6-channel electroencephalogram (EEG); (2) two electrooculogram (first electrode being placed 1 cm above the outer canthus, the second one 1 cm below the inner canthus of the opposite eye, the contralateral mastoid being the neutral reference electrooculography); (3) electromyography (EMG) recordings of the submentalis and both tibialis anterior muscles; and (4) electrocardiography (ECG); (5) sleep respiratory patterns (oral and nasal airflow thermistors), transcutaneous oxygen saturation, and expiratory capnogram (Sankari et al. 2019a). In fact, most sleep laboratories are not equipped to monitor patients with spinal cord injury overnight while managing pressure injuries or other medical problems in patients with spinal cord injury. Sleep laboratories would not have to meet the special needs of a disabled person with labor-intensive regimens of drugs and bowel/bladder/wound care. Additionally, individuals would not have to forgo sleeping in specialized wound care beds or access to specialized equipment for safe lifting and transfers. There is increasing evidence that home-based sleep apnea tests are as effective as facility-

based polysomnography in predicting short-term responses to treatment for obstructive sleep apnea. For home sleep apnea test, oximetry and transcutaneous CO_2 monitoring can be used, with a definition of oxygen desaturation as SPO_2 of ≤88% for ≥5% of the recording time and hypercapnia as tc-PCO_2 of ≥50 mmHg for ≥5% of the recording time (Bauman et al. 2016).

As in the American Academy of Sleep Medicine guidelines (Berry et al. 2012), apneas were defined as ≥10 s with no nasal airflow and hypopneas as ≥10 s of ≥50% reductions in airflow, relative to the pre-event baseline (Table 40.6). The obstructive apnea/hypopnea index (AHI) is expressed as the number of obstructive events (apneas plus hypopneas) per hour of recording time. Events in which baseline airflow was insufficient to measure a 50% reduction were classified as nonspecific hypopnea events. An AHI of ≥5 events/h was chosen as the threshold value for the diagnosis of obstructive sleep apnea (Bauman et al. 2016).

The quantification of periodic leg movements requires a nocturnal polysomnography to record the typical periodic contractions of the tibialis anterior muscle (Levy et al. 2018). During sleep, leg movements were interpreted as periodic leg movement if they lasted 0.5 s with at least 4 consecutive movements, and every 5–90 s (Berry et al. 2012). Periodic leg movements are thus clearly distinct from spasms, clonus, or habitual foot tapping. A pathological periodic leg movement (PLM) index is considered to be equal to or higher than 15 events/h (Levy et al. 2018). Serum levels of iron and ferritin are measured to exclude periodic leg movement and restless legs syndrome secondary to iron deficiency.

Sleepiness is defined as an increased physiologic drive to all asleep. Sleepiness can be assessed either subjectively or objectively. The most common measure of subjective sleepiness is the Epworth Sleepiness Scale, a validated 8-question survey asking the perceived likelihood of falling asleep in various situations (Johns

Table 40.6 Adult scoring rules of sleep and associated events: The 2007 AASM sleep apnea definitions

Respiratory event	Definition (Consensus)
Apnea rule	Score a respiratory event in adults as an apnea if both of the following are met: 1. There is a drop in the peak signal excursion by ≥90% of pre-event baseline using an oronasal thermal sensor (diagnostic study), positive airway pressure device flow (titration study), or an alternative apnea sensor. 2. The duration of the ≥90% drop in sensor signal is ≥10 seconds.
Hypopnea rule	Score a respiratory event as a hypopnea if all of the following are met: 1. The peak signal excursions drop by ≥30% of pre-event baseline using nasal pressure (diagnostic study), PAP device flow (titration study), or an alternative hypopnea sensor. 2. The duration of the ≥30% drop in signal excursions is ≥10 s. 3. There is ≥3% oxygen desaturation from pre-event baseline or the event is associated with an arousal.
Respiratory effort-related arousal rule (RERA)	If electing to score respiratory effort-related arousals, score a respiratory event as a RERA if there is a sequence of breaths lasting at least 10 s characterized by increasing respiratory effort or by flattening of the inspiratory portion of the nasal pressure (diagnostic study) or PAP device flow (titration study) waveform leading to arousal from sleep when the sequence of breaths does not meet criteria for an apnea or hypopnea.
Hypoventilation rule	If electing to score hypoventilation, score hypoventilation during sleep if either of the below occur: 1. There is an increase in the arterial $PaCO_2$ (or surrogate) to a value >55 mmHg for ≥10 min. 2. There is ≥10 mmHg increase in $PaCO_2$ (or surrogate) during sleep (in comparison to an awake supine value) to a value exceeding 50 mmHg for ≥10 min.
Cheyne-stokes breathing rule	Score a respiratory event as Cheyne-stokes breathing if both of the following are met: 1. There are episodes of at least 3 consecutive central apneas and/or central hypopneas separated by a crescendo and decrescendo change in breathing amplitude with a cycle length of at least 40 s (typically 45 to 90 s). 2. There are 5 or more central apneas and/or central hypopneas per hour associated with the crescendo/decrescendo breathing pattern recorded over a minimum of 2 h of monitoring.

1991). The Epworth Sleepiness Scale score ≥ 11 is defined as significant sleepiness. The most commonly used measures of objective sleepiness are the multiple sleep latency test and the maintenance of wakefulness test (Patel et al. 2003).

40.4 Management of Sleep Disorders in Spinal Cord Injuries

40.4.1 Management of Obstructive Sleep Apnea

Obstructive sleep apnea is characterized by recurrent upper airway collapse during sleep, leading to sleep fragmentation and oxyhemoglobin desaturation. Treatment of SDB including obstructive sleep apnea in people with spinal cord injuries is challenging, although substantial symptomatic improvements can be seen in many patients. The most commonly used treatment for SDB is CPAP, which consists of a mask attached to the nose/face that administers a positive pressure to the upper airways to prevent their collapse and obstructive events during sleep and is effective in improving oxygenation (Sankari et al. 2019a). By increasing the intraluminal pressure in the pharynx, CPAP maintains the upper airway patency in patient with obstructive sleep apnea by acting as a pneumatic splint that prevents collapse of the pharyngeal airway. The patency of the pharyngeal airway depends on the balance between the intraluminal and extraluminal forces acting in opposite directions (Bhadriraju and Collop 2012). CPAP can increase upper airway volume by up to 28% (Abbey et al. 1989).

There are many options available when initiating CPAP. The current standard is to perform a single overnight polysomnogram while the patient is monitored so that the attendant can increase the CPAP levels to progressively eliminate breathing disorders. However, split night studies, autotitrating PAP devices, and other empiric methods for initiating CPAP are also available (Bhadriraju and Collop 2012). The CPAP is generally initiated at a setting of 5 cmH2O after appropriate mask fit. The CPAP setting is titrated in increments of 1–2 cmH2O at a time. Obstructive sleep apnea tends to be more severe in the supine position and during REM sleep, and achieving adequate pressure setting in the supine position and during REM sleep is an important consideration. The titration is based on resolution of snoring, resolution or significant improvement of the airflow pattern and apneas and hypopneas, as well as patient's tolerance. Autotitrating PAP (APAP) has been advocated as an alternative to conventional CPAP titration. APAP reduced the mean pressure by 2.2 cmH2O. However, APAP and standard CPAP were similar in terms of adherence and their ability to eliminate respiratory events and to improve subjective sleepiness. Since APAP is more costly than standard CPAP, APAP cannot currently be recommended as a first-line therapy for all patients with obstructive sleep apnea (Ayas et al. 2004).

Other ventilator modes such as bilevel therapy (bilevel PAP, BiPAP) can be used. Bilevel PAP involves setting different inspiratory (IPAP) and expiratory pressures (EPAP). A bilevel setting may be appropriate in patients who have persistent hypoxemia due to obesity hypoventilation syndrome or intrinsic pulmonary disorders. Bilevel PAP is typically initiated by using the CPAP level that eliminated the obstructive apneas as the EPAP and EPAP +3–5 cmH2O as the IPAP (Bhadriraju and Collop 2012). Bilevel PAP may worsen central apneas in patients with obstructive sleep apnea and increase the frequency of Cheyne-Stokes respiration (CSR) and non-CSR central apneas and thus may be less desirable than CPAP for its treatment (Johnson and Johnson 2005).

In addition, lifestyle modifications, including exercise, weight loss, smoking cessation, and avoidance of sedatives, should be encouraged as these have positive effects on SDB in the general population (Bauman et al. 2016; Graco et al. 2018). Patients with untreated obstructive sleep apnea are at increased risk for developing hypertension, and treatment with PAP lowers blood pressure, although the overall effects are relatively modest (about 2 mmHg) (Fatureto-Borges et al. 2016).

40.4.2 Management of Restless Limbs Syndrome

Non-pharmacologic treatments of restless limbs syndrome include improving sleep hygiene, as well as daytime exercise, warm baths, leg massage, and acupuncture. Medications that can worsen restless limbs syndrome should be discontinued, and secondary causes should be investigated and treated as this may improve the degree of symptoms. Iron therapy is recommended for iron deficiency. Vitamin C can improve iron absorption.

Restless limbs syndrome has been treated primarily by four classes of medications, which include dopaminergic agents, anticonvulsants, benzodiazepines, and opioids although other agents have also been used. Levodopa, ropinirole, pramipexole, cabergoline, pergolide, and gabapentin are effective in treating restless limbs syndrome, while rotigotine, bromocriptine, oxycodone, carbamazepine, valproic acid, and clonidine are likely also effective (Badr 2012; Trenkwalder et al. 2008). Levodopa/benserazide or levodopa/carbidopa at dosages of 100/25 to 200/50 mg is considered effective for the treatment of restless limbs syndrome. The dopamine agonists ropinirole and pramipexole are FDA approved for the treatment of restless limbs syndrome. Ropinirole (0.25–4 mg, mean 2 mg) and pramipexole (0.75 mg) are effective in treating restless limbs syndrome in patients with moderate to severe symptoms. Antiepileptics that are used in the treatment of restless limbs syndrome include carbamazepine, gabapentin, pregabalin, and lamotrigine. Of the benzodiazepines, clonazepam is best documented for treatment of restless limbs syndrome (Badr 2012).

40.4.3 Management of Periodic Leg Movements

Periodic leg movements predominate in nonrapid eye movement (NREM) sleep in the general population, but in contrast, a number of case reports and series in spinal cord injury suggest that periodic leg movements are observed during REM sleep and with no clear periodicity (de Mello et al. 1996; Dickel et al. 1994; Ferri et al. 2015; Peters et al. 2018). This observation strongly suggests that periodic leg movement after spinal cord injury occurs peripherally rather than centrally (Sankari et al. 2019a). Periodic leg movement mechanism is not as well understood, but it is likely that dopaminergic descending pathways are involved (Clemens et al. 2006). Accordingly, dopamine agonists are the first line of treatment. Medication treatment for periodic leg movements is similar to that of restless limbs syndrome and includes dopaminergic agents, anticonvulsants, benzodiazepines, and opioids (Badr 2012). One study suggested the possibility that spasticity was, in fact, undiagnosed and/or untreated periodic leg movements, showing significant reduction in periodic leg movement (PLM) index and arousals from sleep in patients with confirmed periodic leg movement ($\geq$15 per hour of sleep) treated with a low dosage of pramipexole (Levy et al. 2018). Periodic leg movement and restless limbs syndrome after physical activity are inhibited during sleep, so physical activity improves the sleep patterns of people with spinal cord injuries (de Mello et al. 1996).

40.4.4 Management of Insomnia

There are several challenges in treating insomnia disorder in people with spinal cord injuries. Pharmacological agents have a number of adverse effects that can be even more significant among people with spinal cord injuries. For example, fall risk among those who ambulate may be further increased and cognition impairment may be exacerbated. Because of these and other concerns, pharmacological therapy is recommended only after attempting cognitive-behavioral therapy for insomnia (CBT-I) (Mehta et al. 2011; Sankari et al. 2019a). CBT is a frequently used treatment for psychosocial issues. CBT incorporates a variety of techniques to facilitate a person's emotional and behavioral change. Several common techniques used in CBT include cognitive restructuring, increasing the person's access and willingness to engage in rewarding activities,

various forms of relaxation training, problem-solving strategies, as well as training in assertiveness and coping skills (Mehta et al. 2011).

Any strategy for the effective treatment of primary and comorbid insomnia should appropriately combine both pharmacological and non-pharmacological measures. In patients with comorbid insomnia, the underlying disorder needs to be assessed and treated appropriately (Monti 2017). Several classes of drugs have been prescribed as hypnotics over the years, including the benzodiazepine receptor agonists (either benzodiazepinic or non-benzodiazepinic agents); melatonin and the melatonin agonist ramelteon; and the tricyclic antidepressant doxepin. Pharmacologic treatments for insomnia including benzodiazepine receptor agonists and a melatonin receptor agonist are summarized in Table 40.7.

A 2008 American Academy of Sleep Medicine (AASM) clinical guideline for the evaluation and management of chronic insomnia recommended short/intermediate acting benzodiazepine receptor agonists (benzodiazepines or benzodiazepine receptor agonistic modulators) or ramelteon as first-line pharmacotherapy. Other drugs, such

Table 40.7 Pharmacologic treatments for insomnia

Medication	Doses (mg)	Half-life (h)	Sleep indications	Common side effects
Benzodiazepines				
Estazolam	1, 2	8–24	Short-term treatment of sleep-onset and sleep-maintenance insomnia	Somnolence, hypokinesia, dizziness, abnormal coordination
Flurazepam	15, 30	48–120	Treatment of sleep-onset and sleep-maintenance insomnia	Dizziness, drowsiness, lightheadedness, staggering, loss of coordination, falling
Quazepam	7.5, 15	48–120	Treatment of sleep-onset and sleep-maintenance insomnia	Drowsiness, headache
Temazepam	7.5, 15, 22.5, 30	8–20	Short-term treatment of sleep-onset insomnia in adults	Drowsiness, dizziness, lightheadedness, difficulty with coordination
Triazolam	0.125, 0.25	2–4	Short-term treatment of sleep-onset and sleep-maintenance insomnia	Drowsiness, headache, dizziness, lightheadedness, pins and needles feelings on skin, difficulty with coordination
Benzodiazepine receptor agonists				
Eszopiclone	1, 2, 3	5–7	Treatment of sleep-onset and sleep-maintenance insomnia	Unpleasant qustatory and metallic taste in mouth, dry mouth, drowsiness, dizziness, headache, symptoms of the common cold
Zaleplon	5, 10	1	Short-term treatment of sleep-onset insomnia	Drowsiness, lightheadedness, dizziness, “pins and needles” feeling on skin, difficulty with coordination
Zolpidem	5, 10	1.5–2.4	Short-term treatment of sleep-onset and sleep-maintenance insomnia	Drowsiness, dizziness, diarrhea, drugged feelings
Melatonin receptor agonist				
Ramelteon	8	1.0–2.6	Treatment of sleep-onset insomnia	Drowsiness, tiredness, dizziness
Heterocyclics				
Doxepin	3, 6	15.3	Treatment of sleep-maintenance insomnia	Somnolence/sedation, nausea, upper respiratory tract infection
Trazodone	50		**Not suggested** as an option for treatment of sleep-onset or sleep-maintenance insomnia	
Orexin (hypocretin) receptor antagonist				
Suvorexant	10, 15, 20		Treatment of sleep-maintenance insomnia	

as sedating antidepressants or anticonvulsants, have been recommended as second- or third-line drugs, especially if there are comorbidities (e.g., mood disorder or epilepsy). Other, non-prescription drugs such as over-the-counter antihistamine sleep aids and herbal/nutritional agents were not recommended due to a lack of proven efficacy and safety concerns (Sateia et al. 2017; Schutte-Rodin et al. 2008). In summary, drugs recommended for treating sleep-onset insomnia are zolpidem, eszopiclone, triazolam, temazepam, ramelteon, and zaleplon. Eszopiclone, zolpidem, doxepin, temazepam, and suvorexant are recommended for the treatment of sleep-maintenance insomnia. However, these drugs such as melatonin, trazodone, diphenhydramine, tiagabine, L-tryptophan, and valerian are not recommended for treating either sleep-onset or sleep-maintenance insomnia.

The British Association for Psychopharmacology consensus in 2017 (Wilson et al. 2019) recommended a shorter acting drug for sleep-onset insomnia such as zolpidem or melatonin, or a slightly longer acting drug such as eszopiclone for those with awakening throughout the night. TCA has little evidence of efficacy. SSRIs, venlafaxine, mianserin, and mirtazapine increase the risk of restless legs syndrome and periodic limb movements during sleep, and SSRIs can induce or worsen sleep bruxism (Wilson et al. 2019). The 2016 American College of Physicians guideline on the management of chronic insomnia indicates insufficient evidence for effectiveness of benzodiazepines, trazodone, and melatonin in the management of chronic insomnia. Benzodiazepine receptor antagonists, doxepin, and suvorexant showed improvement in a number of sleep outcome variables (Qaseem et al. 2016; Sateia et al. 2017).

40.4.5 Management of Circadian Rhythm Sleep-Wake Disorders

Despite the apparent abnormalities of circadian control in spinal cord injuries and the availability of melatonin, little work has been done to understand its potential therapeutic role in spinal cord injuries, particularly in tetraplegia. People with tetraplegia are essentially 180 degrees from the circadian phase all of the time, and as such, exogenous melatonin at an appropriate time can provide unique opportunities for sleep-onset insomnia and sleep phase entrainment (Sankari et al. 2019a). Exogenous melatonin supplementation in tetraplegia normalizes the expression levels of clock gene mRNAs in peripheral blood (Kostovski et al. 2018).

A delayed sleep phase disorder of circadian disorder is defined as a sleep disorder with a delay in sleep period relative to desired sleep and wake times causing insomnia and difficulty waking up. Treatment of this circadian disorder is recommended with 2000–2500 lx of light for 2–3 h before or at rise time (Badr 2012). The mainstay of pharmacotherapy for delayed sleep phase disorder is melatonin. Melatonin, 1–3 mg, is given 5–7 h before sleep time (Burgess et al. 2010).

References

Abbey NC, Block AJ, Green D, et al. Measurement of pharyngeal volume by digitized magnetic resonance imaging. Effect of nasal continuous positive airway pressure. Am Rev Respir Dis. 1989;140:717–23.

Ayappa I, Rapoport DM. The upper airway in sleep: physiology of the pharynx. Sleep Med Rev. 2003;7:9–33.

Ayas NT, Patel SR, Malhotra A, et al. Auto-titrating versus standard continuous positive airway pressure for the treatment of obstructive sleep apnea: results of a meta-analysis. Sleep. 2004;27:249–53.

Ayas NT, Taylor CM, Laher I. Cardiovascular consequences of obstructive sleep apnea. Curr Opin Cardiol. 2016;31:599–605.

Badr MS, editor. Essentials of sleep medicine. An approach for clinical pulmonology. New York: Humana Press; 2012.

Bascom AT, Sankari A, Goshgarian HG, et al. Sleep onset hypoventilation in chronic spinal cord injury. Physiol Rep. 2015;3:e12490.

Bauman KA, Kurili A, Schotland HM, et al. Simplified approach to diagnosing sleep-disordered breathing and nocturnal hypercapnia in individuals with spinal cord injury. Arch Phys Med Rehabil. 2016;97:363–71.

Berlowitz DJ, Brown DJ, Campbell DA, et al. A longitudinal evaluation of sleep and breathing in the first year after cervical spinal cord injury. Arch Phys Med Rehabil. 2005;86:1193–9.

Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of sleep medicine. J Clin Sleep Med. 2012;8:597–619.

Berthon-Jones M, Sullivan CE. Ventilation and arousal responses to hypercapnia in normal sleeping humans. J Appl Physiol Respir Environ Exerc Physiol. 1984;57:59–67.

Bhadriraju S, Collop N. Nasal continuous positive airway pressure (CPAP) treatment. In: Badh MS, editor. Essentials of sleep medicine. An approach for clinical pulmonology. New York: Humana Press; 2012.

Biering-Sørensen F, Biering-Sørensen M. Sleep disturbances in the spinal cord injured: an epidemiological questionnaire investigation, including a normal population. Spinal Cord. 2001;39:505–13.

Bliwise DL, Scullin MK. Normal aging. In: Chokroverty S, editor. Sleep disorders medicine. Basic science, technical considerations and clinical aspects. 4th ed. New York: Springer; 2017.

Bulow K. Respiration and wakefulness in man. Acta Physiol Scand Suppl. 1963;209:1–110.

Burgess HJ, Revell VL, Molina TA, et al. Human phase response curves to three days of daily melatonin: 0.5 mg versus 3.0 mg. J Clin Endocrinol Metab. 2010;95:3325–31.

Castriotta RJ, Murthy JN. Hypoventilation after spinal cord injury. Semin Respir Crit Care Med. 2009;30:330–8.

Castriotta RJ, Wilde MC, Sahay S. Sleep disorders in spinal cord injury. Sleep Med Clin. 2012;7:643–53.

Chokroverty S. Sleep disorders medicine. Basic science, technical considerations and clinical aspects. 4th ed. New York: Springer; 2017a.

Chokroverty S. Overview of normal sleep. In: Chokroverty S, editor. Sleep disorders medicine. Basic science, technical considerations and clinical aspects. 4th ed. New York: Springer; 2017b.

Clemens S, Rye D, Hochman S. Restless legs syndrome: revisiting the dopamine hypothesis from the spinal cord perspective. Neurology. 2006;67:125–30.

Czeisler CA, Klerman EB. Circadian and sleep-dependent regulation of hormone release in humans. Recent Prog Horm Res 1999;54:97–130; discussion 130-2.

de Mello MT, Lauro FA, Silva AC, et al. Incidence of periodic leg movements and of the restless legs syndrome during sleep following acute physical activity in spinal cord injury subjects. Spinal Cord. 1996;34:294–6.

Dickel MJ, Renfrow SD, Moore PT, et al. Rapid eye movement sleep periodic leg movements in patients with spinal cord injury. Sleep. 1994;17:733–8.

Douglas NJ, White DP, Pickett CK, et al. Respiration during sleep in normal man. Thorax. 1982a;37:840–4.

Douglas NJ, White DP, Weil JV, et al. Hypercapnic ventilatory response in sleeping adults. Am Rev Respir Dis. 1982b;126:758–62.

Elliott TR, Frank RG. Depression following spinal cord injury. Arch Phys Med Rehabil. 1996;77:816–23.

España RA, Scammell TE. Sleep neurobiology from a clinical perspective. Sleep. 2011;34:845–58.

Fatureto-Borges F, Lorenzi-Filho G, Drager LF. Effectiveness of continuous positive airway pressure in lowering blood pressure in patients with obstructive sleep apnea: a critical review of the literature. Integr Blood Press Control. 2016;9:43–7.

Ferri R, Proserpio P, Rundo F, et al. Neurophysiological correlates of sleep leg movements in acute spinal cord injury. Clin Neurophysiol. 2015;126:333–8.

Giannoccaro MP, Moghadam KK, Pizza F, et al. Sleep disorders in patients with spinal cord injury. Sleep Med Rev. 2013;17:399–409.

Graco M, McDonald L, Green SE, et al. Prevalence of sleep-disordered breathing in people with tetraplegia-a systematic review and meta-analysis. Spinal Cord. 2021;59:474–84.

Graco M, Schembri R, Cross S, et al. Diagnostic accuracy of a two-stage model for detecting obstructive sleep apnoea in chronic tetraplegia. Thorax. 2018;73:864–71.

Hammell KW, Miller WC, Forwell SJ, et al. Fatigue and spinal cord injury: a qualitative analysis. Spinal Cord. 2009;47:44–9.

Hedemark LL, Kronenberg RS. Ventilatory and heart rate responses to hypoxia and hypercapnia during sleep in adults. J Appl Physiol Respir Environ Exerc Physiol. 1982;53:307–12.

Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med. 2015;3:310–8.

Horner RL. Motor control of the pharyngeal musculature and implications for the pathogenesis of obstructive sleep apnea. Sleep. 1996;19:827–53.

Horner RL. Respiratory physiology: central neural control of respiratory neurons and motoneurons during sleep. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. St Louis: Elsevier Saunders; 2011.

Isono S, Remmers JE, Tanaka A, et al. Anatomy of pharynx in patients with obstructive sleep apnea and in normal subjects. J Appl Physiol. 1985;(82):1319–26.

Isono S, Remmers JE, Tanaka A, et al. Static properties of the passive pharynx in sleep apnea. Sleep. 1996;19(10 Suppl):S175–7.

Johns MW. A new method of measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14:540–5.

Johnson KG, Johnson DC. Bilevel positive airway pressure worsens central apneas during sleep. Chest. 2005;128:2141–50.

Kostovski E, Frigato E, Savikj M, et al. Normalization of disrupted clock gene expression in males with tetraplegia: a crossover randomized placebo-controlled trial of melatonin supplementation. Spinal Cord. 2018;56:1076–83.

Krassioukov A. Autonomic function following cervical spinal cord injury. Respir Physiol Neurobiol. 2009;169:157–64.

Leduc BE, Dagher JH, Mayer P, et al. Estimated prevalence of obstructive sleep apnea-hypopnea syndrome after cervical cord injury. Arch Phys Med Rehabil. 2007;88:333–7.

Levy J, Hartley S, Mauruc-Soubirac E, et al. Spasticity or periodic limb movements? Eur J Phys Rehabil Med. 2018;54:698–704.

Mehta S, Orenczuk S, Hansen KT, et al. An evidence-based review of the effectiveness of cognitive behavioral therapy for psychosocial issues post-spinal cord injury. Rehabil Psychol. 2011;56:15–25.

Monti JM. General principle of treatment of sleep dysfunction and pharmacology of drugs used in sleep disorders. In: Chokroverty S, editor. Sleep disorders medicine. Basic science, technical considerations and clinical aspects. 4th ed. New York: Springer; 2017.

Norrbrink Budh C, Hultling C, Lundeberg T. Quality of sleep in individuals with spinal cord injury: a comparison between patients with and without pain. Spinal Cord. 2005;43:85–95.

Oliven A, Kaufman E, Kaynan R, et al. Mechanical parameters determining pharyngeal collapsibility in patients with sleep apnea. J Appl Physiol. 2010;109:1037–44.

Ohayon MM, Carskadon MA, Guilleminault C, et al. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep. 2004;27:1255–73.

Patel SR, White DP, Malhotra A, et al. Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis. Arch Intern Med. 2003;163:565–71.

Perez MN, Salas RME. Insomnia. Continuum (Minneap Minn). 2020;26:1003–15.

Peters AEJ, van Silfhout L, Graco M, et al. Periodic limb movements in tetraplegia. J Spinal Cord Med. 2018;41:318–25.

Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5:136–43.

Qaseem A, Kansagara D, Forciea MA, et al. Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2016;165:125–33.

Redline S, Kirchner HL, Quan SF, et al. The effects of age, sex, ethnicity, and sleep-disordered breathing on sleep architecture. Arch Intern Med. 2004;164:406–18.

Redline S, Strohl KP. Recognition and consequences of obstructive sleep apnea hypopnea syndrome. Clin Chest Med. 1998;19:1–19.

Sajkov D, Marshall R, Walker P, et al. Sleep apnoea related hypoxia is associated with cognitive disturbances in patients with tetraplegia. Spinal Cord. 1998;36:231–9.

Sankari A, Badr MS. Diagnosis of sleep disordered breathing in patients with chronic spinal cord injury. Arch Phys Med Rehabil. 2016;97:176–7.

Sankari A, Badr MS, Martin JL, et al. Impact of spinal cord injury on sleep: current perspectives. Nat Sci Sleep. 2019a;11:219–29.

Sankari A, Bascom A, Oomman S, et al. Sleep disordered breathing in chronic spinal cord injury. J Clin Sleep Med. 2014;10:65–72.

Sankari A, Vaughan S, Bascom A, et al. Sleep-disordered breathing and spinal cord injury: a state-of-the-art review. Chest. 2019b;155:438–45.

Saper CB, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. Nature. 2005;437:1257–63.

Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014;146:1387–94.

Sateia MJ, Buysse DJ, Krystal AD, et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of sleep medicine clinical practice guideline. J Clin Sleep Med. 2017;13:307–49.

Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med. 2008;4:487–504.

Shafazand S, Anderson KD, Nash MS. Sleep complaints and sleep quality in spinal cord injury: a web-based survey. J Clin Sleep Med. 2019;15:719–24.

Skatrud JB, Dempsey JA. Interaction of sleep state and chemical stimuli in sustaining rhythmic ventilation. J Appl Physiol Respir Environ Exerc Physiol. 1983;55:813–22.

Sowho M, Amatoury J, Kirkness JP, et al. Sleep and respiratory physiology in adults. Clin Chest Med. 2014;35:469–81.

Stepanski E, Lamphere J, Badia P, et al. Sleep fragmentation and daytime sleepiness. Sleep. 1984;7:18–26.

Terson de Paleville DG, McKay WB, et al. Respiratory motor control disrupted by spinal cord injury: mechanisms, evaluation, and restoration. Transl Stroke Res. 2011;2:463–73.

Thijssen DH, Eijsvogels TM, Hesse M, et al. The effects of thoracic and cervical spinal cord lesions on the circadian rhythm of core body temperature. Chronobiol Int. 2011;28:146–54.

Trenkwalder C, Hening WA, Montagna P, et al. Treatment of restless legs syndrome: an evidence-based review and implications for clinical practice. Mov Disord. 2008;23:2267–302.

Wellman A, White DP. Central sleep apnea and periodic breathing. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. St Louis: Elsevier Saunders; 2011.

Wiegand L, Zwillich CW, Wiegand D, et al. Changes in upper airway muscle activation and ventilation dur-

ing phasic REM sleep in normal men. J Appl Physiol. 1985;1991(71):488–97.
Wilson S, Anderson K, Baldwin D, et al. British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: an update. J Psychopharmacol. 2019;33:923–47.
Zeitzer JM, Ayas NT, Shea SA, et al. Absence of detectable melatonin and preservation of cortisol and thyrotropin rhythms in tetraplegia. J Clin Endocrinol Metab. 2000;85:2189–96.

Recommended Additional Reading

Chokroverty S, editor. Sleep disorders medicine. Basic science, technical considerations and clinical aspects. 4th ed. New York: Springer; 2017.
Chokroverty S, Ferini-Strambi L, editors. Oxford textbook of sleep disorders. Oxford: Oxford University Press; 2017.

41 Neurological Deterioration After Spinal Cord Injuries

If the neurological symptoms worsen in patients with acute or subacute phase after spinal cord injuries, the physicians who treat patients with spinal cord injuries are embarrassed and confused about the treatment plan if the cause is unclear. The causes of neurological deterioration after spinal cord injury are not well studied. Neurologic deterioration of acute, subacute, or chronic periods was reported in 2–10% of patients with cervical cord injuries and in 15% of patients with entire spinal cord injuries (Colterjohn and Bednar 1995; Farmer et al. 1998; Marshall et al. 1987; Todd et al. 2015). Many patients with neurologically deterioration with spinal cord injuries are associated with surgical intervention: epidural hematoma not evacuated, attempted reduction of kyphosis, or intraoperative injury (Todd et al. 2015). Additional neurological deterioration may occur after several years, although it may occur in the initial weeks or months after spinal cord injury. It can have a serious negative impact on functional abilities and may lead to anxiety about further loss of functional independence and deterioration of function after adjustment to spinal cord injury.

Neurological deterioration after spinal cord injury can be caused by various neurological causes or complications. Posttraumatic progressive myelopathy is a condition in which the neurological symptoms deteriorate after clinical and neurological stabilization after spinal cord injury. This may be due to spinal cord atrophy, syringomyelia, surgical complications, residual or recurrent spinal cord compression, myelomalacia, hemodynamic complication during acute phase, neurological complication related with medication and pharmacokinetic change, central pontine myelinolysis, metabolic complications, and spinal cord tethering or subarachnoid adhesion. Tethering of the spinal cord and nerve roots or cauda equina due to spinal arachnoiditis may be a cause of late neurological deterioration after spinal cord injuries. The deterioration of neurological symptoms associated with surgery after spinal cord injury has been reported in more than 5 days after the injury (Fried 1974; Gertzbein 1994; Marshall et al. 1987).

This chapter describes the relatively less rare causes of neurological deterioration that are reported or expected in patients with spinal cord injuries.

41.1 Posttraumatic Syringomyelia and Neurological Deterioration After Surgical Intervention for Syringomyelia

The incidence of posttraumatic syringomyelia was reported to be 0.3–3.2% based on radiographic examination and clinical examination (Aito et al. 1999). The incidence examined by

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MRI was 11–22%. If the size of the cavity in the spinal cord is less than 5 mm, it is called an intramedullary cyst, and if it is more than 5 mm, it is defined as a true syrinx (Falci et al. 2009). Although the mechanism of posttraumatic syringomyelia is not well understood, syringomyelia associated with spinal cord injury is often caused by the intramedullary suck and slosh mechanism resulted from the pressure difference between the upper and lower portion of the injured spinal cord. Many pathomechanisms of posttraumatic syringomyelia have been postulated. As the spinal cord moves about 6 cm due to flexion and extension of the spine, a local wound around the spinal cord after trauma of the spinal cord pulls the spinal cord into the dura, which interferes with the cerebrospinal fluid circulation within and around the spinal cord, resulting in a subarachnoid pressure difference (Castillo et al. 1988).

A syringoperitoneal shunt or syringopleural shunt for internal decompression of the spinal cord cavity and surgical untethering of the surrounding of the spinal cord, resulting in an abrupt decrease in syrinx pressure, may lead to neurological worsening (Batzdorf et al. 1998). The changes in neurological symptoms may occur rapidly or gradually after a period of time.

Correction is possible if the worsening of neurological symptoms following surgery to alleviate the symptoms of syringomyelia is due to a functional failure of the shunt. However, when the deterioration of the neurological symptoms is accelerated, it becomes very difficult to deal with it effectively (Schaller et al. 1999). The rate of shunt failure is reported to be approximately 50%. Recently, the surgical treatment of syringomyelia has been limited to the simple dissection of arachnoidal adhesions or expansile duroplasty for pain relief and because of the arachnoidal scarring by placing the shunt. Therefore, the surgery should be carefully considered. Although it is effective in alleviating pain due to the expansion and progression of the syrinx, other symptoms such as abnormal sensation or spasticity are less likely to improve.

41.2 White Cord Syndrome

Overall, posterior cervical decompression is a safe operation with high improvement in patient-reported outcomes, although complication rates are approximately 14% (Fehlings et al. 2016). The most common postoperative complications include C5 palsy, wound infection, and cerebrospinal fluid leak. Neurologic deficits related to the procedure are rare, with a reported rate of 0.18%, and are generally secondary to compressive hematomas or iatrogenic injury. There have been several reports of severe neurological deficits following routine cervical decompression surgeries with no apparent intraoperative complications (Mathkour et al. 2020). Postoperative MRI demonstrates high T2-weighted signal within the spinal cord at the severely compressed segments, which is referred to as "white cord syndrome" (Antwi et al. 2018).

Sudden neurological deterioration following spinal decompression may be attributed to reperfusion injury of the spinal cord as an acute intraoperative "reperfusion injury" (Acharya et al. 2021). On postoperative MRI, cord ischemia and edema are characterized by a hyperintense spinal cord signal (Mathkour et al. 2020; Vinodh et al. 2018). The etiology is attributed to a rapid expansion of the spinal cord with an acutely increased blood supply to the affected area. These sudden changes likely lead to disruption of the blood–brain barrier and the blood–spinal cord barrier, leading to reperfusion injury (Chin et al. 2013). It is important to maintain the postoperative MAP ≥85 mmHg to prevent the ischemic process of the spinal cord.

41.3 C5 Palsy

After cervical spine surgery, a C5 palsy remains a serious complication (Stoops and King 1962). Although the prevalence is low, affected patients suffer from muscle weakness, including deltoid or biceps muscles, brachialgia, and numbness, and are dissatisfied with their surgery (Imagama et al. 2010). Most patients over 95% exhibit uni-

lateral paralysis. The reasons why the C5 nerve root impingement could easily occur after laminoplasty is probably due to the fact that the superior articular process of C5 protrudes in a more anterior direction than at other levels and the rootlets, root of C5 are shorter than those of other segments, and C5 segment is usually the point at which the extent of posterior shift of the cord is greatest (Tsuzuki et al. 1993).

41.4 Surgical Complications of Degenerative Cervical Myelopathy

In case of myelopathy caused by spinal stenosis, the risk of surgery-related damage for decompression is higher than that of normal spinal cord. Neurological deterioration associated with surgery is often due to ischemic injury due to changes in blood flow in the spinal canal with stenosis, as well as physical damage such as graft complications and hematomas. Neurological complications associated with decompression surgery of cervical spondylotic myelopathy are reported to be about 5.5%. (Cybulski and D'Angelo 1988; Farmer et al. 1998).

41.5 Hypotension-Related Ischemic Injury of the Spinal Cord After Surgery

In patients with severe spondylotic myelopathy, myelopathy may rapidly worsen after decompression, including laminectomy. This is known to be related to ischemic spinal cord infarction due to the rapid pressure relief of the spinal cord and the decrease in blood perfusion of the spinal cord in stenosis or compression of blood flow through the stenotic condition. In particular, if sitting or upright posture is suddenly taken without consideration of the postoperative hemodynamic change, the perfusion of the spinal cord may be further reduced, and the symptoms may be worsened (Blumbergs and Byrne 1980). In this case, damage to the medial side, the central gray matter, is more susceptible and may cause spinal cord injury, much like the central cord syndrome.

41.6 Neurological Deterioration by Arteriovenous Malformation

The deterioration of neurological symptoms due to arteriovenous malformation or spinal dural arteriovenous fistula is known to be the main cause of venous congestion in the spinal cord. The presence of a fistula stagnates blood flow and prevents venous drainage of the spinal cord. This increases the venous pressure and directly affects the intrinsic vein of the spinal cord (Kataoka et al. 2001). Therefore, the pressure difference between the arteries and veins decreases, and the perfusion of the blood flow in the spinal cord tissue decreases. If neurological deterioration is recognized, early surgical or interventional therapy can prevent the progression of neurological symptoms.

41.7 Vertebral Artery Injury

Neurological deterioration associated with vertebral artery injury has been reported. Cervical spinal injuries can cause vertebral artery injury due to fracture of the transverse foramen (Deen and McGirr 1992). Damage to the vertebral artery may cause symptoms due to abnormal cervicomedullary blood flow. In most cases, neurological symptoms due to damage of the vertebral artery in spinal cord injuries with vertebral artery injury are often not recognized earlier (Bose et al. 1985; Louw et al. 1990; Schwarz et al. 1991). With sufficient collateral vascular supply, unilateral vertebral artery occlusion may not lead to any neurologic deficits. However, it has been reported that bilateral vertebral artery occlusion in cervical spine injuries results in significant disability and even death (Golinvaux et al. 2015; Strickland et al. 2019; Veras et al. 2000).

41.8 Hemodynamic Change After Acute Spinal Cord Injury

Approximately 5.8% of patients with cervical spinal cord injuries experience neurological deterioration. There is a high risk of neurological complications associated with early surgery, halo, traction therapy, and rotation of the Stryker frame in cervical spinal cord injured patients. In addition to secondary damage from spinal instability, hypotension (systolic blood pressure <90 mmHg) and orthostatic hypotension in the acute phase lead to neurological deterioration due to spinal cord infarction, which is associated with impaired collateral circulation. In the case of sepsis, arterial blood inflow into the vein causes deterioration of spinal cord blood flow and impairment of the circulatory disorder of the injured spinal cord, resulting in worsening of neurological symptoms, causing ischemic injury in the penumbra, and increased cytotoxic edema for infarction.

Other circulatory disorders may lead to an infarction, associated with venous thrombosis at the end of the blood flow of the spinal cord, and aggravate the neurological symptoms. In 80% of patients with complete spinal cord injury, the venous drainage pattern of the spinal cord changes, and the tortuous venous flow in the spinal cord has an anatomical feature that can cause venous stasis and thrombosis. Therefore, anticoagulant therapy is required to maintain adequate blood flow and prevent microthrombosis, unless there is a specific contraindication in the acute phase of spinal cord injury.

41.9 Drugs-Related Neurological Deterioration

In patients with spinal cord injury, changes in pharmacokinetics should be considered. Due to the different drug dynamics from normal people, the occurrence of adverse reactions due to differences in the absorption reactions of intramuscular or oral drugs is high. In particular, the risk of anticholinergic delirium due to diphenhydramine and tricyclic antidepressant is high. Among the commonly used drugs, the effects of oxybutynin on muscarinic receptors, especially M1, may cause serious mental symptoms such as hallucination and cognitive decline in elderly patients (Donnellan et al. 1997).

Psychotropic drug-induced neuroleptic malignant syndrome is an urgent complication with severe symptoms due to increased rigidity and instability of the autonomic nervous system. If a neuroleptic malignant syndrome occurs, bromocriptine is administered at a dose of 2.5 mg bid up to 15 mg/day. In addition, mental symptoms such as hallucinations or disorganized thinking, which are often associated with a sudden withdrawal of baclofen, should be considered. In this case, a small amount of haloperidol helps in relieving the symptoms.

41.10 Osmotic Demyelination Syndrome

In patients with tetraplegia, ECF tends to increase and ICF tends to decrease, probably causing nocturnal natriuresis. The incidence of hyponatremia in spinal cord injured patients is as high as 10–15% compared to 1–2% of normal subjects. This is a phenomenon in which the renin-angiotensin system is activated, and the secretion of ADH is increased to compensate for the occurrence of orthostatic hypotension caused by venous blood pooling in the dependent areas due to reduced sympathetic activity in the blood vessels. When the serum sodium levels do not fall below 120 mEq/L, symptoms usually do not appear, but in severe cases, neurological symptoms such as seizures or psychiatric symptoms occur and rarely result in death (Moore and Midha 1997). In addition, excessive intake of water to prevent kidney stones in spinal cord injured patients may cause hyponatremia.

Increases in serum sodium above 20 mEq/L during the first 48 h should be avoided to correct hyponatremia. In patients with spinal cord injuries, hypoosmolar hyponatremia of less than 130 mEq/L is common, and therefore treatment is required that takes into account the characteristics of electrolyte change in patients with spinal

cord injuries. Rapid correction of hyponatremia results in rapid changes in the sodium level and intracellular influx of sodium in the brainstem cells, leading to central pontine myelinolysis and extrapontine myelinolysis, resulting in decreased consciousness, speech impairment, pseudobulbar palsy, flaccid limb paralysis, locked-in syndrome, and cranial nerve palsy (Boon and Potter 1987).

41.11 Vitamin B12 Deficiency and Nitrous Oxide (N_2O)

The anesthetic nitrous oxide (N_2O) inactivates cyanocobalamin, which rapidly exacerbates the symptoms of vitamin B12 deficiency (Flippo and Holder 1993; Schilling 1986). Therefore, N_2O anesthesia in patients with clinically insignificant vitamin B12 deficiency, especially in elderly patients, can cause subacute combined degeneration of the spinal cord or aggravate the progression of the disease rapidly (Bursell et al. 1999).

References

Acharya S, Kaucha D, Sandhu AS, et al. Misdiagnosis of "White Cord Syndrome" following posterior cervical surgery for ossification of the posterior longitudinal ligament: a case report. Surg Neurol Int. 2021;12:244.

Aito S, El Masry WS, Gerner HJ, et al. Ascending myelopathy in the early stage of spinal cord injury. Spinal Cord. 1999;37:617–23.

Antwi P, Grant R, Kuzmik G, Abbed K. "White Cord Syndrome" of acute hemiparesis after posterior cervical decompression and fusion for chronic cervical stenosis. World Neurosurg. 2018;113:33–6.

Batzdorf U, Klekamp J, Johnson JP. A critical appraisal of syrinx cavity shunting procedures. J Neurosurg. 1998;89:382–8.

Blumbergs PC, Byrne E. Hypotensive central infarction of the spinal cord. J Neurol Neurosurg Psychiatry. 1980;43:751–3.

Boon AP, Potter AE. Extensive extrapontine and central pontine myelinolysis associated with correction of profound hyponatraemia. Neuropathol Appl Neurobiol. 1987;13:1–9.

Bose B, Northrup BE, Osterholm JL. Delayed vertebrobasilar insufficiency following cervical spine injury. Spine. 1985;10:108–10.

Bursell JP, Little JW, Stiens SA. Electrodiagnosis in spinal cord injured persons with new weakness or sensory loss: central and peripheral etiologies. Arch Phys Med Rehabil. 1999;80:904–9.

Castillo M, Quencer RM, Green BA, et al. Acute, ascending cord ischaemia after mobilisation of a stable quadriplegic patient. Lancet. 1988;1:759–60.

Chin KR, Seale J, Cumming V. "White cord syndrome" of acute tetraplegia after anterior cervical decompression and fusion for chronic spinal cord compression: a case report. Case Rep Orthop. 2013;2013:697918.

Colterjohn NR, Bednar DA. Identifiable risk factors for secondary neurologic deterioration in the cervical spine-injured patient. Spine. 1995;20:2293–7.

Cybulski GR, D'Angelo CM. Neurological deterioration after laminectomy for spondylotic cervical myeloradiculopathy: the putative role of spinal cord ischaemia. J Neurol Neurosurg Psychiatry. 1988;51:717–8.

Deen HG Jr, McGirr SJ. Vertebral artery injury associated with cervical spine fracture. report of two cases. Spine. 1992;17:230–4.

Donnellan CA, Fook L, McDonald P, et al. Oxybutynin and cognitive dysfunction. BMJ. 1997;315:1363–4.

Falci SP, Indeck C, Lammertse DP. Posttraumatic spinal cord tethering and syringomyelia: surgical treatment and long-term outcome. J Neurosurg Spine. 2009;11:445–60.

Farmer J, Vaccaro A, Albert TJ, et al. Neurologic deterioration after cervical spinal cord injury. J Spinal Disord. 1998;11:192–6.

Fehlings MG, Tetreault L, Hsieh PC, et al. Introduction: Degenerative cervical myelopathy: diagnostic, assessment, and management strategies, surgical complications, and outcome prediction. Neurosurg Focus. 2016;40:E1.

Flippo TS, Holder WD Jr. Neurologic degeneration associated with nitrous oxide anesthesia in patients with vitamin B12 deficiency. Arch Surg. 1993;128:1391–5.

Fried LC. Cervical spinal cord injury during skeletal traction. JAMA. 1974;229:181–3.

Gertzbein SD. Neurologic deterioration in patients with thoracic and lumbar fractures after admission to the hospital. Spine. 1994;19:1723–5.

Golinvaux NS, Basques BA, Bohl DD, Laurans MS, Grauer JN. Bilateral vertebral artery injury in a patient with upper cervical spine fractures leading to fatal vertebrobasilar infarction: a case report. Orthop Surg. 2015;7:281–5.

Imagama S, Matsuyama Y, Yukawa Y, et al. C5 palsy after cervical laminoplasty: a multicentre study. J Bone Joint Surg Br. 2010;92:393–400.

Kataoka H, Miyamoto S, Nagata I, et al. Venous congestion is a major cause of neurological deterioration in spinal arteriovenous malformations. Neurosurgery. 2001;48:1224–9.

Louw JA, Mafoyane NA, Small B, et al. Occlusion of the vertebral artery in cervical spine dislocations. J Bone Joint Surg Br. 1990;72:679–81.

Marshall LF, Knowlton S, Garfin SR, et al. Deterioration following spinal cord injury. A multicenter study. J Neurosurg. 1987;66:400–4.

Mathkour M, Werner C, Riffle J, et al. Reperfusion "white cord" syndrome in cervical spondylotic myelopathy: does mean arterial pressure goal make a difference? Additional case and literature review. World Neurosurg. 2020;137:194–9.

Moore K, Midha M. Extra pontine myelinolysis in a tetraplegic patient: case report. Spinal Cord. 1997;35:332–4.

Schaller B, Mindermann T, Gratzl O. Treatment of syringomyelia after posttraumatic paraparesis or tetraparesis. J Spinal Disord. 1999;12:485–8.

Schilling RF. Is nitrous oxide a dangerous anesthetic for vitamin B12-deficient subjects? JAMA. 1986;255:1605–6.

Schwarz N, Schwarz N, Buchinger W, et al. Injuries to the cervical spine causing vertebral artery trauma: case reports. J Trauma. 1991;31:127–33.

Stoops WL, King RB. Neural complications of cervical spondylosis: their response to laminectomy and foramenotomy. J Neurosurg. 1962;19:986–99.

Strickland B, Lewis CS, Pham MH. Bilateral vertebral artery occlusion after cervical spine fracture dislocation. World Neurosurg. 2019;124:304–9.

Todd NV, Skinner D, Wilson-MacDonald J. Secondary neurological deterioration in traumatic spinal injury: data from medicolegal cases. Bone Joint J. 2015;97-B:527–31.

Tsuzuki N, Zhogshi L, Abe R, et al. Paralysis of the arm after posterior decompression of the cervical spinal cord. I. Anatomical investigation of the mechanism of paralysis. Eur Spine J. 1993;2:191–6.

Veras LM, Pedraza-Gutiérrez S, Castellanos J, Capellades J, Casamitjana J, Rovira-Cañellas A. Vertebral artery occlusion after acute cervical spine trauma. Spine (Phila Pa 1976). 2000;25:1171–7.

Vinodh VP, Rajapathy SK, Sellamuthu P, et al. White cord syndrome: a devastating complication of spinal decompression surgery. Surg Neurol Int. 2018;9:136.

Recommended Additional Reading

Crock HV, Yoshizawa. The blood supply of the vertebral column and spinal cord in man. New York: Springer-Verlag; 1977.

Hattingen E, Klein JC, Weidauer S, et al., editors. Diseases of the spinal cord. Heidelberg: Springer; 2015.

Jallo J, Vaccaro AR, editors. Neurotrauma and critical care of the spine. 2nd ed. New York: Thieme; 2018.

Thron AK. Vascular anatomy of the spinal cord. In: Radioanatomy as the key to diagnosis and treatment. 2nd ed. Cham: Springer; 2016.

Vaccaro AR, Fehlings MG, Dvorak MF, editors. Spine and spinal cord trauma, evidence-based management. New York: Thieme Medical Publishers; 2011.

Emergency in Chronic Spinal Cord Injuries

42

Acute and long-term secondary medical complications are common in patients with spinal cord injuries. After acute treatment, people with spinal cord injuries may have the same medical problems they experienced in the acute phase, and they may face emergency situations with new medical problems over time. Chronic complications in people with spinal cord injuries such as cardiovascular complications, respiratory complications, urinary and bowel complications, spasticity, pain syndromes, pressure injuries, and bone fractures also have a negative effect on the functional independence and quality of life of the patient as complications are a frequent cause of morbidity and mortality and lead to increased rehospitalization rates and loss of employability (McKinley et al. 1999). Therefore, the prevention, early diagnosis, and treatment of chronic secondary complications in people with spinal cord injuries are critical to limit these complications and improve survival, community participation, and health-related quality of life (Sezer et al. 2015).

The complications associated with an imbalance of the autonomic nervous system, such as autonomic dysreflexia or orthostatic hypotension, persist in chronic spinal cord injuries. These patients have an altered or absent sensation below the level of injury and do not show the typical clinical manifestations of common problems that occur in the neurological level of injury. For example, they will not necessarily be able to feel discomfort as a urinary tract infection or peritonitis develops, nor will they have guarding typically seen in an acute abdomen or fracture (Kupfer et al. 2018). Some of the complications that occur in chronic spinal cord injuries can be serious medical complications that require immediate medical attention, and some can become medically emergent conditions sooner or later because they are not recognized early enough for the event below the neurological level of injury.

42.1 Orthostatic Hypotension

Orthostatic hypotension is defined as a decrease in systolic blood pressure of 20 mmHg or more, or a decrease in diastolic blood pressure of 10 mmHg or more during the first 3 min of the upright position or a head-up tilt of at least 60° on a tilt table, when the body position changes from supine to upright, regardless of whether or not symptoms occur (Gibbons et al. 2017; The Consensus Committee of AAS/AAN 1996). It is usually observed in both acute and chronic phases after spinal cord injuries (Sidorov et al. 2008). Orthostatic hypotension is common early after tetraplegia but tends to improve over time. Asymptomatic systolic blood pressures around 90 mmHg are common in tetraplegia. Therefore, it is important to identify an individual's baseline blood pressure to determine whether a low reading is truly pathologic (Ong et al. 2020). The

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prevalence of orthostatic hypotension and the degree of fall in blood pressure are higher in patients with cervical spinal cord injuries than in patients with thoracic spinal cord injuries. Orthostatic hypotension is less common in spinal cord injuries below the origin of the major splanchnic outflow at T6 and in incomplete lesions (Claydon and Krassioukov 2006; Nobunaga 1998). Orthostatic hypotension is more common in traumatic spinal cord injuries than in nontraumatic spinal cord injuries.

Symptoms associated with orthostatic hypotension in patients with spinal cord injuries, such as lightheadedness or dizziness within a few seconds after sitting or standing, headache, pallor, yawning, sweating, fatigue, blurred vision, weakness, shortness of breath, and syncope, are the same as in the general population. Symptoms of orthostatic hypotension vary based on orthostatic stress, and it is important to recognize subtle symptoms such as fatigue and cognitive impairment. About 40% of patients develop asymptomatic orthostatic hypotension.

When orthostatic hypotension develops, the patient should be placed on supine and leg elevation should be performed. The first thing to do after diagnosing orthostatic hypotension is pharmacologic simplification by reducing or stopping any medications that exacerbate orthostatic hypotension. Many medications, such as drugs for spasticity, bladder, hypertension, and pain, can cause orthostatic hypotension or worsen symptoms of orthostatic hypotension. Abdominal binders and thigh-high compressive stockings can be used to increase venous pressure and reduce venous pooling by reducing the capacity of the legs and abdominal vascular bed. Knee-high compression stockings are not effective. With abdominal binders, compression of 40 mmHg is just as effective as midodrine in the treatment of orthostatic hypotension (Okamoto et al. 2016). Elevating the head of the bed by 5–10 inches (reverse Trendelenburg position) can reduce nocturnal diuresis, morning postural hypotension, morning supine hypertension, and hypovolemia. Postprandial hypotension can occur, and exposure to a hot environment can worsen symptoms of orthostatic hypotension. The most experienced drugs used to treat orthostatic hypotension in spinal cord injuries include salt tablets, midodrine, fludrocortisone, droxidopa, ephedrine, and pseudoephedrine (Krassioukov et al. 2009; Lamarre-Cliché 2002).

42.2 Autonomic Dysreflexia

Autonomic dysreflexia is a well-known medical emergency that occurs in patients with spinal cord injuries at the neurological level of injury of T6 and above, that is, above the major splanchnic outflow (T6-L2). It is reported that the lifetime frequency in people with spinal cord injuries is 19–70% (Hagen et al. 2012). The guidelines of Consortium for Spinal Cord Medicine recommend that autonomic dysreflexia in adults is considered when there is an abrupt elevation in systolic blood pressure of 20–40 mmHg above baseline, while an increase of 15–20 mmHg systolic pressure in pediatric spinal cord injury in response to noxious stimuli below the level of injury (Consortium for Spinal Cord Medicine 2001). Severe autonomic dysreflexia can increase systolic pressures to more than 200 mmHg and cause myocardial infarction, cerebral hemorrhage, seizures, and death. Symptoms can include headache, sweating, and flushing above the level of injury, piloerection, blurry vision, nasal congestion, and bradycardia, but many are asymptomatic (Ong et al. 2020).

Bladder distension is the most common trigger factor for autonomic dysreflexia. The distension can result from urinary retention or catheter blockage and accounts for up to 85% of cases (Sezer et al. 2015; Shergill et al. 2004). The second most common trigger for autonomic dysreflexia is bowel distension due to fecal impaction. Other potential causes include hemorrhoids and anal fissures, acute abdomen such as cholecystitis or appendicitis, ingrown toenails, pressure injuries, fractures, heterotopic ossification, menstruation, pregnancy or labor, deep vein thrombosis, pulmonary embolism, and sexual activity. Medications, especially nasal decongestants and misoprostol (Cytotec®), may also induce auto-

nomic dysreflexia (Blackmer 2003). It is reported that educating patients, caregivers, and family members about autonomic dysreflexia is essential in order to prevent autonomic dysreflexia and identify its occurrence immediately (Vaidyanathan et al. 2012).

When autonomic dysreflexia occurs, initial treatment includes non-pharmacological therapeutic interventions. These interventions include placing the patient in an upright position to take advantage of an orthostatic lowering of blood pressure. The next step must be to loosen tight clothing and/or constricting devices. The blood pressure is checked at least every 5 min until the patient is stable. It is also necessary to find and eliminate the triggering stimulus, most commonly bladder distension or bowel impaction. If the patient does not have a Foley catheter, a straight catheter can be inserted with lidocaine jelly. If non-pharmacological treatment fails and arterial blood pressure is 150 mmHg or greater, pharmacological management should be initiated (Consortium for Spinal Cord Medicine 2001). The predominant drugs are antihypertensive agents with a rapid onset and short duration of action. Long-acting antihypertensive drugs are not recommended, because the elimination of the causative factor can quickly normalize high blood pressure. Nitrates and nifedipine appear to be the most commonly used medications for the treatment of autonomic dysreflexia episodes (Blackmer 2003). If nitroglycerin patch (5 mg) or paste (2% ointment) is used, place 1–2 inches above the lesion of injury. Alternately, a 0.4 mg sublingual nitroglycerin tablet can be administered. Nitroglycerin should be used with caution, as many people with spinal cord injuries take phosphodiesterase inhibitors for erectile dysfunction and interaction of these drugs can result in severe hypotension. Nifedipine, 10 mg, can be provided in capsule form that can be bitten and swallowed (bite-and-swallow) for rapid absorption. Sublingual nifedipine administration may not be absorbed (Phillips et al. 1998). This dose can be repeated in 30 minutes if necessary. Nifedipine should be used with extreme caution in the elderly or in people with coronary artery disease. Hydralazine (Apresoline) lowers blood pressure through peripheral vasodilation. In acute autonomic dysreflexia, administration of 10–20 mg by slow intravenous push is indicated to reduce hypertension. The drug can be used during pregnancy and is a potential therapeutic agent for autonomic dysreflexia in pregnancy and labor (Phillips et al. 1998). β-blockers should be avoided as they can cause excessive α-adrenergic activity. Persistence of autonomic dysreflexia requires transfer to an intensive care unit or emergency room for close hemodynamic monitoring and titration of more aggressive intravenous blood pressure medication, such as hydralazine, nitroglycerin, or nitroprusside (Cruz et al. 2015). An example of treatment algorithm for autonomic dysreflexia is shown in Fig. 42.1.

42.3 Obstruction of the Tracheostomy Tube

Obstruction of the tracheostomy tube may result from mucous plugs, thick secretions, granulation tissue, blood clot formation, kinking or tube dislodgement, or foreign bodies. Attempts to assist with ventilation should be performed, such as the "head tilt, chin lift" maneuver (Nawrocki et al. 2021). Depending on the relative severity of obstruction, these patients may present with mild shortness of breath or even complete respiratory arrest. If the patient has a speaking valve, remove the speaking valve or at least deflate the cuff. Next, the physician or other care provider should attempt to pass a suction catheter. If the suction catheter passes (at least 10 cm or beyond the distal tip of the tube), recheck and observe the adequacy of oxygenation and ventilation (Morris et al. 2013; Nawrocki et al. 2021; Regan and Hunt 2008).

42.4 Accidental Decannulation of the Tracheostomy Tube

Accidental decannulation is a relatively common complication of tracheostomy placement (O'Connor and White 2010; Pattanong 2007). The inadvertent decannulations can be life-

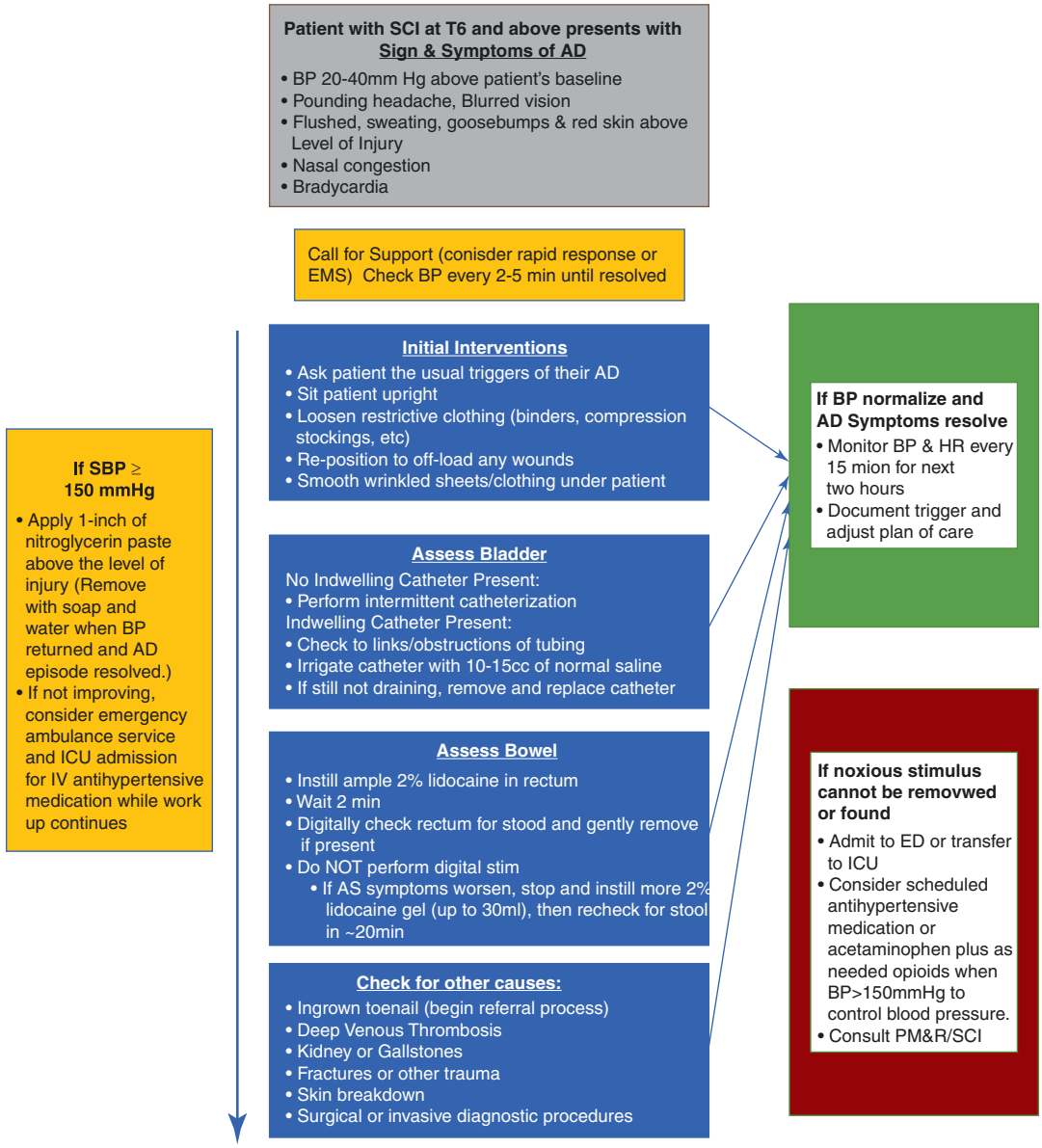

Fig. 42.1 Example of treatment algorithm for autonomic dysreflexia. *AD* autonomic dysreflexia; *BP* blood pressure; *ED* emergency department; *ICU* intensive care unit; *SBP* systolic blood pressure; *SCI* spinal cord injury. From Ong et al. (2020), with permission

threatening, especially if it occurs before the tract between the skin and the trachea has matured. Emergency management of these patients is largely based on two important factors: oxygenation and airway protection and time since tracheostomy placement. If it occurs less than 1 week after placement, the stomal tract is immature and there is therefore a high risk of a false passage into the mediastinum (O'Connor and White 2010). In tubes that have been in place less than 2 weeks, the tract will not yet be mature and surgical consultation may be necessary. If replacement via stoma fails, emergent endotracheal intubation may be required (Nawrocki et al.

2021). Between 1 week and 1 month, the risk of misplacement is proportional to the time passed since initial cannulation. If it has been more than 1 month since initial tracheostomy, the tract is likely well formed and the risk of inadvertent misplacement is low. Once the stomal tract has matured, it can be safely reinserted without image guidance; however, oxygenation should be closely monitored (Morris et al. 2013).

42.5 Chest Pain

Chest pain or discomfort can occur as a result of cardiovascular, pulmonary, gastrointestinal, psychological, or musculoskeletal disorders. Life-threatening causes of chest symptoms such as acute myocardial infarction, pericarditis, aortic dissection, pulmonary embolism, pneumonia, or esophageal rupture must first be ruled out before considering other causes (Amsterdam et al. 2010). Hypertensive and ischemic heart disease is the fourth leading cause of death in people with spinal cord injuries (NSCISC 2021). Certain acute myocardial infarction patients, especially cervical cord injuries, the elderly, women, and diabetics, may not have chest complaints, but rather atypical symptoms such as left shoulder pain or back pain, dyspnea, and nausea.

Classic symptoms of acute coronary syndrome are crushing, substernal chest pain radiating to the left upper extremity, dyspnea, and sweating. Stable angina usually worsens with exercise and relieves with rest, while unstable angina persists regardless of exercise. Pericarditis is usually pleuritic in nature and is typically relieved by leaning forward. Congestive heart failure and bronchospasm can be confused with acute coronary syndrome, as patients with either can experience chest discomfort. Aortic dissections are characterized by tearing back pain or crushing chest pain. Patients with pulmonary embolism classically present with pleuritic chest pain, dyspnea, and tachycardia. Pneumothorax manifests as sudden chest pain and dyspnea and mostly occurs in patients with chest trauma, chronic obstructive pulmonary disease, or a history of pneumothorax, but it can also be a complication of certain procedures such as placement of lines and needle electromyography. Gastrointestinal disorders can often be correlated with meals. Anxiety is a common cause of chest pain, but it is an exclusion diagnosis, and the physician should determine whether the patient became anxious before or after the onset of chest pain. If anxiety is suspected, relaxation techniques and deep breathing should be encouraged while the patient is examined for other causes (Amsterdam et al. 2010; Cruz et al. 2015). Neural causes, such as herpes zoster or intercostal neuralgia, can present as a dermatomal pattern around the chest.

An ECG should be obtained for any patients with chest pain. It should be compared with previous or baseline ECGs, if available, to ensure that any findings found are new (Cruz et al. 2015). Cardiac biomarkers including troponin, creatine kinase, and myoglobin are obtained in patients at risk for cardiac ischemia. Historically, lactate dehydrogenase, or LDH, has also been used, but it is not specific. The enzymes troponin I and troponin T are normal proteins that are important in the contractile apparatus of the cardiac myocyte. The proteins are released into the circulation between 3 and 4 h after myocardial infarction and remain detectable for 10 days afterward. This long half-life enables the late diagnosis of myocardial infarction. There are a number of causes of an increase in troponin that are not related to myocardial infarction. However, troponin elevation is much more sensitive than myoglobin and even creatine kinase. Creatine kinase is a muscle enzyme that is present as isoenzymes. The MB type is specific to myocardial cells, while MM and BB are specific for skeletal muscle and brain tissue, respectively. Creatine kinase level increases approximately 3 to 4 h after a myocardial infarction and remains elevated for 3 to 4 days. Myoglobin is released into the circulation whenever muscle tissue is damaged, including myocardial necrosis. Since skeletal muscles contain myoglobin, this measurement is quite nonspecific for myocardial infarctions. The benefit of myoglobin is that a detectable increase is seen only 30 min after injury, unlike troponin and creatine kinase, which can take

between 3 and 4 h. Other laboratory studies that should be considered include complete blood count, electrolytes, liver function tests, coagulation studies, and levels of brain natriuretic peptide, lipase, and amylase (Amsterdam et al. 2010).

In patients with chest pain, supplemental oxygen should be given and an intravenous line established as soon as possible. If acute myocardial infarction is suspected, 325 mg of aspirin should be administered immediately with nitrates for chest pain while the patient is being prepared for transfer to an acute medical care unit. When aortic dissection is suspected, the patient should be transferred to an acute care unit for monitoring and IV blood pressure control or potential emergent surgical intervention (Cruz et al. 2015).

42.6 Fractures

A fracture below the level of injury is a well-known complication of bone loss after spinal cord injury. Fractures are relatively rare in the first year after spinal cord injury and increase linearly over time. Many fractures have been shown to increase the risk of fractures after spinal cord injury, such as female, age, increased time post-injury, paraplegia, motor complete injuries, low body mass index, low knee BMD, and medications including anticonvulsants, heparin, and opioids. The prevalence of fractures in chronic spinal cord injured population is 25–46%. The most common sites of fractures are the knee (distal femur and proximal tibia), followed by the distal tibia, femoral shaft, femoral neck, and humerus (Friesbie 1997). Most fractures are caused by minor injuries when performing normal activities of daily living such as transfers, range of motion, low-impact collisions, falls, or even stretching. It is known that torsional loads are the major impact of fractures.

Symptoms of acute fractures can vary but may include fever, pain, swelling, increased spasticity, or autonomic dysreflexia. As a rule, work-up with a standard X-ray is sufficient. During the physical examination, the shortening or narrowing of the Bryant's triangle by palpating the lateral hip area in a wheelchair is important for people with spinal cord injury in order to assess the fracture of the femur neck or hip dislocation. For those who are ambulatory, fracture management is similar to the non-spinal cord injury population. For individuals who do not use their lower extremities for functional mobility, the main objective of the treatment is to preserve the function before fracture and maintain a satisfactory alignment while minimizing complications. Surgery, circumferential casting, and external fixation are not indicated as decreased bone mass and risk of recurrent bacteremia, skin breakdown, and osteomyelitis.

Nonsurgical treatment with soft padded splints, such as a well-padded knee immobilizer for femoral supracondylar, femoral shaft, and proximal tibia fractures or a well-padded ankle immobilizer for distal tibia fractures, is generally recommended. The patients can sit in a few days, and the ROM starts in 3–4 weeks. Surgical intervention is generally recommended for proximal femur fracture and severely displaced fractures and rotational deformities. Fracture-related complications after spinal cord injury include nonunion, contracture, skin breakdown, and deep vein thrombosis.

42.7 Acute Abdomen

Spinal cord injuries disrupt connections between the central and peripheral nervous system, leading to somatic motor and sensory deficits, as well as autonomic dysfunctions. The symptoms vary according to the level and severity of the injury. In lesions above T7, the somatic abdominal sensation (T7-L1) is lost (Miller et al. 2001). However, patients with chronic spinal cord injuries may retain some sensation over their anterior abdominal wall, suggesting that some innervation pathways may remain intact (Neumayer et al. 1990). The exact mechanism of the somatic visceral sensation remains unexplained. Visceral sensory fibers could travel with the vague nerve and thus bypass the spinal cord lesion (Neumayer et al. 1990). Acute abdomen, such as gastrointestinal bleeding, appendicitis, intestinal obstruction, cho-

lelithiasis, and pancreatitis that occur in patients with spinal cord injuries, especially cervical cord injuries, are associated with autonomic dysreflexia, shoulder pain, fever, increased spasticity, hypoactive bowel sounds, and nausea. These nonspecific symptoms associated with acute abdominal pathologies result in delayed diagnosis and can lead to a very dangerous situation.

Laboratory tests used to differentiate diagnosis in patients with spinal cord injuries with acute abdomen include a complete blood count, amylase, lipase, liver enzymes, basic chemistry, and urinalysis. Leukocytosis is not specific to acute abdomen as most of these patients are prone to concurrent conditions such as respiratory infections, urinary tract infections, and pressure injuries, which can cause a rise in the leukocyte count. In addition, leukocytosis is only reported in 33–55% of acute abdomens (Miller et al. 2001; Neumayer et al. 1990) Stolarski et al. 2020).

42.7.1 Gastrointestinal Bleeding

Typical findings of an acute intra-abdominal process in patients with spinal cord injuries can be absent or misleading. Because of delayed diagnosis and misdiagnosis, the mortality rate in these patients is 10–15% (Charney et al. 1975). Proper prophylaxis of stress ulcers can reduce the incidence of gastritis, which leads to bleeding. Upper gastrointestinal bleeding occurs in 5–20% of patients with acute spinal cord injuries (El Masri et al. 1982). Gastrointestinal bleeding after spinal cord injury is usually associated with gastroduodenal ulcers (Juler and Eltorai 1985; Walters and Silver 1986). Gastrointestinal bleeding occurs more frequently in patients with cervical or high thoracic cord injuries and increases with complete injuries (Kiwerski 1986; Solerstrom and Ducker 1985).

The symptoms of gastrointestinal bleeding in chronic or acute diseases are often insidious, and there are no early symptoms. Hemodynamic instability and cardiopulmonary dysfunction are common presentations. Upper gastrointestinal bleeding classically shows hematochezia and black tarry stool; if it is massive, it can also show bright red blood per anus. Lower gastrointestinal bleeding is classically accompanied by maroon stools (right side of the colon), bright red blood per rectum (left side of the colon), and melanic (rectocecal). Gastrointestinal bleeding due to perforation in spinal cord injuries may not be detected at first until apparent hemodynamic instability occurs (Leramo et al. 1982). The provocation factors are multifactorial and include stress hormone-mediated ulcerations, diminished supraspinal controls leading to unopposed parasympathetic dysfunction, gastric vascular changes, oxidative stress, as well as the controversial use of steroids for treatment of spinal cord injury (Solerstrom and Ducker 1985). Gastrointestinal bleeding rate in spinal cord injury was 2.77% with 33% mortality with high-dose steroids (Khan et al. 2014). Aspirin and NSAIDs can cause gastritis, and anticoagulants, particularly full-dose heparin, can cause or increase bleeding in the patients with gastritis.

Patient care for spinal cord injury with gastrointestinal bleeding is similar to other patients with intensive care. Hemodynamic stability and attention to cardiopulmonary monitoring are necessary. Blood pressure should be maintained, and coagulopathy should be corrected. Identification of the location of bleeding can be categorized as upper and lower gastrointestinal source. If upper gastrointestinal bleeding is suspected, upper gastrointestinal endoscopy is the test of choice. If lower gastrointestinal bleeding is suspected, fiber-optic flexible colonoscopy should be selected as the first diagnostic tool. Treatment is currently being conducted on anatomic location and pathogenesis underlying gastrointestinal bleeding. The most important treatment for bleeding from stress gastritis is prevention. Lowering the gastric acidity and maintaining intragastric pH 4 to 5 or higher can prevent bleeding. Prophylactic administration of antacids, histamine-2 receptor antagonists, or proton pump inhibitors for the first 4 weeks after spinal cord injury are widely used in intensive care units, and this particular complication is minimized. Long-term use of proton pump inhibitors is associated with an increased incidence of *Clostridium difficile* infection.

42.7.2 Gallbladder Disease

Patients with spinal cord injuries may have an increased prevalence of gallbladder disease. Cholecystitis occurs in 16.7–36% of spinal cord injuries with an acute abdomen and is attributed to a tendency to form gallstones in this population. The mechanism underlying the association between gallstones and spinal cord injury remains unclear. However, there is evidence of gallbladder dysfunction in patients with spinal cord injuries. While gallbladder contraction remains normal in patients with spinal cord injuries, gallbladder relaxation is often impaired in injuries above the T10 level, which leads to a lower resting volume (Ketover et al. 1996; Stolarski et al. 2020; Tandon et al. 1997). Cholelithiasis is more common in patients with spinal cord injuries. In the study, gallstone morbidity in patients with spinal cord injuries increased threefold compared to the control group (Apstein and Dalecki-Chippenfield 1987) and 25% in male patients with chronic spinal cord injuries (Rotter and Larrain 2003). Although the reasons for the increase in cholelithiasis are not well known, there is a possibility of decreased gallbladder motility and bile stasis due to impaired sympathetic innervation, altered enterohepatic circulation of bile acids, and changes in biliary lipid excretion. Acute pancreatitis may result from spasm of the sphincter Oddi as a result of parasympathetic predominance. High doses of steroids can increase risk.

Because of the diagnostic delay of cholecystitis, patients with spinal cord injuries have a higher annual incidence of biliary complications (2.2%) than the general population (0.2% to 1.0%). Although mortality rates are comparable to the general population, patients with spinal cord injuries have a higher complication rate and a higher conversion rate from laparoscopic to open procedures (Moonka et al. 1999). Clinical presentation may not show typical symptoms or signs due to sensory loss. Patients with cervical or high thoracic injuries may have atypical symptoms, such as increased spasticity, abdominal spasms, autonomic dysreflexia, and referring pain to the shoulder.

42.8 Hyponatremia

Hyponatremia is defined as a low serum or plasma sodium (Na^+) concentration, less than 135 mEq/L. Symptoms of hyponatremia can include nausea, muscle cramps, fatigue, lethargy, gait disturbances, forgetfulness, confusion, and, if severe and acute enough, coma or seizures. Asymptomatic chronic hyponatremia for more than 48 h, down to 120 mEq/L, is not a cause for alarm and does not require urgent correction (Norwood 2015).

If hyponatremia is due to volume depletion, if the serum sodium is >120 mEq/L, and if the patient is asymptomatic, hemodynamically stable, and can safely be hydrated orally, the patient can be rehydrated by consumption of water. Patients with serum sodium <120 mEq/L and/or an inability to tolerate oral intake should receive IV fluid boluses of isotonic crystalloids (normal saline or lactated ringers) of at least 2 L as long as the cardiopulmonary status tolerates it. Hypervolemic causes of hyponatremia are managed by treating the underlying disease in addition to free water restriction. Chronic hyponatremia related to syndrome of inappropriate antidiuretic hormone (SIADH) is treated by limiting free water intake to no more than 1 L daily, in addition to treating the underlying cause. In patients with SIADH who do not respond to free water restriction or salt loading alone, the addition of a low-dose loop diuretic such as furosemide 20 mg twice a day orally with salt tablets or IV saline is recommended. Acute hyponatremia, when severe <120 mEq/L and/or associated with neurologic manifestations, requires more urgent correction of serum sodium. This should be done in a monitored setting such as the ICU, where the patient can have frequent neurological checks and timely labs to monitor serum sodium, and is usually accomplished by the administration of IV hypertonic saline (Norwood 2015).

Correction of the sodium concentration should not initially be faster than 0.5–1.0 mEq/L/h until 6–8 mEq/L increase and then should be less than 0.5 mEq/L/h. An increase in sodium concentration of 6–8 mEq/L should be sufficient to significantly decrease symptom. Sodium concentrations in excess of 10–12 mEq/L for the first 24 h or in excess of 20 mEq/L during the

first 48 h are not allowed due to concerns about osmotic demyelination syndrome, which can lead to severe neurological sequelae (Yee and Rabinstein 2010). Initial infusion of 3% saline in 50–100 mL/h is generally safe for a short period of time for an average sized person with severe symptom. Generally, the infusion of 3% saline does not exceed a total of 6–8 h. When sodium is corrected to 6–8 mEq/L, 3% saline is discontinued. The use of 3% saline does not require sodium correction close to the normal range.

42.9 Urinary Tract Infection

Urinary tract infections are common in people with spinal cord injuries and are the leading cause of fever in this population. People with spinal cord injuries have many characteristics that place them at high risk for urinary tract infections, including impaired bladder emptying, instrumentation/catheterization, pressure injuries, and reduced host defense from chronic disease. People with spinal cord injuries usually do not experience the classic symptoms of urinary tract infection such as dysuria, frequency, or urgency due to their loss of sensation. They are more common with vague abdominal discomfort, spasticity, fatigue, fever, or cloudy or malodorous urine. Only 20% of urinary tract infections in spinal cord injuries are caused by *E. coli*. *Enterococci*, *P. mirabilis*, and *Pseudomonas* are more common in this patient population. They also have a high rate of antimicrobial resistance (Patros et al. 2018). Typical antibiotic therapies for urinary tract infection in spinal cord injuries include aminoglycoside plus a penicillin or a third-generation cephalosporin. However, previous culture data must be considered in order to screen for a history of resistant organisms (Dubbs and Sommerkamp 2019). Treatment options, dosage, and duration of treatment are summarized in Table 42.1.

42.10 Pyelonephritis

Pyelonephritis is a bacterial infection of the kidney parenchyma. Most cases are caused by ascension of bacteria through the urinary tract, starting with cystitis. Few cases are caused by hematogenous spread and are associated with virulent organisms such as *S. aureus*, *P. aeruginosa*, *Salmonella*, and *Candida* (Imam 2021). Patients with acute pyelonephritis typically present with fever, flank pain, and vomiting, tenderness in the costovertebral angle, and laboratory diagnosis of urinary tract infection. The Infectious Diseases Society of America (IDSA) recommends that urine cultures with sensitivity testing be performed in all patients with acute pyelonephritis (Gupta et al. 2011). Blood cultures should be requested for patients who appear severely ill. Up

Table 42.1 Empirical antibiotic regimens for uncomplicated urinary tract infection

Nitrofurantoin monohydrate	100 mg	Twice daily	5 d	First line, well-tolerated, inexpensive.
TMP-SMX	160 mg/800 mg	Twice daily	3 d	First line if *E coli* resistance <20%, well-tolerated, inexpensive
Fluoroquinolones				Second line: Falling out of favor because of increasing resistance and adverse side-effect profiles
Ciprofloxacin	500 mg	Twice daily	7d	
Levofloxacin	750 mg	Once daily	5d	
Fosfomycin trometamol	3 g		Once	More expensive, slightly lower efficacy than first-line agents, but may prevent recidivism
Amoxicillin-clavulanate	500 mg/125 mg	Twice daily	3–7 d	Alternative treatment when other agents cannot be used, lower efficacy
Cephalosporins				Alternative treatment when other agents cannot be used, lower efficacy
Cefdinir	300 mg	Twice daily	7 d	
Cefaclor	500 mg	3 times daily	7 d	
Cefpodoxime	100 mg	Twice daily	7 d	
Cefuroxime	250 mg	Twice daily	7–10 d	
Pivmecillinam	400 mg	Twice daily	4–7 d	Availability limited to only some European countries

to 25% of female patients with acute uncomplicated pyelonephritis have positive blood cultures (Velasco et al. 2003), but results from these culture results rarely change management. Diagnostic imaging should be considered, especially if there are concerns for calculi or other obstruction, abscess, emphysematous pyelonephritis, mass, or other mimics of urinary tract infections (Dubbs and Sommerkamp 2019).

Antipyretics and antiemetics are helpful in controlling symptoms. Intravenous fluids can be given if the patient is dehydrated as a result of vomiting or poor oral intake. Antibiotics started should include coverage against *E coli*, which will account for most cases. In patients with recurrent urinary tract infections, indwelling urinary catheters, or a history of instrumentation, coverage against more virulent or resistant organisms should be considered. In areas where uropathogen resistance to fluoroquinolones is less than 10%, ciprofloxacin or levofloxacin is recommended. It is common for patients to receive an intravenous dose of ceftriaxone or aminoglycoside if they are managed in the emergency department, even if they are being discharged on a prescription for an oral fluoroquinolone. The same single-dose parenteral antibiotic regimen is recommended when TMP-SMX or beta-lactams, both second-line agents, are chosen for empiric treatment (Dubbs and Sommerkamp 2019).

42.11 Delirium

Cognitive dysfunction, which is common in older patients with spinal cord injuries, is more likely to be depression than delirium or dementia. Therefore, history and screening for depression are required. In addition, the prevalence of delirium is high due to initial medical problems such as brain damage, the use of opioid analgesics, electrolyte abnormality, hypoglycemia, and drug interactions (Furlan et al. 2009). Therefore, early detection of delirium symptoms and proper treatment are very important. Anticholinergic drugs such as tricyclic antidepressants and diphenhydramine, oxybutynin, and baclofen are also delirium-inducing drugs. Although the cause has been identified and the treatment has been performed, if the delirium persists, a small dose of haloperidol may be used. Haloperidol for delirium should be given 0.5 mg once at night or twice daily in the morning and evening. In severe cases, 0.5–2.5 mg is injected intramuscularly or intravenously. Lorazepam 0.5–1.0 mg can be administered orally. The purpose of haloperidol administration is to stabilize the patient without affecting the level of consciousness. Therefore, if an intramuscular or intravenous injection is given, the patient should be monitored every 30 min and, if necessary, an additional double initial dose should be administered. In addition to delirium and depression, a history of dementia is required. Elderly patients with spinal cord injury who are suspected of delirium, depression, or dementia should be screened for common blood test, urinalysis, electrolyte test, thyroid test, liver function test, serum levels of ammonia, vitamin B12 and folate, ESR and CRP, blood glucose, and brain MRI or CT. In some cases, neuropsychological tests, syphilis tests, and EEG are added.

42.12 Depression and Suicide

Depressive disorders are the most common psychologic distress in people with spinal cord injuries and appear to be more common than in the general population (Fann et al. 2011; Post and van Leeuwen 2012). The estimated prevalence of depression after spinal cord injuries varies widely from study to study. Clinically significant symptom rates range from about 14% to 35% (Frank et al. 1992; Fuhrer et al. 1993), and major depression has been reported in 10% to 15% of people with spinal cord injuries. The percentage of persons with major depressive syndrome in spinal cord injuries ranges from 11.2% in the first post-injury year to 6.4% in the 35th post-injury year (National Spinal Cord Injury Statistical Center 2021). As suicide has been associated with sudden and depressed life events, people with spinal cord injuries may have a higher suicide rate than the general population (Krysinska et al. 2009). The suicide rate is about 3 to 5 times higher than that of the general population, and about 50% of patients with spinal cord injuries report suicidal ideation (Hartkopp et al. 1998). Suicidal mortality among people with spinal cord injuries decreased in the 1990s cohort than in the 1970s cohort, but was still 3 times higher than that of

the general population in the USA (Cao et al. 2014). In a Korean study, suicidal ideation in people with spinal cord injuries was 34.8%, 3 times higher than the general population (Nam et al. 2013). According to the 2020 Annual report of National Spinal Cord Injury Statistical Center (NSCISC), suicide ranks ninth as the primary cause of death of spinal cord injuries (National Spinal Cord Injury Statistical Center 2021). Three risk factors for excessive suicide mortality have been reported in people with spinal cord injuries: non-Hispanic white males, the first 6 years after spinal cord injury, and T1-S3 injury levels with AIS A, B, or C (Cao et al. 2014).

References

Amsterdam EA, Kirk JD, Bluemke DA, et al. Testing of low-risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. Circulation. 2010;122:1756–76.

Apstein MD, Dalecki-Chippenfield K. Spinal cord injury is a risk factor for gallstone disease. Gastroenterology. 1987;92:966–8.

Blackmer J. Rehabilitation medicine: 1. Autonomic dysreflexia. CMAJ. 2003;169:931–5.

Cao Y, Massaro JF, Krause JS, et al. Suicide mortality after spinal cord injury in the United States: injury cohorts analysis. Arch Phys Med Rehabil. 2014;95:230–5.

Charney KJ, Juler GL, Comarr AE. General surgery problems in patients with spinal cord injuries. Arch Surg. 1975;110:1083–8.

Claydon VE, Krassioukov AV. Orthostatic hypotension and autonomic pathways after spinal cord injury. J Neurotrauma. 2006;23:1713–25.

Consortium for Spinal Cord Medicine. Acute management of autonomic dysreflexia: individuals with spinal cord injury presenting to health care facilities. 2nd ed. Washington, DC: Paralyzed Veterans of America; 2001.

Cruz ES, Stolzenberg D, Moon D. Medical emergencies in rehabilitation medicine. In: Maitin IB, editor. Current diagnosis and treatment: physical medicine and rehabilitation. New York: McGraw-Hill Education; 2015.

Dubbs SB, Sommerkamp SK. Evaluation and management of urinary tract infection in the emergency department. Emerg Med Clin North Am. 2019;37:707–23.

El Masri WE, Cochrane P, Silver JR. Gastrointestinal bleeding in patients with acute spinal injuries. Injury. 1982;14:162–7.

Fann JR, Bombardier CH, Richards JS, et al. Depression after spinal cord injury: comorbidities, mental health service use, and adequacy of treatment. Arch Phys Med Rehabil. 2011;92:352–60.

Frank RG, Chaney JM, Clay DL, et al. Dysphoria: a major symptom factor in persons with disability or chronic illness. Psychiatry Res. 1992;43:231–41.

Friesbie JH. Fractures after myelopathy: the risk quantified. J Spinal Cord Med. 1997;20:66–9.

Fuhrer MJ, Rintala DH, Hart KA, et al. Depressive symptomatology in persons with spinal cord injury who reside in the community. Arch Phys Med Rehabil. 1993;74:255–60.

Furlan JC, Kattail D, Fehlings MG. The impact of comorbidities on age-related differences in mortality after acute traumatic spinal cord injury. J Neurotrauma. 2009;26:1361–7.

Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. J Neurol. 2017;264:1567–82.

Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the infectious diseases society of america and the european society for microbiology and infectious diseases. Clin Infect Dis. 2011;52:e103–20.

Hagen EM, Rekand T, Grønning M, et al. Cardiovascular complications of spinal cord injury. Tidsskr Nor Laegeforen. 2012;132:1115–20. English, Norwegian.

Hartkopp A, Brønnum-Hansen H, Seidenschnur AM, et al. Suicide in a spinal cord injured population: its relation to functional status. Arch Phys Med Rehabil. 1998;79:1356–61.

Imam T. Bacterial urinary tract infections. Merk Manual. 2021. https://www.merckmanuals.com/professional/genitourinary-disorders/urinary-tract-infections-utis/bacterial-urinary-tract-infections?redirectid=149. Accessed Aug 27, 2021.

Juler GL, Eltorai IM. The acute abdomen in spinal cord injury patients. Paraplegia. 1985;23:1118–23.

Ketover SR, Ansel HJ, Goldish G, et al. Gallstones in chronic spinal cord injury: is impaired gallbladder emptying a risk factor? Arch Phys Med Rehabil. 1996;77:1136-8.

Khan MF, Burks SS, Al-Khayat H, et al. The effect of steroids on the incidence of gastrointestinal hemorrhage after spinal cord injury: a case-controlled study. Spinal Cord. 2014;52:58–60.

Kiwerski J. Bleeding from the alimentary canal during the management of spinal cord injury patients. Paraplegia. 1986;24:92–6.

Krassioukov A, Eng JJ, Warburton DE, et al. Spinal cord injury rehabilitation evidence research team. A systematic review of the management of orthostatic hypotension after spinal cord injury. Arch Phys Med Rehabil. 2009;90:876–85.

Krysinska K, Lester D, Martin G. Suicidal behavior after a traumatic event. J Trauma Nurs. 2009;16:103–10.

Kupfer M, Kucer BT, Kupfer H, et al. Persons with chronic spinal cord injuries in the emergency department: a review of a unique population. J Emerg Med. 2018;55:206–12.

Lamarre-Cliché M. Drug treatment of orthostatic hypotension because of autonomic failure or neurocardiogenic syncope. Am J Vardiovasc Drugs. 2002;2:23–35.
Leramo OB, Tator CH, Hudson AR. Massive gastroduodenal hemorrhage and perforation in acute spinal cord injury. Surg Neurol. 1982;17:186–90.
McKinley WO, Jackson AB, Cardenas DD, et al. Long-term medical complications after traumatic spinal cord injury: a regional model systems analysis. Arch Phys Med Rehabil. 1999;80:1402–10.
Miller BJ, Geraghty TJ, Wong CH, et al. Outcome of the acute abdomen in patients with previous spinal cord injury. ANZ J Surg. 2001;71:407–11.
Moonka R, Stiens SA, Resnick WJ, et al. The prevalence and natural history of gallstones in spinal cord injured patients. J Am Coll Surg. 1999;189:274–81.
Morris LL, Whitmer A, McIntosh E. Tracheostomy care and complications in the intensive care unit. Crit Care Nurse. 2013;33:18–30.
Nam HS, Kim HR, Ha TH, et al. Suicidal ideation in Korean persons with spinal cord injury. Spinal Cord. 2013;51:789–93.
National Spinal Cord Injury Statistical Center. Complete public version of the 2020 annual statistical report for the spinal cord injury model systems. https://www.nscisc.uab.edu/public/2020%20Annual%20Report%20-%20Complete%20Public%20Version.pdf. Accessed Aug 25, 2021.
Nawrocki O, Hughart J, Morgenstern J. Tracheostomy emergencies. Emergency Medicine Reports, June 15, 2021. https://www.reliasmedia.com/articles/148186-tracheostomy-emergencies. Accessed Aug 23, 2021.
Neumayer LA, Bull DA, Mohr JD, et al. The acutely affected abdomen in paraplegic spinal cord injury patients. Ann Surg. 1990;212:561–6.
Nobunaga AI. Orthostatic hypotension in spinal cord injury. Top Spinal Cord Inj Rehabil. 1998;4:73–80.
Norwood BS. Common laboratory abnormalities. In: Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing; 2015.
O'Connor H, White A. Tracheostomy decannulation. Respiraory Care. 2010;55:1076–81.
Okamoto LE, Diedrich A, Baudenbacher FJ, et al. Efficacy of servo-controlled splanchnic venous compression in the treatment of orthostatic hypotension: a randomized comparison with midodrine. Hypertension. 2016;68:418–26.
Ong B, Wilson JR, Henzel MK. Management of the patient with chronic spinal cord injury. Med Clin North Am. 2020;104:263–78.
Patros C, Sabol M, Paniagua A, et al. Implementation and evaluation of an algorithm-based order set for the outpatient treatment of urinary tract infections in the spinal cord injury population in a VA medical center. J Spinal Cord Med. 2018;41:192–8.
Pattanong P. Dislodged tracheostomy. J Prapokklao Hosp Clin Med Educat Center. 2007;24:304–8.
Phillips WT, Kiratli BJ, Sarkarati M, et al. Effect of spinal cord injury on the heart and cardiovascular fitness. Curr Probl Cardiol. 1998;23:641–716.
Post MW, van Leeuwen CM. Psychosocial issues in spinal cord injury: a review. Spinal Cord. 2012;50:382–9.
Regan K, Hunt K. Tracheostomy management. Contin Educ Anaesth Crit Care Pain. 2008;8:31–5.
Rotter KO, Larrain CG. Gallstones in spinal cord injury (SCI): a late medical complication? Spinal Cord. 2003;41:105–8.
Sezer N, Akkuş S, Uğurlu FG. Chronic complications of spinal cord injury. World J Orthop. 2015;6:24–33.
Shergill IS, Arya M, Hamid R, et al. The importance of autonomic dysreflexia to the urologist. BJU Int. 2004;93:923–6.
Sidorov EV, Townson AF, Dvorak MF, et al. Orthostatic hypotension in the first month following acute spinal cord injury. Spinal Cord. 2008;46:65–9.
Solerstrom CA, Ducker TB. Increased susceptibility of patients with cervical cord lesions to peptic gastrointestinal complications. J Trauma. 1985;25:1030–8.
Stolarski A, He K, Whang E, et al. Diagnostic challenges of acute abdominal emergencies in spinal cord injury patients: a clinical perspective. J Sure Open Access. 2020;6(4) https://doi.org/10.16966/2470-0991.215.
Tandon RK, Jain RK, Garg PK. Increased incidence of biliary sludge and normal gall bladder contractility in patients with high spinal cord injury. Gut. 1997;41:682–7.
Vaidyanathan S, Soni B, Oo T, et al. Autonomic dysreflexia in a tetraplegic patient due to a blocked urethral catheter: spinal cord injury patients with lesions above T-6 require prompt treatment of an obstructed urinary catheter to prevent life-threatening complications of autonomic dysreflexia. Int J Emerg Med. 2012;5:6.
Velasco M, Martínez JA, Moreno-Martínez A, et al. Blood cultures for women with uncomplicated acute pyelonephritis: are they necessary? Clin Infect Dis. 2003;15(37):1127–30.
Walters K, Silver JR. Gastrointestinal bleeding in patients with acute spinal injuries. Int Rehabil Med. 1986;8:44–7.
Yee AH, Rabinstein AA. Neurologic presentations of acid-base imbalance, electrolyte abnormalities, and endocrine emergencies. Neurol Clin. 2010;28:1–16.

Recommended Additional Reading

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing; 2015.
Eltorai IM, Schmitt JK, editors. Emergencies in chronic spinal cord injury patients. 3rd ed. New York: Eastern Paralyzed Veterans Association; 2001.
Maitin IB, editor. Current diagnosis and treatment: physical medicine and rehabilitation. New York: McGraw-Hill Education; 2015.
Noggle CA, Dean RS, editors. Neuropsychological rehabilitation. New York: Springer Publishing Company; 2013.
Rudd MA, Hough S, Wegener ST, et al., editors. Practical psychology in medical rehabilitation. Switzerland: Springer; 2017.

Psychological Problems in Spinal Cord Injuries

43

After spinal cord injury, the patient found that there were dramatic changes in various parts of the body's function. Depending on the level of injury, the patient may have problems with bowel and bladder function, sexual function, and respiratory and cardiac function, as well as voluntary movement and radical changes in the world around them. In addition to the physiological changes, patients experience psychological changes. Each person with spinal cord injury is fully aware of the various issues associated with the injury and its effects on future life at different stages of the treatment process. Each person has a unique approach to coping and problem-solving and presents his/her own pattern of difficulty and distress over the years following the injury onset.

Responses to spinal cord injury vary considerably between individuals, and each person undergoes a unique adjustment process (Chevalier et al. 2009). Previous assumptions on loss response theory are not supported by research in patients with spinal cord injury. No single theory of crisis response or adjustment of disability seems to take into account sufficiently the entire psychological process of the patient (Chevalier et al. 2009). However, a number of theories offer useful insights to consider. The older rehabilitation literature describes the stage theory for this process of psychological reaction to emotional and cognitive reactions as people with spinal cord injury for adjustment. However, there is no universal path for adjustment. In fact, after spinal cord injury, people can go directly to one or more emotional stages without going through the sequential stages of denial, anger, bargaining, depression, and acceptance. There are, however, a number of emotional reactions. Often, these reactions are clinically highly valued in the rehabilitation settings when patients with spinal cord injuries initially encounter their limitations. Adjustment is not an end in itself but a lifelong adaptation process (Chevalier et al. 2009).

Some patients have strong psychological defense mechanisms after spinal cord injury and may appear less anxious and distressed. These psychological defenses can benefit adaptations (mature defenses) and may act as difficulty in adaptations (immature defenses). Understanding this aspect of the patient's adjustment of the psychological defense mechanism can help manage future treatment plans and patient's behavior. Psychological considerations in patients with spinal cord injury are important to provide effective management for all clinicians and disciplines involved in the care of persons with spinal cord injury. Psychologists provide a team of spinal cord injury treatment with the necessary expertise, but all team members need to share information about psychological health of the patient.

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43.1 Psychological Responses and Intervention in the Acute Phase of Spinal Cord Injury

Comprehensive spinal cord injury rehabilitation should begin as soon as possible after injury. This means the introduction of physical, occupational, and speech intervention, as well as psychology and social work, in the intensive care units. In the past, in most of the psychological literature, the patient was assumed to be in a state of shock or denial, with little meaningful emotional change or adaptations having been made (Fordyce 1971). In the acute phase, there is often nonspecific distress and shock from spinal cord injury, which does not usually last for long periods. In some cases, there is no obvious psychological dysfunction. Factors that affect response to spinal cord injury include low environmental reward, external locus of control, chronic pain, and alcohol and substance abuse. Clinical experience seems to support the idea that the process of psychological adjustment starts quite early and early interventions make a significant difference in the short- and long-term process of adjustment (Kemp and Vash 1971).

During the acute phase of spinal cord injury, a wide range of emotional responses include anxiety, depression, overt expression of anger and hostility, denial of the severity of the injury, increased dependency, withdrawal and, in the extreme, muteness and noncompliance. The most profound personal change is the loss of independence. As a patient with spinal cord injury, an adult experiences an incredible loss of control. Depending on the level of injury, the person may need help with breathing, eating, talking, eliminating, bathing, dressing, moving, coughing, and all the other activities. These dependencies range from activities that are absolutely essential for life to small details of comfort and convenience to help them in making life bearable. This loss of control can be extremely difficult for an adult to cope with, but acute care is far from the best of situations. There are many changes in the role of the family and future coping strategies depending on the function and attitude of the patient after the injury.

The phenomenon of regression is perhaps one of the most obvious early consequences of spinal cord injury as becoming more childlike and dependent, losing control, losing reinforcement, becoming egocentric, and becoming focused on more basic levels of need. In addition to regression, various other common early reactions to traumatic spinal cord injury have been observed. Internally, there is considerable confusion about self-esteem and ability to communicate with the surrounding world. Patients with spinal cord injuries experience significant emotional changes. It is important to assess the psychological state of the patient during the initial overall psychological assessment of the patient with spinal cord injury, but it is more important to listen to the patient's personal problems after the injury. The initial psychological state of the patient is expressed as anger, grief, sadness, or rage. Due to its altered physical condition, the loss and fear of the individual are likely to induce social withdrawal indifference or denial, thus making them become socially isolated by feeling of shame (Klyce et al. 2015).

Two other psychological reactions of patients newly injured in the spinal cord have received considerable attention in the literature. They are depression and denial, and both deserve special attention because of the controversy and common misperceptions surrounding them.

No standard approach can be used for every patient during the acute phase of treatment after spinal cord injury. The intervention should be adapted to the individual, the symptoms, and the underlying causes of the symptoms. A general understanding of what the patient and the family are experiencing can lead to some general principles of intervention: knowing the limits of the intervention, allowing the patient to lead, maintaining dignity of the patient, publicizing the new environment or new treatments, facilitating trust in the rehabilitation team, and encouraging positive, realistic expectations.

43.2 Psychological Responses and Intervention in the Rehabilitation Phase

The experience of a serious psychological crisis experienced by the patient continues in the context of rehabilitation care. But the issues of life, death, and physical safety are less prominent. The rehabilitation phase of patients with spinal cord injuries is usually the longest period during the initial hospitalization period. During this time, the patient and family may begin the first steps toward possible adjustment to the disability and the new situation. Sometimes, the patient arrives at rehabilitation without understanding the injury or the prognosis nor any foundation of knowledge to understand what has happened to them.

When confronted with negative or devastating life events, most people want to have the opportunity to ventilate and simply talk about what is happening to them. Allowing the patient to talk about their concerns is one of the most fundamental but important roles that the psychologists perform in the rehabilitation programs. Therapeutic support can provide a positive environment for promoting patient's own identity changes, increasing self-confidence, and providing reinforcement for daily accomplishments. Taking time to listen to the patient thoughts and emotional responses on a regular basis can alleviate the tension of the crisis and help people cope with the difficult tasks.

Many adjustment theories provide useful information. Older literature on rehabilitation explains the theory of the stages of psychological response to emotional and cognitive responses in patients with spinal cord injuries for their adjustment such as shock, denial, anger, depression, and assimilation. However, there is no universal path for adjustment. Psychological interventions perform a variety of functions during the rehabilitation programs, including providing relief from extreme anxiety, fear, and panic; providing relief from overwhelming distress caused by reliving past trauma; teaching adaptive patterns of response; and influencing a positive restructuring of self-image as the meaning of the injury and its impact of life are explored by each patient (Beauregard et al. 2012).

43.3 Psychological Reactions

43.3.1 Depression

Devastating damage, such as spinal cord injury, causes various psychological reactions, ranging from the patient's adjustment reaction to major depressive disorders. The differential diagnosis can include grief associated with to losses, demoralization, adjustment disorder, major depressive disorders, depression secondary to a medical condition, and delirium (Consortium for Spinal Cord Medicine 2020). Depression is often cited as a normal consequence of spinal cord injury and plays an important role in many stage theories of adjustment (Hohmann 1975). The incidence of depression in patients with spinal cord injury is higher than in the general population. Depression is reported in a significant proportion of people with spinal cord injury, which varies from 20% and 30% depending on the results of the study (Bombardier et al. 2012). Because the adjustment reaction is not treated with antidepressants, psychotherapy and support systems by family or friends are needed.

The risk factors for depression after spinal cord injury are divided into modifiable and nonmodifiable groups. Potential modifiable risk factors include fewer rewarding activities, external locus of control, chronic pain, and alcohol and substance abuse (Bombardier et al. 2012). It is particularly important to know the potential modifiable risk factors for developing effective therapeutic strategies that can reduce or prevent depression and promote positive adaptation and coping strategies. Nonmodifiable risk factors include familial history of depression; depression or suicide prior to injury; family problems such as divorce, less than 5 years post-injury; or associated traumatic brain injury (Hagen et al. 2010; Macciocchi et al. 2012).

Depressive behavior can be difficult to distinguish from acceptable reactive depressive episodes, that is, grief due to loss of function and problematic major depression (Graves and Bombardier 2008). Persistent sadness and dysphoria in response to the recognition of functional losses are common. Support, encouragement, and empathic listening are all helpful throughout the process. However, deciding when a person has major depression can be more problematic. Clinical symptoms of depression present as sleep disturbance, weight loss, loss appetite, diminished energy, and diminished interest in sexual functioning (Bhat et al. 2012; Graves and Bombardier 2008). Bereavement or grief reaction after spinal cord injury may be similar to depression, but this usually does not lead to prolonged feelings of guilt, self-reproach, worthlessness, or thoughts of death, as in depressive disorders (Klyce et al. 2015).

43.3.1.1 Assessment for Depression

Risk factors for depression should be identified. Secondary factors that cause depression or exacerbate depression should be determined, such as the effect of medications, pain, or disturbed sleep. Suicide risk is assessed by examining suicidal ideation, plan, or intention, as well as previous attempts (Cuff et al. 2014). Depressive symptoms can occur in a number of contexts, ranging from transient stressful situations, such as transitions in care, anniversaries of the injury, financial or housing difficulty, to chronic stressors such as physical disability, chronic medical illness, and barriers to participation in meaningful or enjoyable activities. Other contributing factors may include medication side effects, delirium, alcohol or drug use, or a comorbid mental health illness, e.g., bipolar disorder, dementia, schizophrenia. Because of this wide range of etiologies and contributors, a thorough history and diagnostic assessment is essential before deciding on a course of action (Consortium for Spinal Cord Medicine 2020).

For people with spinal cord injuries, routine screening for depression should be done. Symptoms that indicate a major depressive disorder include depressed mood or a loss of interest or pleasure in daily activities lasting more than 2 weeks and a change in the person's baseline, impaired functioning, psychomotor retardation, significant change in weight, appetite, and sleep with insomnia or hypersomnia, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, decreased ability to concentrate, and thoughts of death or suicidal ideation or plan (Deak and Winkelman 2012).

43.3.1.2 Screening Tools for Depression

There are several measures to screen for depression, but as screening tools they are long and inefficient. The Patient Health Questionnaire (PHQ)-9 is one of the most commonly used depression scales in patients with spinal cord injuries. It consists of nine items and is shorter than most depression scales. It has been validated in several nonpsychiatric medical conditions including spinal cord injury. The PHQ-9 can overdiagnose a major depressive disorder (false positive) and will therefore require diagnostic interviews and/or reassessment after a short period to ensure that the person meets diagnostic criteria (Consortium for Spinal Cord Medicine 2020). As an indicator of major depressive disorder in spinal cord injuries, overall accuracy is reported to be superior to other depression screening.

The PHQ-2 contains the first two items of the PHQ-9 and can be administered as a prescreen. It is examined how many times a person has experienced a depressed mood and a loss of interest over the past 2 weeks. These symptoms are based on the two essential criteria for the diagnosis of major depressive disorder. It was suggested that physicians could include the PHQ-2 as part of a system review. A positive response to both questions implies an in-depth assessment of depression by a rehabilitation psychologist or other mental health professionals. It is important to note that these measures do not replace a clinical interview for a diagnosing major depressive disorder. Nonspecific effects of spinal cord injury, such as fatigue or reduced energy and sleep disturbance in a hospital setting, can lead to false inflation of scores in depression measures.

43.3.1.3 Management of Depression

Supportive and positive participation of the rehabilitation team can play an important role in promoting success and control during rehabilitation and in promoting adjustment to injury and confidence for individuals with spinal cord injuries. Feelings of sadness and depression are normal response to stress and loss. However, if this and the associated psychological (e.g., anhedonia, guilt, suicidal ideation), cognitive (e.g., poor concentration), and physical (e.g., insomnia, low energy, anorexia) symptoms become severe, prolonged, and impair daily functioning, treatment for a clinically significant depressive disorder is indicated (Consortium for Spinal Cord Medicine 2020). Because of the multiple medical and psychosocial issues faced by individuals with medical comorbidity and the complexity, and often fragmentation, of the current health care system, team-based delivery of evidence-based treatment has emerged as a cost-effective approach to depression care (Huffman et al. 2014). For people with spinal cord injuries, clinicians should offer combined medical and psychosocial treatment for major depression whenever possible (Consortium for Spinal Cord Medicine 2020). Aggressively treatment of comorbidities that may exacerbate depression, such as the use of pregabalin for chronic neuropathic pain and treatment of hypothyroidism or obstructive sleep apnea, may also improve depression (Cardenas and Hooton 2015).

When choosing an antidepressant in patients with spinal cord injuries, possible side effects such as dry mouth, constipation, urinary retention, blurred vision, orthostatic hypotension, and autonomic dysreflexia should be considered. Therefore, tricyclic antidepressants (TCAs) may not be drugs of choice in patients with spinal cord injuries. Antidepressants include selective serotonin uptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase (MAO) inhibitors, and other antidepressants such as bupropion and trazodone. The choice of agent depends on previous response, side effect profile, convenience, cost, patient preference, and drug interaction risk. The primary advantages of SSRI over TCA and MAO inhibitors are safety and tolerability. In people with spinal cord injuries found that venlafaxine extended release (mean dose 186 mg per day), an SNRI, was effective in treating core symptoms of major depressive disorder (depressed mood, anhedonia, guilt, psychomotor agitation, psychomotor retardation, and psychic anxiety) diagnosed an average of 11 years following spinal cord injuries (Consortium for Spinal Cord Medicine 2020). Venlafaxine extended release was also found to significantly decrease nociceptive pain and did not increase spasticity (Consortium for Spinal Cord Medicine 2020). In general, SSRIs and SNRIs are likely the best-tolerated antidepressant classes. However, fluoxetine, an SSRI with a long half-life, should be used with caution because of case study data showing increased risk of spasticity in individuals with spinal cord injuries (Stolp-Smith and Wainberg 1999).

SSRIs such as fluoxetine, sertraline, and paroxetine have different side effects such as stimulation, daytime sleepiness, headache, and sexual dysfunction, but they have much less anticholinergic activity. Among the SSRIs, fluoxetine and paroxetine are most likely to cause drug interactions due to inhibition of metabolism of other drugs through the P450 system. Unlike most SSRIs that are activating throughout the day, paroxetine is sedating and usually taken at night. Tricyclic antidepressants can cause drowsiness and should be used with caution because of the risk of anticholinergic side effects that may exacerbate common spinal cord injury-related symptoms (e.g., hypotension, constipation, urinary retention). Anticholinergic side effects of TCAs may lead to cardiovascular events in patients with heart disease. Also, in people who are at risk for suicide, these should be avoided because of their high lethality in overdoses compared to SSRIs. Trazodone is mainly used as a sleep aid because of sedation and short duration. MAO inhibitors are currently rarely used for depression.

An adequate dose for 6–8 weeks will result in 60–70% of patients responding to commonly used antidepressants. It has been shown that mild to moderate depression responds to cognitive behavior therapy or interpersonal therapy alone,

but takes longer than medications. Antidepressant medication associated with cognitive behavior therapy or interpersonal therapy appears to be the most effective approach.

Psychotherapy must be combined with depression because it is difficult to expect effects from medication alone. Behavior therapy includes social skills training required to build a satisfying relationship with people. This provides them positive reinforcement in interpersonal relationships and learns how to avoid major negative effects such as rejection, ignorance, criticism, and bullying. Cognitive therapy aims to reduce the maladapted thinking of patients and to correct biased cognitive errors. It is known as a cognitive behavior therapy because it is often used with a behavior therapy. If there is a suicidal ideation, suicidal attempt, or other serious psychological/psychiatric conditions, hospitalization may be necessary.

43.3.2 Anxiety

Anxiety is a normal reaction to spinal cord injury, but anxiety can become overwhelming and interfere with daily functioning, which is consistent with anxiety disorders. Anxiety disorders are characterized by anticipation or worry about future threat and are typically accompanied by symptoms such as muscle tension, vigilance, and cautious or avoidant behaviors. These disorders are persistent and usually last 6 months or more (Consortium for Spinal Cord Medicine 2020). Three anxiety screening measures are the Hospital Anxiety and Depression Scale (HADS), the Spinal Cord Injury-Quality of Life (SCI-QOL) Anxiety item bank, and the Generalized Anxiety Disorder 7-item scale (GAD-7).

For the treatment of generalized anxiety disorder and panic disorder in the population without spinal cord injury, the effectiveness of serotonergic antidepressants and cognitive behavioral therapy are roughly equivalent. Therefore, treatment decisions should be based on patient preferences, polypharmacy, medication interactions and potential side effects, and availability from specialized mental health providers (Consortium for Spinal Cord Medicine 2020). Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are considered first-line treatments for generalized anxiety disorders. They have better combined safety and efficacy compared with alternatives such as tricyclic antidepressants and benzodiazepines. The effectiveness of different SSRIs and SNRIs is similar. Therefore, selection medication is based on expected side effects, drug interactions, and patient's treatment history or preferences. Therapeutic dosages of these medications used to treat anxiety are similar to those for treating depression. Clinical improvement is expected on average within 4 weeks, but may range from 2 to 6 weeks (Consortium for Spinal Cord Medicine 2020).

Serotonergic agents may exacerbate spasticity (Stolp-Smith and Wainberg 1999). In that case, buspirone for generalized anxiety disorder and pregabalin are considered second-line treatments. Benzodiazepines, used to treat spasticity and anxiety at the same time, have fallen out of favor because of their potential for tolerance, dependence, and other side effects. The use of benzodiazepines should be reserved for short-term relief of acute severe anxiety or panic disorder (Consortium for Spinal Cord Medicine 2020).

For panic disorder, SSRIs are considered the first-line medical treatment. Other drugs such as SNRIs, tricyclic antidepressants, monoamine oxidase inhibitors, and benzodiazepines have proven effectiveness but are less preferred due to the strength of evidence, side effect profiles, and potential for abuse. Chronic use of benzodiazepines is associated with poorer response to a cognitive behavioral therapy, and prolonged PRN use of benzodiazepine is associated with poorer outcomes generally (Consortium for Spinal Cord Medicine 2020).

43.3.3 Denial

Denial is considered to be a maladaptive attempt to protect oneself from distress. The psychological construction of denial is that reality in the physical or emotional sense is subconsciously ignored or regressed by the individual. Clinically,

patients with spinal cord injuries often have statements that deny the reality of injury, such as "When I walk again…or when I come back to…." These statements are a kind of denial, but the important difference is whether this denial is maladaptive.

43.3.4 Conversion Disorder

Psychogenic or hysterical paralysis is a form of conversion disorder that may have a presentation that superficially resembles a spinal cord injury. Conversion motor paralysis disorder is considered common in young female individuals, although other case series describe predominant occurrence in males (Heruti et al. 2002; Letonoff et al. 2002). The patient has an obvious neurological deficit that is inconsistent with other clinical or radiological findings. It is an exclusion diagnosis that must also meet the criteria for a conversion disorder. Stressful event often precedes the onset of symptoms, suggesting that psychological factors are involved. The patient does not consciously or intentionally simulate the symptoms in a conversion disorder, unlike the case in factitious disorder in which patient assumes a voluntary sick role or simulation or malingering, that is, an intentional fabrication for external gain, which can also be presented in the same way.

Patients who are generally affected show clinical signs and symptoms that are incompatible with defined sites of neuroanatomical injury. The entire limbs are paralyzed in contrast to the central paralysis pattern, which has a flexor hypertonic pattern in the lower extremities and extensor dominant pattern in the upper extremities. It is often referred to as a motor or movement conversion disorder, but additional signs of sensory and autonomic dysfunction are frequently observed. Rectal tone, muscle stretch reflexes, and superficial reflexes are usually preserved. Specific physical examination maneuvers can help diagnose. This includes the Spinal Injuries Center (SIC) test, which the examiner lifts the patient's knees in a passively flexed position with the feet flat on the bed. The test is positive if the patient maintains the knees in the flexed position after support is removed. Hoover's test can be helpful if the patient has unilateral leg paralysis. The patient is asked to raise each leg while patient is in the supine position and examiner supports both limbs from under the heels of the patient. The sign is positive when pressure is felt under the heel of the paralyzed leg when the nonparalyzed leg is raised.

Neurological examinations should be repeated carefully with reviewing baseline imaging. In order not to miss organic causes of paralysis, more definitive tests, such as magnetic resonance imaging or motor evoked potential test, should be considered if the patient does not improve within 2–3 days. MRI of the spine and brain should exclude spinal cord compression or a noncompressive lesion of the spinal cord, cauda equina, or relevant areas in the brain including parasagittal cortical lesions due to anterior cerebral artery stroke or meningioma in the falx. If the patient does not consciously simulate the deficit, direct confrontation of the patient with the source of symptoms may not be productive if there is a conversion disorder. Patients should be gently encouraged to resume normal activity, thus minimizing focus on disability. If symptoms do not spontaneously remit, a short rehabilitation stay with behavioral intervention can be helpful.

43.3.5 Other Affective and Behavioral Responses

Patients with spinal cord injury are subject to various forms of anxiety. Anxiety includes an adjustment reaction with anxiety mood and anxiety related to specific problems such as bowel training or rehabilitation activities (Podell and Torres 2011). Patients using a ventilator become very anxious when the respiratory parameters change or when weaning or changing the respiratory system. Benzodiazepine is very helpful in relieving this situational anxiety with supportive psychotherapy. A judicious use of anxiolytics may be useful as a short-term intervention, but it must be weighted in relation to the involvement of the adjustment to injury. If anxiety affects the

learning required to participate in the rehabilitation program, medication should be considered. Behavioral treatment approaches for the treatment of anxiety, including relaxation training and imagery reconditioning techniques, are also considered. Anxiety in patients with spinal cord injuries is also associated with medications such as antidepressants, steroids, and baclofen, and caffeine should be avoided as it can worsen anxiety.

Panic disorder differs from depression in that it exhibits autonomic dysfunction such as dyspnea, dizziness, dyspnea, tachycardia, diaphoresis, nausea, chest pain, and fear of dying. Panic disorders require antidepressants and anxiolytics in combination with behavioral therapy.

Sometimes there are behavior problems related to anger and hostility toward others, including the medical team. Excessive dependence on others interferes with functional abilities or functional outcomes. Noncompliance with recommended care and reduced motivation to participate in self-care and rehabilitation is a lack of willingness to relate to depression or substance abuse. Serious ethical tension and conflict occur when a patient with high tetraplegia using a ventilator refuses or requires removal of a life support device. Of course, it is a matter for the patient to decide, but it is necessary to evaluate and treat the inherent depression until the decision is made.

43.4 Suicide

Routine suicide screening and systematic suicide risk management in people with spinal cord injuries are supported by the increased reported prevalence of suicidal ideation, suicide attempts, and suicidal deaths in this population. The US studies reported that people with spinal cord injuries were reported to be 3–5 times more likely to die of suicide than the general population (Cao et al. 2014; DeVivo et al. 1991). Suicidal ideations are common after spinal cord injuries. Over 13% of a cohort with spinal cord injuries reported suicidal ideation in the prior 2 weeks in a cross-sectional analysis and 7.4% reported a lifetime suicide attempt (McCullumsmith et al. 2015). While spinal cord injury in itself increases the risk of suicide, a higher risk of death by suicide after spinal cord injury has been associated with certain demographic (non-Hispanic White races) and injury characteristics (paraplegia, T1-S3 level with AIS A, B, or C) as well as a history of drug abuse or current alcohol abuse. Suicide deaths are significantly higher in individuals whose spinal cord injury is caused by an attempted suicide when compared with all other causes of spinal cord injury.

The Columbia Suicide Severity Rating Scale (C-SSRS) is a standardized tool that screens for suicidal ideation, quantifies the severity of suicidal ideation and behavior, and further evaluates for suicidal intent or plan if questions for suicidal ideation generate a positive response.

Warning signs for suicide differ from risk factors (Rudd 2008). Indirect warning signs may include recently increasing or excessive substance abuse, hopelessness (a feeling that nothing can be done to improve the situation); burdensomeness (talking about being a burden to others); purposelessness (no reason for living); feeling trapped with no way out; social withdrawal (from family, friends, society); dramatic mood changes; overwhelming guilt, self-blame, or shame; or neglecting bowel, bladder, skin and other aspects of self-care (Consortium for Spinal Cord Medicine 2020).

43.5 Substance Use Disorders

Mental health disorders and substance use disorders are common comorbidities in people with spinal cord injuries (Kennedy and Evans 2001). These conditions can contribute to the overall suffering and disability of people with spinal cord injuries (Tate et al. 1994), negatively impact outcomes (Craig et al. 2015; Tate et al. 1994), increase the costs, and decrease the efficiency of rehabilitation (Dobrez et al. 2010), and lead to premature death (Craig et al. 2009). A minimum age of 65 years, Latino, and married, as well as injury duration of at least 10 years protect against substance use disorder (Dorstyn et al.

2011; Saunders and Krause 2011; Schandler et al. 1995). It is recommended that the screening include preinjury history of mental health and substance use problems, as people with spinal cord injuries have high rates of pre-injury mental health disorders and substance use disorders, and a history of these disorders is predictive of post-spinal cord injury mental health (Tétrault and Courtois 2014). Mental illness and substance use disorders are often chronic, relapsing conditions that require prolonged treatment, relapse prevention efforts, and ongoing monitoring or rescreening (Frank et al. 1991; Hunt et al. 1971). It is, therefore, of crucial importance to plan continued treatment across transitions in care such as from inpatient rehabilitation to outpatient rehabilitation.

For those with tobacco use disorder, nicotine replacement therapies are approved by the Food and Drug Administration (FDA) and include the nicotine patch, chewing gum, lozenge, oral inhaler, and nasal spray. These therapies help reduce withdrawal symptoms such as anger and irritability, but have little effect on cravings. Bupropion (Zyban, Wellbutrin) is an FDA-approved dopamine-norepinephrine reuptake-blocking antidepressant that is effective for smoking cessation. Varenicline (Chantix, Champix) is a partial nicotine agonist that reduces cravings and withdrawal and facilitates smoking cessation. However, close monitoring is advised, as serious psychiatric symptoms such as increased depression (3–11%) and suicidal behavior/ideation (6–11%) were reported (Consortium for Spinal Cord Medicine 2020). The VA guideline for substance use disorder strongly recommends acamprosate, disulfiram, naltrexone, or topiramate for alcohol use disorders. The VA guideline recommends buprenorphine and methadone for treatment of opioid use disorders, while extended-release injectable naltrexone as well as methadone and buprenorphine are recommended for maintenance phase treatment. Methadone is an opioid agonist that prevents opioid withdrawal, reduces craving, and reduces the effects of illicit opioids (https://www.healthquality.va.gov/guidelines/mh/sud/) (Consortium for Spinal Cord Medicine 2020).

43.6 Mental Status Changes

A changed mental status in patients with spinal cord is not uncommon. Common changes in mental status in patients with spinal cord injuries can be categorized as delirium, dementia, and confusional state, sleep disorders, major psychiatric disorders, and psychological reactions.

The most common causes of delirium in patients with spinal cord injuries are electrolyte abnormalities, sepsis, central nervous system injury, toxic metabolic disorder, alcohol and drug withdrawal or intoxication, and side effects of medications (Morandi and Jackson 2011). Pharmacotherapy of delirium is primarily aimed at controlling agitation and psychotic symptoms. Sometimes the symptoms may not stop even if the underlying cause of delirium is removed. Haloperidol or lorazepam helps reduce agitation. Haloperidol is effective when accompanied by a psychotic symptom. When these drugs are used, it is important to know if there are signs of worsening confusion or signs suggestive of neuroleptic malignant syndrome. Patients should be examined for renal function, liver function, serum ammonia, acid-base status, electrolytes if there is some confusion, and metabolic disorder as is likely to occur during the acute phase of spinal cord injury (Morandi and Jackson 2011). Confusion can be caused by sedative hypnotic intoxication and withdrawal and use of opiates, antidepressants, and minor tranquilizer. In addition, baclofen, diazepam, narcotic analgesics, and anticonvulsants, which are used to treat a variety of neurological symptoms in patients with spinal cord injuries, can cause abnormal mental status. Steroids can also cause emotional changes or paranoid conditions.

43.7 Sleep Disturbance

Sleep disturbances in patients with spinal cord injuries are common with changes in mental status. Symptoms include sleep apnea, sleep deprivation, and reversal of the sleep cycle. Patients with sleep apnea before spinal cord injury can be exacerbated by impaired respiratory function due

to spinal cord injury. In addition, drugs such as baclofen, diazepam, and dantrolene, which are used in spasticity, cause or potentiate sleep apnea (Bhat et al. 2012).

43.8 Long-Term Psychological Considerations

Suicide is higher in people with spinal cord injury than in their age-matched able-bodied people. The risk of suicide in people with spinal cord injury is estimated to be three to five times the general population. The risk is maximum between 2 and 5 years of injury. According to some studies, it will be higher in people with complete paraplegia. One explanation for this seemingly counterintuitive association of suicide with lower level of injury is that the perceived burden of coping capacity may be greater than that of tetraplegia, as people with paraplegia receive less support or are provided less rehabilitation attention. Active suicide gestures or attempts rarely occur during the acute rehabilitation admission, but they are more likely to occur later due to lack of recovery, interpersonal difficulties, financial distress, and significant affective disorders. Substance abuse, such as TCA and trazodone, can also be a trigger for suicide. Suicidal gestures and threats must be taken seriously and responded to with appropriate guidance to ensure safety and adequate treatment.

People with spinal cord injuries often experience significantly reduced emotional distress within the first year of injury. On the other hand, the caregivers, a parent or spouse, often a mother or wife, can have significantly increased distress and the burden. This is because there is a lack of support system for the caregivers provided by others. It is important to have opportunities of care break for the emotional and physical heath of the caregivers.

Many persons with spinal cord injuries do not return to paid employment. Appropriate vocational evaluation and training options should be provided. In the absence of a desire to return to a competitive employment, people with spinal cord injuries should be encouraged to participate in sports activities or meaningful social activities (Beauregard et al. 2012).

43.9 Psychologist Intervention

Psychologist can systematically provide derived information to help patients, families, and staff through structured interviews and formal psychological tests. Some psychologists use standard batteries for psychological testing. Others use combinations of interviews and tests based on specific referral questions and problems. Psychologists can provide information about personality, intellect, affect, mood, and cognition (Green 2007). Recognizing strengths and weaknesses in this area is essential for vocational reintegration, as well as financial and driving competency. This information can be used to guide treatment decisions and discharge plans. Psychologists participate in educational activities for people with spinal cord injuries. Education-focused groups tend to work better than traditional group psychotherapy. Topics commonly discussed include sexuality, body image changes, disability rights, assertiveness, and family relations.

Spinal cord injuries have a negative impact on romantic relationships. Physicians need to identify developing and ongoing stressors, as well as behavioral and emotional difficulties in people with spinal cord injury after discharge. If marital or family difficulties are identified, the psychologist can provide expertise. If additional counseling or therapy is needed, the psychologist can arrange treatment. Alternatively, care can be coordinated with other mental health professionals.

43.10 Quality of Life after Spinal Cord Injury

Quality of life (QOL) and life satisfaction of people with spinal cord injuries have a positive impact on social participation, social support, and perceived control over life. On the other hand, there was no consistent or strong association

between QOL and biomedical factors such as completeness of injury or neurological level of injury (Boakye et al. 2012). QOL improvement is a common goal of spinal cord injury care and rehabilitation, but measuring and defining precision or consistency is a difficult concept. In addition, the usefulness of many popular measures of QOL is limited in people with spinal cord injuries, for example, because of inappropriate questions for people with motor impairments related to walking (Gurcay et al. 2010).

Many components contribute to QOL, only one of which is health-related quality of life (HRQOL). An example of an instrument measuring HRQOL is the Short Form (SF)-36, which is also available in a modified version. Another aspect of QOL is subjective well-being and life satisfaction (Cooper and Cooper 2010). The tool used to describe overall subjective well-being is the Diener Satisfaction with Life Scale (SWLS), which allows the normative data from the Spinal Cord Injury Model Systems and other sources (Boakye et al. 2012).

References

Beauregard L, Guindon A, Noreau L, et al. Community needs of people living with spinal cord injury and their family. Top Spinal Cord Inj Rehabil. 2012;18:122–5.

Bhat S, Gupta D, Chokroverty S. Sleep disorders in neuromuscular diseases. Neurol Clin. 2012;30:1359–87.

Boakye M, Leigh BC, Skelly AC. Quality of life in persons with spinal cord injury: comparisons with other populations. J Neurosurg Spine. 2012;17:29–37.

Bombardier CH, Fann JR, Tate DG, et al. An exploration of modifiable risk factors for depression after spinal cord injury: which factors should we target? Arch Phys Med Rehabil. 2012;93:775–81.

Cao Y, Massaro JF, Krause JS, et al. Suicide mortality after spinal cord injury in the United States: injury cohorts analysis. Arch Phys Med Rehabil. 2014;95:230–5.

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Chevalier Z, Kennedy P, Sherlock O. Spinal cord injury, coping and psychological adjustment: a literature review. Spinal Cord. 2009;47:778–82.

Consortium for Spinal Cord Medicine. Management of mental health disorders, substance use disorders, and suicide in adults with spinal cord injury: clinical practice guideline for heath care providers. Washington, DC: Paralyzed Veterans of America; 2020.

Cooper RA, Cooper R. Quality-of-life technology for people with spinal cord injuries. Phys Med Rehabil Clin N Am. 2010;21:1–13.

Craig A, Tran Y, Middleton J. Psychological morbidity and spinal cord injury: a systematic review. Spinal Cord. 2009;47:108–14.

Craig A, Nicholson Perry K, Guest R, et al. Prospective study of the occurrence of psychological disorders and comorbidities after spinal cord injury. Arch Phys Med Rehabil. 2015;96:1426–34.

Cuff L, Fann JR, Bombardier CH, et al. Depression, pain intensity, and interference in acute spinal cord injury. Top Spinal Cord Inj Rehabil. 2014;20:32–9.

Deak MC, Winkelman JW. Insomnia. Neurol Clin. 2012;30:1045–66.

DeVivo MJ, Black KJ, Richards JS, et al. Suicide following spinal cord injury. Paraplegia. 1991;29:620–7.

Dobrez D, Heinemann AW, Deutsch A, et al. Impact of mental disorders on cost and reimbursement for patients in inpatient rehabilitation facilities. Arch Phys Med Rehabil. 2010;91:184–8.

Dorstyn D, Mathias J, Denson L. Efficacy of cognitive behavior therapy for the management of psychological outcomes following spinal cord injury: a meta-analysis. J Health Psychol. 2011;16:374–91.

Fordyce WE. Behavioral methods in rehabilitation. In: Neff WS, editor. Rehabilitation psychology. Washington, DC: American Psychological Association; 1971. p. 74–108.

Frank E, Prien RF, Jarrett RB, et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder. Remission, recovery, relapse, and recurrence. Arch Gen Psychiatry. 1991;48:851–5.

Graves DE, Bombardier CH. Improving the efficiency of screening for major depression in people with spinal cord injury. J Spinal Cord Med. 2008;31:177–84.

Green P. The pervasive influence of effort on neuropsychological tests. Phys Med Rehabil Clin N Am. 2007;18(43–68):vi.

Gurcay E, Bal A, Eksioglu E, et al. Quality of life in patients with spinal cord injury. Int J Rehabil Res. 2010;33:356–8.

Hagen EM, Eide GE, Rekand T, et al. Traumatic spinal cord injury and concomitant brain injury: a cohort study. Acta Neurol Scand Suppl. 2010;2010:51–7.

Heruti RJ, Reznik J, Adunski A, et al. Conversion motor paralysis disorder: analysis of 34 consecutive referrals. Spinal Cord. 2002;40:335–40.

Hohmann GW. Psychological aspects of treatment and rehabilitation of the spinal cord injured person. Clin Orthop Relat Res. 1975;112:81–8.

Huffman JC, Niazi SK, Rundell JR, et al. Essential articles on collaborative care models for the treatment of psychiatric disorders in medical settings: a publication by the academy of psychosomatic medicine research and evidence-based practice committee. Psychosomatics. 2014;55:109–22.

Hunt WA, Barnett LW, Branch LG. Relapse rates in addiction programs. J Clin Psychol. 1971;27:455–6.

Kemp BJ, Vash CL. Productivity after injury in a sample of spinal cord injured persons: a pilot study. J Chronic Dis. 1971;24:259–75.

Kennedy P, Evans MJ. Evaluation of post traumatic distress in the first 6 months following SCI. Spinal Cord. 2001;39:381–6.

Klyce DW, Bombardier CH, Davis TJ, et al. Distinguishing grief from depression during acute recovery from spinal cord injury. Arch Phys Med Rehabil. 2015;96:1419–25.

Letonoff EJ, Williams TR, Sidhu KS. Hysterical paralysis: a report of three cases and a review of the literature. Spine (Phila Pa 1976). 2002;27:E441–5.

Macciocchi S, Seel RT, Warshowsky A, et al. Co-occurring traumatic brain injury and acute spinal cord injury rehabilitation outcomes. Arch Phys Med Rehabil. 2012;93:1788–94.

McCullumsmith CB, Kalpakjian CZ, Richards JS, et al. Novel risk factors associated with current suicidal ideation and lifetime suicide attempts in individuals with spinal cord injury. Arch Phys Med Rehabil. 2015;96:799–808.

Morandi A, Jackson JC. Delirium in the intensive care unit: a review. Neurol Clin. 2011;29:749–63.

Podell K, Torres K. Affective symptoms in early-onset dementia. Neurol Clin. 2011;29:99–114. viii

Rudd MD. Suicide warning signs in clinical practice. Curr Psychiatry Rep. 2008;10:87–90.

Saunders LL, Krause JS. Psychological factors affecting alcohol use after spinal cord injury. Spinal Cord. 2011;49:637–42.

Schandler SL, Cohen MJ, Vulpe M, et al. Incidence and characteristics of spinal cord injured patients with a family history of alcoholism. J Stud Alcohol. 1995;56:522–7.

Stolp-Smith KA, Wainberg MC. Antidepressant exacerbation of spasticity. Arch Phys Med Rehabil. 1999;80:339–42.

Tate D, Forchheimer M, Maynard F, et al. Predicting depression and psychological distress in persons with spinal cord injury based on indicators of handicap. Am J Phys Med Rehabil. 1994;73:175–83.

Tétrault M, Courtois F. Use of psychoactive substances in persons with spinal cord injury: a literature review. Ann Phys Rehabil Med. 2014;57:684–95.

Recommended Additional Reading

Buchanan LE, Nawoczenski DA, editors. Spinal cord injury-concepts and management approaches. Baltimore, MD: Williams & Wilkins; 1987.

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Kennedy P. The Oxford handbook of rehabilitation psychology. Oxford: Oxford University Press; 2012.

Noggle CA, Dean RS, editors. Neuropsychological rehabilitation. New York: Springer Publishing Company; 2013.

Poręczny AJ, editor. Handbook of health and rehabilitation psychology. New York: Springer Science+Business Media; 1995.

Rudd MA, Hough S, Wegener ST, et al., editors. Practical psychology in medical rehabilitation. Cham: Springer; 2017.

Vodusek DB, Boller F. Neurology of sexual and bladder disorders. In: Aminoff MJ, Boller F, Swaab DF, editors. Handbook of clinical neurology, 3rd series, vol. 130. London: Elsevier; 2015.

Upper Extremity Intervention in Spinal Cord Injuries

44

People with cervical spinal cord injuries have upper extremity dysfunction in performing activities of daily living, including hand function, wheelchair propulsion, transfers, and pressure relief. It is a heterogeneous population characterized by varying levels of cervical cord injury, measurements of neurological deficit such as motor and sensory scores, and severity of neurological impairment. It is therefore important that upper limb outcome measures applied in this population are sensitive to different levels of functioning in individuals (Kramer et al. 2012; Velstra et al. 2015; Velstra et al. 2018). The ability to transfer independently is a key factor for an optimal level of independence, as transfers are required to complete essential daily activities such as bathing, toileting, driving, and getting into and out of bed (Koontz et al. 2011).

Maintaining the function of the upper extremities is of prime importance for the quality of life and social participation of people with spinal cord injuries (Consortium for Spinal Cord Medicine 2005). Despite an overall good prognosis for walking, persons with incomplete tetraplegia have significant residual motor impairment in the upper extremities and need assistance in many areas of self-care (Marino et al. 2011, 2018; Penrod et al. 1990). The highest priority for recovery target in people with tetraplegia was given as restoring upper extremity function (Huh and Ko 2020; Lo et al. 2016; Snoek et al. 2004). Small improvements in upper extremity function can significantly improve quality of life for tetraplegics. The function of the upper extremities in tetraplegia is mainly influenced by motor impairments, which are determined by the level of injury and completeness of injury. Additional causes of dysfunction are secondary complications of spinal cord injuries such as spasticity, pain, and contractures. Independence after tetraplegia is based on upper limb movements and is achieved by both relearning open chain movements such as grasping and by learning closed chain movements such as manual wheelchair propulsion or sitting pivot transfer. Table 44.1 summarizes the muscle function of the upper extremity and the detail of the effects of the neurological level of injury of a spinal cord injury on muscle innervation.

Cervical spinal cord injury leads to extensive sensorimotor dysfunction that affects both somatic and autonomic functions below the level of injury. A C5 spinal cord injury preserves innervation of shoulder and elbow flexors, while C6 injuries also spare wrist extensors and C7 injuries spare elbow extensors in addition. Thus, C5 and C6 injuries impair active elbow extension against gravity, while C5 to C7 injuries prevent active grasping (Woolsey 1985). Fortunately, tenodesis can replace active grasp with passive whole hand and lateral grips if wrist extension is preserved (injury at C6 or below). During tenodesis of wrist extension, tenodesis leads to shortening of flexor digitorum superficialis and

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Table 44.1 Upper extremity muscle function, innervation, and the detail of the effects of spinal cord injury level on muscle innervation

			Innervation		SCI level					
Joint	Muscles	Function	Nerve	Roots	C4	C5	C6	C7	C8	T1
Shoulder scapulo-thoracic	Serratus anterior	Protraction & upward rotation	Long thoracic	C5 C6 C7	–	±	±	±	+	+
	Trapezius upper part	Elevation	Accessory spinal	XI	+	+	+	+	+	+
	Trapezius middle part	Retraction			+	+	+	+	+	+
	Trapezius lower part	Downward rotation			+	+	+	+	+	+
	Pectoralis minor	Depression	Medial pectoral	C8 T1	–	–	–	–	±	±
Shoulder gleno-humeral	Deltoid anterior part & Coracobrachialis	Flexion	Axillary	C5 C6	–	±	±	+	+	+
	Deltoid medial part	Abduction			–	±	±	+	+	+
	Deltoid posterior part	Extension			–	±	±	+	+	+
	Pectoralis major upper part	Flexion/ Adduction/ Medial rotation	Lateral pectoral	C5 C6 C7	–	±	±	±	+	+
	Pectoralis major middle & lower parts	Flexion/ Adduction/ Medial rotation	Medial pectoral	C8 T1	–	–	–	–	±	±
	Latissimus dorsi	Extension/ Adduction/ Medial rotation	Thoracodorsal	C6 C7 C8	–	–	±	±	±	+
	Teres major	Extension/ Adduction/ Medial rotation	Subscapular	C5 C6 C7	–	±	±	±	+	+
	Subscapularis	Medial rotation	Subscapular		–	±	±	±	+	+
	Supraspinatus	Abduction	Suprascapular		–	±	±	±	+	+
	Infraspinatus	Lateral rotation	Suprascapular		–	±	±	±	+	+
	Teres minor	Lateral rotation	Axillary	C5 C6	–	±	±	+	+	+
Elbow	Biceps brachii	Flexion	Musculocutaneous	C5 C6	–	±	±	+	+	+
	Brachialis	Flexion	Musculocutaneous		–	±	±	+	+	+
	Brachioradialis	Flexion	Radial		–	±	±	+	+	+
	Triceps brachii	Extension	Radial	C7 C8 T1	–	–	–	±	±	±
Wrist	Extensor carpi radialis longus & brevis	Extension	Radial	C6 C7 C8	–	–	±	±	±	+
	Extensor carpi ulnaris	Extension	Radial	C7 C8	–	–	–	±	±	+
	Flexor carpi radialis	Flexion	Median	C6 C7	–	–	±	±	+	+
	Flexor carpi ulnaris	Flexion	Ulnar	C7 C8	–	–	–	±	±	+

Table 44.1 (continued)

			Innervation		SCI level					
Joint	Muscles	Function	Nerve	Roots	C4	C5	C6	C7	C8	T1
Fingers & thumb	Flexor digitorum superficialis	Flexion	Median	C7 C8 T1	–	–	–	±	±	±
	Flexor digitorum profundus	Flexion	Median & ulnar	C8 T1	–	–	–	–	±	±
	Extensor digitorum	Extension	Radial	C6 C7 C8	–	–	±	±	±	±
	Flexor pollicis longus & brevis	Flexion	Median	C8 T1	–	–	–	–	±	±
	Extensor pollicis longus & brevis	Extension	Radial	C7 C8	–	–	–	±	±	+
	Abductor pollicis longus	Abduction	Radial		–	–	–	±	±	+
	Abductor pollicis brevis	Abduction	Median	C8 T1	–	–	–	–	±	±
	Opponens pollicis	Opposition	Median		–	–	–	–	±	±
	Adductor pollicis and intrinsic	Adduction	Ulnar	C8 T1	–	–	–	–	±	±
	Abductor digitorum minimi	Abduction	Ulnar	T1	–	–	–	–	–	±

From Mateo et al. (2015), with permission

profundus, which leads to passive finger-to-palm flexion, and of flexor pollicis longus, leading to thumb-to-index lateral adduction (Mateo et al. 2013, 2015). Lack or lost function of the upper extremities can be achieved by rehabilitation or surgical intervention such as tendon transfer, in which transfers a tendon from spared muscles with motor strength above 4, and nerve transfer. The goals of upper extremity surgical reconstruction for tetraplegia are to increase independence and upper extremity function through elbow control for overhead reaching, weight shift, and transfer. Restoration of hand function to allow lateral pinch for self-catheterization, dressing, and activities of daily living (ADLs); and grasp and release for feeding and ADLs (Bednar 2016). It is estimated that approximately 65% to 75% of people with cervical spinal cord injuries would benefit from upper extremity surgery to improve on these functional limitations (Curtin et al. 2005).

44.1 Assessment

The function of the upper extremities of people with spinal cord injuries depends primarily on motor level of injury and sensory functions. Additional factors, including static and dynamic sitting balance, affect the function of the upper extremities. Most of the assessment of upper limb function is mainly about how much each individual's necessary function can be performed using the remaining function. It assesses the degree of ability to perform activities using orthoses or assistive devices, the degree of gross motor functions such as transfers and wheelchair propulsion, and various grasping motion patterns such as lateral pinch, key pinch, tip pinch, three-jaw chuck, and power grip. Prior to the evaluation of upper extremity function including grasp dynamometer, transfers, sitting balance, and wheelchair propulsion should be evaluated. The individualized performance of each activity using

one upper extremity or both upper extremities is also assessed. A neurological assessment based on the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), assessment of activities of daily living related with upper extremity function, Functional Independence Measure, Spinal Cord Independence Measure III, range of motion, and tone evaluation should be performed. For the quantitative evaluation of motor or sensory functions, a grip dynamometer or two-point discrimination evaluation using filament tests can be used. All muscles of the upper extremity are assessed using manual motor testing. Manual motor tests with grading 0 to 5 are based on the British Medical Research Scale. Joints are placed through active and passive range of motion. Contractures or spasticity are noted.

The need for standardized assessment of upper extremity performance arises from advances in interventions that have helped achieve the functional improvements for people with tetraplegia (Backus 2010). Although several upper extremity assessments have been introduced, none have been consistently adopted for research or clinical use so far. The Graded Redefined Assessment of Strength, Sensibility, and Prehension (GRASSP) has been developed for adults with tetraplegia. The GRASSP combines well-established methods of manual muscle strength testing and monofilament sensory testing with observation of grasp and pinch patterns during object manipulation. The Capabilities of Upper Extremity Test (CUE-T) evaluates 19 different performance aspects of upper extremity functions. The CUE-T is a spinal cord injury-specific instrument developed based on the Capabilities of the Upper Extremity Questionnaire (CUE-Q) (Dent et al. 2018).

44.1.1 International Spinal Cord Injury Upper Extremity Basic Data Set

The purpose of the International Spinal Cord Injury Upper Extremity Basic Data Set (Version 1.1) is to standardize the collection and reporting of a minimal amount of information about upper extremity status. The upper extremity function in the data set based on ability to grasp (part of the GRASSP test) (Kalsi-Ryan et al. 2009) (Table 44.2) and shoulder function of reaching ability. In addition, several variables, such as the use of assistive devices (all equipment like splints, adaptive equipment, and FES), spinal cord injury-related complications to upper extremity function like pain, spasms, contractures, and edema, and upper extremity/hand reconstructive surgery were included (Biering-Sørensen et al. 2014; Biering-Sørensen et al. 2015). Each side is scored separately. The international spinal cord injury upper extremity basic data set version 1.1 is found on ISCoS website: https://www.iscos.org.uk//international-sci-upper-extremity-data-sets. The following two changes to the International Spinal Cord Injury Upper Extremity Basic Data Set from Version 1.0 to Version 1.1 are: with regard to the variable 'Basic hand-upper extremity function' the following sentence has been added to the description of the variable: "or functional gain after upper extremity reconstructive surgery or during or after the use of a neuroprosthesis"—this allows the same scoring to be used following these interventions: with regard to the variable "Shoulder function classification," the option "D. Full range of movement (ROM) of shoulder and independent reaching forward and upward" was changed to "D. Ability to reach in all directions including lifting hand above the head reflecting at least grade 3 strength in the shoulder flexors and abductors and elbow extensors." Options A–C in "shoulder function classification" are descriptions of abilities, whereas option D was solely a description of strength even though it was not explicitly stated. In addition, the new definition now distinguishes between active and passive movement for clarity (Biering-Sørensen et al. 2015) (Table 44.3).

The level of basic hand-upper extremity function is specified as follows: 1. No upper extremity function at or below the elbow (i.e., no grasping function, severely limited active placing, or reaching); 2. Passive tenodesis hand (i.e., opening and closing of the hand is only possible by supi-

Table 44.2 Components of the GRASSP and methods for administration

Components of the GRASSP			Method for administration	
Test	Details	Rationale	Position time required	How to test
Sensibility domain: test sites selected by dermatome				
Light touch/SWM	6 palmar/dorsal test sites	Inter/ intra-reliability = 0.965	Supine/ sitting, 10 min	–Apply monofilaments to all test locations –Summate the score for each hand separately
Static 2 Point Disc	3 palmar test sites	Inter/ intra-reliability = 0.989	Supine/ sitting, 5 min	–Apply stimulus to all test locations –Summate score for each hand
Strength and tone domain: muscle selection based on myotomes				
Strength	MMT-4 arm & 7 hand muscles	Inter-reliability = 0.880	Supine/ sitting, 10 min	–Assess each muscle and grade –Summate all scores for each hand
Tone	Modified Ashworth for hand & arm	Inter-reliability = 0.750	Supine/ sitting, 5 min	–Assess elbow and hand for flexor/extensor tone
Prehension domain: segmental influence movement pattern				
Qualitative (descriptive)	3 grasps rated on scale of 0-4		Supine/ sitting, 5 min	–Have subject perform grasps and rate
Quantitative (performance)	5 grasps/6 tasks rated on scale of 0-5	Adapted from Sollerman, inter-reliability = 0.980	Sitting, 15 min	–Set patient up in sitting at table and have patient perform all 6 tasks for each hand separately

GRASSP Graded Redefined Assessment of Strength, Sensibility, and Prehension; *MMT* manual muscle testing; *SWM*, Semmes Weinstein monofilaments
From Kalsi-Ryan et al. (2009), with permission

Table 44.3 International Spinal Cord Injury Upper Extremity Basic Data Set Form (Version 1.1)

Evaluation of the RIGHT and LEFT upper extremity separately:	
Ability to reach and grasp (part of the GRASSP test):	Shoulder function classification:
1. No upper extremity function at or below the elbow No voluntary control of elbow, wrist, or hand muscles; no grasping function; severely limited active placing or reaching of the arm.	**A.** No active placing or reaching of the arm.
2. Passive tenodesis hand Passive hand functions with neither voluntary control of extrinsic and intrinsic hand muscles nor ability to actively extend the wrist. Opening and closing of the hand is only possible by supination or pronation of the forearm (passive tenodesis effect) with no active grasping movements of hand. Bimanual grasping by stabilizing objects between two hands or passive tenodesis grasp is effective only in a limited workspace.	**B.** Severely limited but able to position hand on a desk, without assistance, but not able to reach to the mouth/head (gravity compromises the movements).
3. Active tenodesis hand No voluntary control of extrinsic and intrinsic hand muscles but active wrist extension allowing for passive movements of fingers dependent on a tenodesis effect. Limited single-handed grasping function in a restricted workspace.	**C.** Limited but able to reach mouth/ head, with difficulty or altered movements, e.g. weak or absent pronation-supination or wrist flexion-extension.
4. Active extrinsic hand Voluntary control of wrist and some extrinsic hand muscles allowing for grasping with or without tenodesis enabling some active opening and closing of the hand but reduced dexterity and reduction of workspace.	**D.** Ability to reach in all directions including lifting hand above the head reflecting at least grade 3 strength in the shoulder flexors and abductors and elbow extensors.

(continued)

Table 44.3 (continued)

Evaluation of the RIGHT and LEFT upper extremity separately:	
Ability to reach and grasp (part of the GRASSP test):	Shoulder function classification:
5. Active extrinsic-intrinsic hand Voluntary control of extrinsic and intrinsic hand muscles with full workspace and the ability to perform different grasp forms (e.g., power grip, precision grip, lateral power pinch, precision pinch) but potential limitations of muscle strength and dexterity.	

nation or pronation of the forearm with no active grasping movements of hand); 3. Active tenodesis hand (i.e., no voluntary control of extrinsic and intrinsic hand muscles but active wrist extension allowing for passive movements of fingers dependent on a tenodesis effect); 4. Active extrinsic hand (i.e., voluntary control of wrist and some extrinsic hand muscles allowing for grasping with or without tenodesis but reduced dexterity and reduction of workspace); 5. Active extrinsic–intrinsic hand (i.e., voluntary control of extrinsic and intrinsic hand muscles with full workspace and the ability to perform different grasp forms, e.g., power grip, precision grip, lateral power pinch, and precision pinch, but potential limitations of muscle strength and dexterity).

Shoulder function is classified according to observed function of the shoulder and upper extremity as following 4-point scale: A. No active placing or reaching of the arm; B. Severely limited but able to position the hand on a desk, without assistance, but not able to reach to the mouth/head (gravity compromises the movements); C. Limited but able to reach mouth/head with difficulty or altered movements, e.g., weak or absent pronation–supination or wrist flexion–extension; D. Ability to reach in all directions including lifting hand above the head reflecting at least grade 3 strength in the shoulder flexors and abductors and elbow extensors.

44.1.2 Graded Redefined Assessment of Strength, Sensibility, and Prehension (GRASSP) Test

The GRASSP is a multidimensional assessment and a valid, reliable, and responsive outcome for assessing the upper extremity function in individuals with cervical cord injuries which includes sensation (light touch and static 2-point discrimination), strength (strength and tone), prehension (qualitative and quantitative). The strength and sensibility components are impairment measures. Although the GRASSP is able to detect neurological recovery and changes resulting from interventions, and despite strong psychometric properties (Kalsi-Ryan et al. 2012), its assessment of functional hand performance is limited in scope (lateral pinch, three-jaw chuck, palmar grasp) (Dent et al. 2018). The quantitative prehension scale is a capacity measure in the Activities domain, using the International Classification of Functioning, Disability, and Health (ICF) framework (Kalsi-Ryan et al. 2009; Marino et al. 2018) (Table 44.2). It is recommended that the GRASSP be used in conjunction with other standard spinal cord injury classification or measurement tools such as the International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI) and the Spinal Cord Independence Measure (SCIM). The combination of these outcome tools broadens understanding of the severity and burden of the disease as well as the detection of subtle and clinically meaningful changes in upper limb function and independence from the very acute phase to 1 year after injury (Velstra et al. 2015, 2018).

44.1.3 Capabilities of Upper Extremity Questionnaire

The Capabilities of Upper Extremity Questionnaire (CUE-Q) is a patient-reported assessment of upper extremity functional limitation in tetraplegia (Marino et al. 1998). The CUE-Q asked about limitations in performing

certain actions, such as reaching the right (or left) arm. Patients are asked to rate level of difficulty performing 32 upper limb actions on a scale from 0 (*unable to do*) to 4 (*no difficulty*): arm actions (reaching up, forward and down, pulling and pushing a light and heavy object, extending the wrist and pronating); hand actions, holding items with various grasp patterns; and bimanual items (Oleson and Marino 2014). The CUE-Q is administered immediately prior to CUE-T and is used to examine the association between actual performance (CUE-T) and perceived performance (CUE-Q) (Dent et al. 2018). The CUE-Q form and directions (version 2.1, 2017) are available for download at https://www.spinalcordcenter.org/assessments/cue_quest_v2.1_2017_combined.pdf. There may be differences between patient-reported performance and observed performance of function, especially shortly after spinal cord injury when the person has limited lived experience with a disability (Marino et al. 2018; Oleson and Marino 2014).

44.1.4 Capabilities of Upper Extremity Test

The Capabilities of Upper Extremity Test (CUE-T) is a measure of performance for assessing the function of the upper extremities in people with spinal cord injury based on the CUE-Q (Dent et al. 2018; Marino et al. 2012). In contrast to the limited performance component of the GRASSP, the CUE-T evaluates 19 various performance aspects of upper extremity function, including unilateral, bilateral, proximal, and distal functions (Marino et al. 2012). The CUE-T originally described consisted of 17 items tested on the right and left sides and two bilateral items for a total of 36 items (Marino et al. 2012). The pronation and supination items had poor test–retest reliability. Hence, these items were dropped. The final CUE-T has 32 items, 5-point scale ranging from 0 to 4, where 0 = *unable/complete difficulty* and 4 = *no difficulty*. The total score can be between 0 and 128. The maximum total score (right side + left side + bilateral) is 128 (Marino et al. 2018) (Table 44.4). The CUE-T evaluates objective actions and tasks involving the arm and hand in people with tetraplegia, such as reaching, lifting, pulling, and pushing in addition to various grasp patterns. Test procedures are intended to minimize the effects of functional limitations not involved in a particular test item. In combination, the CUE-T and CUE-Q provide an objective (CUE-T) and self-perceived (CUE-Q) assessment of upper extremity function required for the performance of basic and instrumental activities of daily living (ADL) (Dent et al. 2018). The manual for the CUE-T version 1.1 is available at https://www.spinalcordcenter.org/assessments/cue_t_manual2016_v1.1_publicversion_2018.pdf.

44.1.5 International Classification of Surgery of the Hand in Tetraplegia

If surgery is considered, it is evaluated using The International Classification of Surgery of the Hand in Tetraplegia (ICSHT) (Table 44.5). The ICSHT was developed to evaluate the upper extremity and formulate a treatment plan for patients with tetraplegia (Bednar 2016). The ICSHT includes muscles below the elbow and therefore tendon transfers for elbow extension and proximal movements including shoulder abduction are considered separately (Vova and Davidson 2020). The ICSHT determines the neurological level of injury based on ISNCSCI. In ICSHT, muscle strength and sensory function are evaluated and classified, and the sensory function is evaluated by two-point discrimination of thumb and index finger. If the patient can discriminate two points of less than 10 mm, the sensation is considered normal. In this case, it is marked as Cutaneous (Cu), and if the interval is longer than 10 mm, it is marked as Ocular (O). Intact cutaneous sensibility implies two-point discrimination of 10 mm or less within the thumb and index pulp, which is necessary for lateral pinch without eyesight (Kozin 2008). Ocular sensibility indicates vision as the only afferent. In ISNCSCI, 5 key muscles below the shoulder joint are used, but ICSHT targets the number of mus-

Table 44.4 CUE-T items and scoring

Arm	Raw scoring	Score conversion	Hand	Raw scoring	Score conversion	Bilateral	Raw scoring	Score conversion
Reach forward	Number of repetitions in 30 s	0 = cannot complete 1 = partial completion of 1 repetition 2 = 1–15 repetitions 3 = 16–30 repetitions 4 = 31+ repetitions	Grasp dynamometer	Mean grasp strength of 3 trials measured in kilograms	0 = 0 kg 1 = 0.1–3.0 kg 2 = 3.1–10.0 kg 3 = 10.1–20.0 kg 4 = 20.1+kg	Lift up weight	Based on amount of weight lifted: ½ kg–2 kg	0 = cannot complete 1 = lifts empty 2 = lifts ½ kg 3 = lifts 1 kg 4 = lifts 2 kg
Reach up	Number of repetitions in 30 s	0 = cannot complete 1 = partial completion of 1 repetition 2 = 1–16 repetitions 3 = 16–25 repetitions 4 = 26+ repetitions	Pinch die (two-finger grasp)	Number of repetitions in 30 s	0 = cannot complete 1 = partial completion - 2 repetitions 2 = 3–5 repetitions 3 = 6–8 repetitions 4 = 9+ repetitions	Push down	Based on duration of weight shift: 0–30 s	0=cannot complete 1 = 0.1–4.9 s 2 = 5.0–14.9 s 3 = 15.0–29.9 s 4 = 30 s
Reach down	Number of repetitions in 30 s	0 = cannot complete 1 = partial completion of 1 repetition 2 = 1–10 repetitions 3 = 11–15 repetitions 4 = 16+ repetitions	Pencil (three-finger grasp)	Number of repetitions in 30 s	0 = cannot complete 1 = partial completion - 2 repetitions 2 = 3–5 repetitions 3 = 6–8 repetitions 4 = 9+ repetitions			
Pull weight	Based on weight moved: 0 kg–4 kg	0 = cannot complete 1 = move ½ kg 2 = moves 1 kg 3 = moves 2 kg 4 = moves 4 kg	Key pinch	Mean pinch strength 3 trials measured in kilograms	0 = cannot pinch a credit for at least 5 s & 0 kg 1 = can pinch a credit card for 5 s & 0 kg 2 = 0.1–2.0 kg 3 = 2.1–5.0 kg 4 = 5.1+ kg			

Push weight	Based on weight moved: as above	0 = cannot complete 1 = move ½ kg 2 = moves 1 kg 3 = moves 2 kg 4 = moves 4 kg	Wide grasp	Based on amount of weight lifted and time held give range of weight and time	0 = cannot complete 1 = lift empty 2 = lift ½ kg for <5 s 3 = lift ½ kg for 5 s 4 = lift 1 kg for 5 s			
Wrist up	Number of repetitions in 30 s	0 = cannot complete 1 = partial completion of 1 repetition 2 = 1–30 repetitions 3 = 21–35 repetitions 4 = 36+ repetitions	Manipulate washer	Number of revolutions in 30 s	0 = cannot complete 1 = partial completion of 1 revolution 2 = 1–5 revolutions 3 = 6–10 revolutions 4 = 11+ revolutions			
			Push with index finger	Based on time to complete: 0–90 s	0 = cannot complete 1 = 20.1–90 s 2 = 10.1–20 s 3 = 7.1–10 s 4 = ≤7.0 s			
			Push with thumb	Based on time to complete: 0–90 s	0 = cannot complete 1 = 20.1–90 s 2 = 10.1–20 s 3 = 7.1–10 s 4 = ≤7.0 s			
			Acquire/Release (of grasp dynamometer and container)	Based on ability to acquire and release (yes or no, acquire; yes or no release)	Number of yes (0–4)			

Table 44.5 International Classification for Surgery of the Hand in Tetraplegia (ICSHT)

Sensory	Group	Muscles ≥ grade 4 strength	Function	NLI (ISNCSCI)
Cutaneous (Cu) or ocular (O)	0	No muscles below elbow suitable for transfer		C5
	1	Brachioradialis	Flexion of elbow	C5
	2	+ Extensor carpi radialis longus	Weak wrist extension with radial deviation	C6
	3	+ Extensor carpi radialis brevis	Wrist extension	C6
	4	+ Pronator teres	Forearm pronation	C6, C7
	5	+ Flexor carpi radialis	Wrist flexion	C7
	6	+ Extensor digitorum communis Finger extensors	Extrinsic finger extension at MCP joint	C7
	7	+ Extensor pollicis longus Thumb extensors	Extrinsic thumb IP joint extension	C7, C8
	8	+ Flexor digitorum Partial finger flexors	Extrinsic finger flexion	C8
	9	All muscles except hand intrinsic muscles		C8
	10 (X)	Exceptions		

Sensory (testing for 2-point discrimination)
Cu (cutaneous), if 2-point discrimination in the thumb and index finger ≤ 10 mm (ocular feedback only), if 2-point discrimination in the thumb/index finger > 10 mm or absent
A muscle must be a least grade 4 strength on the Medical Research Council scale to be considered for transfer

cles below the elbow with at least grade 4 strength. In ISNCSCI, it is considered functional when the muscle strength is 3 degree, however, ICSHT defines that it is functional only at 4 degree since at least one level of muscle strength decreases when a muscle is transferred.

44.2 Management

44.2.1 Prevention of Complications Affecting Upper Extremity Function and Orthoses

Early therapy, ideally initiated at the acute care hospital, is used to obtain or maintain joint mobility and to maximize the strength, endurance, and the balance of voluntary muscles (Peljovich 2020). Upper extremity function in people with tetraplegia is mostly determined by the neurological level of injury and completeness of the injury, but it is also affected by spinal cord injury-related complications such as spasticity, joint contracture, and pain. Therefore, it is necessary to reduce spasticity and prevent joint contracture in order to maximize the upper extremity function of a tetraplegic patient. For example, in C5 or C6 spinal cord injury, upper extremity function can be severely limited when the joints are contracted in flexion of the elbow and supination of the forearm. In C6 or C7 injuries, excessive stretching of the finger flexors makes tenodesis grasp difficult. If the claw hand deformity caused by the intrinsic minus in the C8 tetraplegia is not managed, the hand grasp and opening become more impaired. In addition, appropriate assistive devices or orthoses should be used to assist the impaired function, and if necessary, surgery or functional electrical stimulation should be considered. Orthoses can be used to replace lost function or to protect against malpositioning and contracture until recovery occurs. The use of the necessary orthosis depends on the neurological level of injury. In C1–C4 patients with no or little upper extremity muscle strength, the resting hand splint should be extended the wrist by 20–30° and 70° flexed in the MPJ, and the thumb should be kept in abduction with the other finger joints extended. Balanced forearm orthosis (C4 with weak C5), universal cuff (C5, C6, C7), long

opponens orthosis (C5), short opponens orthosis (C6), wrist-driven orthosis (tenodesis splint) (C6, C7), and static hand orthosis with lumbrical bar (C8) are used. The balanced forearm orthosis (BFO) consists of an adjustable forearm trough that is attached to a guidepost arm that articulates with a swivel joint. This supports the weight of the arm and forearm against gravity and is mainly used in patients with high-level tetraplegia. Prerequisites for using BFO are a power source such as neck or trunk muscles or adequate scapular movement (Rahman et al. 2012).

The use of robotic devices in upper extremity rehabilitation in people with cervical spinal cord injuries has gained increasing research interest in an effort to achieve behavioral benefits by facilitating neuroplasticity mechanisms (Singh et al. 2018). Upper limb robotic devices have been used primarily in stroke rehabilitation. Many robotic devices have been proposed primarily for use in motor rehabilitation of arm and hand functions in stroke patients and later introduced for use in other neurological disorders with sensorimotor impairments, including multiple sclerosis. Upper extremity robotic systems can be divided into two main categories: exoskeletons and end-effector robots. Robot-assisted training is emerging as an adjunct modality for labor-intensive and task-specific exercises and for real-time quantified measurement of performance (Rahman et al. 2012; Yozbatiran and Francisco 2019). Additionally, robot-aided therapy can be automated or semiautomated without the need for close supervision or personal assistance from physical/occupational therapists (Yozbatiran and Francisco 2019).

44.2.2 Restorative Surgeries for Upper Extremity Function

There are several factors that are considered in upper extremity surgery on a patient with tetraplegia. Physiatrists need to be familiar with the indications and appropriate timing of referral for upper extremity surgery as this can have a significant impact on the outcome. Early rehabilitation care goals and education must focus on maintaining range of motion through appropriate splinting, spasticity management, and tissue mobilization so as not to limit the potential for neurologic recovery or surgical reconstruction (Vova and Davidson 2020). Appropriate surgical candidates should be selected taking into account not only stabilized neurological recovery, but also cognitive function, spasticity or contracture, and motivation for postoperative rehabilitation treatment. If patients are identified as surgical candidates, they should be evaluated early by a team consisting of the patient, caregivers, physiatrist, occupational therapist, social worker, and hand surgeon. Once a patient's ICSHT level is known and functional goals are established, the team will decide whether the patient is a good surgical candidate. The timing to perform the surgery is a balance between stabilization of the patient's neurologic, emotional, and social recovery from the spinal cord injury and performing surgery, which will temporarily decrease a patient's independence during the rehabilitation process. Surgery is usually delayed for about a year after injury so that the patient can accept the injury and maximize their gains with therapy (Bednar 2016).

The choice of the donor muscle and surgical method should be determined so that the neurological level of injury and functional anatomy can be well understood and the most necessary motion through the surgery can be obtained. Surgical procedures to increase upper extremity function can be divided into procedures to relieve contractures that inhibit upper extremity functions, such as release of elbow flexion contractures or radial osteotomy to correct supination contractures, and reconstructive surgery, including tendon transfers, nerve transfers, and associated procedures, to restore upper extremity function. The goals of reconstructive surgery of the upper extremity are to restore the unavailable function with a general order of priority: elbow extension, wrist extension, lateral pinch and release, and palmar grasp and release (Table 44.6). The reconstructive surgery ladder for the upper extremity function in people with spinal cord injuries requires a basic understanding of kinematics and normal upper extremity and hand

Table 44.6 Priority of reconstructive surgery for upper extremity function in tetraplegia

Priority	Function	Preferred technique
1	Elbow extension	Biceps to triceps or posterior deltoid
2	Wrist extension	BR to ECRB
3	Lateral pinch	BR to FPL
4	Grasp	ECRL to FDP
5	Opening	BR to EDC plus passive intrinsicsplasty
6	Coordinated grasp and opposition	FDS intrinsicsplasty plus ECU opponensplasty

functions. A combination of extrinsic and intrinsic function results in a coordinated grasp pattern, which pattern of synchronous grasp and release is disrupted after spinal cord injury because the extrinsic muscles, intrinsic muscles, or both are affected (Kozin 2008). When selecting a donor muscle for surgery, the donor muscle must have sufficient motor strength ≥4, without compromising existing function through loss of the donor muscle.

44.2.2.1 Tendon Transfer

The mainstay of tetraplegic upper extremity surgery is tendon transfers. Traditionally, it is recommended to perform tendon transfers 1 year after the injury, since by then all possible spontaneous neurological recoveries have already occurred (Titolo et al. 2019). The prognosis for recovery differs considerably depending on the cause, and this should be considered when considering restorative upper extremity reconstruction. Usually, recovery from traumatic spinal cord injury may occur for up to 2 years (Waters et al. 1996). However, most neurological recoveries typically occur within the first 6 months of injury (Lee and Wolfe 2012). The transfer of a muscle either leads to the loss of the original function of the donor muscle or, more often, to a weakening of a movement of the donor muscle due to redundancy of the muscles that contribute to a certain joint movement in the upper extremity (Vova and Davidson 2020). There is also a risk that the transfers or tenodesis will lose strength over time due to progressive stretching, especially in growing pediatric patients, which can alter the biomechanical advantage (Fridén and Gohritz 2015). However, tendon transfers have the advantage over nerve transfers, which are not time sensitive and can be performed once the normal motor recovery has reached a plateau (Vova and Davidson 2020). A tendon transfer involves detaching a functioning muscle and its tendon from its normal insertion and redirecting it to another muscle to restore its desired function. Surgical reconstruction procedures could also include immobilizing joint and/or attaching tendons to bone to passively tighten the anchored tendon to move a distal joint (surgical tenodesis). Surgical interventions of the tetraplegic upper extremity are summarized in Table 44.7. Commonly used upper extremity surgeries in tetraplegia, functional goals, and postoperative rehabilitation were summarized in Table 44.8.

As mentioned above, the ICSHT involves muscles below the elbow. Therefore, tendon transfers for elbow extension and proximal movements including shoulder abduction are considered separately (Vova and Davidson 2020). Proximal upper extremity motor movements, such as shoulder abduction and elbow flexion, are generally not suitable as a reconstructive option for tendon transfer because there is no sufficient proximal donor muscle. Patients with ICHST group 0 function do not have an intact motor below the elbow and therefore no suitable donor muscle for transfer. Static splints and orthoses can be used to assist function, and hand function can only be achieved through neuroprosthetic implantation. Active wrist extension and subsequent gravity-assisted wrist flexion provide passive tenodesis and marginal hand function. This motion combines wrist extension with digital flexion and wrist flexion with digital extension (Kozin 2008). If a C5 tetraplegia, who has no means of producing tenodesis and is unable to acquire, grasp, or release objects, wants to regain

Table 44.7 Surgical interventions for upper extremity function in tetraplegia

NLI (INSCSCI)	ICSHT group	Tendon transfer, Tenodesis	Function goal
C5	1	• BR to ECRB • FPL tenodesis • Biceps to triceps or posterior deltoid to triceps	• Active wrist extension • Static thumb pinch • Active elbow extension
C6	1 or 2	• BR to FPL • EPL tenodesis • Biceps to triceps or posterior deltoid to triceps	• Active thumb pinch • Static thumb extension • Active elbow extension
	3	• BR to FPL • ECRL to FDP • EPL tenodesis • Biceps to triceps or posterior deltoid to triceps	• Static thumb extension • Static finger extension • Active elbow extension
C7	4 or 5	• BR to FPL • EPL tenodesis • ECRL to FDP • PT to EDC	• Active thumb pinch • Static thumb extension • Active finger flexion • Active finger extension
	6	• BR to FPL • PT to EPL • ECRL to FDP	• Active thumb flexion • Active thumb extension • Active thumb flexion
	7	• BR to FPL • Opponensplasty via PT • ECRL to FDP	• Active thumb flexion • Active thumb opposition • Active finger flexion
C8	8 or 9	• Zancolli Iasso procedure	• Prevents MP hyperextension

NLI neurological level of injury, *ISNCSCI* International Standards for Neurological Classification of Spinal cord Injury, *ICSHT* International Classification for Surgery of the Hand in Tetraplegia, *BR* brachioradialis, *ECRB* extensor carpi radialis brevis, *FPL* flexor pollicis longus, *EPL* extensor pollicis longus, *ECRL* extensor carpi radialis longus, *FDP* flexor digitorum profundus, *PT* pronator teres, *MP* metacarpophalangeal joint

Table 44.8 Summary of commonly used upper extremity surgeries to achieve functional goals and postoperative rehabilitation

Ability goal	Functional goal	Procedure	Rehabilitation
Stabilizing elbow in space, reaching overhead objects, pushing wheelchair, stabilizing trunk	Elbow extension	Reconstruction of triceps function	
		Posterior deltoid-triceps	4-wk in cylinder cast with elbow fully extended
		Biceps-triceps	4-wk orthosis
Use of utensils, handwriting, pushing wheelchair	Grip	Reconstruction of grip Reconstruction of passive key grip	
		BR-ECRB FPL-radius	4 wk with arm in cast with flexed thumb and wrist
		CMC I arthrodesis Reconstruction of active key grip	4–10 wk active exercise
		BR-FPL CMC I arthrodesis Split FPL-EPL tenodesis	4 wk in orthosis with active key pinch but restriction of wrist extension

(continued)

Table 44.8 (continued)

Ability goal	Functional goal	Procedure	Rehabilitation
Reaching for objects, e.g., cup or glass positioning of thumb and fingers for improved grasp control	Opening of the hand	Reconstruction of thumb and finger extensors	
		Passive opening	4 wk wrist and thumb in cast
		CMC I arthrodesis	
		EPL to extensor retinaculum attachment	
		Active opening	4 wk wrist, fingers, and thumb in cast
		PT-EDC and EPL/APL	
		Reconstruction of intrinsics	
		Zancolli-lasso tenodesis	4 wk of immobilization in intrinsic plus position. Thumb actively exercised 1st postoperative day
		House tenodesis	
		EDM-APB	

APB abductor pollicis brevis, *APL* abductor pollicis longus, *BR* brachioradialis, *CMC* carpometacarpal, *ECRB* extensor carpi radialis brevis, *EDC* extensor digitorum communis, *EDM* extensor digiti minimi, *EPL* extensor pollicis longus, *FPL* flexor pollicis longus, *PT* pronator teres. From Fridén and Gohritz 2012, with permission

wrist extension, the patient is in the ICHST 1 group, and the brachioradialis is transferred to the ECRB tendon (House and Shannon 1985). Grasp and release are done by tenodesis, which can be enhanced by an orthotic device. The BR and ECRL are functioning in the ICHST 2 group. The ECRL is retained for active wrist extension. The BR is transferred to the FPL to provide active pinch (Fridén and Gohritz 2012). The IP joint of the thumb is stabilized with a screw or wire. In the absence of an active thumb extension, the EPL and EPB tendons are tenodesed to the metacarpal (Waters et al. 1985). In C5 or C6 patients, they belong to the ICHST group 1, 2, 3, and the biceps muscle can be transferred to the triceps muscle or the posterior deltoid muscle can be transferred to the triceps muscle to allow the elbow extension (Lamb and Chan 1983). When performing a biceps-to-triceps transfer, a patient must have intact brachialis and supinator muscles to maintain elbow flexion and forearm supination postoperatively (Bednar 2016; Kuz et al. 1999). Their assessment requires a careful physical examination of elbow flexion and forearm supination strength. However, the biceps transfer tends to weaken the elbow flexion, but the functional importance is not so great that the biceps transfer is more beneficial to achieve a stronger elbow extension than the posterior deltoid transfer (Kozin 2008; Mulcahey et al. 2003).

In activities of daily living, far more tasks are performed with lateral pinch than grasp. This fact underscores the importance of lateral pinch reconstruction for object manipulation, such as holding a toothbrush, pen, fork, or computer disk. A more sophisticated form of pinch (i.e., opposition or pulp-to-pulp pinch) requires an opposing thumb with good control and sensibility. In tetraplegia, unless the spinal cord injury is at a lower level with preservation of extrinsic function and isolated loss of intrinsic function, opposition is often beyond the scope of restorability. Synchronous grasp uses extrinsic and intrinsic muscle activity and is usually not achievable in tetraplegia. An extrinsic grasp via a tendon transfer to restore FDP function is a realistic goal in ICSHT group 3 with the BR, ECRL, and ECRB function. There is controversy concerning whether hand reconstruction should be for pinch and grasp or only pinch. When reconstructing to restore pinch and grasp, the BR is transferred to the FPL and the ECRL is transferred to the FDP. The ECRB is left to provide centralized wrist extension (Bednar 2016). This palmar grasp offers the possibility of holding objects, although the digital roll-up impedes the acquisition of objects with considerable diameter, such as a cup. Individuals with tetraplegia compensate for acquisition by using wrist flexion and concomitant finger extension tenodesis to encircle the

item, followed by active wrist extension and active finger flexion to hold the object in the hand (Kozin 2008).

Finger and thumb extension can often be achieved by wrist flexion (active or passive) and simultaneous tenodesis of the passive finger extension. In ICSHT group 4, BR, ECRL, ECRB, and PT are functional. The goals of upper extremity reconstruction in these patients are pinch, grasp, and release. The functions required in this group are finger extension, thumb extension, intrinsic function, finger and thumb flexion, and thumb carpometacarpal stability (Bednar 2016). The isolated tendon transfer to the extrinsic finger extensors leads to metacarpophalangeal (MCP) joint extension with minimal interphalangeal (IP) joint extension.

Group 5 patients have the addition of FCR, which is generally retained for better wrist control and better finger extension secondary to active wrist flexion (Bednar 2016). Intrinsic function is the last priority in hand reconstruction, although some form of passive intrinsic reconstruction is usually part of finger extension reconstruction. Active intrinsic reconstruction is only indicated in the case of lower-level tetraplegia (ICSHT groups 6 or greater) (Kozin 2008). Individuals with intact extensor digitorum function (C7) and absent finger flexion (C8) are prone to develop MCP joint extension deformities (intrinsic minus hand, true claw hand deformity). Prophylactic night-time splinting in an intrinsic plus hand position will prevent the development of these contractures (Kozin 2008).

Postoperative Care

The duration of immobilization following tendon transfer varies depending on the procedure, but averages about 4 weeks. At this point, the patient begins active and passive mobilization. After surgery, the patient has to learn new functions with a muscle that was previously used for a different function. For example, after transfer of the brachioradialis muscle to the extensor carpi radialis brevis, the patient must learn to extend the wrist without elbow flexion (Vova and Davidson 2020).

44.2.2.2 Nerve Transfer

The trauma patterns that lead to the spinal cord injury vary and superimposed injuries to the brachial plexus or peripheral nerves, subsequent compression neuropathy as well as problems with overuse and instability (with shoulder dysfunction and pain) and spasticity can further complicate the clinical scenario. Traditional surgeries to restore upper extremity function in spinal cord injuries include combinations of tendon transfers, tenodesis, and fusion procedures. Nerve transfers have some disadvantages as well. Nerve transfers are time sensitive and require the surgeon to sacrifice intact neural structures (Vova and Davidson 2020). When the pattern of injury is established and no further spontaneous recovery of function is expected, nerve transfer surgery may be a treatment option. Through the use of peripheral nerve transfer techniques, the volitional control of previously absent motion, such as elbow extension and finger flexion and/or extension, provides improved function and quality of life. The timing of nerve transfers for tetraplegia is still debated (Titolo et al. 2019). There are two basic time schedules for nerve transfer: time independent and time dependent (Fox 2016; Hill and Fox 2019) (Fig. 44.1). The nerve transfer from the intact segments proximal to the injured segments to the caudal segments distal to the injured segment is a time-independent nerve transfer that is performed to restore volitional control of motor function or bypass the zone of spinal cord lesion (Fox 2016; Titolo et al. 2019). This transfer can be done at any time after spinal cord injury. Muscle groups with intact lower motor neurons but damaged upper motor neurons may have the opportunity for intervention beyond 12 months of injury (Khalifeh et al. 2019). The nerve transfer from the intact segments proximal to the injured segments is a time-dependent rescue transfer performed to restore volitional control and reinnervate nonfunctioning muscles. Denervated muscles should benefit from early surgery, before the onset of muscle atrophy (Cain et al. 2015). After nerve transfer, the nerve must regenerate from the coaptation site to the target muscle at a rate of approximately 2.5 cm/month

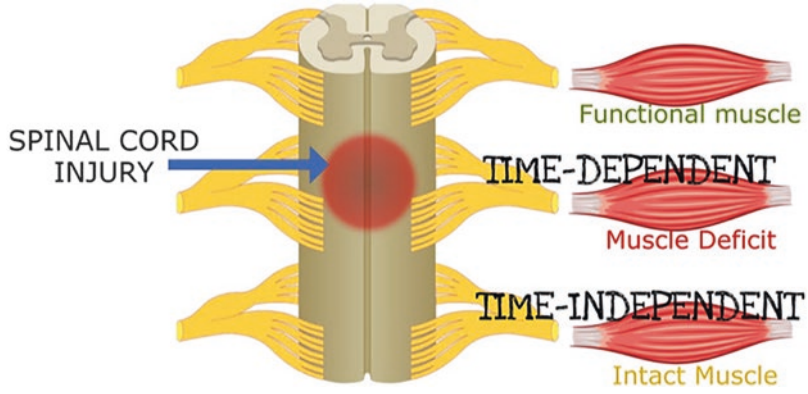

Fig. 44.1 Time-dependent and time-independent nerve transfer based on spinal cord injury level. Over the lesion, the muscle is functional. At the level of injury, the muscle is not directly innervated by spinal cord and function restoration is time dependent. Under the level of injury, the muscle is still innervated by spinal cord. The function restoration is time independent. From Titolo et al. (2019), with permission

(1 inch/month), depending on the length. Therefore, clinical evidence of muscle reinnervation and functional strength after nerve transfer can take 6 to 12 months or more, and success rates are not as high as those for tendon transfers (Fox et al. 2018; Vova and Davidson 2020).

Nerve transfer means the coaptation of an expendable pure motor axon donor with the recipient branch over the shortest possible distance (Fridén and Gohritz 2012). The most common nerve transfers, theoretically suitable donor nerves that are used in cervical spinal cord injuries, are as follows: (1) Transfer of branches of the axillary nerve (C5C6), usual donor includes branches to the teres minor or posterior deltoid, to the triceps branches of the radial nerve, which restores elbow extension; (2) Transfer of branches of the musculocutaneous nerve (to the coracobrachialis or brachialis muscle) can be used to restore wrist extension or finger flexion; (3) Transfer of the supinator branch of the radial nerve may be used to restore finger and thumb extension and abduction by reinnervation of the posterior interosseous nerve branch or wrist extension by reinnervation of the nerve to extensor carpi ulnaris (Fox 2016; Fridén and Gohritz 2012; Hill and Fox 2019). Nerve transfers for the tetraplegic upper extremity are summarized in Table 44.9.

Postoperative Care

Tendon transfers typically require weeks of immobilization postoperatively, whereas nerve transfers do not require strict immobilization (Vova and Davidson 2020). Immediate resumption of light use of the effected extremity for activities of daily living, such as eating, self-catheterizing, and grooming, is permitted, since all nerve transfers are completed in a tension-free fashion. However, there are limitations in repetitive movements at the surgical site to avoid serum formation (Fox et al. 2018). The dressing is removed after 48 h and routine bathing will resume. Drains are removed when drain output is less than 30 mL per day. Full weight-bearing activity, such as using the extremity for transfers or manual wheelchair propulsion, is permitted 2–4 weeks after surgery. Motor reeducation can be initiated at this point. Sports and strengthening exercises are allowed 4 weeks after surgery if there are no complications (Fox 2016).

Table 44.9 Summary of nerve transfers for tetraplegic upper extremity

Function	Donor	Recipient
Elbow extension	Selected deltoid branch of axillary nerve Teres minor branch of axillary nerve	Triceps branch of radial nerve
Wrist extension	Brachialis branch of musculocutaneous nerve	Extensor carpi radialis longus
	Supinator branch of radial nerve	Extensor carpi ulnaris
Finger flexion	Brachialis branch of musculocutaneous nerve	Flexion branches of median nerve (anterior interosseous nerve), anterior interosseous, flexor carpi radialis, flexor digitorum profundus
	Brachioradialis nerve	Flexion branches of median nerve (anterior interosseous nerve), anterior interosseous, flexor carpi radialis flexor digitorum profundus
	Extensor carpi radialis brevis nerve	Flexion branches of median nerve (anterior interosseous nerve), anterior interosseous, flexor carpi radialis flexor digitorum profundus
Finger extension	Supinator branch of radial nerve	Posterior interosseous nerve Extensor carpi ulnaris

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References

Backus D. Exploring the potential for neural recovery after incomplete tetraplegia through nonsurgical interventions. PM R. 2010;2(12 suppl 2):S279–85.

Bednar MS. Tendon transfers for tetraplegia. Hand Clin. 2016;32:389–96.

Biering-Sørensen F, Bryden A, Curt A, et al. International spinal cord injury upper extremity basic data set. Spinal Cord. 2014;52:652–7.

Biering-Sørensen F, Bryden A, Curt A, et al. International spinal cord injury upper extremity basic data set version 1.1. Spinal Cord 2015;53:890.

Cain SA, Gohritz A, Fridén J, et al. Review of upper extremity nerve transfer in cervical spinal cord injury. J Brachial Plex Peripher Nerve Inj. 2015;10:e34–42.

Consortium for Spinal Cord Medicine. Preservation of upper limb function following spinal cord injury: a clinical practice guideline for healthcare professionals. 2005.

Curtin CM, Gater DR, Chung KC. Upper extremity reconstruction in the tetraplegic population, a national epidemiologic study. J Hand Surg Am. 2005;30:94–9.

Dent K, Grampurohit N, Thielen CC, et al. Evaluation of the capabilities of upper extremity test (CUE-T) in children with tetraplegia. Top Spinal Cord Inj Rehabil. 2018;24:239–51.

Fox IK. Nerve transfers in tetraplegia. Hand Clin. 2016;32:227–42.

Fox IK, Miller AK, Curtin CM. Nerve and tendon transfer surgery in cervical spinal cord injury: Individualized choices to optimize function. Top Spinal Cord Inj Rehabil. 2018;24:275–87.

Fridén J, Gohritz A. Novel concepts integrated in neuromuscular assessments for surgical restoration of arm and hand function in tetraplegia. Phys Med Rehabil Clin N Am 2012;23:33–50, ix-x.

Fridén J, Gohritz A. Tetraplegia management update. J Hand Surg Am. 2015;40:2489–500.

Hill EJR, Fox IK. Current best peripheral nerve transfers for spinal cord injury. Plast Reconstr Surg. 2019;143:184e–98e.

House JH, Shannon MA. Restoration of strong grasp and lateral pinch in tetraplegia: a comparison of two methods of thumb control in each patient. J Hand Surg Am. 1985;10:22–9.

Huh S, Ko HY. Recovery target priorities of people with spinal cord injuries in Korea compared with other countries: a survey. Spinal Cord. 2020;58:998–1003.

Kalsi-Ryan S, Curt A, Fehlings MG, et al. Assessment of the hand in tetraplegia using the graded redefined assessment of strength, sensibility and prehension (GRASSP): impairment versus function. Top Spinal Cord Inj Rehabil. 2009;14:34–46.

Kalsi-Ryan S, Beaton D, Curt A, et al. The graded redefined assessment of strength sensibility and prehension: reliability and validity. J Neurotrauma. 2012;29:905–14.

Khalifeh JM, Dibble CF, Van Voorhis A, et al. Nerve transfers in the upper extremity following cervical spinal cord injury. Part 2: preliminary results of a prospective clinical trial. J Neurosurg Spine. 2019:1–13.

Koontz AM, Kankipati P, Lin YS, et al. Upper limb kinetic analysis of three sitting pivot wheelchair transfer techniques. Clin Biomech (Bristol, Avon). 2011;26:923–9.

Kozin SH. Pediatric onset spinal cord injury: implications on management of the upper limb in tetraplegia. Hand Clin. 2008;24:203–13.

Kramer JL, Lammertse DP, Schubert M, et al. Relationship between motor recovery and independence after sensorimotor-complete cervical spinal cord injury. Neurorehabil Neural Repair. 2012;26:1064–71.

Kuz JE, Van Heest AE, House JH. Biceps-to-triceps transfer in tetraplegic patients: report of the medial routing technique and follow-up of three cases. J Hand Surg Am. 1999;24:161–72.

Lamb DW, Chan KM. Surgical reconstruction of the upper limb in traumatic tetraplegia. A review of 41 patients. J Bone Joint Surg Br. 1983;65:291–8.

Lee SK, Wolfe SW. Nerve transfers for the upper extremity: new horizons in nerve reconstruction. J Am Acad Orthop Surg. 2012;20:506–17.

Lo C, Tran Y, Anderson K, et al. Functional priorities in persons with spinal cord injury: using discrete choice experiments to determine preferences. J Neurotrauma. 2016;33:1958–68.

Marino RJ, Shea JA, Stineman MG. The capabilities of upper extremity instrument: reliability and validity of a measure of functional limitation in tetraplegia. Arch Phys Med Rehabil. 1998;79:1512–21.

Marino RJ, Burns S, Graves DE, et al. Upper- and lower-extremity motor recovery after traumatic cervical spinal cord injury: an update from the national spinal cord injury database. Arch Phys Med Rehabil. 2011;92:369–75.

Marino RJ, Patrick M, Albright W, et al. Development of an objective test of upper-limb function in tetraplegia: the capabilities of upper extremity test. Am J Phys Med Rehabil. 2012;91:478–86.

Marino RJ, Sinko R, Bryden A, et al. Comparison of responsiveness and minimal clinically important difference of the capabilities of upper extremity test (CUE-T) and the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP). Top Spinal Cord Inj Rehabil. 2018;24:227–38.

Mateo S, Revol P, Fourtassi M, et al. Kinematic characteristics of tenodesis grasp in C6 quadriplegia. Spinal Cord. 2013;51:144–9.

Mateo S, Roby-Brami A, Reilly KT, et al. Upper limb kinematics after cervical spinal cord injury: a review. J Neuroeng Rehabil. 2015;12:9.

Mulcahey MJ, Lutz C, Kozin SH, et al. Prospective evaluation of biceps to triceps and deltoid to triceps for elbow extension in tetraplegia. J Hand Surg Am. 2003;28:964–71.

Oleson CV, Marino RJ. Responsiveness and concurrent validity of the revised capabilities of upper extremity-questionnaire (CUE-Q) in patients with acute tetraplegia. Spinal Cord. 2014;52:625–8.

Peljovich A. Hand reconstruction in children with spinal cord injury. Phys Med Rehabil Clin N Am. 2020;31:471–98.

Penrod LE, Hegde SK, Ditunno JF Jr. The effect of age on prognosis for functional recovery in acute traumatic central cord syndrome (CCS). Arch Phys Med Rehabil. 1990;71:963–8.

Rahman T, Basante J, Alexander M. Robotics, assistive technology, and occupational therapy management to improve upper limb function in pediatric neuromuscular diseases. Phys Med Rehabil Clin N Am. 2012;23:701–17.

Singh H, Unger J, Zariffa J, et al. Robot-assisted upper extremity rehabilitation for cervical spinal cord injuries: a systematic scoping review. Disabil Rehabil Assist Technol. 2018;13:704–15.

Snoek GJ, IJzerman MJ, Hermens HJ, et al. Survey of the needs of patients with spinal cord injury: impact and priority for improvement in hand function in tetraplegics. Spinal Cord. 2004;42:526–32.

Titolo P, Fusini F, Arrigoni C, et al. Combining nerve and tendon transfers in tetraplegia: a proposal of a new surgical strategy based on literature review. Eur J Orthop Surg Traumatol. 2019;29:521–30.

Velstra IM, Curt A, Frotzler A, et al. Changes in strength, sensation, and prehension in acute cervical spinal cord injury: European multicenter responsiveness study of the GRASSP. Neurorehabil Neural Repair. 2015;29:755–66.

Velstra IM, Fellinghauer C, Abel R, et al. The graded and redefined assessment of strength, sensibility, and prehension version 2 provides interval measure properties. J Neurotrauma. 2018;35:854–63.

Vova JA, Davidson LT. Nerve and tendon transfers after spinal cord injuries in the pediatric population: clinical decision making and rehabilitation strategies to optimize function. Phys Med Rehabil Clin N Am. 2020;31:455–69.

Waters R, Moore KR, Graboff SR, et al. Brachioradialis to flexor pollicis longus tendon transfer for active lateral pinch in the tetraplegic. J Hand Surg Am. 1985;10:385–91.

Waters RL, Sie IH, Gellman H, et al. Functional hand surgery following tetraplegia. Arch Phys Med Rehabil. 1996;77:86–94.

Woolsey R. Rehabilitation outcome following spinal cord injury. Arch Neurol. 1985;42:116–9.

Yozbatiran N, Francisco GE. Robot-assisted therapy for the upper limb after cervical spinal cord injury. Phys Med Rehabil Clin N Am. 2019;30:367–84.

Recommended Additional Reading

Hirt B, Seyhan H, Wagner M, et al. Hand and wrist anatomy and biomechanics. A comprehensive guide. New York: Thieme; 2017.

Saunders RJ, Astifidis RP, Burke SL, et al., editors. Hand and upper extremity rehabilitation: a practical guide. 4th ed. St. Louis: Elsevier; 2016.

Skirven TM, Osterman AL, Fedorczyk JM, et al., editors. Rehabilitation of the hand and upper extremity. 6th ed. Philadelphia: Elsevier; 2011.

Walking in Spinal Cord Injuries

45

Spinal cord injury usually results in conditions that affect motor, sensory, and autonomic functions. In addition to the injuries associated with the musculoskeletal system, these primarily affect the mobility of the patient in the early stages of rehabilitation. During rehabilitation, improvements of motor and sensory deficits are important to maintain independence in activities of daily living such as ambulation. Improvements can be attributed to recovery of neuronal structure and function and the adoption of compensatory strategies (Levin et al. 2009).

The ability to walk again is often the ultimate goal of rehabilitation for patients with spinal cord injuries. Ambulation in patients with spinal cord injury is influenced by the level of injury and the different levels of muscle paralysis, sensory impairment, the lack of trunk control, and spasticity (Hardin et al. 2013). Abnormalities of walking in patients with spinal cord injuries were the absence of active movement of the sagittal plane motions in the hip and knee joints, increased ankle plantar flexion during swing phase, and an inability to position the lower extremity for initial foot contact, and the foot drop or foot slap resulted from paralysis of ankle dorsiflexor muscles. The reason for standing or walking is that starting earlier standing exercises after spinal cord injury allows for training of spinal neural circuits involved in generation of stepping movements. Other systems, such as cardiovascular or musculoskeletal systems, can also benefit from this intervention, which prevents secondary deterioration by nonuse (Wirz et al. 2001). However, the long-term goal of locomotor training is to achieve overground ambulation.

Depending on the level and completeness of the spinal cord injury, the motor function available is the main determinant of waking ability. Several other factors, including muscle tone, proprioception, endurance, age, range of motion, and additional impairments or comorbidities, are also important in determining options available for walking after spinal cord injury. But this is not a long-term ambulatory option for many of these people. There are several potential medical, psychological, and practical benefits, but high energy requirements and excessive demands on the upper extremities for weight-bearing are the major factors that limit its use for long-term functional ambulation in patients with spinal cord injuries even with the use of orthoses and assistive devices (Hardin et al. 2013). On the other hand, wheelchair propulsion has energy costs and speeds similar to normal walking.

There is a reliable prognostic factor for the potential ambulatory function, but at the end of treatment, the patient does not need a wheelchair for all mobility-related activities, a wheelchair for long-distance travel only, or no wheelchair at all. Useful definitions of various mobility modes include wheelchair users and wheelchair-

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dependent patients for daily mobility. Therapeutic walkers are usually patients who use wheelchairs, but occasionally they can walk a limited distance. Functional walkers are patients who have recovered a certain ambulatory function allowing them to walk in daily life with or without walking aids or orthoses. These patients do not need a wheelchair.

Walking using an orthosis or advanced high-tech walking tool including an exoskeletal walking assist robot system has psychological and medical advantages, but it also has a high load on the upper extremity and high energy demand. Rather, it is advantageous that wheelchair use requires energy consumption similar to normal walking. All spinal cord injury patients can be candidates for gait and gait training, but gait training and gait cannot replace important rehabilitation exercises such as mobilities, bed training, exercise training for daily living, or wheelchair use training.

45.1 Measurements of Ambulatory Function

To adapt the content and intensity of training to the goals of rehabilitation, it is recommended to regularly evaluate patients, for example, every 2 weeks. Assessments must comprehensively assess the condition and therefore the disability, as well as the possible areas of activity: assessing impairment, range of motion, muscle strength, and sensory function and for activity assessments, such as Walking Index for Spinal Cord Injury II (WISCI II), Spinal Cord Independence Measure, 10-m walk test, 6-min walk test, Timed Up and Go test, 50-foot walk test, Spinal Cord Injury-Functional Ambulation Inventory (SCI-FAI), Functional Independence Measure-Locomotor (FIM-L), and Berg Balance Scale. WISCI II and 10-m walk test are the most valid and clinically useful tests as primary outcome measures for gait and ambulation for incomplete spinal cord injury, as they have showed criterion-oriented validity, reliability, and sensitivity to change (Alexander et al. 2009).

45.1.1 Walking Index for Spinal Cord Injury (WISCI)

The Walking Index for Spinal Cord Injury (WISCI) is a functional measure for clinical use and for research to evaluate improvement in walking of individuals with spinal cord injuries. In the second version (WISCI II), with two additional levels, the walking capability is rated from 0 to 20 depending on the dependence of the individual using assistive devices, orthoses, or walking aids and personal assistance (Ditunno and Ditunno 2001). The examiner observes the patient walking 10 m and assesses the level considered safe. The use of the WISCI is limited when assessing persons with only minor walking impairment due to a ceiling effect. Walking endurance is not reflected in WISCI.

45.1.2 Spinal Cord Independence Measure

The Spinal Cord Independence Measure, version III (SCIM III), designed specifically for people with spinal cord injuries, is a comprehensive disability measure. The assessment reflects three aspects of self-care management, medical conditions, and mobility. The first section assesses the item of self-care (feeding, bathing, dressing, and grooming) with a total score of 20 points. The second section refers to activities of respiration, bladder sphincter management, and bowel sphincter management and collects up to 40 points. The third section presents all aspects of mobility as a total of 40 points. All subitems can reach a maximum of 100 points.

45.1.3 Spinal Cord Injury Functional Ambulation Inventory (SCI-FAI)

This gait assessment is limited to spinal cord injury, and it is easy to assess and evaluate three components of walking: gait pattern with maximum of 20 points, the use of assistive devices with a maximum of 14 points, and walking

modalities such as speed, frequency, and distance with 5 possible points. Higher scores indicate a higher level of walking ability (Field-Fote et al. 2001).

45.1.4 6-Minute Walk Test

The 6-minute walk test measures the distance a patient can walk on a flat surface as quickly as possible in 6 min. The patient may stop and rest, but is not allowed to sit, during the test, and the use of auxiliary equipment is also permitted. The test was originally designed for patients with respiratory impairment. The 6-min walk test is particularly suitable for recording further improvements for people with minor impairment.

45.1.5 Timed Up and Go

Timed Up and Go (TUG) is a timed walk test, originally developed to assess the sense of balance in elderly people and the risk of falling. The TUG records the time, in seconds, during which the patient has to get up from a chair, walk 3 m, turn around when he/she reaches the 3-m line, walk back, and sit on the chair. If the patient takes more than 30 s to complete the task, the patient usually needs assistance in transfers and going upstairs, and the patient will not go out alone. Use of auxiliary equipment is permitted.

45.1.6 10-Meter Walk Test

For the 10-meter walk test (10 MWT), the patient should be able to walk for at least 14 m since this is the total distance covered by this test. It measures the time in seconds required for a patient to walk 10 m. Use of assistive devices is permitted.

45.1.7 Berg Balance Scale

Originally developed for the elderly, the Berg Balance Scale (BBS) is now also used for patients with stroke and spinal cord injuries, multiple sclerosis, etc. It comprises a total of 14 items each rated on a 5-point scale. The total number of points is from 0 (severely impaired balance) to 56 points (excellent balance).

45.2 Wheelchair Mobility

Wheelchairs are essential for independent mobility for most people with spinal cord injuries. People can ambulate with an assistive device indoors and use a wheelchair for community mobility. Others may use manual wheelchairs for short distances and power wheelchairs for longer distances. Wheelchair and seating systems should maximize function. A properly fitted system optimizes the function of the upper extremity and distributes seat pressure to minimize the risk of pressure injuries. Proper fitting of the wheelchair will minimize the obliquity of the pelvis and accompanying scoliosis and kyphosis.

Wheelchairs can be self-propelled (power) or propelled by the occupants (manual). Manual wheelchairs may have rigid or folding frames. Folding wheelchairs are smaller, easier to transport, and less expensive. By moving the wheel axle forward, maneuverability is improved. However, this reduces stability by narrowing the base of support. Proper seat height can make transfers easier. In general, it is usually easiest to transfer between surfaces of the same height. The control mechanisms of power wheelchairs are joystick, head control, chin control, and sip-and-puff.

Tilt or reclining indicates the movement of the seating surface relative to the floor surface. However, in the tilt settings, the angle between the seat and backrest remains constant. The back angle (angle of the backrest), that is, the recline, refers to the angle between the seat and backrest. This angle can be adjusted to accommodate patient comfort, tone, stability, function, as well as joint range of motion. Many power wheelchairs are equipped with power tilt and recline to relieve pressure. Power recline is convenient for certain self-care tasks such as intermittent cathe-

terization. However, reclining can cause shear forces that can contribute to pressure injuries and can increase spasticity.

45.3 Therapeutics for Spinal Cord Injury Walking

Approaches to facilitating walking after spinal cord injuries can be divided into two main categories. Compensatory strategies include the use of assistive devices and lower extremity orthoses, functional electrical stimulation (FES), or a combination of both to compensate for the loss of muscle strength necessary for walking. Locomotor training uses techniques that facilitate the recovery of walking by promoting plasticity in the central nervous system, central pattern generator.

45.3.1 Orthoses

Overall, there were three types of walking orthoses for patients with spinal cord injuries: mechanical orthoses, hybrid orthoses, and power orthoses (exoskeleton).

45.3.1.1 Mechanical Orthoses

Mechanical orthoses in this category include ankle–foot orthoses, knee–ankle–foot orthoses, hip–knee–ankle–foot orthoses, reciprocating gait orthoses and medial linkage orthoses.

The purpose of an orthosis that aids walking is stability during standing posture, to improvement of swing, or both. Factors affecting spinal cord injury walking may influence the choice of orthotic prescription. Additional considerations include adjustability, potential for skin damage, cosmoses, weight of the orthosis, ease of donning and doffing, durability, and cost.

Ankle–Foot Orthoses

Ankle–foot orthoses (AFOs) are used for people who have enough strength of the quadriceps to stabilize their knee during stance but need the orthosis to control the ankles. The controls required for the ankle depend on the available motor function.

When the dorsiflexors are weak, a dorsiflexion assist or a posterior leaf spring ankle-foot orthosis prevents excess plantar flexion during swing and prevents toe drag. Plantar flexion stop should be used to increase the tone of plantar flexion instead of using a dorsiflexion assistance, as the latter may become overwhelmed by the spastic plantar flexors and may induce triggering spasticity due to rapid stretch of the plantar flexors. Plantar flexion stop, however, can increase the flexion moment at the knee during the early stance phase, increasing the demand for the quadriceps and causing knee buckling. Weakness of the ankle flexors may require a dorsiflexion stop that limits dorsiflexion to 10° to prevent excessive ankle dorsiflexion and knee flexion during stance.

In addition to controlling ankle motion, an AFO can also be used to control the knee. AFO, which limits dorsiflexion, may help prevent knee flexion during stance and partly can compensate for weak quadriceps with stabilization of the knee, through AFO ground reaction. AFO limiting plantar flexion of the ankle has the opposite effect on the knee and can be used to limit the recurrence of genu recurvatum by adjusting the ankle angle.

Knee–Ankle–Foot Orthoses

Knee–ankle–foot orthosis (KAFO) are often prescribed for people with a lower level spinal cord injury (T4 and below) (Merati et al. 2000). A KAFO generally consists of thigh cuffs attached medially and laterally to metal bars that are connected to an ankle-foot orthosis (AFO) or to a shoe. Knee–ankle–foot orthoses are used when the knees and ankle need to be stabilized while walking. Scott-Craig KAFO is a type of KAFO with metal upright braces that is designed to ensure the stability of the ankle and foot while maintaining balance when standing without the support of the upper extremities. It has offset knee joints with a bail knee lock, adjustable ankle joint between 5° and 10° dorsiflexion, an extended foot plate embedded in the shoe sole,

and a cushion heel. KAFOs can be metal or thermoplastic. In order to walk with bilateral KAFO, there is no need for significant lower extremity contractures and good upper extremity strength. Due to the high energy cost of walking with bilateral KAFOs, the percentage of not use is high. The advantage of KAFOs is that they are easier to don/doff as compared to RGOs or HKAFOs because they do not go above the hips (Chafetz et al. 2005).

Hip–Knee–Ankle–Foot Orthosis

A hip–knee–ankle–foot orthosis (HKAFO) is an orthotic device that has components that stabilize or lock the joints at and below the waist. A subcomponent of the HKAFO is the knee–ankle–foot orthosis (KAFO) section. The typical HKAFO is made up of two KAFOs that are linked above the hip with either a pelvic band, lumbar sacral orthotic, or thoracic lumbar sacral orthotic (TLSO) section (Chafetz et al. 2005). A simple hip joint with one degree of freedom was usually in the hip-knee-ankle–foot orthosis. HKAFOs include orthotic control of the hip in addition to the more caudal joints of the lower limb. An assistive device is required for ambulation with HKAFOs. They are more difficult and cumbersome for transfers or curb/step walking and have a high energy cost, which render them impractical for community ambulation for adults with spinal cord injuries (Hirokawa et al. 1990). Paraplegic patients use a swing through walking pattern while walking with this type of orthoses (Merritt and Yoshida 2000). A variant of the HKAFO is the hip guidance orthosis, also called the Parawalker.

Reciprocal Gait Orthoses

Reciprocal gait orthosis (RGO) is a type of HKAFO that uses a mechanical system that connects each side of the brace by either an isometric bar, a double cable, or a single cable system (Chafetz et al. 2005). To achieve a reciprocal gait, a person shifts their weight forward and laterally while extending the hip and upper trunk. The ultimate goal of reciprocal gait orthoses is to mobilize the lower limb by trunk extension. One hip extension creates hip flexion in the other side. Using this kind of orthosis, patients can walk reciprocally and can doff and don the orthosis independently but cannot stand up without help (Nene et al. 1996). It is also difficult for paraplegic patients to walk on a ramp and incline. To solve this problem, the hip joints of this orthosis must have two conditions of locking systems: in a full extension locking position and in 20° flexion from the first position for walking on ramp and incline (Nene et al. 1996). It is generally suggested that an HKAFO may be best used by those interested in increased speed for play activities or keeping up with friends, while an RGO may be most beneficial for stability and for those with weaker upper extremities (Thomas et al. 2001).

A modified version of RGOs is advanced reciprocating gait orthosis (ARGO) with one pull-push cable in the pelvic section designed to assist walking in individuals with paraplegia. Hip guidance orthosis (HGO), RGO and ARGO showed the same motion in pattern and magnitude, but in using the ARGO the pelvic had a pattern of jerky movement. A more developed RGO is defined as isocentric reciprocating gait orthosis (IRGO) and introduced by Motlock in 1992 (Motlock 1992).

Medial Linkage Orthosis

Another type of mechanical orthosis is medial linkage orthosis (MLO). There are variations in this type of orthosis, which include the WalkAbout™, Moorong™, and PrimeWalk™ and the hip and ankle linked orthosis (HALO). These orthoses are based on a medial single hip joint, which provides artificial hip joint movements.

Donning and doffing with this type of orthosis, however, is difficult due to its bulky structure and increased weight. MLOs have less donning and doffing time and light structure compared to IRGOs, but these types of orthoses do not have a reciprocating gait mechanism and pelvic rigid structure. Therefore, the users are forced to use high energy consumption during walking, which in turn can create a poor posture compared to walking with IRGO conditions (Harvey et al. 1997, 1998).

Walking with mechanical orthoses is not ideal for spinal cord injury patients and is a view based on the associated problems during walking with them that includes high loads on upper limb joints and high rate of energy consumption. Some authors have also stated that walking with mechanical orthoses is boring and exhausting (Bernardi et al. 1995; Johnson et al. 2009).

45.3.1.2 Hybrid Orthoses

Hybrid orthoses are a kind of functional electrical stimulation (FES)-activated orthoses. FES is the application of external electrical stimulation to paralyzed muscles to restore their function (Nene et al. 1996). The first reported use of FES to facilitate walking for people with spinal cord injuries improved the stability of the quadriceps muscle stimulation during the stance phase was in 1980. Although hybrid orthosis has certain advantages, there are some limitations associated with the use of orthoses, FES, or hybrid orthoses, in particular by premature muscle fatigue, erroneous triggering of nearby muscles, and heavy and bulk orthoses.

Two kinds of hybrid orthoses are available: hybrid orthosis based on available mechanical designs, such as RGO, ARGO, and MLO, and hybrid orthoses based on the new designs such as modular hybrid, wrapped spring clutch, and spring brake orthoses.

Electrical stimulation of the lower limbs during the corresponding gait phase was used to facilitate walking in people with spinal cord injuries, either used alone or in a hybrid system in combination with orthoses. These systems can be directed to just one movement, for example, electrical stimulation to prevent foot drop in patients with ankle dorsiflexor weakness, or the system can be more complicated. For example, the Parastep system is a neuroprosthetic system approved by US FDA for people with T4 to T12 complete paraplegia. It uses electrical stimulation at several sites, including the quadriceps, gluteal muscles, and peroneal nerves. When used in conjunction with a rolling walker, which is operated via finger-activated control switches, it allows independent standing and ambulation. However, the system is cumbersome and inefficient and more appropriate for exercise than as a primary purpose for ambulation (Giszter 2008).

When electrical current is applied to contract muscles, large-diameter (type II) muscle fibers, which are easily fatiguable, are preferably stimulated. This is in contrast with the normal activation of motor units by the central nervous system, whereby smaller fibers (type I) are stimulated, which are less susceptible to fatigue. Thus, muscle fatigue is a significant limiting factor of these FES systems.

45.3.1.3 Power Orthoses (Exoskeleton)

Body weight-supported treadmill training and exoskeletal robotic walking system are an intervention that may result in ambulatory function of the patients. Robotic systems are equipped with driven leg joints and sensors to measure the torque and position of the joints. The advantage of robotic systems is that it can extend the training session and consequently of performing a higher number of repetitions (Esquenazi et al. 2012).

Spinal cord injury patients do not use their mechanical orthoses, with abandonment rates of 61–90% for children with myelomeningocele (Katz-Leurer et al. 2004; Sykes et al. 1995) and 46–54% in adults with spinal cord injury (Jaspers et al. 1997), due to the high level of energy expenditure needed to ambulate. One of the main reasons for the development of PGOs was to potentially reduce energy consumption when walking with an orthosis. A healthy subject walks with 0.176 mL/kg/m energy expenditure (Bernardi et al. 1999), and a spinal cord injury subject walks with weight-bearing control orthosis (WBCO) 5.41 J/kg/s energy expenditure (Kawashima et al. 2003).

Powered gait orthoses (PGOs, exoskeleton) can be used as a gait training system to facilitate ambulation both in the clinical situation and in the home via an external power supply using electric motors and pneumatic and/or hydraulic actuators. Powered orthoses are a type of orthoses that are activated with an external power supply. The mechanical orthoses have a simple structure and user-friendly design. This type of

orthoses has not progressed in development in recent years, however, because technology of the powered orthoses is seen a major focus of research on rehabilitation and assisted walking in patients with spinal cord injuries (Arazpour et al. 2012, 2016).

45.3.2 Locomotor Training

Locomotor training may restore walking by promoting plasticity in the central nervous system. The theory of locomotor training has the potential that repetitive task-specific training can activate neural circuits, that is, central pattern generator (Rossignol and Dubuc 1994) in the spinal cord and improves neural plasticity. There are several modes to provide locomotor training including manual-assisted body weight-supported treadmill training (BWSTT) (Hornby et al. 2005), robotic BWSTT, and locomotor training in conjunction with FES. Proposed guiding principles for locomotor training include (1) maximizing weight-bearing on the legs and minimizing or eliminating weight-bearing through the arms; (2) optimizing sensory cues compatible with standing or walking; (3) postural control and optimizing trunk, limb, and pelvic kinematics for walking and associated motor tasks; and (4) maximizing recovery and use of normal movement patterns and minimizing the use of compensatory movement strategies (Morawietz and Moffat 2013; Swinnen et al. 2010; Sykes et al. 1995).

References

Alexander MS, Anderson KD, Biering-Sorensen F, et al. Outcome measures in spinal cord injury: recent assessments and recommendations for future directions. Spinal Cord. 2009;47:582–91.

Arazpour M, Chitsazan A, Hutchins SW, et al. Design and simulation of a new powered gait orthosis for paraplegic patients. Prosthetics Orthot Int. 2012;36:125–30.

Arazpour M, Bani MA, Mousavi ME, et al. Orthoses for spinal cord injury patients. In: Fuller H, Gates M, editors. Recovery of motor function following spinal cord injury. London: IntechOpen; 2016. p. 259–76. http://www.intechopen.com/books/recovery-of-motor-function-following-spinal-cord-injury.

Bernardi M, Canale I, Castellano V, et al. The efficiency of walking of paraplegic patients using a reciprocating gait orthosis. Paraplegia. 1995;3:409–15.

Bernardi M, Macaluso A, Sproviero E, et al. Cost of walking and locomotor impairment. J Electromyogr Kinesiol. 1999;9:149–57.

Chafetz RS, Johnston TE, Calhoun CL. Outcomes in upright mobility in individuals with a spinal cord injury. Top Spinal Cord Injury Rehabil. 2005;10:94–108.

Ditunno PL, Ditunno JF Jr. Walking index for spinal cord injury (WISCI II): scale revision. Spinal Cord. 2001;39:654–6.

Esquenazi A, Talaty M, Packel A, et al. The ReWalk powered exoskeleton to restore ambulatory function to individuals with thoracic-level motor-complete spinal cord injury. Am J Phys Med Rehabil. 2012;91:911–21.

Field-Fote EC, Fluet GG, Schafer SD, et al. The spinal cord injury functional ambulatory inventory (SCI-FAI). J Rehabil Med. 2001;33:177–81.

Giszter SF. Spinal cord injury: present and future therapeutic devices and prostheses. Neurotherapeutics. 2008;5:147–62.

Hardin EC, Kobetic R, Triolo RJ. Ambulation and spinal cord injury. Phys Med Rehabil Clin N Am. 2013;24:355–70.

Harvey L, Davis G, Smith M, et al. Energy expenditure during gait using the walkabout and isocentric reciprocal gait orthoses in persons with paraplegia. Arch Phys Med Rehabil. 1998;79:945–9.

Harvey LA, Smith MB, Davis GM, et al. Functional outcomes attained by T9-12 paraplegic patients with the walkabout and the isocentric reciprocal gait orthoses. Arch Phys Med Rehabil. 1997;78:706–11.

Hirokawa S, Grimm M, Solomonow M, et al. Energy consumption in paraplegic ambulation using the reciprocating gait orthosis and electric stimulation of the thigh muscles. Arch Phys Med Rehabil. 1990;71:687–94.

Hornby TG, Zemon DH, Campbell D. Robotic-assisted, body-weight-supported treadmill training in individuals following motor incomplete spinal cord injury. Phys Ther. 2005;85:52–66.

Jaspers P, Peeraer L, Van Petegem W, et al. The use of an advanced reciprocating gait orthosis by paraplegic individuals: a follow-up study. Spinal Cord. 1997;35:585–9.

Johnson W, Fatone S, Gard S. Walking mechanics of persons who use reciprocating gait orthoses. J Rehabil Res Dev. 2009;46:435–46.

Katz-Leurer M, Weber C, Smerling-Kerem J, et al. Prescribing the reciprocal gait orthosis for myelomeningocele children: a different approach and clinical outcome. Pediatr Rehabil. 2004;7:105–9.

Kawashima N, Sone Y, Nakazawa K, et al. Energy expenditure during walking with weight-bearing control (WBC) orthosis in thoracic level of paraplegic patients. Spinal Cord. 2003;41:506–10.

Levin MF, Kleim JA, Wolf SL. What do motor "recovery" and "compensation" mean in patients following stroke? Neurorehabil Neural Repair. 2009;23:313–9.

Merati G, Sarchi P, Ferrarin M, et al. Paraplegic adaptation to assisted-walking: energy expenditure during wheelchair versus orthosis use. Spinal Cord. 2000;38:37–44.
Merritt J, Yoshida M. Knee ankle foot orthoses: indications and practical applications of long leg braces. Phys Med Rehabil State Art Rev. 2000;14:395–422.
Morawietz C, Moffat F. Effects of locomotor training after incomplete spinal cord injury: a systematic review. Arch Phys Med Rehabil. 2013;94:2297–308.
Motlock WM. Principles of orthotic management for child and adult paraplegia and clinical experience with the isocentric RGO. In: Proceeding of 7th world congress of the international society in prosthetic and orthotics, Chicago, 1992.
Nene A, Hermens H, Zilvold G. Paraplegic locomotion: a review. Spinal Cord. 1996;34:507–24.
Rossignol S, Dubuc R. Spinal pattern generation. Curr Opin Neurobiol. 1994;4:894–902.
Swinnen E, Duerinck S, Baeyens JP, et al. Effectiveness of robot-assisted gait training in persons with spinal cord injury: a systematic review. J Rehabil Med. 2010;42:520–6.
Sykes L, Edwards J, Powell ES, et al. The reciprocating gait orthosis: long-term usage patterns. Arch Phys Med Rehabil. 1995;76:779–83.
Thomas SS, Buckon CE, Melchionni J, et al. Longitudinal assessment of oxygen cost and velocity in children with myelomeningocele: comparison of the hip-knee-ankle-foot orthosis and the reciprocating gait orthosis. J Pediatr Orthop. 2001;21:798–803.
Wirz M, Colombo G, Dietz V. Long term effects of locomotor training in spinal humans. J Neurol Neurosurg Psychiatry. 2001;71:93–6.

Recommended Additional Reading

Bromley I. Tetraplegia and paraplegia: a guide for physiotherapists. New York: Churchill Livingstone; 1976.
Harrison P. Managing spinal injury: critical care. The international management of people with actual or suspected spinal cord injury in high dependency and intensive care unit. London: The Spinal Injury Association; 2000.
Harvey L. Management of spinal cord injuries: a guide for physiotherapists. Philadelphia, PA: Churchill Livingstone; 2008.
Lusardi MM, Jorge MM, Nielsen C. Orthotics and prosthetics in rehabilitation. 3rd ed. Philadelphia: Elsevier; 2013.
Somers MF. Spinal cord injury. Functional rehabilitation. 3rd ed. New York: Pearson; 2010.
Webster JB, Murphy DP. Atlas of orthoses and assistive devices. 5th ed. Philadelphia: Elsevier; 2019.

Wheelchairs and Wheelchair Mobility in Spinal Cord Injuries

46

The wheelchairs are the essential tool of mobility for most individuals with spinal cord injuries (Michael et al. 2020). One of the most important recommendations for people with spinal cord injuries is the type of wheelchair and the accessories needed to enable maximum functionality, including maximizing independent mobility, maximizing independent functioning, preventing and minimizing deformity or ensuring stable positioning, and projecting a healthy, vital, and attractive body image (Weiss et al. 2010). When the capacity and fit of a wheelchair are matched to the needs and abilities of individuals with spinal cord injuries, health, function, community participation, and quality of life can be maximized (Michael et al. 2020). In principle, wheelchairs must meet certain criteria depending on the neurological level of injury, the remaining muscles and their strength, the patient's height and weight, the patient's functional level, the type of terrain, and the occupation and home adaptation of the patient. Improved wheelchairs have enabled people to play a more active role in sports, along with the greater desire of people with disabilities to be more active in all aspects of life.

Wheelchairs are becoming lighter, more user-friendly with precision bearings in all four wheels, and more individually adjustable. Despite the fact that there are already excellent models in production, the development of the wheelchair must be closely monitored in the future to ensure that the most efficient wheelchair is recommended to the patient. The function, management, balance, and safety of people with spinal cord injuries must be considered when selecting a wheelchair. There are some important general considerations in the choice of a wheelchair. There were only three basic genotypes for wheelchairs: manual wheelchairs, electrically powered wheelchairs, and scooters. Of course, there are a multitude of varieties within each of these genotypes (Cooper et al. 2006). A wheelchair prescription consists of two core components: a wheelchair base (manual or power) and the seating interface (seat cushion and backrest). The weight of the wheelchair depends on the functional level of each patient. A standard upright wheelchair weight is 50 to 55 pounds (23–25 kg). A lightweight wheelchair weighs approximately 40 pounds (18 kg) and is suitable for those with weaker upper extremities so that they can get in and out of the chair or get into the car. In addition, prescribing an appropriate wheelchair and its accompanying components requires consideration of the patient's individual medial needs, physical activities, preferences, individual's posture, functional needs or activities, expected use of the wheelchair, the prognosis for change in the patient's condition, physical environment at home and in the community, availability of accessible transportation, and available financial resources (Hughes et al. 2005; Michael et al. 2020). When

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choosing a wheelchair, the specific needs of each individual wheelchair user must be considered (Boninger et al. 2005). Prescribing a wheelchair should be just as precise as prescribing medication (Yasukawa et al. 1994). All movements including manipulation and mobilization of the wheelchair in this chapter are described based on motor complete tetraplegic patients.

46.1 Manual Wheelchair Option Selection

A wheelchair is made up of a seating system (the postural support structure), a frame (the supporting structure), and a mobility system (the propelling structure) (Ventura and Bendix 2020) (Fig. 46.1). Manual wheelchairs are mainly divided into classes according to frame weight and adjustability of the rear axle. The two most commonly prescribed classes for people with spinal cord injuries are K0004 (high strength lightweight) and K0005 (ultra-lightweight) of the Medicare categories (Gebrosky et al. 2018). The lightweight wheels offer a lower moment of inertia, which allows quicker acceleration and lower rotating weight (Hughes et al. 2005).

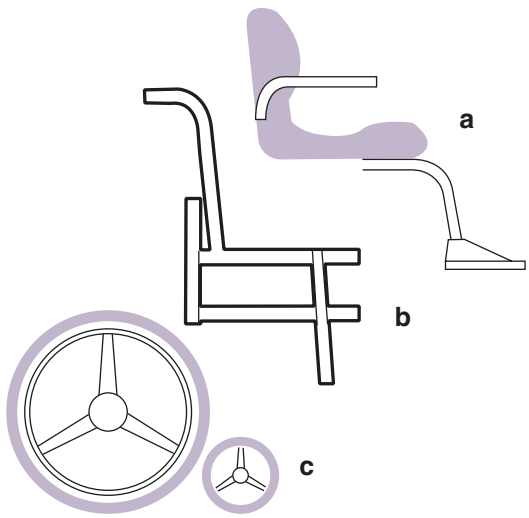

Fig. 46.1 The three components of the wheelchair include the postural support structure (**a**), the supporting structure (**b**), and the propelling structure (**c**). From Ventura and Bendix (2020), with permission

Customization of the lightest possible wheelchair has been recommended by clinical practice guidelines of Consortium for Spinal Cord Medicine (Consortium for Spinal Cord Medicine 2005) in order to delay the onset and progression of the shoulder and wrist pain. The recommendation of the clinical practice guidelines can only be achieved with a K0005. The clinical practice guidelines recommend placing the rear wheel as far forward as possible without loss of stability and positioning the wheel so that the user's elbow is flexed 90–120° when the hand is at the top of the handrim, dead center of the handrim (Consortium for Spinal Cord Medicine 2005).

Since the patient with a spinal cord injury spends many hours a day in the wheelchair, it must fit well for reasons of comfort, safety, and skin protection. For correct and initial measurements, the patient must sit in the normal sitting position, with the head in midline, trunk erect, hips flexed 90° and knees 90–100°, and feet in neutral position when the patient is sitting in the wheelchair (Weiss et al. 2010). The patient should also sit on a cushion of the thickness that they will be using. The importance of correct fit of the wheelchair must be assured so that the user can achieve maximal comfort, stability, function, and safety (Pierson and Fairchild 2008). The patient must be involved in the wheelchair selection process so that their ideas and desires are taken into account and so that they learn about the considerations involved in wheelchair prescription and will be able to make educated selections in the future. These considerations include balance and safety, propulsion, transfers, and future plans, such as sports activity and vocation. Selecting a wheelchair very early is not always advisable as balance, strength, and the extent of possible recovery are not always known. For example, some patients may need a tall back in the early stages that may not be needed later and affect their wheeling ability. It is desirable to have a selection of rental wheelchairs available so that patients can learn the difference between various types and may progress from one step to another as they become more adept. The components of the standard manual wheelchair are shown in Fig. 46.2.

Fig. 46.2 Features and components of a standard manual wheelchair. Photo of the wheelchair taken from https://www.clasphub.org/products/transport-wheelchairs/transport-wheelchair/

46.1.1 Frame Material

As manual wheelchair technology has advanced over time, four key features have emerged almost simultaneously. These features are decreased weight, decreased shocks and vibrations, improved transportability, and increased durability (DiGiovine et al. 2006). The frame mass is an important factor in choosing a manual wheelchair. Aluminum is widely used in wheelchairs because it has a better strength-to-weight ratio than steel (Liu et al. 2010; Medola et al. 2014). Recently, titanium and carbon fiber have been used to make wheelchair frames. Titanium has advanced properties in terms of shock and vibration absorption and a better strength-to-weight ratio than aluminum (Flemmer and Flemmer 2016; Liu et al. 2010; Medola et al. 2014). Similarly, carbon fiber has a much higher strength-to-weight ratio than aluminum and steel. However, both titanium and carbon fiber are more expensive than aluminum and require special manufacturing techniques (DiGiovine et al. 2006; Flemmer and Flemmer 2016).

46.1.2 Seat Height

The seat height is measured from the bottom of the heel to the posterior thigh with 90° knee flexion and 2 inches is then added to allow clearance for the footrest (Brown and Banks 2014; Pierson and Fairchild 2008). The thickness of the cushion and its relative additional height should be considered. Ideally, the patient should sit in a standard height wheelchair on the cushion that they will be using. The feet should be positioned as if they were on the footplate. If the heel is at least 2 to 2½ inches (6 cm) above the floor, then a standard height wheelchair can be ordered. If the heel is more than 5 inches (13 cm) above the ground, a lower frame chair should be considered. The seat height of the standard adult wheelchair is 19.5 to 20.5 inches (50–52 cm) from the ground.

If the seat is too high, the user may experience insufficient trunk support and difficulties in propelling the wheelchairs. If the seat is too low, it can be difficult for the user to perform a standing or lateral swing transfer because the person's center of gravity is lower, making it difficult to

lift the body and result in improper weight distribution while sitting (Pierson and Fairchild 2008), and causing the patient's feet to drag and raising the thigh and knee, increasing pressure on the ischial tuberosity.

46.1.3 Seat Width

The seat width is measured across the widest point of the hips with clothing and any orthosis and add 2 inches (5 cm) to this measurement for the total seat width. The correct seat width allows for one hand width (approximately 1 inch) on either side of the trochanters. In general, when assessing the width of a wheelchair, a flat hand should slip between the patient's hips and the wheelchair arms. The hand should be in slight contact with the user and the armrest panel or wheelchair handrims when the user is seated in the center of the seat (Pierson and Fairchild 2008). This allows the wheelchair user to easily reach the handrims and places the arm in a position with greater leverage. The width should allow room for the patient to twist in the chair when changing position and should provide space for winter clothing. The patient may also need space to place his or her hands on the cushion to change position, do a push-up, or initiate a transfer. If the patient is dependent, space is needed for a helper's hands to adjust his or her position, clothing, and so forth. Patients with lower extremity orthoses usually do not need a wider chair because their orthoses fit below the trochanters. If the wheelchair is too narrow, transfers and wheelchair access become difficult and pressure injuries along the hips and thighs from the armrest guard are more likely to occur. A small wheelchair may prohibit the use of orthotics or coats. If the seat is too wide, trunk support is impaired, leading to scoliosis, back pain, and difficulty propelling the wheelchair (Weiss et al. 2010) as the distance to the handrims increases, leading to leaning to one side of the wheelchair while propelling and resulting in uneven weight distribution (Brown and Banks 2014). The seat width is 18 inches (46 cm) for a standard adult wheelchair and 16 inches (41 cm) for a narrow adult wheelchair.

46.1.4 Seat Depth

The seat depth is the distance from the front of the seat upholstery to the back of the seat upholstery. The seat depth is measured from the most posterior aspect of the buttocks to the popliteal fossa, and 2 inches (5 cm) is then subtracted from this measurement to allow for clearance of the hamstring tendons. If a back cushion is to be used, measure the depth with the cushion in place or add the thickness of the cushion to the measurement. While not a critical measurement, the width of a fist between the back of a patient's knees and the seat front allows sufficient length of cushion to support the thighs adequately while the person can twist or maneuver in the wheelchair. That is, the correct seat depth should ideally be 2 to 4 inches from the popliteal space or approximately one hand width. It is important that the edge of the seat should not contact the back of the knees. If the seat depth is too shallow, ischial pressure is increased and the stability of the chair decreases (Weiss et al. 2010). A standard wheelchair is 16 inches (41 cm) deep for most adults. The person with a longer thigh may need a sports model with an 18 inches (46 cm) or 20 inches (51 cm) depth.

If the front to the back of the seat is too short, the user may experience decreased trunk stability as the thighs are less supported, increased weight bearing on the ischial tuberosities as the body weight is shifted posteriorly due to the lack of support to the thighs, and poor balance because the base of support has been reduced. If the seat is too long from the front to the back, the user may experience increased pressure in the popliteal area, causing skin discomfort or impaired circulation as the seat upholstery is longer than the thighs (Pierson and Fairchild 2008). In addition, a long seat can prevent the patient from sliding back fully into the seat, preventing the patient from being properly seated on the wheelchair and resulting in a slumped posture (Brown and Banks 2014).

46.1.5 Backrests and Backrest Height

An optimally fitted backrest supports the posture of the body segment and minimizes trunk movement and energy losses during dynamic use of the arms. In manual wheelchairs, the standard backrest is nonadjustable sling upholstery that stretches over time, promotes kyphotic deformity and posterior pelvic tilt, and can reduce propulsion efficiency (Krey and Calhoun 2004; Michael et al. 2020; Yoo 2015).

The determination of the backrest height depends on the patient's level of functional mobility, the type of wheelchair prescribed (Brown and Banks 2014), comfort, stability, and control of the wheelchair. In general, people with minor mobility impairments prefer a lower backrest height. A lower backrest height allows more freedom of movement such as leaning or turning and is less restrictive when propelling wheelchair but offers less support than a high backrest. Propelling with the backrest height lower than 16 inches (40.6 cm) enables a larger range of movement for the shoulder, an increased stroke angle and push time, and a reduced cadence (stroke frequency) regardless of the level or slope propelling, resulting in a reduced risk of upper limb overuse-related injuries (Yang et al. 2012). When assessing the height of the backrest, the cushion required must be included. A standard wheelchair backrest height is 16 inches (41 cm) and is measured from the seat of chair to the floor of the axilla with the user's shoulder flexed to 90°, and then subtracting approximately 4 inches (10 cm) (Pierson and Fairchild 2008), or from the bottom of the patient's cushion to the inferior angle of the scapula (Yasukawa et al. 1994). The backrest height varies according to the patient's needs. Some wheelchairs have a modular back that comes in 8.5 inches (22 cm), 11 inches (28 cm), 13.5 inches (34 cm), and 16.5 inches (42 cm) heights. The correct backrest height for the patient with impaired trunk control should be positioned 1 inch below the inferior angle of the scapula. Those with intact trunk control should use lower backrests, taking the top of the lumbar spine as a reference (Cherubini and Melchiorri 2012). A modular backrest can be useful in determining the height required by a tetraplegic patient, and it will be useful for the patient who requires a high back at first for balance but then progresses to a lower back. A patient with impaired balance should have their back height at least 1 inch above the inferior angle of the scapula (Ford and Duckworth 1987).

A higher backrest provides better support, but limits shoulder extension and impairs manual wheelchair propulsion by blocking scapular movement (Medola et al. 2014), as excessive skin irritation can occur over the inferior angles of the scapulae as they rub against the upholstery (Pierson and Fairchild 2008), can push a patient too forward to tend to fall, and a lower backrest will often correct this problem. On the other hand, the lower backrest is beneficial for the patient as they can move their shoulder freely, which can push hard on the handrims with a greater push angle and push time, thus reducing push frequency (Yang et al. 2012), but back support and posterior stability are limited (Medola et al. 2014). The patient in a wheelchair with a low back can fall backward.

46.1.6 Armrests

Armrests have a number of different functions for the wheelchair user (Cooper et al. 2010; Cooper et al. 2000). Armrests are often used to support pressure relief through push-up. There are three basic styles of armrest: wrap-around, full-length, and desk-length. A wrap-around armrest gets its name because it is attached to the frame of the wheelchair back below the backrest. Full-length armrests support almost the entire forearm (Cooper et al. 2010). Full-length armrests provide good support for the upper extremities, but they can make it difficult to get close to some tables and desks. The high-level tetraplegic patient will likely need height-adjustable desk armrest or full-length armrest with detachable arm troughs. These help with positioning and balance, protection of the shoulder joint, and the hand and wrist positioning. Desk armrests allow the patient to approach a desk or table. In addition to different lengths, the armrests can also be

fixed, adjustable, or removable. When adjustable, the armrests can move up and down to fit the length of the user's trunk and arms. Removable armrests are recommended for users who perform a lateral swinging or sliding transfer in a seated posture (Pierson and Fairchild 2008).

46.1.7 Armrest Height

The armrest height is measured from the seat to the olecranon process with the user's elbow flexed to 90°, and then approximately 1 inch is added if a seat cushion is to be used. The standard height of the armrest is 9½ inches (24 cm). The patient must sit on the cushion that he or she will be using. For patients with tetraplegia, an adjustable armrest is usually used to allow working at different heights. The adjustable armrest can be adjusted from 8 to 13 inches (20–33 cm) in height and can be used with very tall and very short people. Many paraplegic patients do not use armrests.

If the armrest is too high, it may be difficult for the user to propel the wheelchair as it is difficult to reach the high armrest to grasp the handrims, can lead to postural deviation due to an elevated shoulder when resting the forearm on the armrest, and limit the use of the armrests caused by discomfort when trying to use them, leading to decreased trunk stability and fatigue, and causing the shoulders to be pushed upward, causing pressure and pain in the glenohumeral joint (Brown and Banks 2014; Pierson and Fairchild 2008). If the armrest is too low, the user may experience poor posture and back discomfort, which is caused by excessive trunk forward leaning to place the forearms on the armrest (Pierson and Fairchild 2008) and can lead to upper trapezius strain and shoulder subluxation (Yasukawa et al. 1994).

46.1.8 Seat Tilt (Seat Angle)

The seat tilt (reclining the seat angle) is a common procedure used to improve a user's sitting balance and functional reach (Medola et al. 2014). The seat angle can range from 0 to 20°. It should be noted that the back of the seat of a standard wheelchair is approximately 1 inch (2.5 cm) lower than the front. Tilting the seat toward the backrest allows the user to fit more securely in the chair, and the chair is more responsive to the user's movements. The seat angle also gives the user some pelvic tilt, which ensures greater trunk stability. If an increased tilt is required due to spasticity, patient positioning, or slipping forward, a wedge cushion can be used. Although there is a decrease in pressure on the ischial tuberosity, there is an increase in peak pressure on the sacrococcygeal region.

46.1.9 Legrests

The footrest and legrest are collectively referred to as front rigging (Weiss et al. 2010). The legrests are used to provide support to the lower extremities, and the footrest provides support to the feet. A standard swing away removable legrest is convenient for the patient transferring to the bathtub. It is also convenient for being close to bed or toilet, for easy stowing in the trunk of a small car, or for negotiating tight corners on occasion. The helper of a dependent patient may need to remove a legrest to get close enough to ease the transfer. A locking lever mechanism can usually be operated by a person who can remove a leg from the footrest to enable the legrest to swing out. Occasionally the lever needs to be lengthened or curved out to make it easier to reach. Some patients are required to have elevating legrests, usually because of dependent edema or because they use power recliner wheelchairs. Elevating legrests lengthen the wheelchair and reduce maneuverability.

46.1.10 Footrests (Footplates)

Footrest length is measured from the fibular head to the bottom of the shoe. Remember to add in the height of the cushion. These are available in various sizes depending on the patient's needs or as adjustable footrests that allow the foot to be

positioned in dorsiflexion or plantar flexion. Since the width of the footrest depends on the width of the wheelchair, an adaptation to the wheelchair's width may make it necessary to change the size of the footrest. Footrests are often the first part of the wheelchair to come in contact with an obstacle. Therefore, they should be durable. Footrests can be fixed, foldable, or swing away. Rigid footrests are used during sports activities and are suitable for people who are very active in their wheelchairs.

The height of the footrest is important for the positioning of the patient. As a rule of thumb, a flat hand can easily be inserted under the thighs. The goal is to apply even pressure along the length of the thighs to relieve some pressure from the buttocks. In general, the footrest is positioned in such a way that the angle of the knees ranges from 90° to 120°. If the footrests are too high, the buttocks will be pressed too much. If the foot support is too low, the pressure on the seat interface tends to increase with the weight of the legs, the feet push the thighs down and press them against the seat, and circulation to the lower leg can be impeded or the weight of the legs over the front edge of the cushion can cause the patient out of the wheelchairs. When the feet are not properly supported, gravity will bend the ankles down, facilitating the shortening of the calf muscles (Medola et al. 2014). If it is properly adjusted, the footrest must have a clearance of 2 inches from the floor. If it is beneficial for the patient to be able to recline slightly to improve balance, the caster spindle may have an overlying socket to elevate the front part of the wheelchair. If there are several positions for the rear wheel axles on the wheelchair, the axles can be placed in a higher position. This will also tilt the wheelchair backward and raise the footrests.

46.1.11 Leg Straps

One or two detachable leg straps or an H-strap can be attached with Velcro or a post and loop, one strap behind the heel and another optional one at about the mid calf. The heel loop prevents the foot from sliding backward.

46.1.12 Recliner Back

A recliner wheelchair has both a high backrest and a headrest. Patients who are prone to pressure injuries, cannot sit fully upright, and have poor sitting balance, poor endurance, orthostasis, or respiratory needs, or who otherwise must be able to adjust the backrest, may benefit from a recliner or tilt mechanism. These systems add weight and bulk and require a longer wheelbase to maintain adequate stability when the chair is reclined. In addition, shear forces are usually increased (Weiss et al. 2010). A headrest is required for head support and control of the recliner wheelchair (Brown and Banks 2014). This type of wheelchair can have manual or power controls. A manual recliner wheelchair is difficult to maneuver and should not be ordered unless absolutely necessary (Ford and Duckworth 1987).

Semireclining wheelchairs allow the back of the chair to be adjusted in various positions, from fully upright position to 30°. The chair back will usually be higher than that of a standard wheelchair, and a removable head component is necessary to support the user's head when reclined. Elevating legrests are necessary components of this chair for user comfort and to maintain chair stability (Pierson and Fairchild 2008). Fully reclining wheelchairs allow the back to be adjusted to various positions, from vertical to fully horizontal. A headrest and elevating legrests are necessary components, as previously described. In addition, the rear wheels will be located further back than on a standard wheelchair, or they may move back as the wheelchair is reclined to increase the base of support and stability of the chair (Pierson and Fairchild 2008).

46.1.13 Wheels

Wheel components include the type of tire, handrim (pushrim), tire rim, Mag (magnesium) wheel or wire spoke wheel, and the hub (Brown and Banks 2014). The rear wheels play an important role in mass and vibration transmission. Heavier wheels make it difficult to start moving from a standing position; lighter wheels allow

faster acceleration (Hughes et al. 2005). Traditionally, rear wheels were made from either plastic or steel. Standard wheels are 20–24 inches (51–61 cm) in diameter. Mag wheels are the most common wheels. They are made of plastic or metal, but were initially made of magnesium, thus their name (Weiss et al. 2010). Recently, carbon fiber has been used to make lighter wheels. In addition to reducing weight, carbon fiber wheels minimize the transmission of vibration to the user's body (Digiovine et al. 2006). Mag wheels require less maintenance than spoke wheels. Spoke wheels are lighter, are easier to propel, and have improved shock absorbance. However, they tend to bend and loosen (Weiss et al. 2010).

46.1.14 Tires

Tires can be obtained as solid, pneumatic, or semipneumatic tires. If a tire is hard, it rolls easier than a soft tire, but the pneumatic tire can be as comfortable. Pneumatic tires have been shown to significantly reduce rolling resistance compared to solid tires, and this facilitates manual propulsion by keeping the wheels rolling for a longer distance (Kwarciak et al. 2009; McLaurin and Brubaker 1991). Rolling resistance is the force that counteracts the movement of a tire as it rolls over surface (Kwarciak et al. 2009). The balance between ease of wheeling and comfort must be decided on an individual basis. Despite the advantages of pneumatic tires, solid tires are still widely used because they require almost no maintenance and there is no risk of being deflated by flat tires (Kwarciak et al. 2009). A narrow tire has less resistance, is easy to propel on a hard surface, and is well suited for sports activities. These tires are designed for speed, maneuverability, and endurance. But a wider tire is required for pushing over soft or rough ground and is more suitable for outdoor use (Brown and Banks 2014). This is especially important for front tires (casters).

46.1.15 Casters and Caster Locks

Casters are the small wheels in the front of the wheelchair. The casters are used to steer the wheelchair and are available in a diameter of 2, 5, or 8 inches (5, 13, or 20 cm) (Weiss et al. 2010). Similar to the rear wheels, solid rubber, pneumatic, or semipneumatic caster wheels are commercially available. Although pneumatic wheels have been shown to reduce rolling resistance, they require special attention regarding pressure control and maintenance. Therefore, solid casters are still the most commonly used type of caster in manual wheelchairs (Medola et al. 2014). The larger the caster diameter, the easier it is to push the wheelchair over rough surfaces, but the smaller caster diameter allows it to be turned on a hard surface and makes the wheelchair more maneuverable. The smaller diameter wheels increase rolling resistance, so the user has to push harder to maintain an average speed (Medola et al. 2014). The position of the caster in the wheelchair is an important aspect of wheelchair mechanic. The shorter the distance between the rear wheel and caster, the lower the rolling resistance due to the increased weight on the rear wheels (Digiovine et al. 2006). A shorter distance between the rear wheel and caster, however, requires a shorter wheelchair length, which can affect the system stability. An important aspect is the stability of the wheelchair when the caster is turned forward, and the larger caster provides a longer wheelbase and therefore more stability. For these reasons, most tetraplegic patients choose an 8 inches (20 cm) caster. An extremely efficient caster made of molded plastic has precision bearing on both spindle and axle, and a pneumatic tire that ensures a softer ride.

Caster locks are used to lock the caster wheels to prevent them from turning (Pierson and Fairchild 2008). Caster locks on both sides can be used to ensure stability during transfer. These should always be locked in the forward position with the casters. The locking lever can be adjusted with a loop or an extension for easier handling.

46.1.16 Axle Position of the Rear Wheels

Many wheelchairs have multi-axle positions. The position of the wheel is important for efficient propulsion. The anterior–posterior position of the rear wheels influences two important aspects of wheelchair mobility: stability and manual propulsion (Medola et al. 2014). When the rear wheel is mounted forward, more weight is placed on the rear wheels and less on the front caster. This makes it easier to roll the wheelchair and often places the wheel in a more suitable position for the patient's arm thrust. When the rear wheels are moved forward, push angle and shoulder ROM are increased, thus reducing both push frequency and handrim forces and minimizing the risk of upper limb injuries (Boninger et al. 2005; McLaurin and Brubaker 1991). However, the wheelchair is less stable in this position, and the learner may require anti-tipping extensions. While positioning the wheels rearward improves stability, it limits the user's ability to reach the handrims in this rearward position, thus reducing the push angle (Medola et al. 2014).

If the rear wheels are mounted higher or lower, the tilt of the wheelchair will change. The vertical distance between the rear wheels and the seat has a major impact on the biomechanics of manual propulsion. A lower seat by shifting the axle upward benefits manual propulsion as it leads to an increased push angle. However, it leads to increased ROM of the upper extremities, which is potentially harmful if physiological limits are exceeded (van der Woude et al. 1989). On the other hand, if the user is too high above the wheels, he or she can only push the handrims over a short distance (small push angle), and in order to maintain the desired speed, the user has to increase push frequency, which leads to muscular fatigue (Boninger et al. 2000, 2005; Medola et al. 2014). The optimal seat height is determined by the elbow angle when the user holds the handrim at its top position. Elbow angles ranging from 100° to 120° are associated with improved propulsion efficiency and lower energy expenditure (van der Woude et al. 1989, 2009).

46.1.17 Camber of the Rear Wheels

The camber is the wheel angle against the vertical axis (Fig. 46.3). Camber of the rear wheels makes it easier to propel the wheelchair, increases stability, makes turning easier, tightens the turning radius, and enhances maneuverability. The disadvantages are increased overall width of the chair, increased wheelbase, increased tire wear, and lower seat height, which can increase wear of the shoulder joint (Perdios et al. 2007; Weiss et al. 2010). Camber angles are usually between 0 and 15°, mostly between 7 and 12°. Six degrees is the optimal angle for rear wheel camber in terms of lateral stability in inclined planes, comfort during handrim propulsion, maneuverability, and the general preferences of manual wheelchair users (Medola et al. 2014; Perdios et al. 2007). If the camber is extreme, the wheelchair may be too wide at the base for narrow doorways, the top of the wheel may scrape the patient's hips, and the wheels may be so close at the top that the patient's wheeling will be inefficient. Camber is not available on K0004 (high strength lightweight) chairs. Therefore, K0005 (ultralightweight) chair should be prescribed for camber of the rear wheels (Michael et al. 2020).

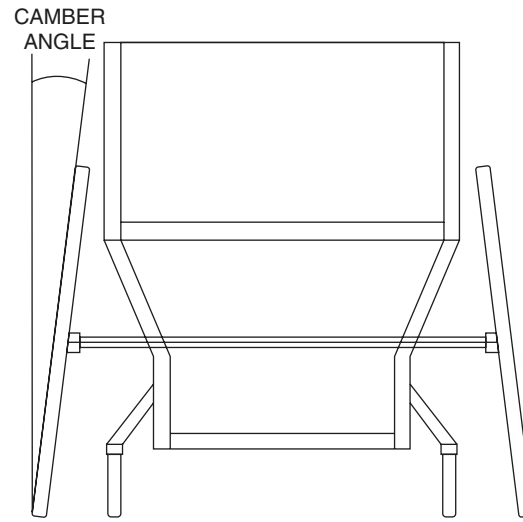

Fig. 46.3 Rear wheel camber. From Medola et al. (2014), with permission

46.1.18 Anti-Tippers

These devices prevent the wheelchair from tipping over backward. They are usually found on the back of the wheelchair near the floor. Most have tiny wheels on the ends. Anti-tippers are optional equipment on most manual wheelchairs and recliner wheelchairs. The disadvantage of anti-tippers is that they can prevent climbing over curbs or other small obstacles. Rear anti-tippers may need to be manually rotated upward if the wheelchair is tipped backward to transverse curbs (Brown and Banks 2014).

46.1.19 Handrims (Pushrims)

The handrims are attached to the outside of the rear wheels to allow safe propulsion and control without touching the tire directly, to avoid getting the hands dirty. In the majority of manual wheelchairs, the handrims are two metallic round tubes of 20 mm diameter, located on the outer side of the wheels (Medola et al. 2014). Larger diameter handrims are easier to grasp and propel, but they are heavier and cause distance to decrease with each stroke (McLaurin and Brubaker 1991). The small size of conventional handrims leads to two main problems: increased pressure on the areas of the hand surface where contact with the handrim occurs and reduced mechanical efficiency due to inability to hold the handrim with the entire hand, which requires additional muscle contraction to stabilize the hands on the handrim (Medola et al. 2014; van der Woude et al. 2003). In order to enlarge the diameter of the handrim and to increase the coefficient of friction, plastic-coated handrims are used, whereby the force necessary to propel the wheelchair can be generated more easily (DiGiovine et al. 2006).

Handrims are available with various projections (e.g., knobs, bumps, or nubs) that are intended to improve wheelchair propulsion. Handrims with projections are beneficial for patients with poor hand grip who cannot grasp a regular-sized handrim. The projections are evenly distributed around the handrim in a vertical, a horizontal, or an oblique direction, and enable patients with severe hand weakness to propel the wheelchair using their palms (Brown and Banks 2014).

46.1.20 Retainer Straps

Most injuries of wheelchair users result from tipping and fall accidents. Many of these accidents occur while climbing a curb, climbing a 45° curb, or descending a 5° ramp. Seat belts provide stability and safety to the patient, and the type of seat belt prescribed is based on the patient's preference and upper extremity strength and functional ability (Brown and Banks 2014).

46.1.20.1 Chest Strap

A chest strap may be required for safety in patients with high-level lesion, especially when starting treatment or when wearing a halo orthosis. The chest strap is attached to the frame of the chair at midchest level to increase trunk stability, prevent the user from falling out of the chair, and keep the body upright (Pierson and Fairchild 2008).

46.1.20.2 Safety Belt (Lap Belt)

A 2-inch (5 cm) safety belt can be attached to the second retainer screw up on both sides of the back between the upholstery and the back upright. It can be fastened in front with a car safety belt buckle or a Velcro D-ring fastening.

46.1.20.3 Knee Strap

Occasionally, a knee strap may be needed to restrain patients with gross extensor spasms who can slide under a waist safety strap. A strap passing across the shins, just below the knees, is attached to the front uprights of the wheelchair.

46.1.20.4 Ankle Strap

If extensor spasms only occur in the legs, the strap can be attached to the frame of the legrests. Skin checks must be made regularly and the strap may need to be padded.

46.1.20.5 Toe Loops

Toe loops are rarely necessary and can lead to leg injuries in a fall. They can also be inconvenient for an independent person. The toe loop is being used in conjunction with a modified shoe to help to correct a deformity or extreme inversion of the foot.

46.1.21 Wheelchair Cushions

Wheelchair cushions are designed for comfort; some also improve pressure distribution and prevent pressure injuries or improve pelvic stability. The type of cushion prescribed for wheelchair users should be based on the individual patient's needs, a combination of clinical knowledge, pressure mapping, history of skin tolerance, history of pressure injuries, and other individual characteristics (Consortium for Spinal Cord Medicine 2014). Factors to consider in a cushion evaluation include pressure redistribution and shear reduction qualities, comfort, postural support, level of functional activity, ADL performance, heat reducing properties (Knox et al. 1994), adaptability, cost, care, and maintenance needs (Consortium for Spinal Cord Medicine 2014). Wheelchair-bound patients who are unable to transfer and stand independently need a more complex seat cushion that prevents pressure injuries and provides truncal and pelvic stability. The use of donut-shaped ring cushions should be avoided, as with bed supports.

The wheelchair cushions were mainly developed for pressure management in the ischial tuberosity (Metring et al. 2012). By using the non-postural muscles to compensate for the functional loss of the spine erector muscles and the different location of the center of gravity, the posture of people with spinal cord injuries usually changes (Aissaoui et al. 2001). Although various wheelchair cushions such as gel, foam, and egg crate seat cushion are used, they are not very helpful in changing static sitting posture to prevent or correct these expected postural abnormalities in patients with spinal cord injuries (Metring et al. 2012).

There are many types of cushions on the market today. No cushion is suitable for every patient. There are two basic types of seating systems for wheelchairs: linear systems and contoured systems (Gilsdorf et al. 1991). Linear seating systems are planar in that the seat and back surfaces are flat and only conform to the weight of the user. Contour measurements for custom contoured cushions can be made using vacuum-forming or seating contour measurement systems. Custom contoured seat cushions were developed to completely relieve pressure on bony areas with redistribution at another area (Consortium for Spinal Cord Medicine 2014). For many wheelchair users, a simple linear seating system or a standard contour is very effective (Gilsdorf et al. 1990). Foam, viscoelastic fluid, dry floatation (air) cushions, gel, and honeycomb (thermoplastic cellular matrix) are the most common cushion materials (Ferguson-Pell et al. 1986). Various densities and types (e.g., polyurethane, urethane, latex, T-Foam, Sun-Mate) of foam are commonly used in linear seating systems. The densities are divided into extra-high, high, medium, and low. As the density increases, the cushion becomes firmer. Patients with very prominent ischial tuberosities need a higher density foam cushion for support. Due to different needs, polyurethane foam is preferred because it can be easily modified for each patient. A laminated cushion is available for sufficient stability and comfort. It is made of 1 inch high-density polyurethane foam on an extra high-density polyurethane foam cushion. The thickness of cushions is from 2 inches to 5 inches. The cushion should be as thin as possible while providing safe sitting pressure. The usual thickness is 3 or 4 inches. Cushion use reduces the maximum subcutaneous stress below the ischial tuberosity. However, increasing the cushion thickness beyond 3 inches (8 cm) is ineffective in further reducing subcutaneous stress (Ragan et al. 2002).

46.1.21.1 Cushion Selection

In the selection of cushion, pressure distribution, corrective or accommodative postural support, weight, durability, air flow, temperature regulation, different builds, different types of skin,

allergies, perspiration problems, flaccidity or spasticity, and different degrees of independence must be considered (Krey and Calhoun 2004; Michael et al. 2020). Patients who are careful with their skin inspection, skin care, weight shifts, and nutrition will have fewer skin problems. Sitting-acquired pressure injuries mainly occur over the ischial tuberosity resulting from the effects of the pelvic position on the displacement of the ischium (Hobson and Tooms 1992; Pompeo and Baxter 2000).

A wheelchair cushion is usually a compromise between several different needs. The patient learning independent transfers requires a firm cushion with a low friction surface. A person who sits for a long time requires a cushion which is soft or molded so that the patient's weight is evenly distributed on any portion of the cushion, thereby allowing good circulation. However, it can be difficult for the patient to maintain balance on the softer cushion, especially on air- or water-filled cushions. Moisture absorption is another important consideration in cushion selection for the incontinent patient or for the patient who perspires excessively. Ideally moisture should pass through the cushion without being absorbed, like a closed-cell foam or an ROHO cushion. If incontinence is a major problem, a cushion with a water barrier covering may be required. A material such as ensolite, which has a fatty texture, or a waterproof cloth that can breathe, such as "Gore-Tex," will protect the cushion. A foam rubber cushion needs protection as washing destroys the chemicals and the cushion loses density.

If the patient perspires excessively, the cushion and cover materials should allow air circulation. ROHO cushions and egg-crate type cushions meet this requirement: the egg-crate type cushions have to be replaced frequently as the convolutions flatten and their effectiveness is lost. Some types of cushions are very suitable for cold climate. Cushions like foam rubber or ensolite can be excellent in a cold climate, whereas air-filled neoprene rubber cushions such as ROHO can be too cold unless other insulation such as sheepskin is added. The foam becomes hard and brittle in cold climate and "flows" in a hot climate.

The weight of the cushion is important for the independent person who must lift the cushion as in car transfers. Water or gel-type cushions are generally heavy. A 3 inches (8 cm) thick extra firm density foam rubber cushion is well tolerated by most patients and is certainly the easiest to use for learning to transfer. Thinner cushions may not provide adequate protection for the skin.

46.1.21.2 Pressure Relief

A variety of interventions have been recommended for the prevention of sitting-induced pressure injuries in people with spinal cord injuries, including pressure redistribution cushions, pressure-relieving activities such as push-ups and leaning forward, and wheelchair tilt-in-space and recline (Consortium for Spinal Cord Medicine 2014). The tilt-in-space and recline of the wheelchair are particularly suitable for people with tetraplegia who cannot perform pressure-relieving activities on their own (Dicianno et al. 2009). Cushions can be customized by layering different types of foam or by placing different types of foam under bony areas. Gel-filled cushions range from basic cushions to individually modified seat cushions for patients with high risk for skin breakdown (Brown and Banks 2014). Foam cushions can be adapted by plucking or carving out pressure relief areas. Areas of excessive pressure can be located by feeling the pressure area between the buttocks and the cushion with a flat hand, or pressure sensors can be used. Since it is difficult to place a patient in exactly the same place each time when the patient is transferred or moved, any pressure relief cutouts must be made large enough to accommodate this.

46.1.21.3 Wedge Cushions

Patients who need moderate positioning assistance can benefit from an air cushion with multiple air cells. This type of cushion can be used with or without a contoured silicone foam base, which additionally provides lateral and preischial contoured support (Brown and Banks 2014). Application of additional cushions such as abduc-

tion wedges or other wedge cushions may be required for posturing or balance, but these may interfere with transfers. The wedge cushion, which is higher at the front than at the back, may be necessary to prevent the patient from sliding forward, or it may help to prevent extensor spasticity. The footrests must be raised to accommodate the increased height of the wedge. Knee abduction wedges can be useful to reduce adduction and extensor spasticity. An abduction wedge can be useful for the flaccid patient to position their legs to help prevent foot deformities, to avoid knee pressure areas, and to relieve pressure on the genitals or urinary system. A person with scoliosis may require a laterally wedged cushion in conjunction with lateral supports. It is very difficult to attempt to correct or accommodate scoliosis while maintaining normal pressure over the ischial tuberosity. Often a compromise must be made and carefully monitored to maintain comfort, function, pressure relief, and position (Pierson and Fairchild 2008).

46.1.21.4 Cushion Cover

Some cushions may be used without a cover to allow direct skin contact. This is sometimes desirable when treating pressure areas. A cover will be required for general use. Cushion covers should not be substituted by pillowcases, towels, plastic bags, or other cover surfaces (Consortium for Spinal Cord Medicine 2014). A light soft canvas cover is often used because it has been washed and is good for absorption of perspiration. A nylon taffeta cover over the canvas cover will facilitate sliding. The direction of weave of the material can affect sliding. It is possible to select the smooth direction of the material by passing a thumbnail across the material in two directions and listening for the softer sound. This will be the smooth direction that should be from side to side for easier sideways transfer. A two-way stretch material makes a most desirable cushion cover because it does not exert a shear force on the skin. However, this type of material is not as easy to move on as nylon taffeta. "Gore-Tex" is a breathable and waterproof material that can be stretched in two directions and fairly slippery.

46.1.22 Wheelchair Accessories

46.1.22.1 Wheelchair Bags

Most patients will find a back hanging from the push handles very useful, especially when wheelchair arms are not used. The bag must be hung low for the patient to access it.

46.1.22.2 Lapboards

A lapboard is useful for most tetraplegics. The advantages of the tray are simple attachment, stability, and appearance. Lapboards provide increased work surface for activities. A transparent plastic tray allows patients to check their foot position and their clothing.

46.1.23 Brakes

Brakes are essential for stability during transfers and many other activities, such as working at the table or eating. A brake extension provides more leverage but requires a larger range of motion of the upper extremities. The types of wheel brakes prescribed for a patient are determined by upper extremity strength, hand grip, and functional dexterity (Brown and Banks 2014).

46.1.23.1 Applying Brakes

Pushing forward (toggle lock) is the preferred movement to apply locking brakes because it is easier to maintain balance. The lock should be engaged before any transfer to stabilize the chair and to add patient safety (Pierson and Fairchild 2008). In tetraplegic patients, the motion to apply and release the brakes of manual wheelchair is modified in various ways depending on the neurological level of injury. To maintain balance, some patients apply a brake with one hand using the other arm as a counterbalance. A patient can hook one elbow over the push handle and use it as an anchor point to develop more momentum to push against the brake. The hand position is determined by the degree of external rotation required and the presence or absence of wrist extensors. The brakes can be operated with the wrist extension and/or shoulder external rotation. The palm of the hand or the fingers push against

the brake when elbow flexion and shoulder external rotation are used for braking.

46.1.23.2 Releasing Brakes

Releasing brakes use the same methods of maintaining balance as the brakes are applied, except that pulling action makes it more difficult to maintain balance. The brakes can be released simultaneously, usually using adduction and internal rotation of the shoulders. The brakes can also be released by a chopping action by hitting the brake handle with the side of the hand.

46.2 Propelling Manual Wheelchair

Patients must be properly positioned in the wheelchair before they are ready to learn the techniques of propelling the wheelchair. Manual wheelchair users should propel with long smooth strokes that maximize the stroke length or contact angle (Consortium for Spinal Cord Medicine 2005). The wheelchair user should try to impact the handrim smoothly and adjust the speed of the hand to the rotating speed of the handrim. During the recovery phase of the propulsive stroke, the user should let the hand drop below the handrim and remain below the handrim until they are ready to start propulsion again (Boninger et al. 2002). As the patient gradually becomes familiar with the propelling and basic movements of the manual wheelchair, wheelchair mobility skills become important in daily life. In order to function independently, manual wheelchair users must have various wheelchair skills to be able to deal with the physical barriers they encounter in various environments in daily life (Fliess-Douer et al. 2010; Webster et al. 1989). Manual wheelchair skills of people with spinal cord injuries are positively associated with activities and participation (Kilkens et al. 2005).

46.2.1 Wheeling Forward

The patient places the palms of both hands as far back as possible on the handrims to propel wheelchair forward. Activity in the push phase begins in late recovery and ends in early to late push (Mulroy et al. 2004). There are two functional synergies of muscle activity in forward propelling: push (anterior deltoid, pectoralis major, supraspinatus, infraspinatus, serratus anterior, biceps) and recovery (middle and posterior deltoid, supraspinatus, subscapularis, middle trapezius, triceps) (Mulroy et al. 2004). The shoulders are internally rotated and the elbow slightly flexed initially. A pushing action is developed through adduction and external rotation of the shoulders. The upper trunk is extended to maintain balance as the hands move forward. Patients try to move their hands just a short distance until they learn to synchronize these movements. With practice, more speed and balance are developed. In some cases, a patient may not be able to maintain balance in the chair while wheeling and may not tolerate a safety belt across the chest. In such cases, they can wheel while placing one or both arms behind the push handles. However, this limits their shoulder flexion and causes them to lose a significant amount of their propelling power.

46.2.2 Wheeling Backward

The patients using handrims will propel the wheelchair backward by placing their hands as far forward as they can reach, with elbows slightly flexed. With the back resting against the back of the wheelchair, they adduct and internally rotate their shoulders while they are elevated and retract their shoulder girdles. This creates a pulling motion that does not cause them to fall forward. Some patients using this technique also extend the upper trunk for additional pull and maintaining balance. The patient who is unable to maintain balance when wheeling backward must place one or both arms over the back of the wheelchair.

46.2.3 Hand Adaptations

46.2.3.1 Covered Handrims

If the patient's hands slip on the handrims, the handrims can be taped temporarily. Plastic-covered rims or rubber-covered rims are commercially available.

46.2.3.2 Pusher Mitts

The patient who does not obtain sufficient support on the handrims can push directly on pneumatic tires. In this case, the patient will likely need pusher mitts to protect the hands and increase friction. A plastic spoke guard may also be used so that the fingers do not get caught in the spokes. A well-maintained spoked wheel is lighter and easier to propel, but a molded plastic wheel is easier to maintain and less likely to catch the fingers.

46.2.3.3 Wide Spacers

The patient who cannot gain friction on the tire or handrim may push on wide spacer. The patients place their thumbs on the handrims with their thumbs against the spacer. It is possible to propel the chair using this method even though the shoulder adductors are weak. To customize this wheelchair, replace the four 3/4-inch (1.91 cm) spacers with eight 1½-inch (3.8 cm) spacers.

46.2.3.4 Vertical Extensions

If the patient cannot position the hand to utilize spacers, vertical extensors can be added. Eight to twelve extensions will be necessary. Horizontal extensions are not recommended as they are hazardous and will widen the wheelchair. Angled or oblique extensions also widen the wheelchair but may be necessary for some patients.

46.2.3.5 Pushing Splints

A molded splint, extending from behind the metacarpophalangeal joints to the mid-forearm, will stabilize a weak wrist. Pushing hooks, appropriately positioned and bent for each patient, can be attached to the molded splint. The patient can push against spacers, wide spacers, or vertical extensions of the handrims.

46.2.3.6 Grade Aids

Many tetraplegic patients need grade aids to allow them to push up a hill. The grade aids hold the chair still until the hands can be repositioned. They can also be useful for a helper when pushing a chair up a steep slope.

46.3 Weight Relief Methods in the Wheelchair

A seated person who has anesthesia of the buttocks must have pressure relief, especially from the bony areas, the ischial tuberosities, and the sacrum area. In early rehabilitation, weight relief is carried out at least every 25 or 30 min, but individual tolerance can be assessed and increased through frequent skin inspections. The skin condition, patient weight, and type of seating required vary widely and tolerance must be carefully adjusted. The following methods of relieving weight in the wheelchair are available.

46.3.1 Pushing Up

Pushing on the wheelchairs is the most effective method of relieving weight from the buttock.

46.3.2 Leaning Forward

The person can lean forward and rest their trunk on their knees or on a table surface to relieve weight from the buttock.

46.3.3 Leaning Sideways

The person can lean the trunk sideways on the armrest of the wheelchair to relieve the weight, leaning first to one side and then to the other.

46.3.4 Leaning Backward

The person can relieve the weight by leaning back on the chair back. The chair can be tipped backward to relieve the weight of the patient's buttocks. This position may also be very useful for the patient with dizziness (postural hypotension). If the person needs to be reclined for longer periods, the chair can be tipped back and the push handles rest on a bed.

46.4 Electrically Powered Wheelchair and Option Selection

A patient who can propel a manual wheelchair can use a power wheelchair as a second wheelchair to cover the distances for shopping, school, and social activities. It should be noted that it is very difficult to climb stairs or sidewalks with a power wheelchair, usually not easy to transport in a family car, and the family may need to purchase a van with a lift. Many tetraplegic patients who use a power wheelchair as their primary wheelchair may still need a manual wheelchair for greater mobility on outings where architectural barriers are likely to be encountered and also because they may perform the exercise from wheeling. Various controls (access devices or interface) are available to operate the chair, including those operated by the patient's hand, chin, head, tongue, or mouth (Pierson and Fairchild 2008). Power wheelchairs are divided into groups according to performance requirements (Table 46.1). The groups most commonly prescribed for people with spinal cord injuries are Groups 2, 3, and 4 (Michael et al. 2020). If an electrically powered tilt-in-space or recline position is available, the position at 35° tilt-in-space and 120° recline should be used and the tilted and reclined position should last 3 min rather than the clinically recommended 30 s every 30 min (Consortium for Spinal Cord Medicine 2014) for effective skin perfusion to minimize ischemia of the weight-bearing soft tissues (Jan et al. 2013). Ischial pressure decreases in response to increasing the tilt-in-space and recline, but coccygeal pressure increases (Chen et al. 2014).

Table 46.1 Classification of power wheelchairs

	Group 2 (standard plus use)	Group 3 (general use)	Group 4 (high activity use)
Performance requirements			
Minimum range	7 miles	12 miles	16 miles
Minimum obstacle climb	40 mm	60 mm	75 mm
Dynamic stability incline	6°	7.5°	9°
Health and mobility components			
Drive wheel suspension	Not available	Available	Available
Number of power seating functions accommodated	Generally one	3 or more	3 or more

From Michael et al. (2020), with permission

Power assist wheelchairs (e.g., pushrim-activated power-assisted wheelchair) are manual wheelchairs with motors that supplement the user's push that are classified as hybrid wheelchairs (Algood et al. 2004). These motors are either embedded in the rear wheels or attached to the rear axle via a quick release module. They are suitable when a person cannot functionally propel a manual wheelchair but needs the compactness, maneuverability, and portability of a manual wheelchair. It has been shown that the use of the pushrim-activated power-assisted wheelchair reduces energy consumption by 17–43% during 3-minute propulsion bouts (Algood et al. 2004; Haubert et al. 2005). Power assist wheelchairs cannot be equipped with power-adjustable seat functions including tilt-in-space and recline (Michael et al. 2020).

46.4.1 Joystick Control

Joystick control is the most common access device for power wheelchair systems. The normal method to control an electrically powered wheelchair is to use a small joystick that can be attached to the right or left chair armrest. Various adaptations can be used to effectively control the joystick control. A thicker or longer removable plastic, wood, or metal dowel can be added. The joystick can be customized with a T-bar or a J-shaped handle.

46.4.2 Alternate Controls

Some people unable to control the joystick may need alternative wheelchair control mechanisms using a different body part, including chin con-

trol, head control, sip and puff, speech control, tongue control, mouthpiece, myoelectric, or a custom-designed device (Brown and Banks 2014). All of these controls are interfaces with microswitches, with the exception of the head and chin controls, which are themselves direct proportional controls and therefore do not require an interface. When proportional controls can be used, they provide finer maneuverability of the wheelchair. However, head control cannot be used with a recliner wheelchair because a headrest is required in the recliner position. Head, breath, and chin controls require exact positioning of the patient, especially at the beginning of learning.

46.4.2.1 Head Control

Head control is base mounted in the headrest, which is activated by moving the head to control maneuvering of the wheelchair. This steering mechanism requires good head control. The patient who does not need a recliner wheelchair may find the head control very acceptable. All proportional controls require on/off switches, which are usually controlled with a shoulder shrug to operate a lever arm. Alternatively, this switch can be positioned so that it can be operated by pressing the lever with the cheek.

46.4.2.2 Sip and Puff Control

The wheelchair is controlled by a sequence of pulling and pushing air through the straw with the mouth. The patient must be able to move her head enough to reach forward for the tube when using a sip and puff interface. The user controls the movement of the power wheelchair by sipping (inhaling) or puffing (exhaling) into a pneumatic tube. When sipping, a negative pressure is created on the tube, and puffing results in a positive pressure. Generally, the user will sip a certain number of times to indicate a direction and puffs to confirm the choice and activate the movement of the wheelchair.

46.5 Wheelchair Selection Based on Neurological Level of the Spinal Cord Injury

The selection of the power or manual wheelchair and the accessories and conditions required for each wheelchair should be considered based on the patient's neurological level of injury and conditions such as muscle strength and spasticity. In general, people with spinal cord injury at C6 or below do not need or want a power wheelchair. The standard of care for a manual wheelchair for people with low-level spinal cord injuries is a lightweight customized wheelchair. However, young, active paraplegic people with low-level spinal cord injuries and good trunk stability often prefer a sports-type wheelchair for mobility due to its sporty and ease of maneuverability (Brown and Banks 2014). A summary of wheelchair requirements for different levels can be found in Tables 46.2 and 46.3.

46.5.1 C1-C2-C3

Patients with complete lesions are dependent on full-time ventilatory support because of complete paralysis of the primary respiratory muscles. A power wheelchair with tongue control and an underslung tray for both ventilator and batteries can give the person some mobility and independence. This wheelchair must be custom-made and have a fully powered recliner. The frame of the wheelchair must be a non-folding reclining type with no crossbars. This means that the tray under the seat can accommodate the ventilator with its accessory battery and charger as well as two batteries for the motors to operate the wheelchair.

Due to skin problems over the ischial tuberosities, a power reclining back is indicated, which can be operated on several times per hour by the patient or attendant in order to relieve pressure over these areas. All persons with spinal cord

Table 46.2 Power wheelchair for people with spinal cord injuries

	C1, 2, 3	C4	C5	C6	C7 and below
Frame					
Non-folding with tray for ventilator	✓	*			
Folding		✓	✓	✓	NA
Power reclining	✓	✓	*		
Upright			✓	✓	
Controls					
Lip/Tongue	✓				
Chin with power swing away		✓			
Hand			✓	✓	
Power recliner	✓	✓			
Emergency call	✓	*			
Casters					
1¾ semipneumatic caster wheel	✓	✓	✓	✓	
Shock absorbing suspension fork	✓	✓	✓	✓	
Large wheel					
2-inch pneumatic tire with zero-pressure tubes	✓	✓	✓	✓	
Foot supports					
Elevating legrests	✓	✓			
Elevating legrests (linkage to power recliner back)	*	*			
Standard footrest			✓	✓	
Heel loops (standard footrest only)			*	*	
H-strap (for severe spasticity)			*	*	
Arm supports					
Troughs attached to back	✓	*			
Desk armrest, adjustable			✓	✓	
Full-length armrest, adjustable	✓	✓			

✓ = for most patients, * = for some patients

Table 46.3 Manual wheelchairs for people with spinal cord injuries

	C1-3	C4	C5	C6	C7, C8	T1-8	T9-12	L1-2	L3-5
Frame									
Recliner	✓	✓	*						
Upright			✓	✓	✓	✓	✓	✓	✓
Weight									
Standard	✓	✓				✓	✓	✓	✓
Lightweight stainless			✓	✓	✓	*	*	*	*
Arm supports									
Full length	✓	✓				✓	✓	✓	✓
Desk length			✓	✓	✓	✓	✓	✓	✓
Adjustable	✓	✓	✓	✓	✓				
Nonadjustable						✓	✓	✓	✓

Table 46.3 (continued)

	C1-3	C4	C5	C6	C7, C8	T1-8	T9-12	L1-2	L3-5
Foot supports									
Elevating legrests	✓	✓							
Standard footrest	*	*	✓	✓	✓	✓	✓	✓	✓
Heel loops			✓	✓	✓	✓	✓	✓	✓
H-strap (for severe spasticity)			*	*	*	*	*		
Handrims									
12 vertical projections			*						
8 vertical projections			✓	*					
Friction				✓	*				
Standard					✓	✓	✓	✓	✓
Locks									
Caster locks			✓	✓	✓	*			
Hill holders			*	*					
Brake extensions									
Tires									
Hard rubber	✓	✓							
Pneumatic tires with zero-pressure tubes			✓	✓	✓	✓	✓	✓	✓

✓ = for most patients; * = for some patients

injuries of C4 and above should have a power recliner wheelchair (Yasukawa et al. 1994). Most models can be tilted from −5° to 50°. However, some tilt-in-space wheelchairs can be tilted up to 120°. Tilting and reclining increase the seating surface area over the buttocks and back, which prevents pressure injuries (Brown and Banks 2014). The standard back height of the reclining wheelchair is 24 inches, and the necessary head extension is 10 inches high. The seat cushion should be a 4 inches thick laminated foam made up of 1 inch high-density foam and 3 inches extra-high-density foam. The back cushion should be 1½ inches thick and extend at least up to the scapular spine. The wheels should be of the "mag" type (no wire spokes) with pneumatic tires to absorb shocks over bumps such as doorways and side-walk cracks. The tires must be of the puncture-proof type to prevent flats. The casters should be the 1¾ inches wide semi-pneumatic type, which are puncture proof and yet absorb shocks. The casters are 8 inches in diameter.

The armrests should be removable, should be height-adjustable, and should be full length, not desk-type, to better support lapboards. The arm troughs or the lapboard should be attached to the back frame of the wheelchair with a swivel joint so that they will follow the patient back as the wheelchair reclines. In general, elevating legrests are placed to control lower extremity edema. An H-strap is required to keep the feet on the footrests. Occasionally, toe straps are required to keep the foot on the footrests in patients with excessive quadriceps spasticity. Two seat belts with Velcro closures are required. One should be placed at the chest and the other at the pelvis.

Since the patient has no head control or upper extremity function at this level, the power wheelchair must be controlled with the chin, lips, or tongue. This can be done with a sip-puff control. Proportional control using the chin, lips, or tongue except sip-puff control is preferred, which provides smooth acceleration and any selected speed within the speed range.

46.5.2 C4

Most patients at this level do not need a ventilator. A standard folding reclining wheelchair

frame cannot be used. With the exception of the controls and frame, the wheelchair is the same as that described for C1–3. The control for this level of injury is a chin or head control since the neck muscles are now innervated. The chin control can be attached to a manual swing away or a power arm attached to the upright of the wheelchair back. The power control for the swing away arm can be operated by the innervated shoulder elevator or by lateral bending of the head.

46.5.3 C5

Ability of the patient with C5 neurological level of injury to relieve ischial pressure should be assessed. In general, a patient with F+ motor strength of the biceps or normal elbow proprioception can perform an independent forward raise using loops attached to the wheelchair backrest uprights. The wheelchair can be manual or power, depending on both the patient's ability to propel the manual wheelchair and their jobs. When a power wheelchair is ordered, it should have a standard upright frame, removable adjustable desk armrests, and a standard swing away footrest with heel loops or H-strap. The H-strap should be used when hamstring spasticity is so severe that the feet ride over the heel loops. Then the heel loops should be removed.

The back height should be as low as possible, but high enough to support the patient's back. The most common back height is 18 inches (46 cm), but if the spine is overstretched or if the patient is unusually tall, then the height can be up to 22 inches (56 cm). The patient will usually not need a back cushion. However, if there is a tendency for excessive pressure on the sacrum, a sacral back pad 1½ inches thick should be ordered. The width of the back cushion should be 2 inches narrower than the width of the chair so that it fits between the metal uprights.

To help the patient to use the hand control, a modification of the joystick can be made by fabricating a yoke to support the patient's wrist due to the weakness of the wrist muscles. If a manual wheelchair is ordered, it must also be an upright frame with the same accessories as the power wheelchair. The handrails should have 8 to 12 peg projections. These projections should always be vertical when ordering and then bend outward according to the patient's needs. The pegs often bend approximately 20–30 degrees outward as the patient begins to learn to propel the wheelchair. Later, as the patient's function increases, the pegs can be bent to a more vertical position. Caster locks can be ordered to assist the family if they plan to perform dependent sliding board transfers with the patient.

Another important aspect of this level of injury is the weight of the manual wheelchair. A lightweight wheelchair should be ordered if the manual wheelchair is the primary one that will be used. If the manual wheelchair is a backup of the power wheelchair, an inexpensive model can be purchased regardless of weight.

46.5.4 C6–C7

Most patients at this level do not need a power wheelchair for mobility. They can easily propel a manual wheelchair. People with spinal cord injury at C6 and below are most functional in a lightweight manual wheelchair unless they have other limiting factors such as age, obesity, upper extremity contractures, asymmetrical upper extremity muscle functions, arthritis, or pulmonary and cardiovascular diseases (Yasukawa et al. 1994). If the patient is attending school or has to travel long distances for work, their energy level may not allow them to propel a manual wheelchair over those distances and a power wheelchair can be needed. The power wheelchair should be a standard upright with a standard joystick proportional control. The patient should be equipped with a lightweight wheelchair with an upright frame. The lightweight wheelchair makes it easier for patients with tetraplegia to propel and allows them the opportunity to lift the wheelchair into the car independently (Kreutz 2002).

The height of the wheelchair backrest must be high enough to allow adequate stabilization of the trunk. Ideally, the height of the wheelchair

backrest should be at least 1 inch below the inferior angle of the scapulae. It is not uncommon for the back height to be 3–4 inches below the inferior angle of the scapulae. This allows maximum mobility of the scapulae when propelling the wheelchair and allows easy access to the push handles. Patients at this level use the push handles to readjust to the body in the wheelchair, readjust the legs for foot positioning on the footrest, and relieve sitting pressures. Patients at this level generally prefer friction handrails over projection handrails. The friction handrails are necessary because the patient does not have a strong grasp power.

The wheelchair must have swivel locks on the casters to stabilize the wheelchair during a lateral transfer. The footrest should be swing away and non-elevating. The footrests should have either heel loops or an H-strap. The H-strap is indicated for severe hip and knee flexion spasticity, as the feet can climb over the heel loops. The armrest must be removable and adjustable desk arms so that the patient can get closer to tables and desks. Pneumatic tires with puncture-proof inner tubes are recommended.

46.5.5 C8 and Below

A standard upright wheelchair is provided to patients with a neurological level of injury of C8 and below. However, individual needs can be very important. A lightweight wheelchair is recommended for most female and elderly patients. Most of these patients or their families will find it easier to get the wheelchair in and out of the car and with 10 pounds (4.5 kg) less weight. The standard back height is usually adequate (Kreutz 2002). However, this may not apply to the very tall or the very short person. It is important to maintain trunk balance and should have scapulae mobility.

Ideally, wrap-around armrests should be ordered if possible. This feature reduces the overall wheelchair width by approximately 1 inch, while only decreasing the internal seat width between the trochanters by 3/8 inch or less, although the seat upholstery width remains the same. This allows easier clearance through doorways. Standard non-adjustable armrests are routinely ordered. Most of these patients have good trunk balance and choose not to use the armrest. Footrests are standard swing away with either heel loops or H-strap. It is important to recognize that the heel loops are for the person who has little or no spasticity. The H-strap is for the patients with spasticity who will pull their feet over the heel loops. For persons with quadriceps and knee proprioception, nothing may be required.

The 1¼-inch pneumatic tire with the puncture-proof zero-pressure tube is recommended. The standard tube pneumatic tire is not recommended due to maintenance problems such as flat tires. However, the pneumatic tire is preferred by patients who participate in athletics. They prefer pneumatic tires because they have better control of the wheelchair during sports activities. Wheelchair accessories such as caster locks and hill holders are not recommended for these patients.

46.5.6 Sports Wheelchairs for Low-Level Spinal Cord Injuries

Active and young paraplegic patients with good trunk stability often prefer a sports wheelchair for reasons of sporty styling, mobility, and better maneuverability. A sports wheelchair has easy turning, higher speed, and lower rolling resistance than a standard wheelchair. The rear wheels have cambers that allows the wheels to be tilted by up to 16°. The tilted wheels increase the base width of the wheelchair and allow for higher speed and faster turns (Brown and Banks 2014). A manual sports wheelchair is made of lightweight titanium or carbon fibers, and the type of the wheelchair depends on the functional status of the patient and the type of sport being played such as tennis, cycling, basketball, and recreational activities.

The wheels are variable depending on the sport: two large rear wheels (22–27 inches,

Fig. 46.4 Manual sports wheelchair tire type. (**a**) clincher tire, (**b**) slick pneumatic tire, and (**c**) Kavlar tire

56–68 cm) and one or two small casters (3 inches, 7.6 cm) for basketball or tennis and two large rear wheels (28 inches, 71 cm) and one smaller caster (20 inches, 51 cm) for cycling. The choice of the tire type of sports wheelchair depends on speed, maneuverability, and endurance. Clincher is high performance for basketball, tennis, and cycling. It is designed with inserts that prevent the pneumatic tire from becoming completely flat after a flat tire. Slick pneumatic tires are designed for high speeds. A Kevlar tire made of material used for bulletproof vest is high performance and ideal for sports (Fig. 46.4). Sports wheelchairs usually do not have armrests as they increase the weight of the wheelchair, decrease freedom of motion, and reduce maneuverability. Armrests also interfere with wheelchair propulsion over long distances (Brown and Banks 2014).

46.5.7 Standing Wheelchairs

Standing wheelchairs lift a person from a sitting position to a standing position. The standing wheelchair supports the legs and trunk and enables the patient to stand. The benefits of standing include improved circulation, improved urinary and bowel function, and increased bone density (Brown and Banks 2014). A standing wheelchair can be manual or motorized.

References

Aissaoui R, Boucher C, Bourbonnais D, et al. Effect of seat cushion on dynamic stability in sitting during a reaching task in wheelchair users with paraplegia. Arch Phys Med Rehabil. 2001;82:274–81.

Algood SD, Cooper RA, Fitzgerald SG, et al. Impact of a pushrim-activated power-assisted wheelchair on the metabolic demands, stroke frequency, and range of motion among subjects with tetraplegia. Arch Phys Med Rehabil. 2004;85:1865–71.

Boninger ML, Baldwin M, Cooper RA, et al. Manual wheelchair pushrim biomechanics and axle position. Arch Phys Med Rehabil. 2000;81:608–13.

Boninger ML, Koontz AM, Sisto SA, et al. Pushrim biomechanics and injury prevention in spinal cord injury: recommendations based on CULP-SCI investigations. J Rehabil Res Dev. 2005;42(3 Suppl 1):9–19.

Boninger ML, Souza AL, Cooper RA, et al. Propulsion patterns and pushrim biomechanics in manual wheelchair propulsion. Arch Phys Med Rehabil. 2002;83:718–23.

Brown A, Banks K. Wheelchairs and assistive devices. In: Maitin IB, editor. Current diagnosis and treatment physical medicine and rehabilitation. 1st ed. New York: McGraw-Hill Education; 2014.

Chen Y, Wang J, Lung CW, et al. Effect of tilt and recline on ischial and coccygeal interface pressures in people with spinal cord injury. Am J Phys Med Rehabil. 2014;93:1019–30.

Cherubini M, Melchiorri G. Descriptive study about congruence in wheelchair prescription. Eur J Phys Rehabil Med. 2012;48:217–22.

Consortium for Spinal Cord Medicine. Preservation of upper limb function following spinal cord injuries: a clinical practice guideline for health-care profession-

als. Washington DC: Paralyzed Veterans of America; 2005.

Consortium for Spinal Cord Medicine. Pressure ulcer prevention and treatment following spinal cord injury: a clinical practice guideline for health-care professionals. 2nd ed. Washington DC: Paralyzed Veterans of America; 2014.

Cooper RA, Cooper R, Boninger ML, et al. Wheelchairs and seating for people with spinal cord injuries. In: Lin VW, editor. Spinal cord medicine. Principle and practice. 2nd ed. New York: Demosmedical; 2010.

Cooper RA, Cooper R, Tolerico M, et al. Advances in electric-powered wheelchairs. Top Spinal Cord Injury Rehabil. 2006;11:15–29.

Cooper RA, Rentschler AJ, O'Connor TJ, et al. Wheelchair armrest strength testing. Assist Technol. 2000;12:106–15.

Dicianno BE, Arva J, Lieberman JM, et al. RESNA position on the application of tilt, recline, and elevating legrests for wheelchairs. Assist Technol 2009;21:13–22; quiz 24.

DiGiovine CP, Koontz AM, Boninger ML. Advances in manual wheelchair technology. Top Spinal Cord Inj Rehabil. 2006;11:1–14.

Ferguson-Pell M, Cochran GV, Palmieri VR, et al. Development of a modular wheelchair cushion for spinal cord injured persons. J Rehabil Res Dev. 1986;23:63–76.

Flemmer CL, Flemmer RC. A review of manual wheelchairs. Disabil Rehabil Assist Technol. 2016;11:177–87.

Fliess-Douer O, Vanlandewijck YC, Lubel Manor G, et al. A systematic review of wheelchair skills tests for manual wheelchair users with a spinal cord injury: towards a standardized outcome measure. Clin Rehabil. 2010;24:867–86.

Ford JR, Duckworth B. Physical management for the quadriplegic patient. 2nd ed. Philadelphia: F.A. Davis Company; 1987.

Gebrosky B, Pearlman J, Cooper R. Comparison of high-strength aluminum ultralight wheelchairs using ANSI/RESNA testing standards. Top Spinal Cord Injury Rehabil. 2018;24:63–77.

Gilsdorf P, Patterson R, Fisher S. Thirty-minute continuous sitting force measurements with different support surfaces in the spinal cord injured and able-bodied. J Rehabil Res Dev. 1991;28:33–8.

Gilsdorf P, Patterson R, Fisher S, et al. Sitting forces and wheelchair mechanics. J Rehabil Res Dev. 1990;27:239–46.

Haubert L, Requejo P, Newsam C, et al. Comparison of energy expenditure and propulsion characteristics in a standard and three pushrim-activated power-assisted wheelchairs. Top Spinal Cord Inj Rehabil. 2005;11:64–73.

Hobson DA, Tooms RE. Seated lumbar/pelvic alignment. A comparison between spinal cord-injured and noninjured groups. Spine (Phila Pa 1976) 1992). 17;293–298.

Hughes B, Sawatzky BJ, Hol AT. A comparison of Spinergy versus standard steel-spoke wheelchair wheels. Arch Phys Med Rehabil. 2005;86:596–601.

Jan YK, Liao F, Jones MA, et al. Effect of durations of wheelchair tilt-in-space and recline on skin perfusion over the ischial tuberosity in people with spinal cord injury. Arch Phys Med Rehabil. 2013;94:667–72.

Kilkens OJ, Post MW, Dallmeijer AJ, et al. Relationship between manual wheelchair skill performance and participation of persons with spinal cord injuries 1 year after discharge from inpatient rehabilitation. J Rehabil Res Dev. 2005;42(3 Suppl 1):65–73.

Knox DM, Anderson TM, Anderson PS. Effects of different turn intervals on skin of healthy older adults. Adv Wound Care. 1994;7(48–52):54–6.

Kreutz D. Life care planning for spinal cord injury: seating and mobility consideration. Top Spinal Cord Inj Rehabil. 2002;7:28–37.

Krey CH, Calhoun CL. Utilizing research in wheelchair and seating selection and configuration for children with injury/dysfunction of the spinal cord. J Spinal Cord Med. 2004;27(Suppl 1):S29–37.

Kwarciak AM, Yarossi M, Ramanujam A, et al. Evaluation of wheelchair tire rolling resistance using dynamometer-based coast-down tests. J Rehabil Res Dev. 2009;46:931–8.

Liu HY, Pearlman J, Cooper R, et al. Evaluation of aluminum ultralight rigid wheelchairs versus other ultralight wheelchairs using ANSI/RESNA standards. J Rehabil Res Dev. 2010;47:441–55.

McLaurin CA, Brubaker CE. Biomechanics and the wheelchair. Prosthetics Orthot Int. 1991;15:24–37.

Medola FO, Elui VM, Santana Cda S, et al. Aspects of manual wheelchair configuration affecting mobility: a review. J Phys Ther Sci. 2014;26:313–8.

Metring NL, Gaspar MI, Mateus-Vasconcelos EC, et al. Influence of different types of seat cushions on the static sitting posture in individuals with spinal cord injury. Spinal Cord. 2012;50:627–31.

Michael E, Sytsma T, Cowan RE. A primary care provider's guide to wheelchair prescription for persons with spinal cord injury. Top Spinal Cord Inj Rehabil. 2020;26:100–7.

Mulroy SJ, Farrokhi S, Newsam CJ, et al. Effects of spinal cord injury level on the activity of shoulder muscles during wheelchair propulsion: an electromyographic study. Arch Phys Med Rehabil. 2004;85:925–34.

Perdios A, Sawatzky BJ, Sheel AW. Effects of camber on wheeling efficiency in the experienced and inexperienced wheelchair user. J Rehabil Res Dev. 2007;44:459–66.

Pierson FM, Fairchild SL. Principles & techniques of patient care. 4th ed. St. Louis: Saunders; 2008.

Pompeo M, Baxter C. Sacral and ischial pressure ulcers: evaluation, treatment, and differentiation. Ostomy Wound Manage. 2000;46:18–23. Erratum in: Ostomy Wound Manage 2000;46:9.

Ragan R, Kernozek TW, Bidar M, et al. Seat-interface pressures on various thicknesses of foam wheelchair

cushions: a finite modeling approach. Arch Phys Med Rehabil. 2002;83:872–5.
van der Woude LH, Bouw A, van Wegen J, et al. Seat height: effects on submaximal hand rim wheelchair performance during spinal cord injury rehabilitation. J Rehabil Med. 2009;41:143–9.
van der Woude LH, Formanoy M, de Groot S. Hand rim configuration: effects on physical strain and technique in unimpaired subjects? Med Eng Phys. 2003;25:765–74.
van der Woude LH, Veeger DJ, Rozendal RH, et al. Seat height in handrim wheelchair propulsion. J Rehabil Res Dev. 1989;26:31–50.
Ventura SH, Bendix K. Prescription wheelchairs: seating and mobility systems. In: Chui KK, Jorge MM, Yen S, et al., editors. Orthotics and prosthetics in rehabilitation. 4th ed. St. Louis: Elsevier; 2020.
Webster JS, Cottam G, Gouvier WD, et al. Wheelchair obstacle course performance in right cerebral vascular accident victims. J Clin Exp Neuropsychol. 1989;11:295–310.
Weiss LD, Weiss JM, Porree T, editors. Oxford American handbook of physical medicine and rehabilitation. Oxford: Oxford University Press; 2010.
Yang YS, Koontz AM, Yeh SJ, et al. Effect of backrest height on wheelchair propulsion biomechanics for level and uphill conditions. Arch Phys Med Rehabil. 2012;93:654–9.
Yasukawa L, Stevens S, Ueberfluss J. Wheelchairs. In: Yarkony GM, editor. Spinal cord injury. Medical management and rehabilitation. Gaithersburg: Aspen Publishing, Inc.; 1994.
Yoo I. The effects of backrest thickness on the shoulder muscle load during wheelchair propulsion. J Phys Ther Sci. 2015;27:1767–9.

Recommended Additional Reading

Hsu JD, Michael JW, Fisk JR. AAOS atlas of orthoses and assistive devices. 4th ed. Philadelphia: Mosby; 2008.
Chui KK, Jorge MM, Yen S, et al. Orthotics and prosthetics in rehabilitation. 4th ed. St. Louis: Elsevier; 2020.
Cooper RA. Wheelchair selection and configuration. New York: Demos; 1998.
Redford JB, editor. Orthotics etcetera. 2nd ed. Baltimore: Williams & Wilkins; 1986.
Wilson AB Jr. Wheelchairs: a prescription guide. 2nd ed. New York: Demos; 1992.

Orthoses in Spinal Cord Injuries

47

An orthosis is defined as "an externally applied device that is used to modify the structural and functional characteristics of the neuromuscular and skeletal systems." Orthotics is defined as "the science and art involved in the treatment patients by the use of an orthosis" (Condie 2008). Orthoses are classified according to the anatomical segments and joints that include them, such as wrist-hand-finger orthosis (WHFO), ankle–foot orthosis (AFO), and lumbosacral orthosis (LSO). Orthoses for people with spinal cord injuries can be divided into two broad categories: static orthoses and dynamic orthoses. A static orthosis stabilizes the joint and prevents movement. A dynamic orthosis involves movement across the joint(s).

Orthotic intervention can be one of the most important parts of rehabilitation for people with spinal cord injuries. People with spinal cord injuries benefit from the use of properly prescribed and fitted upper extremity orthoses, lower extremity orthoses, or spinal orthoses. The general goals of orthoses in people with spinal cord injuries are to stabilize the joints, to prevent unwanted contractures of the joints or shortening of the muscles, especially 2-joint muscles, to increase desired motion, or to induce contractures in order to target specific movements support.

47.1 Upper Limb Orthoses for People with Spinal Cord Injuries

Upper limb orthoses are an important treatment to ensure proper positioning and prevent edema and irreversible changes in the muscle-tendon-bone architecture of the extremity. Treatments such as upper extremity orthoses, reconstruction surgery, or FES are assessed and determined based on the International Standards for Neurological Classification for Spinal Cord Injury (ISNCSCI) and the International Classification of Surgery of the Hand in Tetraplegia (ICSHT) (Hsu et al. 2008). The functional level of the patient determines the types of orthoses required. Other important considerations are the person's goals, motivation, support systems, and resources (Atkins et al. 2010). Upper limb orthoses play an important role in an effort to maximize upper limb utilization in people with tetraplegia.

As mentioned above, static orthoses are used for position and dynamic orthoses are used for function. The dynamic orthoses designs were used most frequently with people with spinal cord injuries of C6 and C7. The static hand splint serves several purposes in the treatment of tetraplegia, including avoiding overstretching, espe-

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cially the wrist extensors, maintaining the functional position, preventing deformities, such as claw hand, and protecting and stabilizing the flail joint (Krajnik and Bridle 1992). A wrist-hand orthoses (WHO), which is often referred to as a resting hand splint in rehabilitation of spinal cord injury, is used to position the wrist and hand in a functional position. The static WHO is often indicated as a positional orthosis for C1–5 tetraplegics with zero wrist extensors and an intrinsic minus hand. Static hand and WHO is used to prevent deformities and should maintain the thumb opposition, thumb web space, and palmar arch as well as proper angulation between the hand and forearm. The WHO may also be indicated to protect a hand from injury and is usually worn at night when it is less likely to interfere with activities of daily living skills and so that it can be worn for a longer duration without interruption (Mulcahey et al. 2015). A standard WHO or wrist-hand-finger orthoses (WHFO) maintains the wrist in approximately 45° extension, the metacarpophalangeal (MCP) joints in 80–90° flexion and the interphalangeal (IP) and distal interphalangeal (DIP) joints in natural. These orthoses are indicated for those with complete C5 tetraplegia or those with weak wrist against gravity for functional tasks. Alternatively, a custom dorsal or volar-based cock up splint can be used. The WHO or WHFO can be used with universal cuffs that make it easier to hold utensils, typing peg, or writing instrument (Mulcahey et al. 2015). A long opponens splint is indicated as a pre-tenodesis splint for people with complete C5 tetraplegia with gravity-eliminated wrist extension. Opponens splints keep the thumb in opposition to the first two fingers. A long opponens splint is needed when the wrist is flaccid. A short opponens splint is used when there is good wrist movement (Krajnik and Bridle 1992).

Tenodesis skills may not be as effective for object manipulation and release, even with good wrist extensors. An option for nighttime use could be a volar- or dorsal-based modified resting hand type splint that positions the wrist in approximately 45° flexion while maintaining the MP joints in 90° flexion. This option could be used to help individuals with excessive tightness of long finger flexors or other impairments that would not allow effective passive release of an object during tenodesis skill. The person with C6 and C7 spinal cord injury who has a wrist extension can benefit from a short opponens splint to position the thumb in an approximated lateral pinch position and assist a more effective tenodesis grasp (Mulcahey 2008).

Dynamic orthoses, such as the wrist-driven, wrist-hand orthosis (WDWHO) (also known as the wrist-driven, flexor-hinge splint or tenodesis splint) offer prehension to increase independence in activities of daily living (Atkins et al. 2010; Krajnik and Bridle 1992). The WDWHO is a dynamic prehension orthosis for power transmission from the wrist extensors to the fingers. The WDWHO is designed to improve tenodesis skills by improving the strength of a pinch pattern. Active wrist extension provides grasp and gravity-assisted wrist flexion enables the patient to open the hand. The WDWHO holds the thumb in an opposition position to the second and third finger of the hand and offers a stronger three-jaw chuck pinch as a wrist extension (Johanson and Murray 2002). The strength of the wrist extensor should be at least grade 3+ and proximal strength should be functional. WDWHO candidates have a functional level of C5 with some returns C6, C6, and C7 tetraplegia. Individuals with C5 tetraplegia who have little active wrist extension can use a ratchet mechanism in the tenodesis splint, locking their hands into a closed posture (Knutson et al. 2006).

It is very important to prevent pressure injuries caused by orthoses when using orthoses in upper limb with sensory dysfunction in people with spinal cord injuries. The orthosis is first placed on the hand for 30 min, then it is removed and 1 h later any red areas are noted and reassessed. Once the orthosis is removed, any redness should resolve after 20 min. With normal results on routine skin examinations, wearing time is gradually increased (Lavis and Codamon 2019). If the redness has not disappeared, adjustments may be needed. The patient should be aware of the importance of skin inspection to avoid exces-

sive pressure and skin breakdown. The wear tolerance is gradually increased until an optimal tolerance is reached (Atkins et al. 2010).

When prescribing upper limb orthoses in spinal cord injuries, many factors including motor strength of the neurological level of injury and adjacent distal segments, sensory function, contracture, spasticity, and motivation of the patient should be considered. The following is orthotic management for people with tetraplegia based on the neurological level of injury (Table 47.1). Figure 47.1 is an algorithm for making decisions the treatment of upper limb orthoses in people with tetraplegia.

Table 47.1 Upper limb orthoses according to neurological level of spinal cord injury

Orthosis	Level of spinal cord injury	Rationale
Dynamic orthoses		
Mobile arm support (Balanced forearm orthosis, Ball-bearing feeder)	Weak C5Incomplete injuriesAlso indicated with shoulder weakness (internal-external rotator muscle grades 2− to 3/5; bicep-supinator muscle grades 2−/5)	Function Assists in reaching in horizontal and vertical planes Increases functional ROM and strength Independence with feeding and hygiene after setup Provides support to allow correct movement patterns
Overhead rod and sling	Weak C5Incomplete injuriesAlso indicated with shoulder weakness (internal-external rotator muscle grades 3 to 3+/5; bicep/supinator muscle grades 3/5)	Function Increases functional ROM and strength Independence with wheelchair driving after setup Independence with feeding and hygiene after setup Provides support to allow correct movement patterns
Static splints, casts, or orthoses		
Resting hand splint	C1–C7	Position Prevents joint deformityPreserves web spacePreserves balance with intrinsic and extrinsic musculature
Intrinsic plus splint	C12–C7	Position Same as resting hand splint but places finger MP joint in more flexion Long term, allows better tenodesis alignment of first digit and thumb
Elbow extension splints, bivalve cast	C5–C6	Position Prevents elbow contracture from muscle imbalance and/or hypertonicity
Dorsal wrist support splints	C5	Function (e.g., slot for utensils) and position Prevents severe wrist drop and ulnar deviationIf positioning is needed long term, may consider permanent splint fabricated by orthotist
Long opponens orthosis	C5	Position and function Can be dorsal or volar Prevents wrist drop and ulnar deviationPreserves web space and supports thumb, reducing subluxation Slot may be fabricated for function
Wrist cock-up orthosis	C5 Incomplete injuries	Position and function Supports wrist in slight extensionAllows finger movement for incomplete injuries
Short opponens orthosis	C6–C7	Position and function Supports thumb to prevent subluxation Improves tenodesis and prehension
Tenodesis orthosis	C6–C7	Function Enhances natural tenodesis in either tip-pinch or lateral pinch May consider permanent splint fabricated by orthotist
MP (metacarpophalangeal) block orthosis	C8-T1	Position Prevents “claw hand” or hyperextension of the MP joints Protects weak intrinsic musculature

From Atrice et al. (2020), with permission

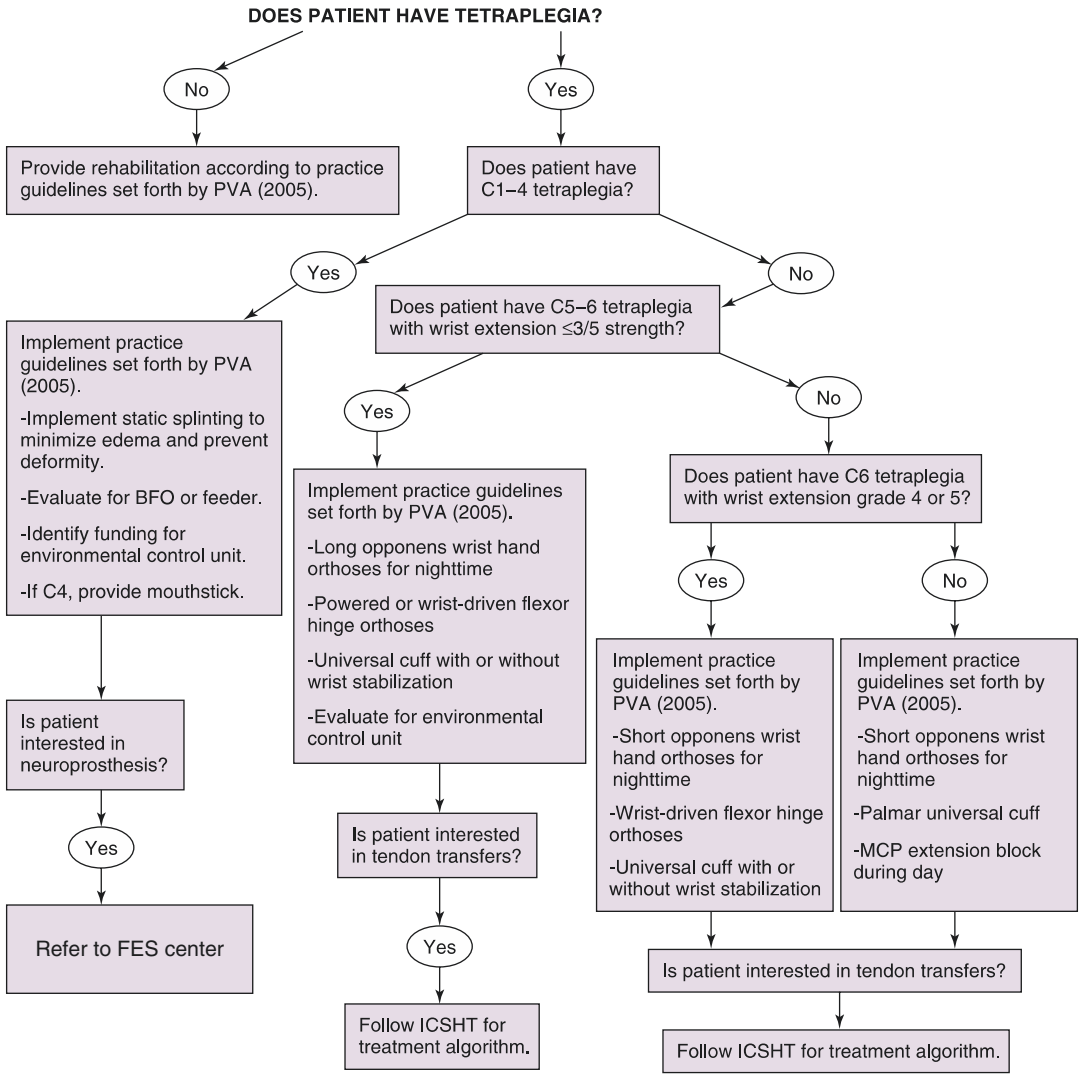

Fig. 47.1 Algorithm for treatment decisions of upper limb orthoses in people with tetraplegia. From Tubbs and Pound (2019), with permission

47.1.1 Neurological Level of Injuries: C1–C4

Orthoses for people with high tetraplegia are intended to avoid complications and ensure the comfort of the patient as well as preservation of the esthetic appearance of the upper extremity including the hand. Custom-molded or prefabricated static wrist-hand orthoses (WHO) help to maintain the functional position of the wrist and hand and to prevent contractures or deformities. Common static hand splints include the resting hand splint, wrist extension splint, and long and short opponens splint. A long opponens WHO should be used to support the proximal and distal transverse arch and the longitudinal arch of the hand. The wrist should be positioned in 30° extension and the thumb in full abduction and extension. Nighttime splinting supports the arches and keeps the thumb in full abduction and extension, but the fingers and the hand in an intrinsic plus posture.

A mouth stick, not an upper limb orthosis, enables some functions such as typing, page turn-

ing or writing. Automatic, mechanical, and powered feeders can be prescribed. Developments in robotic technology enable the use of robotic arms as functional assistive devices for persons with tetraplegia (Tubbs and Pound 2019).

47.1.2 Neurological Level of Injury: C4

A mobile arm support (known as the balanced forearm orthoses (BFOs) or ball-bearing forearm orthoses) enable people with weak or paralyzed arm and shoulder musculature (C3–C5 tetraplegia) to move their arms in a horizontal plane and raise or lower their hands (Knutson et al. 2006). A mobile arm support (known as the balanced forearm orthosis, BFO) mounted on the wheelchair supports the weight of the arm and provides the horizontal movement of the arm and elbow at the shoulder and elbow through a linkage of bearing joints. It allows the hand to be positioned for activities. The mobile arm support consists of a mounting bracket, a proximal arm, a distal arm, and a forearm support trough (Baumgarten 1985).

The patient is recommended to wear a static orthosis at night. The resting hand splint and the long opponens splint support the wrist and allow the fingers and thumb to rest in their functional position.

47.1.3 Neurological Level of Injury: C5

Person with C5 spinal cord injury have good elbow flexors but poor or absent wrist extensors. The wrist is supported by a static orthosis to prevent excessive stretching of the weak or absent wrist extensors. Resting hand splints, dorsal wrist splints, and long and short opponens splints are commonly used orthoses (Hoffer et al. 1981). If there is no wrist extensors that enable tenodesis effect, the finger flexors should be stretched, as a natural finger flexion position facilitates the development of flexor tendon tightness. A ratchet variation of the tenodesis splint can produce a tenodesis effect in people with C5 tetraplegia having with little or no wrist extension, which can lock the hand in a closed position in order to sustain grasp (Knutson et al. 2006). The elbow must be kept in extension to avoid flexion contractures. Elbow flexion contractures of more than 25° can affect functional independence, such as transfer activity (Bryden et al. 2004; Dalyan et al. 1998). If there is no active elbow extension, elbow extension splints are used to prevent contracture at night. The universal cuff is often used for feeding and hygiene. The universal cuff is often combined with an orthosis that supports the wrist in a functional position.

47.1.4 Neurological Level of Injuries: C6–C7

The focus in hand management for persons with C6 or C7 level is on optimizing the biomechanics of the wrist and hand on order to promote an effective tenodesis grip and pinch. Tenodesis is the passive closing of the fingers when the wrist is extended and the opening of the hand when the wrist is flexed (Atkins et al. 2010). Individuals with neurological level of injury at the C6 have intact wrist extensors, as well as some strength in the serratus anterior and clavicular pectoralis muscles. Pectoralis muscle strength provides the ability to bring the arm across the chest to midline, enabling activities that require bilateral arm use. The intact wrist extensors allow the person to use the tenodesis action at the wrist to achieve dynamic prehension for feeding, hygiene, and similar activities. Various orthoses are prescribed to promote the adaptive shortening of the flexor digitorum profundus, superficialis, flexor pollicis longus, and to protect the web space (Harvey 1996). Such orthoses wrap the fingers as in a boxing glove and place the thumb in lateral pinch against the index finger.

The wrist-driven, wrist-hand orthosis (WDWHO) is a dynamic orthosis that transmits force from the wrist extensors to the fingers for prehension. The WDWHO provides a strong pinch for activities such as self-catheterization. Prehension with the WDWHO is produced by active wrist extension, which transfers power

from the wrist extensors to flex the index and middle fingers against the thumb. The gravity-assisted wrist flexion creates hand opening.

47.1.5 Neurological Level of Injury: C8

The person with C8 spinal cord injury neurological level of injury at C8 has intact extrinsic finger muscles but weak or absent intrinsic muscles. The goal of orthosis for the patient is to preserve the natural architecture of the hand and prevent deformities due to muscle imbalance between the extrinsic and intrinsic hand muscles. The activity of the long flexors with absent lumbricals creates a claw hand deformity. Prehension without initial metacarpalphalangeal flexion is therefore less effective. A static hand orthosis with a metacarpalphalangeal extension stop (lumbrical bar) helps substitute for the intrinsic minus hand to prevent the clawing of the hand and to improve hand opening. In practice, most people with the C8 level would not use orthoses.

47.2 Lower Limb Orthoses for People with Spinal Cord Injuries

People with spinal cord injuries with a variety of motor or sensory deficits who could benefit from the use of lower limb orthoses. Lower limb orthoses in people with spinal cord injuries are used as upper limb orthoses to protect deformities or shortening of the muscles, to stabilize a joint or to move an extremity. Lower limb orthoses for spinal cord injuries are not as important in rehabilitation as the upper limb orthoses. A large percentage of people with ASIA C and D recover some degree of functional ambulation, most will require the use of orthotic devices. People with ASIA A and B have much less potential for independent ambulation and do so at an extremely high energy expenditure (Atrice 2000). The energy cost is highest for people with complete paraplegia who use a swing through gait pattern and lowest for persons who use bilateral ankle–foot orthoses (AFO) (Atrice 2000). The most common purpose of the lower limb orthoses for spinal cord injuries is to stabilize the joints and to make it easier to stand or walk. Basically, lower limb orthoses should be used minimally in order to stabilize the joints and to apply three-point pressure system. Figure 47.2 shows an example of a three-point pressure system applied in an ankle–foot orthosis.

If the orthoses are used for standing or walking, walking aids such as a cane or canes, a walker or crutches may be required. As a reference, levels of ambulation can be divided into

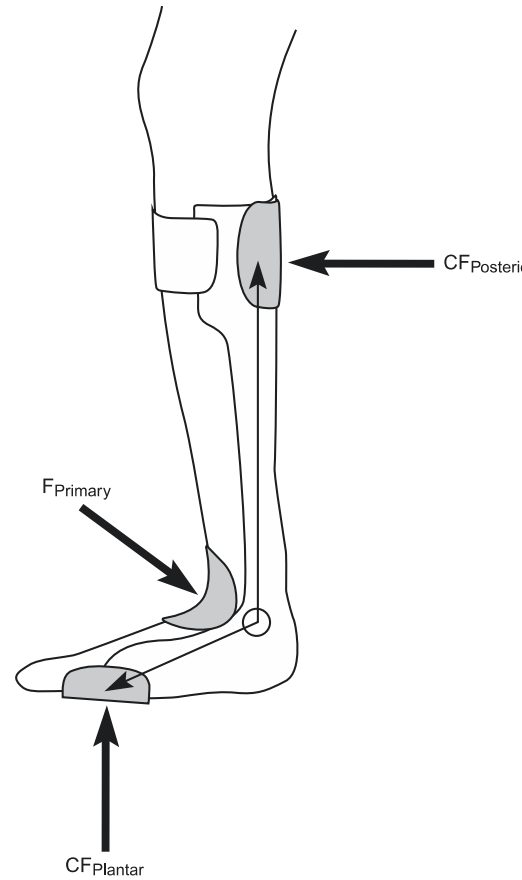

Fig. 47.2 An example of a three-point pressure system applied in an ankle-foot orthosis. Plantarflexion control system acts during swing phase in an ankle-foot orthosis. The large primary force (Fprimary) is applied in a posterior-inferior direction and two counterforces are applied in an upward (CFplantar) and anterior (CFposterior) direction. From Lusardi (2020), with permission

four categories: standing only; exercise, which ambulates short distances for the purpose of regular exercise; household, which ambulates inside home or work, uses wheelchair much of the time; community, independent on all surfaces, does not use wheelchair (Atrice 2000). Currently, several advanced orthoses have been developed for people with spinal cord injuries that use hydraulic or pneumatic control systems or electrical power sources including robotic exoskeleton gait systems (HAL, Ekso, Indigo, Rewalk, ExoAtlet) to aid in moving the legs forward during the swing phase or stabilizing the weight bearing during the stance phase. Lower limb orthoses ambulation level related to injury level are presented in Table 47.2.

47.2.1 Ankle–Foot Orthosis (AFO)

An ankle–foot orthosis (AFO) supports the ankle and foot joints. AFOs are usually prescribed for people with lesions between L4 and S2 to allow safe and effective ambulation by supporting the weakened muscles around the ankle. Solid-ankle AFO, posterior leaf spring AFO, and articulated AFO are commonly prescribed AFOs for spinal cord injuries. The solid-ankle AFO is the most commonly prescribed and is made of plastic with a rigid construction and promotes maximum support and stability in all planes by preventing both dorsiflexion and plantarflexion. The posterior leaf spring AFO is less rigid than the solid-ankle AFO and allows some ankle flexibility. The artic-

Table 47.2 Lower limb orthoses and ambulation level for complete spinal cord injuries

Level of injury	Orthosis	Features	Ambulation class
T_1–T_5	Bilateral KAFOs; with pelvic band (HKAFO); Scott-Craig KAFOs	Hip joints and locks; pelvic band	Standing; exercise; primarily pediatrics
T_1–T_{12}	Reciprocating gait orthosis (RGO); Scott-Craig KAFOs	Molded plastic pelvic band; thoracic extension with anterior and posterior straps; hip joints and bilateral knee joints; polypropylene posterior thigh cuffs and AFO sections	Exercise; primarily pediatrics; limited adult use
T_{12}–L_1	Scott Craig KAFOs; RGO	Thigh cuff high laterally for increased hip stability; bail lock at knees; posterior offset knee joints; double adjustable ankle joints; double strut stirrup	Standing; exercise
T_{12}–L_2	Conventional KAFOs	Medial upright 2 in. below perineum; variety of knee lock options; double action ankle joints; corrective knee straps for varum or valgum	Standing; exercise; limited household
T_{12}–L_2	Polypropylene KAFOs	Medial upright 2 in. below perineum; variety of knee lock options; variety of trim lines (medial/lateral); variety of ankle support options	Standing; exercise; limited household
L_3–L_4	Conventional AFO, metal	Accommodates fluctuating edema; variety of ankle joint options	Household; limited community
L_3–L_4	Custom polypropylene AFO, solid ankle	Custom-contoured construction; hindfoot-neutral alignment; dorsiflexed ankle may eliminate/reduce toe drag and genu recurvatum; limited accommodation for fluctuation edema; variety of foot plate options	Household; limited community
L_3–L_4	Custom polypropylene AFO, articulated ankle	Custom-contoured construction; articulation allows better accommodation for stair climbing, unlevel terrain; adjustable plantar flexion stop (optional); dorsiflexed angle to eliminate/reduce toe drag and genu recurvatum; limited accommodation for fluctuating edema; variety of foot plate options	Household; limited community; community

KAFO knee-ankle-foot orthosis; *HKAFO* hip-knee-ankle-foot orthosis; *AFO* ankle-foot orthosis

ulated AFO has medial and lateral hinge joints (ankle plantarflexion stop or ankle dorsiflexion stop) of the ankle that are closely aligned with the anatomical ankle joint (Lavis and Codamon 2019). AFO can be made of plastic, metal, carbon fiber, or a combination of these materials. AFOs can add stability to the knee during stance by adjusting the angle of the ankle. Plantarflexion makes knee extension easier, and more dorsiflexion makes knee flexion easier. The main purpose of AFO is to stabilize the ankle by keeping the ankle in a static position to prevent foot drop while walking (Mulcahey et al. 2015). The most common use of AFO is the control of the ankle joint in the sagittal plane. The AFO with a plantarflexion stop is intended to provide clearance of the foot during swing phase if the ankle dorsiflexors are not strong enough: the tibialis anterior and extensor digitorum longus. A dorsiflexion stop in an AFO is used to limit ankle dorsiflexion and substitutes for weak ankle plantarflexors: the gastrocnemius and soleus. The stop provides stability in the sagittal plane by limiting the dorsiflexion ROM of the talocrural joint. Limiting dorsiflexion to neutral or slightly plantarflexion influences the extension stability of the knee and is helpful when the quadriceps strength is grade 3- (Fair minus).

47.2.2 Knee–Ankle–Foot Orthosis (KAFO)

The KAFO is usually prescribed when other types or forms of bracing like AFOs cannot adequately control knee instability due to quadriceps weakness or laxity (Lavis and Codamon 2019). The knee–ankle–foot orthoses (KAFO) are often used for people with the lower thoracic or lumbar spinal cord injuries (T9-L1) to ensure the ability to stand and/or walk. KAFO's knee joints are divided into offset free motion knee joints and joint with locking mechanisms. The offset knee joint provides increased knee stability by moving the mechanical knee axis posterior to the anatomical knee joint, allowing the individual to position the center of gravity or weight line anterior to the knee joint axis. The advantages of using this type of joint are lower energy consumption, easier transition from sitting to standing, and an improved gait pattern. The disadvantages are instability when going down a slope or walking on uneven terrain. Locked joints such as the bail lock, drop ring lock, and lever release maintain the knee in a locked position throughout the gait cycle and create compensation strategies for clearing the floor by circumduction, hip hiking, lateral tilting of the trunk to the contralateral side, and vaulting. A swing through gait pattern with the KAFO and walking aids such as Lofstrand crutches is often used. The Scott-Craig orthosis is a KAFO alternative designed to facilitate a swing through gait. Using bilateral KAFOs and crutches for walking requires high energy costs. Therefore, patients who choose to use bilateral KAFOs must be motivated, physically fit, and have good upper limb strength (Mulcahey et al. 2015). In fact, patients who have used bilateral KAFOs do not use the orthoses because of high energy consumption. However, bilateral KAFOs may be recommended for therapeutic use.

47.2.3 Hip–Knee–Ankle–Foot Orthosis (HKAFO)

The hip–knee–ankle–foot orthoses (HKAFO) is used to stabilize the hips as well as the knee, ankle, and foot. The typical HKAFO is a pair of KAFOs linked above the hip with a pelvic band, lumbosacral orthosis, or TLSO. There are many different types of HKAFO, such as reciprocating gait orthosis (RGO), Walk-A-Bout orthosis, Parawalker, or hip guidance orthosis. Exoskeletal HKAFO is also now available.

47.3 Spinal Orthoses for Spinal Trauma, Spinal Fracture, or Postoperative Care

Considerations of orthotic management for spinal injuries are based on stability, fracture type, comorbidity, and expected outcome (Malas et al. 2008). The main objective of the spinal orthoses is to protect the spinal column from stresses that

may lead to a progression of the spinal deformity and prevent adequate healing of the injury (Patwardhan et al. 1990). To achieve this goal, the orthoses must be able to limit gross vertebral motion of the spinal column, limit intersegmental motion at the injured site, and provide proper spinal alignment/realignment of the spine to the injured site (Malas et al. 2008). Postoperatively, additional loads such as a sitting or upright posture should not damage the surgical construct of a spine. Thus, the splint effect of the orthosis can be helpful in protecting the surgical construct, bone-construct interface, and possibly the biological fusion. The role of postoperative orthoses is still controversial today. On the other hand, surgical failures still occur, especially if postoperative orthoses are omitted from the treatment plan (Malas et al. 2008). The selection of spinal orthoses for trauma and postoperative care includes prefabricated and customized devices. However, definitive answers to the fundamental questions of when to use spinal orthoses and whether they are effective remain incomplete, and more research is needed. Spinal orthoses are described in terms of the anatomical regions of the spine, such as cervical orthosis (CO), cervicothoracic orthosis (CTO), lumbosacral orthosis (LSO), thoracolumbosacral orthosis (TLSO), or cervicothoracolumbosacral orthosis (CTLSO). The trauma or fracture type of the cervical and thoracolumbar spine, the mechanism of injury, and the orthotic management are summarized in Table 47.3.

47.3.1 Cervical Orthosis (CO)

Cervical spine orthoses can be limited to the subaxial spine itself, in the form of a cylinder that fits around the neck with a trimline at the occiput, mandible, and sternoclavicular structures, or it may extend proximally and distally (halo vest) or just distally over the thoracic cage for additional control (cervicothoracic orthosis, CTO) (Leahy and Maccord 2020). In general, increasing the stiffness and length of a CO improved its ability to restrict motion. However, lateral flexion and rotation over the entire cervical spine, as well as flexion-extension at the upper levels, are not well controlled by any of the conventional COs (Johnson et al. 1977).

The CO soft collar tends to be the most comfortable of available cervical collars, but it does not substantially control the motion of the cervical spine, it provides kinesthetic reminder to limit motion. The soft collar allows up to 75–80% of normal cervical motion (Hartman et al. 1975;

Table 47.3 Trauma or fracture types of the cervical and thoracolumbar spine, injury mechanism, and orthotic management

Level		Type		Injury mechanism	Remarks	Orthoses
Upper cervical	C1	Jefferson		Axial load	Triplanar instability	Halo vest
	C2	Hangman		Hyperextension plus distraction	Traumatic spondylolisthesis, triplanar instability	Halo vest
		Odontoid		Shear plus compression	Type I: Stable; type II and III: Unstable	Halo vest
Lower cervical	C3-7	Anterior compression		Hyperflexion	Most common level at C5, possible brachial plexus involvement	Rigid collar
		Whiplash		Hyperextension	Soft tissue injury to anterior longitudinal ligament likely, long-term risk for chronic forward head posture	Soft collar

(continued)

Table 47.3 (continued)

Level		Type		Injury mechanism	Remarks	Orthoses
Cervicothoracic junction injuries spanning this level require a CTO or CTLSO						
Upper thoracic	T1-8	Denis classification applies to all thoracic and lumbar levels	Denis I: Anterior compression	Flexion plus compression	Three fourths of thoracolumbar fractures are of this type, two thirds of those occur at T12–L1–2. Anterior column damage only in most cases. Posterior ligamentous injury may indicate instability.	Hyperextension is the mechanism of action. Common choices: Corsets, Jewett (milder injuries), and TLSOs (custom or prefabricated).
			Denis II: Burst	Compression plus flexion	Anterior and middle columns are damaged. Fracture of superior endplate is more common. There may be retropulsion of one or more fragments from the posterior wall.	
Lower thoracic	T9–12		Denis III: Chance and slice	Flexion plus distraction (seat belt injury)	Chance: Posterior and middle column damage to vertebral body. Slice: Posterior and middle column damage to intervertebral disc. Surgery is indicated.	
Thoracolumbar junction (T12-L1–2) are very common fracture sites and require a TLSO						
Upper lumbar	L1–2		Denis IV: Fracture dislocation	Translation, flexion, rotation, shear	Complete disruption of anterior, middle, and posterior columns. Surgery is indicated.	N/A
Lower lumbar	L3–5	Other	Spondylolysis and spondylolisthesis	May be a sports-related injury from gymnastics. In adults, may cause chronic LBP.	Common in the lower lumbar spine, especially L4–5 and L5–S1. Spondylolisthesis usually requires posterior pelvic tilt in the orthosis.	Custom LSO or TLSO

From Romanoski et al. (2019), with permission

Johnson et al. 1977; Richter et al. 2001). Therefore, the soft collar is contraindicated for any injury involving significant damage to the ligamentous or bony structures of the cervical spine during the initial treatment phase. The plastic or universal collar is made from less flexible polyethylene and provides some control of flexion motion in the midcervical spine. It is not believed to be effective in controlling extension, lateral flexion, or rotation (Fisher et al. 1977). The Philadelphia collar extends more distally and more proximally than the plastic collar. It encap-

sulates the mandible and occiput, extends anteriorly below the sternal notch and posteriorly to approximately T3. The conventional Philadelphia collar allows 30–44% of normal flexion and extension, approximately 44% of normal rotation, and up to 66% of lateral flexion (Johnson et al. 1977). More effective versions of the Philadelphia collar that provide improved stabilization include the Marlin Aspen®, Malibu®, and Miami® collars.

47.3.2 Cervicothoracic Orthosis (CTO)

CTOs include the Yale, sternal occipital mandibular immobilizer (SOMI), two-poster, four-poster, and halo orthosis. The Yale orthosis is largely thermoplastic and extends down to 2 cm proximal to the xiphoid process and is very effective in controlling both flexion and extension. The SOMI brace is a highly effective cervical thoracic orthosis that can be applied in the supine position with minimal disruption. The SOMI controls flexion quite well, but is less effective in controlling extension and lateral flexion (Johnson et al. 1977). The two-poster and four-poster CTOs are usually made of aluminum and thermoplastics. Such poster designs have a sternal plate that is rigidly connected to a mandibular support. The custom-molded Minerva provides excellent control for thoracic and cervical regions without the need for invasive skull pins. It is not as effective as halo in controlling lateral flexion (Maiman et al. 1989). The Minerva brace is the most effective method for immobilizing C1–2 and has been shown to limit flexion/extension by approximately 79%, axial rotation by 88%, and lateral bending by 51% (Sharpe et al. 1995).

It is widely believed that the halo vest provides maximum cervical control compared to all other cervical orthoses. The halo vest eliminates 90% of normal cervical motion (Johnson et al. 1977). The highest percentage of normal motion occurred at the C2–C3 level (42% of normal), and the least amount of motion occurred at the C7-T1 level (20% of normal) (Botte et al. 1996). In the conventional halo vest, four pins are screwed into the skull and tightened to a recommended torque. Care must be taken to properly place the halo on the head, which should be located 1 to 2 cm posterior to the ears and 1 cm above the lateral third of the eyebrows. This is to avoid the frontal sinus, supraorbital and supratrochlear nerves, and temporals muscle, minimizing the risk of loosening and avoiding pain during mastication (Botte et al. 1996; Garfin et al. 1986) (Fig. 47.3). Four pins are inserted with 6 to 8 lb./in of torque (Bono 2007). Movement and cellular necrosis can cause loosening and degeneration of the periosteum around the screws, which should be checked after 24 h and weekly thereafter. The halo vest is associated with a high rate of complications, such as pin loosening, pin infection, pressure injuries located on the trunk, nerve injury, dysphagia, or dural penetration. Halo-associated dysphagia is the result of immobilization of hyperextension, requiring repositioning of the neck to less extension (Botte et al. 1995; Garfin et al. 1986). A higher rate of complications occurs in older patients. A cervical orthosis is recommended as the initial treatment option for the elderly population, as higher incidences of morbidity and mortality have been reported in this population group when using the halo vest (Glaser et al. 1986).

47.3.3 Thoracolumbosacral Orthosis (TLSO)

The three-point hyperextension TLSO includes Jewett and CASH (cruciform anterior spinal hyperextension) orthoses. These may be sufficient to provide an extension moment to prevent further kyphosis or deformity in single-column compression fractures with minimal loss of the original anterior height of the vertebra. When height loss exceeds 85%, the three-point hyperextension TLSO does not appear to effectively prevent deformity progression (Patwardhan et al. 1990). If limiting lateral flexion is required, the Jewett orthosis is the orthosis of choice, as the CASH orthosis poorly controls lateral flexion. The Jewett is most effective in preventing flexion and extension between T6 and L1. The TLSO

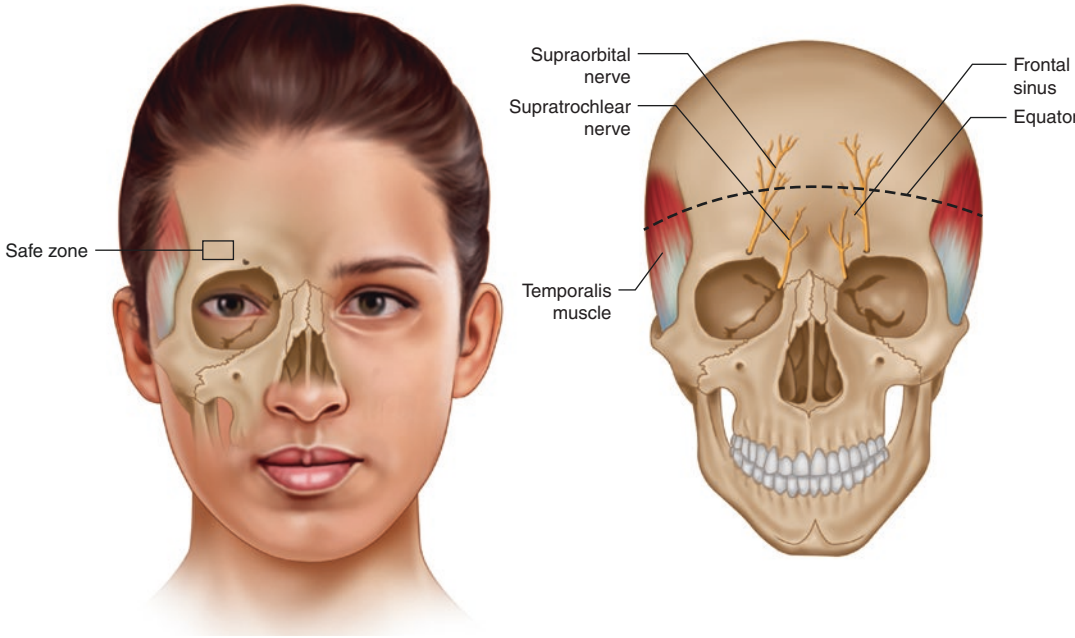

Fig. 47.3 Drawing showing the safe zone for the anterior halo-pin placement. Laterally, the pin should be placed anterior to the temporalis muscle and fossa, to avoid possible painful mastication or penetration through thin cranial bone. Medially, the pin should be kept in lateral one third portion of the superior orbital rim, to avoid the supraorbital and supratrochlear nerves or the frontal sinus. Superiorly, the pin should be kept below the level of the greatest skull circumference (skull equator), to avoid cephalad migration of the pin. Inferiorly, the pin should be kept above the supraorbital ridge to prevent displacement or penetration into the orbit. Adapted from Botte et al. (1996) and Garfin et al. (1986)

body jacket is a custom-molded orthosis for a maximum balance between comfort and efficiency in controlling the movement of the thoracic spine. Indications for the custom-molded TLSO body jacket are post-surgical thoracic protection and chronic instability. However, it is difficult to don and doff, and since it can migrate on the body, it requires frequent adjustment of position. Bivalve TLSO remains the most convenient option for donning and doffing as the patient is likely to be fit in a recumbent position.

When the postoperative TLSO are used, it should be extended four to five levels above and below, if possible, for optimal stabilization in all planes (Abudou et al. 2013; Romanoski et al. 2019). For people with fractures or instrumentation at or above T3, it is important to consider using over-the-shoulder straps to extend the lever to discourage further vertebral sway and increase stability. Typically, patients remain in a thoracolumbar orthosis for 8 to 12 weeks or until biological fusion occurs. Early weaning or lowering the original height of the TLSO may have the negative effect of adding functional stress and making the fusion more susceptible to failure (Romanoski et al. 2019).

References

Abudou M, Chen X, Kong X, et al. Surgical versus non-surgical treatment for thoracolumbar burst fractures without neurological deficit. Cochrane Database Syst Rev. 2013;6:CD005079.

Atkins MS, Clark D, Waters RL. Upper limb orthoses. In: Lin VW, editor. Spinal cord medicine: principles and practice. 2nd ed. New York: Demos Medical Publishing; 2010.

Atrice MB. Lower extremity orthotic management for the spinal-cord-injured client. Top Spinal Cord Inj Rehabil. 2000;5:1–10.

Atrice MB, Ackerman PM, Webber K, et al. Traumatic spinal cord injury. In: Lazaro RT, Reina-Guerra SG, Quiben MU, editors. Umphred's neurological rehabilitation. 7th ed. St. Louis: Elsevier; 2020.

Baumgarten JM. Upper extremity adaptations for the person with quadriplegia. In: Adkins HV, editor. Spinal cord injury clinics in physical therapy. New York: Churchill Livingston; 1985.

Bono CM. The halo fixator. J Am Acad Orthop Surg. 2007;15:728–37.

Botte MJ, Byrne TP, Abrams RA, et al. The halo skeletal fixator: current concepts of application and maintenance. Orthopedics. 1995;18:463–71.

Botte MJ, Byrne TP, Abrams RA, et al. Halo skeletal fixation: techniques of application and prevention of complications. J Am Acad Orthop Surg. 1996;4:44–53.

Bryden AM, Kilgore KL, Lind BB, et al. Triceps denervation as a predictor of elbow flexion contractures in C5 and C6 tetraplegia. Arch Phys Med Rehabil. 2004;85:1880–5.

Condie DN. International Organization for Standardization (ISO) terminology. In: Hsu JD, Michael JW, Fisk JR, editors. AAOS atlas of orthoses and assistive devices. 4th ed. Philadelphia: Mosby; 2008.

Dalyan M, Sherman A, Cardenas DD. Factors associated with contractures in acute spinal cord injury. Spinal Cord. 1998;36:405–8.

Fisher SV, Bowar JF, Awad EA, et al. Cervical orthoses effect on cervical spine motion: roentgenographic and goniometric method of study. Arch Phys Med Rehabil. 1977;58:109–15.

Garfin SR, Botte MJ, Waters RL, et al. Complications in the use of the halo fixation device. J Bone Joint Surg Am. 1986;68:320–5.

Glaser JA, Whitehill R, Stamp WG, et al. Complications associated with the halo-vest. A review of 245 cases. J Neurosurg. 1986;65:762–9.

Hartman JT, Palumbo F, Hill BJ. Cineradiography of the braced normal cervical spine. A comparative study of five commonly used cervical orthoses. Clin Orthop Relat Res. 1975;109:97–102.

Harvey L. Principles of conservative management for a non-orthotic tenodesis grip in tetraplegics. J Hand Ther. 1996:238–42.

Hoffer MM, Braun R, Hsu J, et al. Functional recovery and orthopedic management of brachial plexus palsies. JAMA. 1981;246:2467–70.

Hsu JD, Michael JW, Fisk JR. AAOS atlas of orthoses and assistive devices. 4th ed. Philadelphia: Mosby; 2008.

Johanson ME, Murray WM. The unoperated hand: the role of passive forces in hand function after tetraplegia. Hand Clin. 2002;18:391–8.

Johnson RM, Hart DL, Simmons EF, et al. Cervical orthoses. A study comparing their effectiveness in restricting cervical motion in normal subjects. J Bone Joint Surg Am. 1977;59:332–9.

Knutson J, Audu M, Triolo R. Interventions for mobility and manipulation after spinal cord injury: a review of orthotics and neuroprsthetic options. Top Spinal Cord Injury Rehabil. 2006;11:61–81.

Krajnik SR, Bridle MJ. Hand splinting in quadriplegia: current practice. Am J Occup Ther. 1992;46:149–56.

Lavis TD, Codamon L. Lower limb orthoses for person with spinal cord injury. In: Webster JB, Murphy D, editors. Atlas of orthoses and assistive devices. 5th ed. Philadelphia: Elsevier; 2019.

Leahy TE, Maccord S. Orthoses for spinal dysfunction. In: Chui KK, Jorge MM, Yen S, et al., editors. Orthotics and prosthetics in rehabilitation. 4th ed. St. Louis: Elsevier; 2020.

Lusardi MM. Principles of lower extremity orthoses. In: Chui KK, Jorge MM, Yen S, et al., editors. Orthotics and prosthetics in rehabilitation. 4th ed. St. Louis: Elsevier; 2020.

Maiman D, Millington P, Novak S, et al. The effect of the thermoplastic Minerva body jacket on cervical spine motion. Neurosurgery 1989;25:363–367; discussion 367–8.

Malas BS, Meade KP, Patwardhan AG, et al. Orthoses for spinal trauma and postoperative care. In: Hsu JD, Michael JW, Fisk JR, editors. AAOS atlas of orthoses and assistive devices. 4th ed. Philadelphia: Mosby; 2008.

Mulcahey MJ. Upper limb orthoses for the person with spinal cord injury. In: Hsu JD, Michael JW, Fisk JR, editors. AAOS atlas of orthoses and assistive devices. 4th ed. Philadelphia: Mosby; 2008.

Mulcahey MJ, Betz RR, Bryden A, et al. Orthotic management. In: Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. New Delhi: Wolter Kluwer; 2015.

Patwardhan AG, Li SP, Gavin T, et al. Orthotic stabilization of thoracolumbar injuries. A biomechanical analysis of the Jewett hyperextension orthosis. Spine (Phila Pa 1976). 1990;15:654–61.

Richter D, Latta LL, Milne EL, et al. The stabilizing effects of different orthoses in the intact and unstable upper cervical spine: a cadaver study. J Trauma. 2001;50:848–54.

Romanoski N, Schults S, Garter DR Jr. Orthoses for spinal trauma and postoperative care. In: Webster JB, Murphy D, editors. Atlas of orthoses and assistive devices. 5th ed. Philadelphia: Elsevier; 2019.

Sharpe KP, Rao S, Ziogas A. Evaluation of the effectiveness of the Minerva cervicothoracic orthosis. Spine (Phila Pa 1976). 1995;20:1475–9.

Tubbs JT, Pound D. Upper limb orthoses for persons with spinal cord injuries and brachial plexus injuries. In: Webster JB, Murphy D, editors. Atlas of orthoses and assistive devices. 5th ed. Philadelphia: Elsevier; 2019.

Recommended Additional Reading

Chui KK, Jorge MM, Yen S, et al. Orthotics and prosthetics in rehabilitation. 4th ed. St. Louis: Elsevier; 2020.

Lazaro RT, Reina-Guerra SG, Quiben MU. Umphred's neurological rehabilitation. 7th ed. St. Louis: Elsevier; 2020.

Webster JB, Murphy D, editors. Atlas of orthoses and assistive devices. 5th ed. Philadelphia: Elsevier; 2019.

White A, Panjabi M. Clinical biomechanics of the spine. 2nd ed. Philadelphia: JB Lippincott; 1990.

Follow-Up and Long-Term Care of Spinal Cord Injuries

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With the COVID-19 pandemic lasting than expected, hospital visits for people with disabilities, including spinal cord injuries, are inevitably limited, requiring new strategies for patient management, discharge planning, and follow-up care. Follow-up care for patients with spinal cord injuries and their families must be a continuous and lifelong process. Once discharged, the person is faced with the reality of a spinal cord injury and its effects on all physical activity, daily life, and family life. A discharge plan, starting in the acute phase and continuing during the rehabilitation phase, should aim to promote and respond to the need for education and adjustment of individuals and the families. People with spinal cord injuries have multiple impairments that can pose safety risks (Shatzer 2012). These educational components include management of the medical and functional aspects of the disability; to be an expert in performing, delivering, and directing care; to recognize the need to seek medical help; to inform themselves about all aspects of equipment needs and use; and to identify, seek support, and cope with stressors of the disability. At the time of discharge, people with spinal cord injuries should adopt new routines and changed lifestyle that reflects the multiple aspects of disability. Some of the most common problems encountered visiting primary care providers include pressure injury wound management, bowel and bladder dysfunctions, shoulder pain, spasticity, and autonomic dysreflexia. Before discharge, patients should be given accessibility information such as an accessible parking, elevator, restroom access (Lee et al. 2020).

One of the main objectives of a follow-up program is to provide services, options and guidelines that help the individuals and families achieve and maintain a high level of health and independence (Sandin and Klaas 2013). Follow-up care should provide a link between a comprehensive care center and the community, including local nursing homes, crisis intervention centers, recreational/vocational programs, independent living centers, and drug abuse programs (Beauregard et al. 2012; Sandin and Klaas 2013). It should have easy access to healthcare providers, including physiatrists, medical consultants, primary care providers, therapists, social workers, psychologists, nurses, and insurance providers. The common goal shared by the follow-up services and these providers is to promote independence and optimal health of the individual. In addition to follow-up on main medical complications of people with spinal cord injuries, counseling and management on nutrition, physical activity, mind-body, sleep, substance abuse, and positive psychology emphasized in lifestyle medicine are needed (Phillips et al. 2020).

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48.1 Clinic Visits

It is advisable to evaluate the patient after discharge in a clinic visit at 1, 3, 6, and 12 months and then once a year. Throughout the follow-up process, rehabilitation team must provide ongoing support for basic medical needs, including drug prescriptions and software and durable equipment. Each time patients visit the follow-up system, the patient must be evaluated by a physiatrist, nurse, and social worker. If necessary, the patient can be evaluated by a physical or occupational therapist, rehabilitation psychologist, rehabilitation counselor, vocational evaluator and counselor, or recreational therapist. Laboratory studies should be performed regularly during the follow-up phase, according to patient need. Special emphasis should be placed on the genitourinary system and other major organ systems that are susceptible to serious complications.

From the first follow-up visit to the clinic, patients with spinal cord injuries should be performed repeated neurological and functional assessments. These parameters are required to establish an accurate diagnosis and prognosis. Diagnosis focuses on neurological level of injury and completeness. Improvement or deterioration can be determined by repetitive, accurate examinations with documentation. The main types of assessments are motor and sensory examinations based on the International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI) and reflex examination.

The motor testing is more reliable and objective than sensory examination. The motor and sensory examinations should include all key muscles and major muscles and pinprick/light touch of the key areas according to ISNCSCI, as well as anal tone and anal sensation including deep anal pressure. In addition, optional examinations include abdominal muscles, the diaphragm, non-key muscles, proprioceptive senses, etc.

Tendon reflexes should be examined and recorded, including the biceps, brachioradialis, triceps, knee and ankle jerks, tibialis posterior reflex, and hip adductor reflex. Plantar response indicating upgoing toe and downing toe or no response should be checked. The bulbocavernosus reflex, anocutaneous reflex, cremasteric reflex, and dartos reflex must also be tested. Basic neurological assessment is supplemented by assessment of spasticity, clonus, pattern movement, or movement dominance.

48.2 Medical and Function Complications in Follow-Up

48.2.1 Genitourinary System

Urinary tract infections are often observed in patients with spinal cord injuries during the follow-up phase of care. Many males return home voiding spontaneously or on intermittent catheterizations. The incidence of infection may increase in individuals using urethral indwelling catheters and external collecting devices. All patients with indwelling catheters are likely to develop bacteriuria within 48 h of insertion. Decisions to treat individuals are based on positive cultures and symptomatology. Patient hygiene, use of clean versus sterile technique, frequency of catheterization, hydration, and evidence of vesicoureteral reflux are other factors influencing the development of bladder infections. Symptoms of autonomic dysreflexia may indicate vesicoureteral reflux, stones, and outlet obstruction.

48.2.2 Gastrointestinal System

Difficulties associated with bowel routines in the follow-up population may be related to changes in diet, level of activity, method and changes of bowel routine, as well as problems with attendant care. Assistance to modify the program according to their new needs is provided by the follow-up system. Once at home, persons with spinal cord injury need to rearrange their lifestyle, eating habits, and activity habits according to the family life, caregivers, work, or school schedule. Individuals must be familiar with all aspects of

the routine, including problem-solving activities. During the follow-up period, individuals may be gradually withdrawn from bowel medications until digital stimulation and increasing abdominal pressure and abdominal massage producing effective results. Gastrointestinal disorders include stress ulcers, gallbladder disease, hiatal hernia, and liver or pancreas disease.

48.2.3 Pressure Injuries

Skin problems are a major follow-up issue affecting not only the individual's health condition but also his or her entire social and psychological health. Pressure injuries disrupt the lifestyle of the person, often delaying or loss of work or school days, requiring repeated and long-term hospitalization.

48.2.4 Musculoskeletal System

Spasticity can help the person with their activities of daily living, but spasticity remains a major problem for patients with spinal cord injuries over a period of years of follow-up. People with severe spasticity may have skin breakdown; sleep disturbances; contractures; and interference with grooming, dressing, positioning, and transfers. Causes of spasticity should be determined because of increased spasticity in the presence of an infection, pressure injuries, or other medical problems including acute abdomen.

During follow-up, heterotopic ossification may be observed. Common etiologies include local trauma, edema, and vascular changes. Early signs and symptoms may include a reduction in range of motion, local swelling, and local heat. Clinicians who suspect heterotopic ossification should also consider the possibility of a deep vein thrombosis, as symptomatology presented is often similar. To manage issues related to heterotopic ossification, initiation or adjustment of the medication, outpatient physical therapy, and emphasis on the importance of range of motion activities for the individual and caregivers are required.

Joint and muscle pain is seen in people with spinal cord injuries and can result from inadequate posture and positioning, improper wheelchair fit, other daily activities, and the degenerative diseases of aging. Assessing a person's position, use of lapboards, proper wheelchair propulsion, and daily activities provide the information needed to respond to this problem. Contractures that occur due to lack of daily range of motion exercise or spasticity make the health and daily activity of the person more complicated. Preventing contractures through proper positioning and monitoring of the prescribed exercise programs should be part of the person's daily living.

48.2.5 Cardiovascular System

Cardiovascular complications, including changes in blood pressure control, such as orthostatic hypotension and autonomic dysreflexia, and dependent edema, are common problems in years of follow-up. Informing the person about preventive measures such as gradual change of position, use of abdominal binder and compression stockings, and maintaining adequate salt and fluid intake helps control blood pressure. Deep vein thrombosis and/or pulmonary emboli are seen infrequently during the follow-up years but appear more serious and life-threatening problem. It may occur even 2–3 years or more after the initial injury. During follow-up, peripheral arterial pulses should be routinely palpated to exclude arterial occlusion.

48.2.6 Respiratory System

Respiratory diseases, including upper and lower respiratory tract infections, are common in patients with tetraplegia and high-level paraplegia. It is important to maintain good lung hygiene by practicing deep breathing and assisted coughing techniques. Recognition of early symptoms and rapid intervention of respiratory tract infection should be strongly encouraged.

48.2.7 Sexual Function

Sexual and reproductive problems are a common concern for spinal cord injury patients in the years of follow-up. These problems become more important when people return home or in an environment that facilitates building relationships. Concerns include fertility, performance issues, and sexual adjustment to the different components of disability including bladder and bowel routines. Women with spinal cord injuries should receive adequate and appropriate contraceptive information and advice. Providing instructions on breast and testicular examinations, emphasizing the need for annual pelvic examinations, and providing information about sexually transmitted diseases are important roles in maintaining good health.

48.2.8 Medication Control and Polypharmacy

Patients with spinal cord injury should continue to administer medication, including medication for spasticity, pain, bladder, or bowel. Patients with spinal cord injuries should understand the purpose, action, and side effects of the drugs and should immediately report suspected or adverse reactions. The role of the physician in drug management should be to assess the effectiveness of the treatment regimen and, if necessary, correct or modify it. Close supervision of drug therapy and prevention of overmedication are essential.

The use of multiple medications is common in treating complications following spinal cord injury. Patients with spinal cord injuries often require long-term health management for secondary complications and are at increased risk for several chronic comorbidities such as diabetes and heart disease over the course of their lives. Polypharmacy is associated with numerous negative health consequences, including an increased risk of falls, adverse drug events, hospitalization, mortality, declines in functional status, and impaired cognition (Hand et al. 2018). The most common medication-related problems are ineffective medications, adverse drug effects, and underusing and overdosing (Patel et al. 2017). Polypharmacy often has overlapping pharmacological mechanisms or targets, which increases the risk of drug-related problems.

48.2.9 Psychosocial Problems

In order to cope with the psychosocial reality and complexity of disability adaptation, continuous comprehensive support, the use of peer support groups, and psychological counseling are required (Yurgelun-Todd et al. 2007). Helping patients and their families develop appropriate coping and problem-solving skills can also help reduce the occurrence of maladaptive behaviors such as substance abuse.

48.2.10 Functional Aspects

The mobility problem of the patient with spinal cord injury during follow-up is especially related to wheelchair usage and ambulation training. The patient may need additional evaluation of equipment or other mobility issues. Throughout the years of follow-up, the equipment will need to be repaired and may need to be evaluated for new equipment as the person's functional condition changes.

48.3 Telerehabilitation

The use of remote assessment and intervention technologies in rehabilitation has grown exponentially, paving the way for the advancement of telerehabilitation (Galea 2019). Telehealth and telerehabilitation or contactless care for people with disabilities, including spinal cord injuries, are of particular importance in this Covid-19 pandemic. Telerehabilitation has been used to shorten hospital stay, facilitate home discharge, and educate and support patients and caregivers (Nelson et al. 2017; Nix and Comans 2017; Tsavourelou et al. 2016). It has been shown that telerehabilitation strengthens the patient-provider connection by (1) enhancing the knowledge of the patients

and their contextual factors, (2) facilitating the exchange of information and education, and (3) establishing shared goal setting and action planning (Galea 2019; Wang et al. 2016).

References

Beauregard L, Guindon A, Noreau L, et al. Community needs of people living with spinal cord injury and their family. Top Spinal Cord Inj Rehabil. 2012;18:122–5.

Galea MD. Telemedicine in Rehabilitation. Phys Med Rehabil Clin N Am. 2019;30:473–83.

Hand BN, Krause JS, Simpson KN. Polypharmacy and adverse drug events among propensity score matched privately insured persons with and without spinal cord injury. Spinal Cord. 2018;56:591–7.

Lee J, Varghese J, Brooks R, et al. A primary care providers's guide to accessibility after spinal cord injury. Top Spinal Cord Rehabil. 2020;26:79–84.

Nelson M, Bourke M, Crossley K, et al. Telerehabilitation versus traditional care following total hip replacement: a randomized controlled trial protocol. JMIR Res Protoc. 2017;6:e34.

Nix J, Comans T. Home quick - occupational therapy home visits using mHealth, to facilitate discharge from acute admission back to the community. Int J Telerehabil. 2017;9:47–54.

Patel T, Milligan J, Lee J. Medication-related problems in individuals with spinal cord injury in a primary care-based clinic. J Spinal Cord Med. 2017;40:54–61.

Phillips EM, Frates EP, Park DJ. Lifestyle Medicine. Phys Med Rehabil Clin N Am. 2020;31:515–26.

Sandin KJ, Klaas SJ. Assessment and evaluation of primary prevention in spinal cord injury. Top Spinal Cord Inj Rehabil. 2013;19:9–14.

Shatzer M. Patient safety in the rehabilitation of the adult with a spinal cord injury. Phys Med Rehabil Clin N Am. 2012;23:371–5.

Tsavourelou A, Stylianides N, Papadopoulos A, et al. Telerehabilitation solution conceptual paper for community-based exercise rehabilitation of patients discharged after critical illness. Int J Telerehabil. 2016;8:61–70.

Wang S, Blazer D, Hoenig H. Can eHealth technology enhance the patient-provider relationship in rehabilitation? Arch Phys Med Rehabil. 2016;97:1403–6.

Yurgelun-Todd DA, Sava S, Dahlgren MK. Mood disorders. Neuroimaging Clin N Am. 2007;17:511–21.

Recommended Additional Reading

Bromley I. Tetraplegia and paraplegia: a guide for physiotherapists. New York: Churchill Livingstone; 1976.

Buchanan LE, Nawoczenski DA, editors. Spinal cord injury-concepts and management approaches. Baltimore, MD: Williams & Wilkins; 1987.

Cardenas DD, Hooton TM, editors. Medical complications in physical medicine and rehabilitation. New York: Demos Medical Publishing, LLC; 2015.

Cardenas DD, Dalal K, editors. Spinal cord injury rehabilitation. Physical medicine and rehabilitation clinics of North America. Philadelphia, PA: Elsevier; 2014.

Chhabra HS, editor. ISCoS textbook on comprehensive management of spinal cord injuries. Wolters Kluwer: New Delhi; 2015.

Green D, editor. Medical management of long-term disability. 2nd ed. Boston, MA: Butterworth-Heinemann; 1996.

Harvey L. Management of spinal cord injuries: a guide for physiotherapists. Philadelphia, PA: Churchill Livingstone; 2008.

Rudd MA, Hough S, Wegener ST, et al., editors. Practical psychology in medical rehabilitation. Switzerland: Springer; 2017.

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