CHAPTER ONE

Understanding Spinal Cord Injury and Advances in Recovery

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In a moment, your life is completely changed. Yes, life will go on; yes, you can still be functional; but nothing will ever be the same again. Understanding that fact will be the most difficult lesson you will ever learn. Nothing is easy anymore, the simple tasks you used to do seem like they are impossible now. In rehab, you will learn about your bladder, bowels, skin, and nutrition. You will learn how to be functional in a wheelchair, maybe even how to be independent. But at the end of the day, it all comes down to one question—do you want to go on living? As you ponder that question, think about family, friends, a hug from your son or daughter, a kiss from your lover, sunsets, your favorite food. Whatever you need to think about to choose life—just do it. You'll have all the time in the world to learn about SCI once you've chosen life.
Tara (T12 SCI)

The multidisciplinary spinal cord injury (SCI) rehabilitation team includes physicians who specialize in SCI medicine. This specialty depends on a thorough knowledge of spinal cord neuroanatomy and spine anatomy that endows an understanding of the neurological sequelae associated with SCI and spinal cord disease. SCI physicians are responsible for managing medical and rehabilitation care. They must know how to prognosticate the degree to which a patient is likely to recover from complete and incomplete injuries and are responsible for prescribing medications or procedures to manage problems related to SCI that may affect body systems, such as pain, bowel and bladder symptoms, spinal stability, spasticity, and autonomic dysreflexia.

The physician coordinates patient care with the rehabilitation team through discharge to the home or to an alternate living environment. This involves working closely with physical, occupational, speech, and respiratory therapists; nurses; psychologists; urologists; wheelchair seating and orthotic specialists; social service representatives; and case managers. Social service and case management representatives provide the skilled investigation of reimbursement for care and equipment during the patient's transition into the home, community, and workplace environments. This chapter supplies the foundation of knowledge about SCI from a historical and epidemiological aspect. In addition, it presents the anatomy of the spinal cord and defines how to diagnose complete and incomplete injuries. Algorithms for predicting outcomes on the basis of patient presentation early after injury are provided. Finally, an overview of pharmaceutical and surgical clinical trials to promote recovery are discussed.

HISTORY AND EPIDEMIOLOGY

The earliest reference to SCI was approximately 5000 years ago by an unknown Egyptian physician in the so-called Edwin Smith Papyrus as "an ailment not to be treated."[1] Only during the past half century have individuals with SCI been given hope for survival. Before World War II, life expectancy for a person with SCI was rarely greater than 2 years; most succumbed to septic infections, renal failure, and pressure ulcers. With the advent of antibiotics and improved therapeutic techniques, remarkable progress has been made toward effectively preventing and managing the numerous medical complications of SCI. Improved acute-care management and early provision of comprehensive rehabilitation services have helped individuals with SCI maximize their self-care and mobility skills, which usually permits them to reintegrate into their communities. As the annual incidence of SCI has remained unchanged in the United States, with decreased mortality each year after injury, there has been a gradual increase in the prevalence and the importance of this condition as a health issue for society has occurred.

Traumatic SCI has an incidence of approximately 11,000 patients per year in the United States with a prevalence of 250,000,[2] thus affecting a small but significant portion of the population over the years. Although the overall incidence has remained constant in the last few decades, the epidemiology has changed (Box 1-1). Motor vehicle crashes (MVC) are still the primary cause of SCI, followed by falls and violence-related causes.[2] The proportion of injuries related to sports has decreased over time, whereas the proportion of injuries from falls has increased. Acts of violence caused 13% of SCI before 1980, and peaked between 1990 and 1999 at 25% before declining to 14% since 2000. The mean age at traumatic SCI has increased to 37.6 years, although the majority of injuries still occur in 16- to 30-year-olds.[2-4] The percentage of people older than 60 years has increased from 5% before 1980 to 11% among injuries since 2000. The etiology of the injury differs in the various age groups, with violence and sports-related injuries more common in the younger individuals and falls higher in the older population.

Males are predominately affected, with African Americans and Hispanics disproportionally affected relative to their percentages in the general population.[2-4] There is a greater incidence of injuries in the warmer months and on weekend days. There has been a recent trend toward an increased number of incomplete lesions, possibly as a result of changes in etiology (i.e., falls are more likely to cause an incomplete injury and violence a complete injury), improved treatment at the site of injury by emergency medical technicians, and subsequent immediate medical care. At the time of injury, more than 50% of people with SCI are at least high school graduates and employed. The majority are single at the time of injury, with fewer than one third being married (30%).[4] Approximately one half of all traumatic SCIs are cervical lesions, and one third are thoracic. The most common neurological level of injury (NLI) is C5, followed by C4 and then C6 in the cervical region, and T12 is the most common level of paraplegia[3,4] (Box 1-2).

BOX 1-1 | Epidemiology of Traumatic Spinal Cord Injury

Incidence: 11,000/year
Prevalence: 250,000
Average age: 37.6 years
Sex: 80% male
Ethnicity: Disproportionally African Americans and Hispanics
Etiology: Motor vehicle crashes (MVCs) (48%), falls (23%), violence (14%), sports (9%), other (6%)

Adapted from Spinal cord injury: facts and figures at a glance, *J Spinal Cord Med* 28:379-380, 2005.

BOX 1-2 | Percentage of Injuries by ASIA Classification

Incomplete tetraplegia (34.5%)
Complete paraplegia (23.1%)
Complete tetraplegia (18.4%)
Incomplete paraplegia (17.5%)

Adapted from Spinal cord injury: facts and figures at a glance, *J Spinal Cord Med* 28:379-380, 2005.

ANATOMY

To understand SCI and its treatment, it is imperative to understand the basic anatomy of the vertebral column, the spinal cord, coverings, the spinal cord and associated nerves, its vascular supply, the spinal tracts with the spinal cord, and the autonomic nervous system.

Vertebral Column

The vertebral column (Figure 1-1) is composed of seven cervical, twelve thoracic, five lumbar, five sacral, and four coccygeal vertebrae. Each vertebrae consists of a body and an arch. The arch or lamina is connected to the vertebral body by the pedicle. Spinous processes project posteriorly from the lamina and the transverse processes project laterally (Figure 1-2). Each vertebra articulates with the vertebrae superiorly and inferiorly by the superior and inferior articular process. The spinal cord is then protected within the vertebral foramen, which is formed by the vertebral body and arch.

The intervertebral discs separate each vertebra and constitute 20% to 33% of the vertebral column. The disc is composed of the nucleus pulposus, which is the central aspect and composed of fine fibrous strands in a mucoprotein gel of mucopolysaccharides. The water content is 70% to 90% and decreases with age. In the lumbar spine the nucleus lies more posterior than in the cervical spine. The annulus fibrosis forms the outer boundary of the disc, and it is composed of fibrous tissue in concentric laminated bands, which is arranged in a helix. The fibers in each adjacent band run in opposite directions. The peripheral bands attach to the vertebral body and are called Sharpey's fibers, which form a much stronger attachment than those fibers attached centrally.

The ligaments function to stabilize the vertebral column (Figure 1-3). The anterior longitudinal ligament (ALL) connects the anterior aspect of the vertebral bodies, and the posterior longitudinal ligament (PLL) attaches the posterior aspect of the vertebral bodies. These ligaments act to limit flexion and extension, respectively. Both the ALL and PLL are thicker in the thoracic region. Unlike the ALL, the PLL is connected to the intervertebral disc. The ligamenta flava extend from the anterior inferior border of the laminae above to the posterosuperior borders of the laminae below, thereby connecting the borders of adjacent lamina from the second cervical vertebrae to the first sacral vertebrae.

The interspinous ligaments connect adjacent spines. They are narrow and longer in the thoracic region and wider and thicker in the lumbar region and only somewhat developed in the cervical region. The supraspinous ligament originates in the ligamentum nuchae and is attached to the tip of the spinous processes down to the sacrum. These are thicker and broader in the lumbar region than in the thoracic region. Intertransverse ligaments pass between the transverse processes in the thoracic region and connect with the deep muscles in the back. The capsular ligaments attach the adjacent articular processes. These are more taut in the thoracic and lumbar regions.

Coverings of the Spinal Cord

The coverings (i.e., meninges) of the spinal cord include the dura mater, arachnoid membrane, and pia mater (Figure 1-4). The spinal dura is located between the meningeal layer of the dura and the vertebra and is single layered, unlike the cranial dura. The venous plexuses are located in this space and are used clinically for the administration of epidural anesthesia. Caudally, the spinal dura ends at the level of the second sacral vertebra, where the dura becomes a thin extension (i.e., the coccygeal ligament or filum terminale externum) and serves to anchor the spinal dura to the base of the vertebral canal. The arachnoid membrane loosely invests the spinal cord and is connected to the dura by connective tissue trabeculae. The arachnoid extends from the foramen magnum and surrounds the cauda equina (i.e., nerve roots of the spinal nerves caudal to the second lumbar vertebra). The subarachnoid space contains cerebrospinal fluid (CSF). The spinal pia is a vascular membrane that projects into the ventral fissure of the spinal cord. At intervals, dentate ligaments (i.e., ligaments of pial tissue) extend from the lateral surfaces of the spinal cord, serving to anchor the spinal cord to the arachnoid and through it to the dura. The pia mater extends from the cranial pia mater to the filum terminale that anchors the spinal cord to the dura at the level of the second sacral vertebra.

Spinal Cord

The spinal cord is a cylindrical structure that extends from the medulla oblongata rostrally and ends at the lower border of the first lumbar vertebra (Figure 1-5). At the caudal end, the spinal cord is conical and is known as the conus medullaris. A filament extending from the conus medullaris is called the filum terminale. This filament is enclosed in pia and consists of glial cells, ependymal cells, and astrocytes. The coccygeal ligament is an extension of spinal dura. This ligament surrounds the filum terminale internum of the spinal cord and attaches to the coccyx to anchor the spinal cord.

The spinal cord initially occupies the entire length of the vertebral canal. After the third month of life, however, the spinal cord lengthens at a slower rate than the vertebral column. By adulthood, the spinal cord occupies only the upper two thirds of the vertebral column, with its caudal end located at the level of

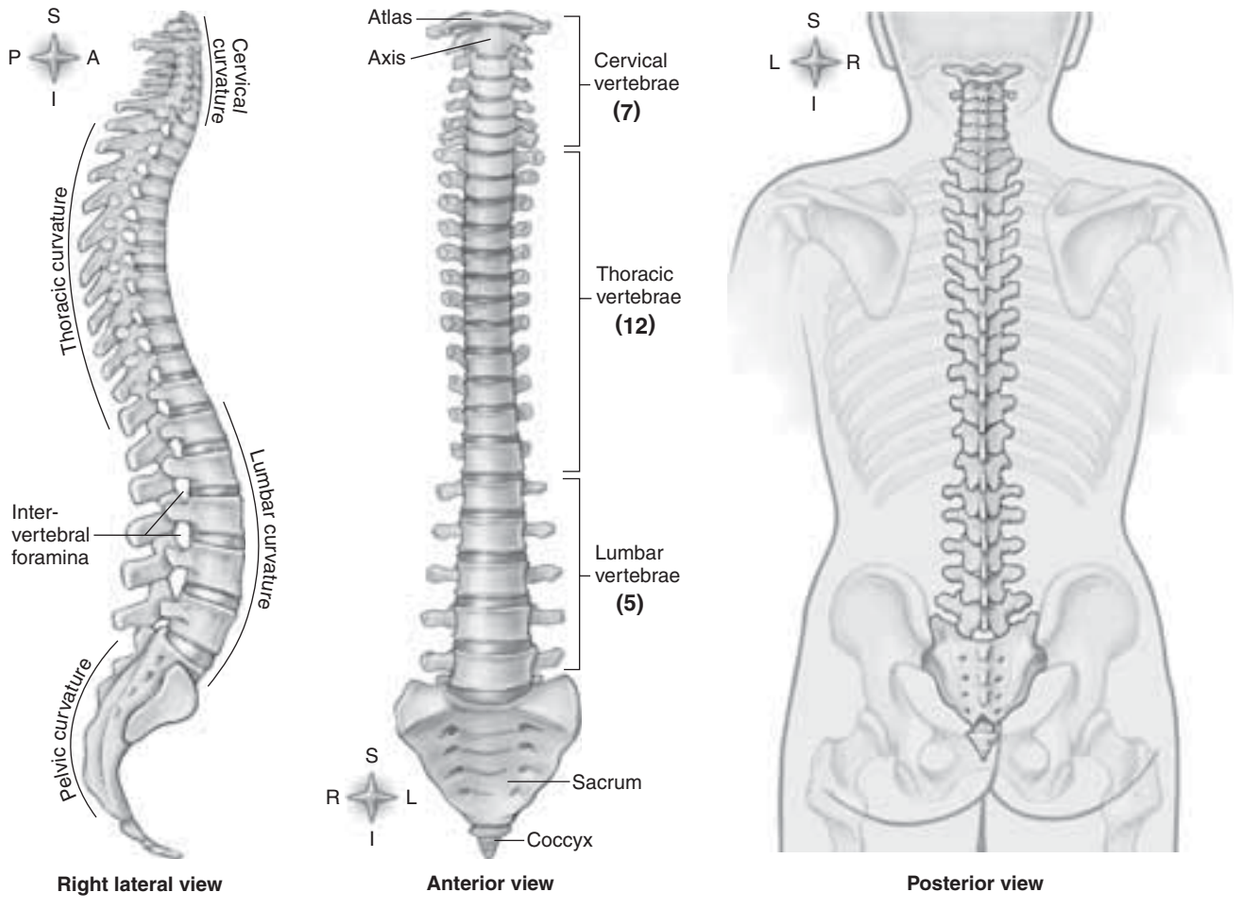


FIGURE 1-1 The vertebral column (three views) (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 8-13, p. 233.)

the first lumbar vertebra. For this reason, it is necessary for the lumbar and sacral nerve roots to descend some distance within the vertebral canal to exit from their respective intervertebral foramina. The filum terminale is surrounded by lumbosacral nerve roots that resemble a horse's tail, and it is called the cauda equina (see Figure 1-5).

The lumbar cistern extends from the caudal end of the spinal cord at the L2 vertebra to the second sacral vertebra. The subarachnoid space is widest at this site and contains the filum terminale internum and nerve roots of the cauda equina. Because of the large size of the subarachnoid space and relative absence of neural structures, this space is most suitable for the withdrawal of CSF by lumbar puncture (LP). The LP is usually preformed between the third and fourth lumbar vertebra (L3 to L4).

Spinal Nerves

Thirty-one pairs of spinal nerves emerge from the spinal cord and at each level of the spinal cord and exit through the intervertebral foramina. The 31 segments include 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal pairs of spinal nerves. In the thoracic level and below the spinal cord, nerves exit through the intervertebral foramina just caudal to the vertebra of the same name. In the cervical region, however, these nerves exit through the intervertebral foramina just rostral to the vertebra of the same name. This is because there are eight cervical nerve roots and only seven cervical vertebrae; the eighth cervical spinal nerve exits through the intervertebral foramen just rostral to the first thoracic vertebra.

Each spinal nerve consists of a dorsal root, which contains afferent fibers, and a ventral root, which contains efferent fibers. The dorsal root is absent in the first cervical and coccygeal nerves. The dorsal and ventral roots enter the intervertebral foramen, but because of the length difference between the spinal cord and the vertebral column, cervical and upper thoracic roots run at right angles to the spinal cord, whereas lower thoracic and more caudal roots are increasingly oblique. Within the intervertebral foramen is the dorsal root ganglion.

The dorsal and ventral roots then join to form the common spinal nerve trunk (see Figures 1-4, *B* and 1-5). Usually the following four branches (i.e., rami) arise from the common spinal nerve trunk: (1) the dorsal ramus, which innervates the muscles and skin of the back; (2) the ventral ramus, which innervates the ventrolateral part of the body wall and all limbs; (3) the meningeal branch, formed by several small branches arising from the common nerve trunk and the ramus communicantes, which re-enters the intervertebral foramen and innervates the meninges, blood vessels, and vertebral column; and (4) the ramus communicans, which consists of the white and gray portions. The white ramus

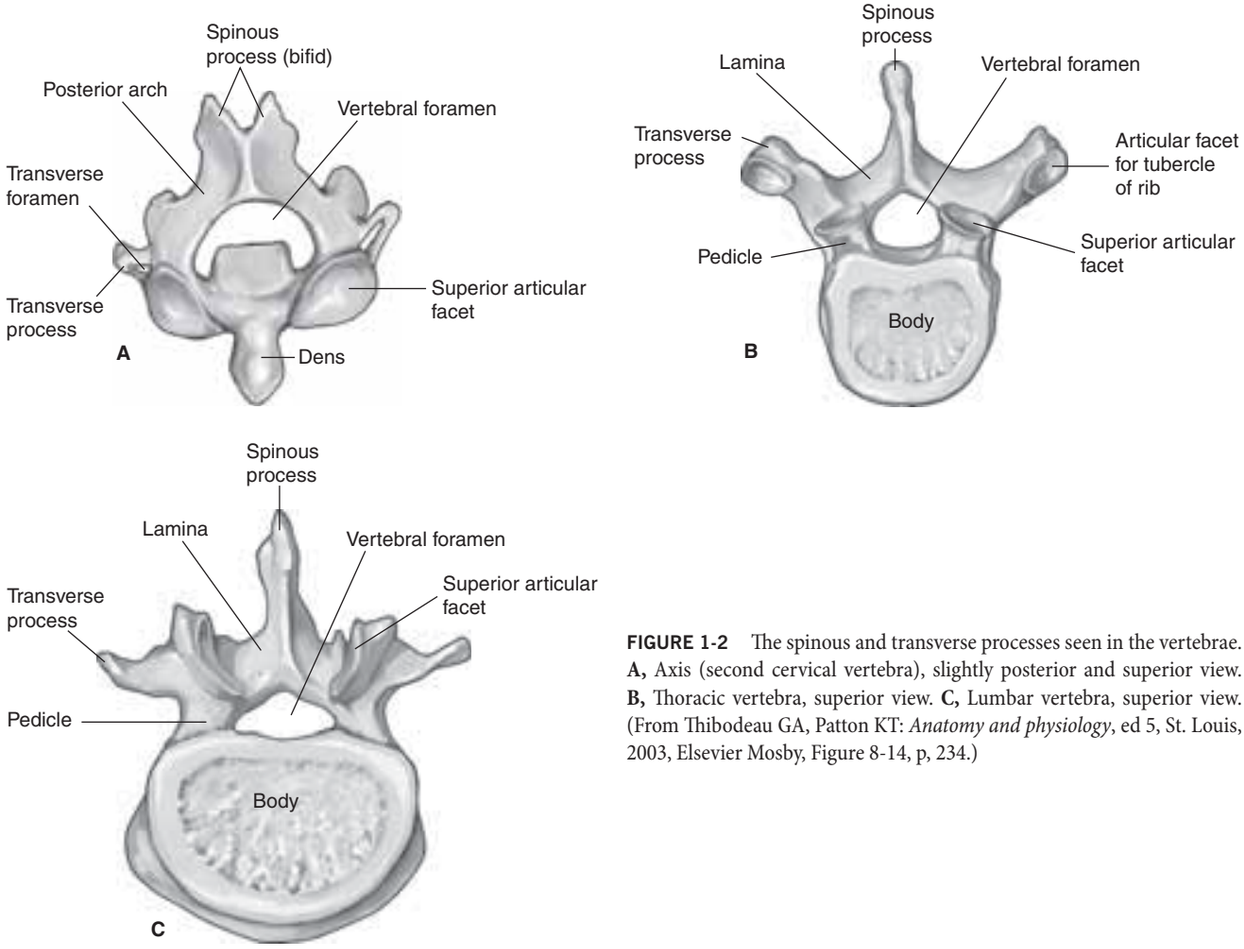


FIGURE 1-2 The spinous and transverse processes seen in the vertebrae. **A,** Axis (second cervical vertebra), slightly posterior and superior view. **B,** Thoracic vertebra, superior view. **C,** Lumbar vertebra, superior view. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 8-14, p, 234.)

communicans carries myelinated preganglionic fibers from the spinal cord to the sympathetic ganglion, whereas the gray ramus communicans contains the unmyelinated postganglionic fibers.[5]

The spinal cord has two enlargements; cervical and lumbar (see Figure 1-5). The cervical enlargement includes the C5 through T1 nerve roots to form the brachial plexus, which innervates the upper limbs. The lumbar plexus, comprising nerve roots L1 to L4, and the lumbosacral plexus, consisting of nerve roots from L4 to S2, emerge from the lumbar enlargement. The lumbar plexus innervates the lower limbs. The sacral spinal nerves emerge from the conus medullaris and contain parasympathetic and somatic motor fibers innervating the muscles of the bladder wall and external sphincter, respectively.

Vascular Supply

The spinal cord receives its blood supply from one anterior and two posterior spinal arteries and anterior and posterior radicular arteries. The anterior spinal artery arises in the upper cervical region and is formed by the union of two small branches of the vertebral arteries. The anterior spinal artery supplies the anterior two thirds of the spinal cord, including the gray matter and anterior and anterolateral white matter. It travels in the ventral median fissure for the entire length of the spinal cord. The anterior spinal artery varies in diameter according to its proximity to a major radicular artery. It usually is narrowest in the T4 to T8 region of the spinal cord. There are two posterior spinal arteries, which originate as a small branch of either the vertebral artery or the posterior inferior cerebellar artery. The posterior spinal arteries supply the posterior one third of the spinal cord, consisting of posterolateral and posterior white matter of the spinal cord.

The blood supply from the anterior and posterior arteries is sufficient for the upper cervical segments. Segmental arteries that arise from the aorta supply the anterior and posterior spinal arteries in the thoracic and lumbar regions. The radicular arteries supply the remaining segments of the spinal cord. These arteries arise from the vertebral, cervical, intercostal, lumbar, and sacral arteries. They have anterior and posterior divisions that supply the vertebrae, meninges, and spinal arteries. The posterior arteries are joined by communicating vessels except in the area of the conus medullaris. The major radicular artery that supplies the lumbosacral enlargement of the spinal cord is known as the artery of Adamkiewicz. It arises from the left intercostal or lumbar artery at the level of T6

to L3 and provides the main blood supply to the lower two thirds of the spinal cord. There are fewer radicular arteries supplying the midthoracic region of the spinal cord; they are smaller in diameter and therefore create a watershed zone of the spinal cord at this level. In clinical situations where there is low blood flow to the spinal cord, this level of the cord is most affected at the T4 to T6 level.

Spinal Tracts

The internal structure of the spinal cord is such that a transverse section of the spinal cord reveals a butterfly-shaped central gray matter surrounded by white matter (see Figure 1-5). The gray matter of the spinal cord contains cell bodies and primarily neurons, dendrites, and myelinated and unmyelinated axons, which are either exiting from the gray matter to the white matter or projecting from the white matter to innervate neurons located in the gray matter. Autonomic neurons are located laterally and exit by the ventral root and innervate smooth muscle. Lower motor neurons are located ventrally, exit by the ventral roots, and innervate striated muscle. The white matter consists of ascending and descending bundles of myelinated and unmyelinated axons (i.e., tracts or fasciculi). The ascending pathways relay sensory information **to** the brain (Figure 1-6), whereas the descending pathways relay motor information **from** the brain (Figure 1-7).

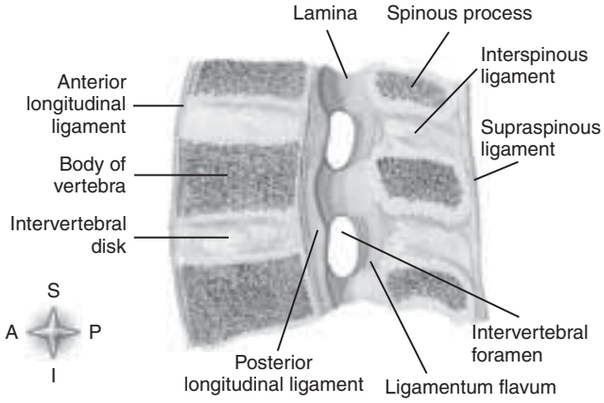


FIGURE 1-3 Vertebrae and their ligaments. Sagittal section of two lumbar vertebrae and their ligaments. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 9-11, p, 266.)

Ascending Pathways

Sensory tracts or ascending pathways are composed of bundles of axons that are continuations of the peripheral sensory nerves whose cell bodies are located in the dorsal root ganglion and ascend toward the brainstem (Figure 1-6). The lateral spinothalamic tract transmits pain and temperature sensation. Receptors for pain and temperature travel from the dermis and epidermis of the skin toward the spinal cord and synapse in the dorsal horn of the gray matter. The fibers cross over within one or two vertebral segments and then travel in the lateral spinothalamic tract and ascend to the ventral posterolateral nucleus of the thalamus. The fibers then ascend in the internal capsule to reach the postcentral gyrus, which is the primary somatic sensory area of the brain.

The nerve fibers of the receptors in the dermis of the skin for pressure and light touch enter the cord in the same fashion; however, on entering, the axons pass into the ipsilateral dorsal white column and bifurcate. One branch immediately enters the dorsal horn gray matter, synapses, and crosses over within one or two segments, and the other branch remains ipsilateral and ascends in the dorsal column for as many as 10 spinal segments. The ipsilateral branch ultimately enters the dorsal horn, synapses, and crosses over to join the other branch in the ventral white column. This bundle of fibers forms the ventral spinothalamic tract. These axons travel in the same pathway as the lateral tract to reach the post central gyrus, which interprets these sensations.

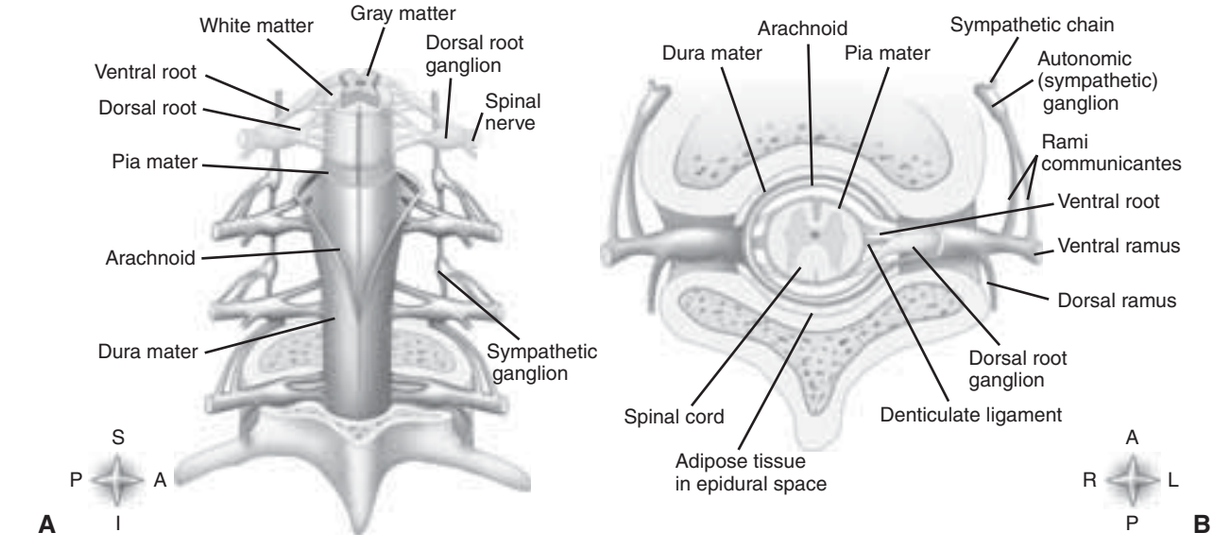


FIGURE 1-4 **A,** The meninges, the inner coverings of the spinal cord, are composed of three distinct layers. The dura mater extends to cover the spinal nerve roots and nerves and sheaths the arachnoid membrane and the pia mater. **B,** Rami arising from the common spinal nerve trunk (dorsal, ventral, and communicantes). (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 13-3, p. 377.)

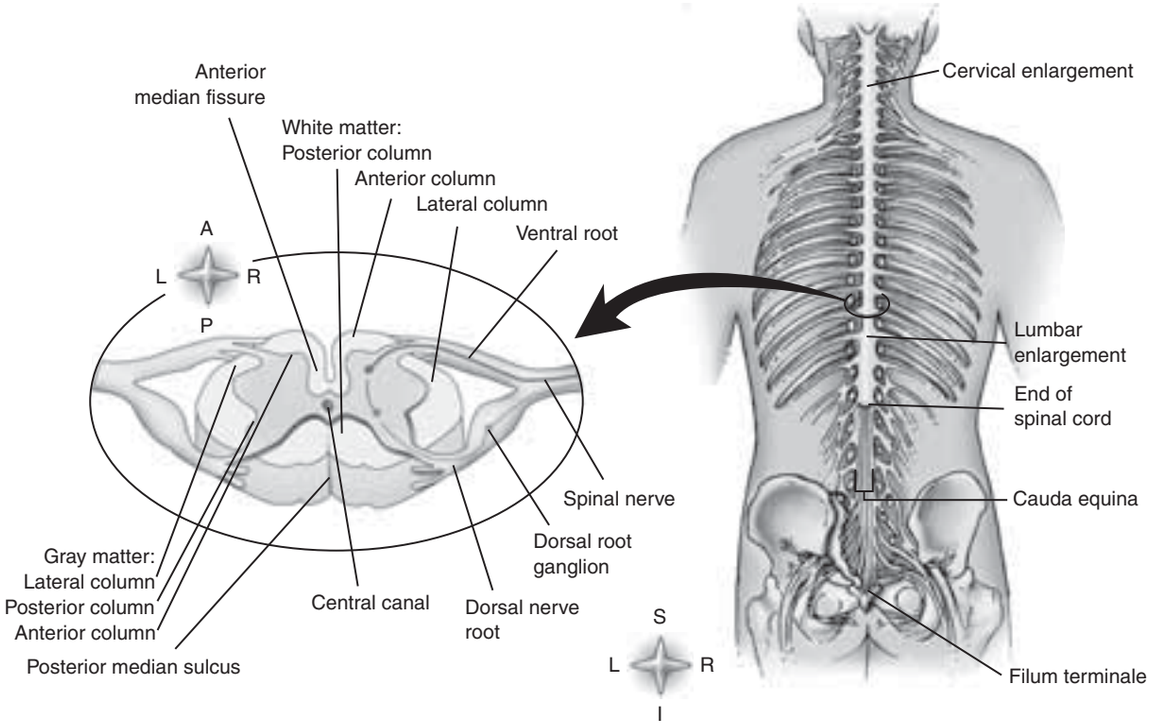


FIGURE 1-5 Spinal cord. *Inset,* A transverse section of the spinal cord in the broader view. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 13-6, p. 381.)

The posterior columns transmit three different sensations: proprioception (conscious awareness of movement), fine touch, and vibration sense. The receptors for proprioception are located in muscles, tendons, and joints, whereas those for fine touch and vibration are located in the dermis. Their nerve fibers reach the dorsal root ganglion in the same manner as the above tracts. Once the axons enter the spinal cord they immediately pass into the ipsilateral dorsal white columns and ascend to the medulla. Axons that enter the cord at the sacral and lumbar levels are situated in the medial part of the dorsal column, called the fasciculus gracilis, and convey information from the lower part of the body. Those axons that enter at the thoracic and cervical levels are situated in the lateral part of the column, termed the fasciculus cuneatus, and convey information from the upper part of the body. Both axons of each fasciculus synapse in the medulla and form a bundle termed the medial lemniscus. These axons also ascend by the same pathway as the above tract to reach the postcentral gyrus.

The cerebellum is the control center for the coordination of voluntary muscle activity, equilibrium, and muscle tone. The spinocerebellar pathways supply information regarding the condition of the muscles, the amount of tone, and the position of the body by unconscious proprioceptive fibers, whose receptors are found in joints, tendons, and muscles. This enables an individual to walk and perform other complex acts subconsciously without having to think about which joints are flexed and extended.

Descending Pathways

The lateral corticospinal tract is the main tract for voluntary muscle activity. Its origin is the precentral gyrus of the frontal lobe of the brain, where large pyramidal-shaped cell bodies are located (Figure 1-7). Their axons exit the cortex and descend through the internal capsule to the medulla oblongata. At this point approximately 80% to 90% of the axons cross at the pyramidal decussation to the contralateral side of the medulla and descend in the lateral white columns of the spinal cord in the lateral corticospinal tract. At each level of the spinal cord the axons from the lateral tract peel off and enter the gray matter of the ventral horn and synapse with secondary neurons. The 10% to 20% of uncrossed axons that continue down on the same side of the cord travel in the ventral corticospinal tract. The axons of the ventral tract then cross over at the corresponding level of muscles that it innervates. Both tracts travel from the precentral gyrus to the ventral horn as a single uninterrupted neuron and are termed upper motor neurons (UMN), whereas the secondary neurons that they synapse on are termed lower motor neurons (LMN). Injury to the UMN versus the LMN presents with different effects on the muscles they innervate.

Autonomic Nervous System

The autonomic nervous system regulates involuntary functions such as blood pressure, heart rate, respiration, digestion, glandular secretion, reproduction, and body temperature. The autonomic nervous system is divided into three divisions: sympathetic, parasympathetic, and enteric. Preganglionic neurons of the sympathetic nervous system originate in the intermediolateral cell column from the first thoracic to second lumbar (T1 to L2) area. Generally, the axons of these preganglionic neurons exit the spinal cord through the ventral roots and enter the main trunk of the spinal nerve. The axons of the sympathetic preganglionic neurons exit through the white ramus and reach one of the sympathetic ganglia to ultimately innervate its target organ.

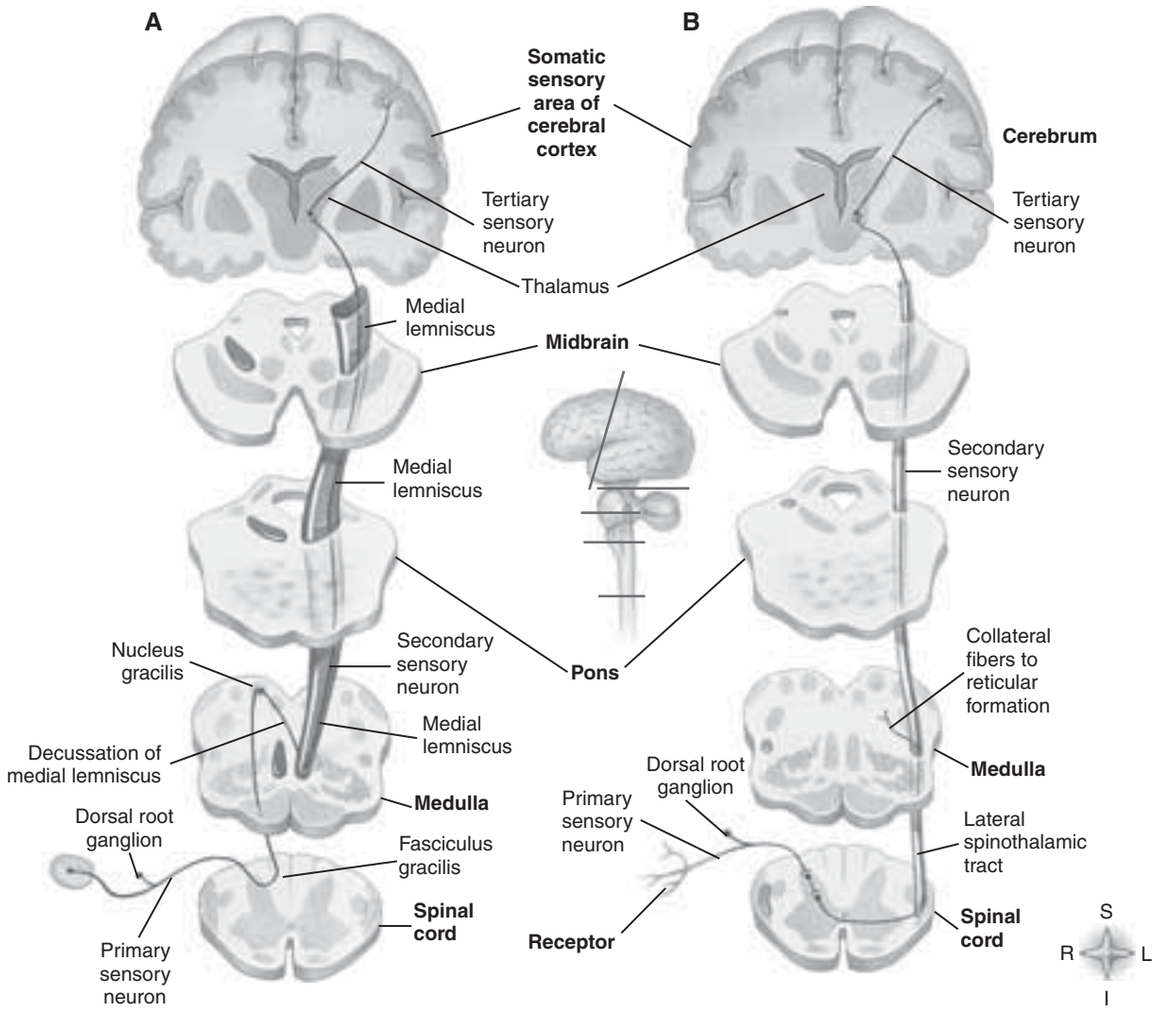


FIGURE 1-6 Examples of somatic sensory ascending pathways. **A,** A pathway of the medial lemniscal system that conducts information about discriminating touch and kinesthesia. **B,** A spinothalamic pathway that conducts information about pain and temperature. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 13-22, p. 399.)

The sympathetic division of the autonomic nervous system is activated in stressful situations, resulting in increases in heart rate, blood pressure, blood flow in the skeletal muscles, blood sugar, and pupillary dilatation. All of these responses prepare the individual for fight or flight. For example, an increase in blood flow in the skeletal muscles will help in running away from the site of danger (i.e., flight), an increase in heart rate and blood pressure will help in better perfusion of various body organs, an increase in blood sugar will provide energy, and pupillary dilatation will provide for better vision under these circumstances.[5]

For the parasympathetic nervous system, the preganglionic neurons arise from the brainstem, which includes the midbrain, pons and medulla oblongata, and the sacral region (S2 to S4) of the spinal cord, therefore often referred to as the craniosacral division. From the spinal cord, the axons exit through the ventral roots, travel through pelvic nerves, and synapse on postganglionic neurons that are located close to or within the organs being innervated. The postganglionic parasympathetic nerve fibers are very short compared with the sympathetic postganglionic nerve fibers.

Activation of the parasympathetic division of the autonomic nervous system results in conservation and restoration of body energy. For example, decreases in heart rate by the parasympathetic system will also decrease the demand for energy while the increased activity of the gastrointestinal (GI) system will promote restoration of body energy. The effects of parasympathetic activation are localized and last for a short time.

The enteric nervous system consists of neurons in the wall of the gut (i.e., intrinsic innervation), which regulates GI motility and secretion. The GI system is also controlled by sympathetic and parasympathetic innervation (i.e., extrinsic innervation). The extrinsic system can override the intrinsic system under certain conditions.

CLINICAL ASSESSMENT OF SPINAL CORD INJURY

The most accurate way to assess SCI is to perform a standardized physical examination based on the *International Standards for Neurological Classification of Spinal Cord Injury*,[6,7] previously referred to as the American Spinal Injury Association (ASIA) guidelines.

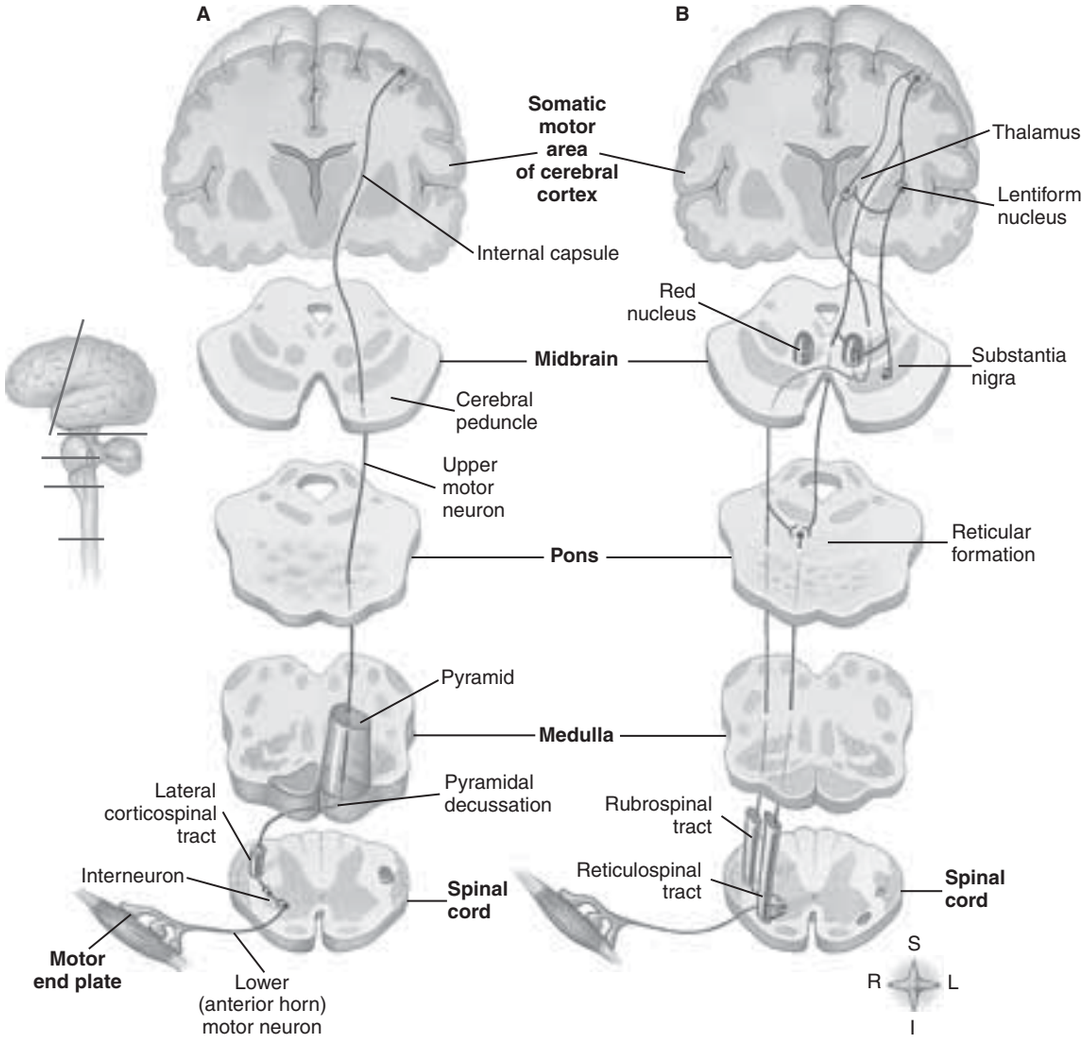


FIGURE 1-7 Examples of somatic motor descending pathways. **A,** A pyramidal pathway, through the lateral corticospinal tract. **B,** Extrapyramidal pathways, through the rubrospinal and reticulospinal tracts. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 5, St. Louis, 2003, Elsevier Mosby, Figure 13-22, p. 401.)

This allows the examiner to determine the motor, sensory, and neurological level of injury (NLI) and the degree of completeness of the injury and to determine the ASIA Impairment Scale (AIS).

The neurologic examination of a person with SCI has two main components: the sensory and motor, with certain required and optional elements. The required elements include determination of the sensory, motor, and neurological levels, generation of sensory and motor scores, and determination of the completeness of the injury. Also required is a rectal examination that tests for voluntary anal contraction and anal sensation. This information should be recorded on the standardized neurological flow sheet (see Figure 1-8), which can be included in the medical records. The optional elements involve aspects of the neurological examination that may better describe the patient's clinical condition but that are not used for numerical scoring and include testing of additional muscles, proprioception, and reflexes. To learn how to use the international standards, an instructional manual and video tapes are available through the ASIA office in Atlanta, Georgia. These standards provide basic definitions of the most common terms used by clinicians in the assessment of SCI and describe the neurological examination.

The international standards are the most valid and reliable classification to assess SCI and are used by the Model System Spinal Cord Injury database. This database, which is maintained by specially designated SCI model system centers in the United States, tracks information regarding the injury, functional, and behavioral status from the time of injury through follow-up over the years. Key terms frequently used in the treatment of SCI are defined in Box 1-3.

Twenty-eight key dermatomes are used for the sensory examination (i.e., C2 to S4-5), each separately tested for pinprick with a safety pin and light touch with a cotton-tipped applicator (Figure 1-8). A numerical scale is used, with 0 representing absent sensation, 1 representing impaired sensation, which is defined as partial or altered sensation including hyperesthesia, and 2 representing normal sensation, with the face being the normal reference point (Figure 1-8).

BOX 1-3 | Key Terms Important to the Assessment of Spinal Cord Injury

Key muscle groups: Ten muscle groups that are tested as part of the standardized spinal cord examination.

Root Level	Muscle Group
C5	Elbow flexors
C6	Wrist flexors
C7	Elbow extensors
C8	Long finger flexors
T1	Small finger abductors
L2	Hip flexors
L3	Knee flexors
L4	Ankle dorsiflexors
L5	Long toe extensor
S1	Ankle plantar flexors

Motor level: The most caudal key muscle group that is graded 3/5 or greater with the segments cephalad graded normal (5/5) strength.
Motor index score: Calculated by adding the muscle scores of each key muscle group; a total score of 100 is possible.
Sensory level: The most caudal dermatome to have normal sensation for both pinprick and light touch on both sides.
Sensory index score: Calculated by adding the scores for each dermatome; a total score of 112 is possible for each pinprick and light touch.
Neurological level of injury: The most caudal level at which both motor and sensory modalities are intact.
Complete injury: The absence of sensory and motor function in the lowest sacral segments.
Incomplete injury: Preservation of motor or sensory function below the neurological level of injury that includes the lowest sacral segments.
Sacral sparing: Presence of motor function (voluntary external anal sphincter contraction) or sensory function (light touch, pinprick at S4/5 dermatome, or anal sensation on rectal examination) in the lowest sacral segments.
Zone of partial preservation: All segments below the neurological level of injury with preservation of motor or sensory findings; used only in complete SCI.

For the pinprick examination the patient must be able to distinguish between the pin (i.e., sharp) and dull edge of the safety pin (dull). The inability to distinguish between the two yields a score of 0. A score of 1 for impaired response to the pinprick testing is given when the patient can distinguish between sharp and dull, but the pin is not felt as sharp as on the face. The normal score of 2 is only given if the pin is felt as sharp as when tested on the face.

For light touch, a cotton-tipped swab is used, with a normal score of 2 being the same touch sensation as on the face and an impaired score of 1 indicating less sensation than on the face. The sensory level is defined as the most caudal dermatome to have normal sensation for both pinprick and light touch on both sides of the body. Sensory index scoring is calculated by adding the scores for pinprick and light touch separately, for each dermatome, for a total score possible of 112 (56 on each side).

To test deep anal sensation, a rectal digital examination is performed. The patient is asked to report any sensory awareness, touch or pressure, with firm pressure of the examiner's digit on the rectal wall. Deep anal sensation is recorded as either present or absent. The optional elements of the sensory examination include proprioception (i.e., joint position and vibration), temperature, and deep pressure sensations.

If accurate sensory testing in any dermatome cannot be performed, "not tested" (NT) should be recorded, or an alternate location within the dermatome can be tested with notation that an alternate site was used. If NT has been documented, then a sensory score cannot be calculated.

The required elements of the motor examination consist of testing 10 key muscles on each side of the body, five in the upper limb and five in the lower limb (see Box 1-3). Muscles should be examined in a rostral to caudal sequence, starting with the elbow flexors (i.e., C5 innervated muscles), and finishing with ankle plantarflexors (Sl). All muscles are tested with the patient in the supine position and graded on a numerical scale from 0 to 5 (see Figure 1-8). Although most muscles are innervated by more than one nerve root segment, the muscles tested have been chosen because of their consistency for being innervated primarily by the segment indicated and for their ease of testing in the supine position. If a particular muscle has a grade of 3/5, it is considered to have full innervation by at least one of its innervating segments, in SCI the more cephalad segment. A muscle graded 5 (i.e., normal) is considered to be fully innervated by both its spinal root segments. A muscle with strength greater than 3 has antigravity strength and is considered useful for functional activities.[8] A number of optional muscles (e.g., diaphragm, deltoids, abdominal muscles, and hip adductors) may also be tested, which may be helpful in determining involvement of certain regions of the spinal cord, but are not used to obtain a motor score.

In addition to the key muscles, the external anal sphincter should be tested by digital examination to sense for voluntary contraction. Care must be taken not to confuse a reflex contraction of the anal sphincter with voluntary contraction.

The motor level is defined as the most caudal key muscle group that is graded 3 or greater with the segments cephalad to it graded normal in strength.[6] Motor scores for each muscle are entered on a standard form and the motor index score is calculated. The maximum total motor score is 50 on each side, for a total of 100. Often the patient's clinical condition may prevent the completion of an accurate examination, such as when a patient is comatose from an associated traumatic brain injury, has injury to the brachial or lumbosacral plexi, or has a limb immobilized because of a fracture. When the patient is not fully testable for any reason, the examiner should record NT for not tested instead of a numerical score.

The NLI is the most caudal level at which both motor and sensory modalities are intact on both sides of the body. For example, if the motor level is C7 and the sensory level is C8, the overall NLI is C7. The motor or sensory level may be different from side to side, and therefore it is recommended to record each separately if it presents a clearer picture of the patient's status (i.e., right C6 motor, C7 sensory, left C7 motor, C6 sensory). The motor level and upper limb motor score better reflect the degree of function and the severity of impairment and disability, relative to the NLI, after motor complete tetraplegia.[9]

CLASSIFICATION OF SPINAL CORD INJURY

In 1969, Frankel et al[10] introduced a five-grade system of classifying traumatic SCI, with a division into complete and incomplete injuries. This scale was adapted by ASIA in 1982. A

complete injury was defined as the patient having no preservation of motor or sensory function more than three levels below the NLI. The three levels distal to the NLI were termed the zone of partial preservation (ZPP). In an incomplete injury, there was preservation of motor or sensory function below the ZPP. The amount of preserved sensory or motor function determined the specific Frankel classification. Changes were subsequently made to the Frankel classification and the 1982 ASIA Guidelines.[7] The Frankel classification was replaced in 1992 by the ASIA Impairment Scale (AIS),[11] which was revised in 1996[12] and 2000[6] and reprinted in 2006 with corrections to the 2000 edition.

Tetraplegia, the preferred term instead of quadriplegia, is defined as loss of motor or sensory function in the cervical segments of the spinal cord. It does not include brachial plexus lesions or injury to the peripheral nerves outside the neural canal. Paraplegia is defined as an impairment of motor or sensory function in the thoracic, lumbar, or sacral segments of the cord. With paraplegia, neurological function in the upper limbs is spared, but depending on the level of injury, the trunk, legs, and pelvic organs may be involved. Paraplegia can refer to cauda equina and conus medullaris injuries but not to lumbosacral plexus lesions or injuries to peripheral nerves outside the neural canal. Use of the terms quadriparesis, tetraparesis, and paraparesis are discouraged because they describe incomplete lesions imprecisely.

A complete injury is defined as the absence of sensory or motor function in the lowest sacral segments (i.e., no sacral sparing). An incomplete injury is defined as preservation of motor function or sensation below the NLI that includes the lowest sacral segments (i.e., sacral sparing). Sacral sparing is tested by light touch and pinprick at the anal mucocutaneous junction (S4 to S5 dermatome), on both sides, and testing voluntary anal contraction and deep anal sensation as part of the rectal examination. If any of these are present, indicating sacral sparing, the individual has a neurologically incomplete injury. According to this definition, a patient with cervical SCI can have sensory and motor function in the trunk or even in the legs, but unless sacral sparing is present, the injury must be classified as complete with a large ZPP (Clinical Note: Classification of Spinal Cord Injury). The ZPP is now defined as the segments below the NLI with preservation of sensory or motor findings and is used only in patients with a complete (ASIA A) SCI.[6] The ASIA Impairment Scale, which describes five categories of SCI, is listed in Box 1-4.

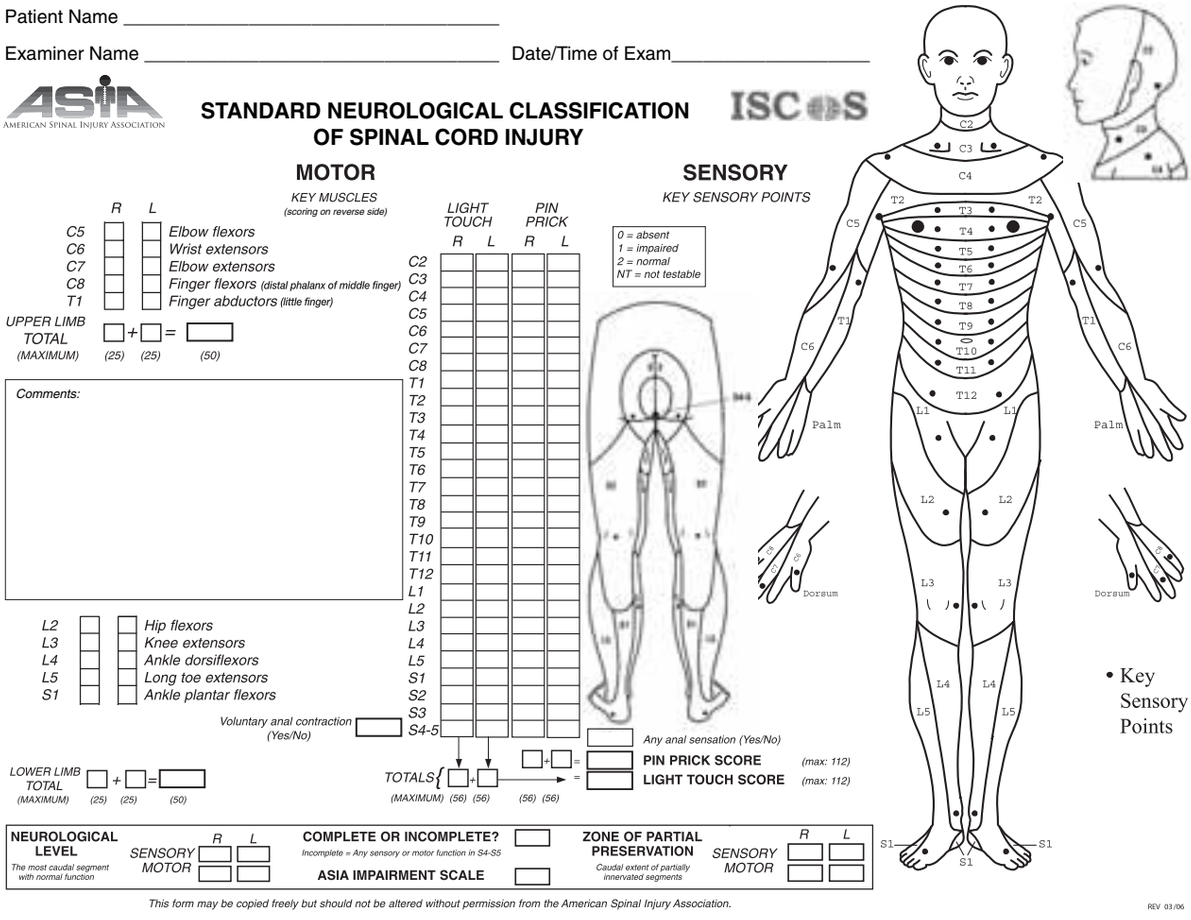
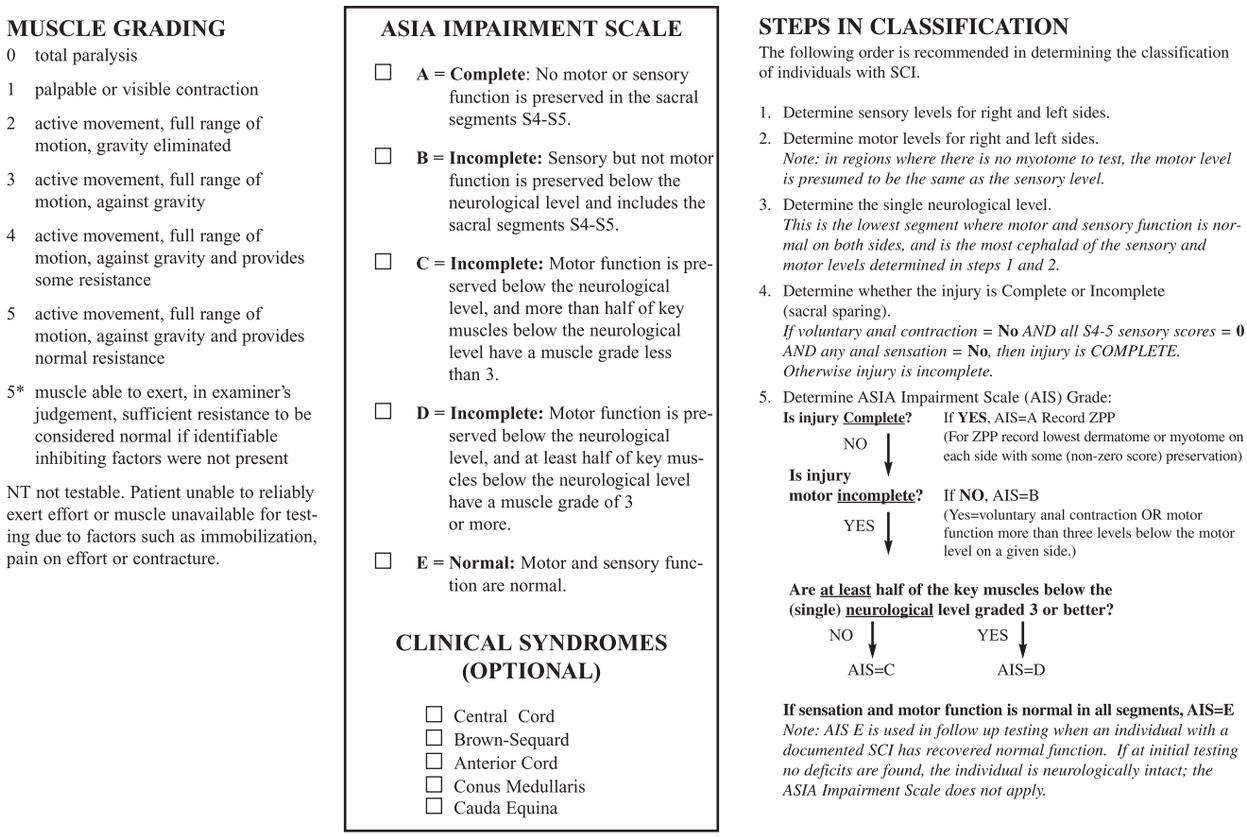


FIGURE 1-8 American Spinal Injury Association (ASIA) Standard Neurological Classification of Spinal Cord Injury. (Courtesy American Spinal Injury Association, Atlanta, GA, 2006.)



MUSCLE GRADING

0 total paralysis

1 palpable or visible contraction

2 active movement, full range of motion, gravity eliminated

3 active movement, full range of motion, against gravity

4 active movement, full range of motion, against gravity and provides some resistance

5 active movement, full range of motion, against gravity and provides normal resistance

5* muscle able to exert, in examiner's judgement, sufficient resistance to be considered normal if identifiable inhibiting factors were not present

NT not testable. Patient unable to reliably exert effort or muscle unavailable for testing due to factors such as immobilization, pain on effort or contracture.

ASIA IMPAIRMENT SCALE

☐ **A = Complete**: No motor or sensory function is preserved in the sacral segments S4-S5.

☐ **B = Incomplete:** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.

☐ **C = Incomplete:** Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.

☐ **D = Incomplete:** Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.

☐ **E = Normal:** Motor and sensory function are normal.

CLINICAL SYNDROMES (OPTIONAL)

☐ Central Cord
☐ Brown-Sequard
☐ Anterior Cord
☐ Conus Medullaris
☐ Cauda Equina

STEPS IN CLASSIFICATION

The following order is recommended in determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
2. Determine motor levels for right and left sides.
   Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level.
3. Determine the single neurological level.
   This is the lowest segment where motor and sensory function is normal on both sides, and 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 (sacral sparing).
   If voluntary anal contraction = **No** *AND all S4-5 sensory scores* = **0** *AND any anal sensation* = **No**, *then injury is COMPLETE. Otherwise injury is incomplete.*
5. Determine ASIA Impairment Scale (AIS) Grade:

Is injury Complete? If **YES**, AIS=A Record ZPP (For ZPP record lowest dermatome or myotome on each side with some (non-zero score) preservation)

NO ↓

Is injury motor incomplete? If **NO**, AIS=B (Yes=voluntary anal contraction OR motor function more than three levels below the motor level on a given side.)

YES ↓

Are at least half of the key muscles below the (single) neurological level 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; the ASIA Impairment Scale does not apply.

FIGURE 1-8, cont'd American Spinal Injury Association (ASIA) Standard Neurological Classification of Spinal Cord Injury. (Courtesy American Spinal Injury Association, Atlanta, GA, 2006.)

INCOMPLETE SPINAL CORD INJURY

Different clinical syndromes of SCI are frequently referred to by clinicians and in the literature, including central cord, Brown-Sequard, anterior cord, conus medullaris, and cauda equina syndromes. In general, these syndromes do not accurately describe the extent of the neurological deficit (Table 1-1).

Central Cord Syndrome

The most common of the incomplete syndromes is central cord syndrome (CCS). CCS is characterized by motor weakness in the upper limbs greater than the lower limbs, in association with sacral sparing. In addition to the motor weakness, other features include bladder dysfunction and varying sensory loss below the level of the lesion. In his original description, Schneider and others[14] noted that the etiologic factor was hyperextension with simultaneous compression of the cord by anterior osteophytes and posterior impingement caused by buckling of the ligamentum flavum. Although CCS most frequently occurs in older adults with cervical spondylosis with hyperextension injuries, the syndrome may occur in individuals of any age and is associated with other etiologies, predisposing factors, and injury mechanisms. The pathology of central cord syndrome is commonly believed to result from an injury that primarily affects the center of the spinal cord. Depending on the degree and severity of the lesion, there may be paralysis of both the upper and lower limbs, with relatively more involvement of the upper limbs. This is due to the proposed lamination of the fibers in the corticospinal tract, with the cervical fibers most centrally located in relation to the thoracic, lumbar, and sacral fibers.[13,14] Others have not, however, found this lamination to exist in humans.[15,16] Quencer et al,[17] in a study that used magnetic resonance imaging (MRI) and pathological observations, found that CCS is predominantly a white matter peripheral injury and that intramedullary hemorrhage is not a common feature. Central cord syndrome generally has a favorable prognosis.[18-21] The typical pattern of recovery usually occurs earliest and to the greatest extent in the lower limbs, followed by bladder function, upper limb (proximal), and intrinsic hand function. Although there is a reported generally good outcome for persons with CCS, the prognosis for functional recovery should consider the patient's age, with a less optimistic prognosis in older relative to younger patients.[20] Specifically, younger people (less than 50 years of age) are more successful in becoming independent in ambulation than are older adults (97% versus 41%). Similar differences are seen between the younger and older patients in independent bladder function (83% versus 29%), independent bowel function (63% versus 24%), and dressing (77% versus 12%).[20] All patients, regardless of age, whose injuries initially are classified as ASIA D within 72 hours, are usually able to regain ambulatory function.[21]

CLINICAL NOTE **Classification of Spinal Cord Injury**

The following steps should be followed to classify a patient's SCI:

- Perform sensory examination in 28 dermatomes bilaterally for pinprick and light touch including S4-S5 dermatome and test for anal sensation
- Determine sensory level (right and left) and total sensory score
- Perform motor examination in the 10 key muscle groups including anal contraction
- Determine motor level (right and left) and motor index score
- Determine NLI
- Classify injury as complete or incomplete
- Categorize according to the ASIA Impairment Scale (see Box 1-4)
- Determine zone of partial preservation if ASIA A

BOX 1-4 | ASIA Impairment Scale

A = **Complete**: No motor or sensory function is preserved in the sacral segments S4-S5.
B = **Incomplete**: Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.
C = **Incomplete**: Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.
D = **Incomplete**: Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.
E = **Normal**: Motor and sensory function are normal.

American Spinal Injury Association (ASIA) Standard Neurological Classification of Spinal Cord Injury. (Courtesy American Spinal Injury Association, Atlanta, GA, 2006.)

TABLE 1-1 | Incomplete Clinical Syndromes

Syndrome Recovery	Main Symptoms	Prognosis
Central cord	Greater weakness in the upper limbs than in the lower limbs Occurs almost exclusively in the cervical region Frequently seen in older adults and those with cervical stenosis	Favorable prognosis for walking and activities of daily living on the basis of age (<50 years old greater improvement than >50 years) Recovery occurs earliest in legs, followed by bladder, then proximal upper extremity muscles, and intrinsics last
Brown-Sequard	Greater ipsilateral proprioceptive and motor loss and contralateral loss of sensitivity to pain and temperature	Best prognosis for ambulation Recovery starts in ipsilateral proximal extensors then the distal flexors
Anterior cord	Variable loss of motor function and pain and temperature, while preserving proprioception	Poor prognosis for recovery of lower limb function and ambulation
Cauda equina	Injury to the lumbosacral nerve roots resulting in an areflexic bladder, bowel, and lower limbs	A lower motor neuron injury Regrowth is possible, but better prognosis for proximal muscles
Conus medullaris	Injury of the sacral cord and lumbar nerve roots Sacral segments may show preserved reflexes (e.g., bulbocavernosus with high conus lesions) Results in areflexic bladder, bowel, and lower limbs with a low lesion	As above Depends on the level of injury to the conus

Data from Kirshblum S, O'Connor K: Levels of injury and outcome in traumatic spinal cord injury, *Phys Med Rehabil Clin North Am* 11:1-27, 2000.

Brown-Sequard Syndrome

Brown-Sequard syndrome (BSS) consists of asymmetric paresis with hypalgesia more marked on the less paretic side. It accounts for 2% to 4% of all traumatic SCIs.[22-24] In the classical presentation, BSS consists of the following:

- Ipsilateral loss of all sensory modalities **at** the level of the lesion
- Ipsilateral flaccid paralysis **at** the level of the lesion
- Ipsilateral loss of position sense and vibration **below** the lesion
- Contralateral loss of pain and temperature **below** the lesion
- Ipsilateral motor loss **below** the level of the lesion

Neuroanatomically, this is explained by the crossing of the spinothalamic tracts, which carry pain and temperature fibers, in the spinal cord, as opposed to the corticospinal (i.e., motor tract fibers) and dorsal columns (i.e., light touch), which cross for the most part in the brainstem.

Only a limited number of patients have the pure form of BSS; Brown-Sequard plus syndrome (BSPS) is much more common.[25] BSPS refers to a relative ipsilateral hemiplegia with a relative contralateral hemianalgesia. Although BSS has traditionally been associated with knife injuries, stab wounds are rarely the cause of BSPS. A variety of etiologies, including those that result in closed spinal injuries with or without vertebral fractures may be the cause.

Despite the variation in presentation, considerable consistency is found in the prognosis of BSS. Recovery takes place in the ipsilateral proximal extensors and then the distal flexors.[26,27] Motor recovery of any limb having a pain and temperature sensory deficit occurs before the opposite limb and these patients may expect voluntary motion, strength, and functional gait recovery by 6 months.

Overall, patients with BSS have the best prognosis for functional outcome. Many patients ambulate independently at discharge from rehabilitation (75%) and nearly 70% perform functional skills and activities of daily living independently.[25] The most important predictor of function is whether the upper or lower limb is the predominant site of weakness: when the upper limb is weaker than the lower limb, patients are more likely to ambulate at discharge. Recovery of bowel and bladder function is also favorable, with continent bladder and bowel function achieved in 89% and 82%, respectively.[25]

TABLE 1-2 | **Comparison of Epiconus, Conus Medullaris, and Cauda Equina Lesions**

Symptom	Epiconus	Conus Medullaris	Cauda Equina
Pain	Uncommon	Uncommon	Very common and may be severe
Bowel and bladder reflexes	Present	Absent	Absent
Anal and BC reflex	Present	Absent*	Absent
Muscle tone	Increased	†	Decreased
MSRs	Increased‡	†	Decreased
Symmetry of weakness	Yes	Yes	No
Sensation	In dermatomal distribution	Absent in saddle distribution and may be dissociated	In root distribution
Recovery prognosis	Limited	Limited	Possible

Data from Kirshblum S, Donovan WH: Neurological assessment and classification of traumatic spinal cord injury. In Kirshblum S, Campagnolo DI, DeLisa JA, editors: *Spinal cord medicine,* pp. 82-95, Philadelphia, 2002, Lippincott Williams & Wilkins.
*Unless a high conus lesion.
†Depends on whether nerve roots are affected. If so, then is decreased.
‡Ankle plantarflexors and hamstrings, not knee jerks.
BC, Bulbocavernosus; *MSR,* muscle stretch reflexes.

Anterior Cord Syndrome

Anterior cord syndrome involves a lesion affecting the anterior two thirds of the spinal cord while preserving the posterior columns. This may occur with retropulsed disc or bone fragments,[28] direct injury to the anterior spinal cord, or with lesions of the anterior spinal artery, which provides the blood supply to the anterior spinal cord.[29] Lesions of the anterior spinal artery may result from diseases of the aorta, cardiac or aortic surgery, embolism, polyarteritis nodosa, or after an angioplasty. There is a variable loss of motor and pinprick sensation with a relative preservation of light touch, proprioception, and deep pressure sensation. Usually patients with an anterior cord syndrome have only a 10% to 20% chance of muscle recovery, and even in those with some recovery there is poor muscle power and coordination.[30]

Conus Medullaris and Cauda Equina Injuries

The conus medullaris, which is the terminal segment of the adult spinal cord, lies at the inferior aspect of the L1 vertebrae. The segment above the conus medullaris is termed the epiconus, consisting of spinal cord segments L4 to S1. Nerve roots then travel from the conus medullaris caudal as the cauda equina.

Lesions of the epiconus will affect the lower lumbar roots supplying muscles of the lower part of the leg and foot, with sparing of sacral segments. The bulbocavernosus reflex and micturition reflexes are preserved, representing a UMN lesion. Spasticity will most likely develop in sacral innervated segments including the toe flexors, ankle plantar flexors, and hamstring muscles. Recovery is similar to other UMN SCIs.

The conus medullaris consists of neural segments S2 and below. Injuries to the conus will present with LMN deficits of the anal sphincter and bladder as a result of damage to the anterior horn cells of S2 to S4. Bladder and rectal reflexes are diminished or absent, depending on the exact level of the lesion. Motor strength in the legs and feet may remain intact if the nerve roots (L3 to S2) are not affected. The lumbar nerve roots may be spared partially or totally in the conus medullaris; this is referred to as root escape. If the roots are affected as they travel with the sacral cord in the spinal column, this will result in LMN damage with diminished reflexes. In low conus lesions, the S1 segment is not involved and therefore the ankle jerks are normal, a finding accounting for most instances of failure to make the diagnosis. Because of the small size of the conus medullaris, lesions are more likely to be bilateral compared with those of the cauda equina. With conus medullaris lesions, recovery is limited.

Injuries below the L1 vertebral level do not cause injury to the spinal cord but rather to the cauda equina or nerve roots supplying the lumbar and sacral segments of the skin and muscle groups. This usually produces motor weakness and atrophy of the lower limbs (L2 to S2) with bowel and bladder involvement (S2 to S4) and areflexia of the ankle and plantar reflexes. Often the patient may have spared sensation in the perineum or lower limbs but complete paralysis. In cauda injuries there is loss of anal and bulbocavernosus reflexes and impotence.

There is consensus that cauda equina injuries have a much better prognosis for recovery than other SCI syndromes. This is most likely because the nerve roots are more resilient to injury and because many of the biochemical processes that occur in the spinal cord and produce secondary damage occur to a much lesser extent in the nerve roots. Progressive recovery may occur over a course of weeks and months.

Separation of cauda equina and conus lesions in clinical practice is difficult because the clinical features of these lesions overlap. Isolated conus lesions are rare because the roots forming the cauda equina are wrapped around the conus. The conus may be affected by a fracture of L1, whereas a fracture of L2 or lower can impinge on the cauda equina. Sacral fractures and fractures of the pelvic ring also frequently damage the cauda equina. Bullet wounds can penetrate the bony structures to traumatize the cauda equina and conus. Differences between these lesions are outlined in Table 1-2.

PROGNOSIS FOR RECOVERY AND PREDICTION OF OUTCOME

The physical examination is the most important component in determining future neurological improvement after injury. After classification of the patient's injury is made, prognostication early after the injury can be determined. There are a number of clinical methods to assist in prognosticating neurological recovery after

BOX 1-5 | Prognostic Indicators of Complete Tetraplegia

- From 1 week to 1 year after injury, 30% to 80% of patients will regain one motor level
- Initial strength of the muscle is a significant predictor of its rate of recovery and its prognosis for achieving antigravity strength
- The faster an initially 0/5 muscle starts to recover some strength, the greater the prognosis for recovery
- Most upper limb recovery occurs during the first 6 months, with the greatest rate of change during the first 3 months
- Most patients with some initial strength plateau earlier but at a higher level than patients who are initially 0/5
- Motor recovery can continue with lesser gains seen in the second year, especially for patients with initial 0/5 strength

SCI, including the neurological examination and the use of radiological and electrodiagnostic tests.[31,32]

The most important determinant of recovery is whether the person has a neurological complete or incomplete injury as determined by the neurological examination. Other key determinants on examination include the initial level of injury, the initial strength of the muscles, and the age of the individual. Box 1-5 lists some generalizations regarding prognostication based on an early examination.

Individuals with a motor complete injury will usually regain one motor level of recovery by 1 year after injury. Recovery of strength is greater and earlier in those patients with some initial motor strength immediately caudal to the level of injury. The greater the initial strength of the muscle, the faster the muscle will recover to strength of greater or equal to 3/5. Those with an initially incomplete injury have a better prognosis for future ambulation if there is motor sparing as opposed to sensory sparing only. For individuals with an initially sensory incomplete lesion, sparing of pinprick sensation may be a better predictor of functional ambulation at 1 year relative to those with light touch alone spared. Approximately 70% of individuals with a diagnosis of an incomplete cervical injury may regain the ability to ambulate at 1 year, with approximately 46% regaining the ability for community ambulation.

Recovery from injuries below the cervical spine, resulting in paraplegia, has not been studied to the degree of tetraplegia, but some of the generalizations regarding prediction of recovery is the same. In thoracic level and high lumbar level injuries (NLI above L2), the clinician can usually only test for sensory modality change to document an improvement in NLI because there are no corresponding key muscle groups between T1 and L2. The prognosis for regaining functional ambulation in people with complete paraplegia is 5%; however, the lower the level of injury, the greater the potential functional capability. Individuals with incomplete paraplegia have the best prognosis for ambulation. Eighty percent of individuals with incomplete paraplegia regain hip flexors and knee extensors at 1 year.

For the purposes of prognostication, MRI is the most superior of all radiological tests. A number of studies have related MRI findings to the neurological status and recovery after SCI and found that the degree and type of MRI change correlates with the severity and prognosis of the injury. A hemorrhage displayed on the initial MRI correlates with the poorest prognosis, followed by contusion, and edema. A normal study (no MRI abnormality) correlates with the best prognosis. If a hemorrhage is initially seen, this usually suggests a complete injury. If a hemorrhage is present in patients with an incomplete injury, those patients usually have less chance of recovery relative to patients with other MRI findings. If no hemorrhage is seen on the initial MRI, those patients will most likely have an incomplete lesion and have a significantly better prognosis for motor recovery in the upper and lower limbs as well as improvement in the ASIA Impairment Scale classification. The degree and extent of cord edema on MRI has an inversely proportional effect as a prognostic indicator for initial impairment level and future recovery. If the edema involves multiple levels, there is a poorer prognosis and a greater chance of having a complete lesion. In general, MRI can be used to augment the physical examination in prognosticating recovery of patients with a cervical SCI; however, by itself it is not as accurate a predictor as the physical examination.

There are a number of electrophysiological tests that have been used in the acute period after SCI to assess the level and severity of the SCI and to prognosticate neurological and functional outcomes. Techniques include nerve conduction studies, late responses (H-reflex and F-wave), somatosensory evoked potentials, motor evoked potentials, and sympathetic skin responses, all of which can supplement clinical and neuroradiological examinations.[32] These tests, however, are most useful in differentiating lesions of the central and peripheral nervous system and in uncooperative or unconscious patients because they do not require the cooperation of the patient. They are not recommended as a routine part of the acute workup of a newly injured individual to offer prognosis for neurological or functional outcome.

PHARMACOLOGICAL AND SURGICAL INTERVENTIONS TO ENHANCE RECOVERY AND REGENERATION

After the initial injury, numerous changes occur within the spinal cord that hinder return of function.

Table 1-3 lists areas of research in each of the categories of treatment after SCI. The text summarizes recently completed trials, trials currently in progress, or human clinical trials planned for the near future.

Over the last few decades there have been a number of pharmacological strategies in the initial treatment of SCI to enhance recovery. Methylprednisolone (MP) was initially studied in the National Acute Spinal Cord Injury Study (NASCIS) I, which randomized patients into high- versus low-dose regimens.[33] No statistical difference in neurological or functional outcome was found between the two regimens at 6 months or 1 year; however, the high dose used was below the theoretical therapeutic threshold. The NASCIS II study randomized patients with acute SCI into placebo, high MP, and naloxone treatment groups.[34] Patients with penetrating wounds and cauda equina injuries were excluded. This study found that MP given within 8 hours after the injury (30 mg/kg bolus and 5.4 mg/kg/hour for 23 hours) improved neurological recovery at 6 weeks, 6 months, and 1 year, although functional recovery was not clearly studied. Patients treated after 8 hours demonstrated

TABLE 1-3 | **Overview of Spinal Cord Injury Research**

Category of Treatment	Areas of Research
Protection	Previously studied: Methylprednisolone, naloxone, calcium channel blockers, GM-1 Present and future studies: Minocycline, erythropoietin, riluzole, sulfonylureas, hyperdynamic therapy, and CSF drainage
Stimulating axonal growth	Electrical stimulation (oscillating field stimulator [OFS], IN-1 (Nogo-blocking antibody), MAG (myelin-associated glycoprotein), OMgp (oligodendrocyte myelin glycoprotein), Rho inhibitors (e.g., BA-210 [Cethrin]), activated macrophages, chondroitin sulfate proteoglycans (CSPGs), inosine, heparan sulfate proteoglycans (HSPGs), keratan sulfate proteoglycans (KSPGs), nerve growth factors, estrogen and serotonin selective reuptake inhibitors
Bridging	Peripheral nerve grafts, Schwann cells, olfactory ensheathing glial cells, nanotubes
Enhancing axonal transmission	Schwann cells, olfactory ensheathing glial cells, 4-aminopyridine, HP-184, neuroprogenitor cell transplants (stem cells)
Rehabilitation	Electrical stimulation, weight supported ambulation

no beneficial effect. Although the initial report of NASCIS II indicated no beneficial effects of naloxone, a subsequent report found that patients with incomplete lesions treated with naloxone within 8 hours had significantly greater recovery than patients treated with placebo.[35] One of the keys to NASCIS II was the evidence that medication may improve neural recovery, thus indicating that secondary injury (i.e., injury occurring after the initial trauma to the cord) occurs. Mechanisms of action for MP include improving blood flow to the spinal cord, preventing lipid peroxidation, being a free radical scavenger, and having anti-inflammatory function.

NASCIS III randomized patients into 24- or 48-hour treatment with MP or tirilizad mesylate.[36] Tirilizad is a potent steroid with no glucocorticoid effect, thus offering the positive effects of MP (e.g., lipid peroxidation and antioxidant activity) without the side effects. This study concluded that patients treated within 3 hours of the injury should receive 24 hours of steroids and those treated between 3 to 8 hours after injury should receive 48 hours of treatment. This newer protocol using 48 hours of treatment has not been universally accepted, and there are a number of recent reports that question the current routine use of steroids.[37-39]

GM-1 ganglioside (Sygen) is present in high concentrations in the central nervous system (CNS) and forms the major component of cell membranes. It is thought that GM-1 ganglioside can augment neurite outgrowth and decrease CNS tissue damage, prevent glutamate-induced neuronal excitotoxicity, and stimulate and preserve protein kinases. An initial small study treating patients within 48 hours of injury for an average of 26 days found greater mean recovery at 1 year including some improved recovery in muscles with no strength at entry of the study.[40] A subsequent large multicenter study reported a trend toward improvement in neurological recovery in ASIA B individuals at 26 weeks after being treated for 8 weeks and a significant effect in individuals who received GM-1 ganglioside but who did not have surgery relative to those who did have surgery and did not receive GM-1 ganglioside. No significant effect was noted at the principal end point of 26 weeks in the total group of patients studied.[41]

A medication trial was performed for subjects with chronic incomplete spinal cord injury with fampridine-SR, a long-acting formulation of 4-aminopyridine (4-AP). 4-AP is a potassium (K^+) channel blocker that blocks fast internodal axonal K^+, which blocks conduction of the nerve action potentials. Preliminary work in SCI (Phase II studies) showed trends toward improvement in pain and spasticity.[42-44] Phase III multicenter trials were completed but did not show significant results, although there were improvements in multiple sclerosis trials and further study is currently underway.

A Phase II trial was also performed with HP-184. This medication is a potassium (K^+) and sodium (Na^+) channel blocker that in a Phase I trial in 48 subjects with chronic incomplete SCI resulted in increased motor index scores.[45] The Phase II trial recruited 240 subjects with chronic incomplete SCI (ASIA C, D) with injury levels C4-T10. Outcome measures include motor index score and gait improvement. Results have not been published to date.

The study with ProCord (activated macrophages) (Proneuron Biotechnologies, Ness-Ziona, Israel) was an international multicenter trial for individuals with an acute neurologically complete SCI (ASIA A). The basis of this study was to impose an appropriate inflammatory response encouraging a self-operating chain of reactions needed for spinal cord regeneration and regrowth. Macrophages isolated from the patient's own blood were activated through Proneuron's proprietary process and then injected directly into the patient's injured spinal cord by day 14 after injury. In a Phase I trial in Israel initiated in 2000, five of 16 subjects showed an AIS improvement from ASIA A to incomplete status, with three subjects to ASIA C and two to ASIA B by 1 year.[46] The Phase II trial, however, was halted because of financial restraints after approximately two thirds of the subjects were recruited. Results should be forthcoming.

A Phase 1 clinical trial was performed on 10 subjects with oscillating field electrical stimulation (OFS) for individuals with a neurologically complete SCI. Their levels of injury were between C5 and T10, with no evidence of cord transection demonstrated on MRI. Implantation of the OFS was within 18 days of the injury and the subjects underwent evaluation every 2 weeks after implantation; the unit was removed at 15 weeks. At 1 year, their degree of pain as measured by the visual analog scale pain score was decreased, with improvement noted in light touch and pinprick sensation and some muscle strength improvement as well.[47] The use of OFS treatment in patients with acute SCI was found to be safe and perhaps efficacious, and the Food and Drug Administration has given permission for enrollment of 10 additional acutely injured patients. Further results and clinical trials in this area are expected.

A recently initiated trial is using BA-210 (Cethrin), a Rho pathway antagonist that may promote neuroregeneration and neuroprotection in the CNS. This is applied to the surface of the dura mater of the spinal cord together with a fibrin sealant normally used to repair small dural tears, within 7 days of injury. The study is being performed in a number of centers in the United States and Canada for individuals with a neurologically complete SCI. Minocycline, a semisynthetic tetracycline antibiotic, showed good improvement in hind limb function and strength in animal model studies, and human trials have begun.[48]

A number of surgical procedures using either fetal stem cells (Huang in China) or adult olfactory cell transplants (Lima in Portugal) are being performed. Although Huang has reported some results,[49] this was not a prospective research project and many questions remain regarding these results. Additional results are pending from these surgical approaches.[50]

There has been great excitement within the field of SCI medicine regarding research that has moved from the laboratory to human clinical trials. Despite the excitement with respect to cure and the optimism regarding the development of therapies, at present no pharmacological, surgical, or rehabilitative therapy exists that can cure all of the impairments caused by the injury. Most likely a combination of the above mentioned treatments will be required to address the complex issues of SCI. Further study is required to not only find treatments to enhance neurological and functional recovery but also to decrease medical complications and optimize the quality of lives of persons with SCI.

SUMMARY

While the overall incidence of traumatic spinal cord injury has remained relatively stable, there has been a change in the epidemiology of SCI. Although MVCs remain the primary cause of SCI, falls rank second, primarily among older adults, and injury related to violence, most often seen in young men, is third. There also is a recent trend toward an increased number of incomplete lesions, possibly the result of changes in etiology and improved treatment at the site of injury by emergency medical technicians and subsequent immediate care.

Understanding the neurological anatomy of the spinal cord is essential to comprehension of the mechanisms of SCI. In addition, knowledge of the autonomic nervous system anatomy and function is critical to appreciation of the impairments of the multiple body systems that it controls.

Classification of an SCI enables the determination of impairment and helps prognosticate outcomes and plan for the patient's ongoing needs. The ASIA examination is the standard neurological examination for SCI and is used to determine the neurological level of injury, the motor impairment scale, the sensory impairments, and the zone of partial preservation. There are several types of incomplete injuries and classification of these types also aids in determining outcomes. Clinical mastery of methods for prognosis of functional recovery is important to give the patient a realistic picture of his future. In the acute stages after injury, however, patients and their families may focus completely on this information and every attempt must be made to avoid depleting all hope of recovery.

Finally, some completed and new clinical trials concentrating on spinal cord injury cure and recovery are reviewed. Research is constantly changing as new technologies in the basic and clinical sciences emerge. Thus, the field of rehabilitation must continue to build and maintain the physical capacity of individuals with SCI so that when a cure becomes available their body systems will be in optimal condition.

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