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453 Diseases of the Spinal Cord

In infectious cases, prompt administration of broad-spectrum antibiotics, drainage of any abscess cavities, and identification of the offending organism are essential. Anticoagulant therapy may benefit cases of primary thrombosis. Repair or occlusion of the carotid artery may be required for treatment of fistulas or aneurysms. Tolosa-Hunt syndrome is characterized by onset, over days or a few weeks, of severe orbital pain with variable ophthalmoparesis and numbness of the upper face (V1 and V2 divisions of the tri geminal nerve) and by a dramatic clinical response to glucocorticoids. Although distinctive, the presentation can be mimicked by numerous other conditions that involve the cavernous sinus and orbit, includ ing sarcoid (Chap. 379), vasculitis (Chap. 375), IgG4-related disease (Chap. 380), lymphoma, and fungal infections. MRI can suggest the presence of granulomatous inflammation, but biopsy is sometimes required for diagnosis. A dramatic improvement in pain is usually evident within a few days; oral prednisone (60 mg daily) is usually con tinued for 2 weeks and then gradually tapered over a month, or longer if pain recurs. Occasionally an immunosuppressive medication, such as azathioprine or methotrexate, needs to be added to maintain an initial response to glucocorticoids. Lesions in the superior orbital fissure and orbital apex cause more prominent vision loss than those in the cavernous sinus due to com pression of the optic nerve; the second branch of the trigeminal nerve is usually spared. The cause is often an invasive fungal infection, frequently due to osseous erosion through the wall of the maxillary, sphenoid, or ethmoid sinuses. Infiltrative processes such as amyloi dosis, granulomatosis with polyarteritis, an idiopathic granulomatous inflammation similar to Tolosa-Hunt, and IgG4-related disease are additional causes. Biopsy is often necessary for diagnosis. As noted above, Guillain-Barré syndrome commonly affects the facial nerves bilaterally. In the Fisher variant of Guillain-Barré syn drome, oculomotor paresis occurs with ataxia and areflexia in the limbs (Chap. 458). Wernicke’s encephalopathy can cause a severe ophthalmoplegia combined with other brainstem signs (Chap. 318). Progressive bulbar palsy is a slowly progressive purely motor disor der affecting multiple cranial nerve nuclei. Weakness of the face, jaw, pharynx, neck, and tongue is usually present accompanied by atrophy and fasciculations. It is a form of motor neuron disease (Chap. 448). Pure motor syndromes without atrophy raise the question of myas thenia gravis (Chap. 459), and when rapidly evolving, Guillain-Barré syndrome, diphtheria, and poliomyelitis are additional considerations. Glossopharyngeal neuropathy in conjunction with vagus and acces sory nerve palsies may occur with herpes zoster infection or with a tumor or aneurysm in the posterior fossa or in the jugular foramen, through which all three nerves exit the skull. Hoarseness due to vocal cord paralysis, some difficulty in swallowing, deviation of the soft pal ate to the intact side,

anesthesia of the posterior wall of the pharynx, and weakness of the upper part of the trapezius and sternocleidomas toid muscles make up jugular foramen syndrome. Paralysis of the vagus and hypoglossal nerves (Tapia syndrome) can rarely follow endotracheal intubation and has been reported during the COVID-19 pandemic; symptoms consist of dysphonia and tongue deviation and usually resolve within a few months. An idiopathic form of multiple cranial nerve involvement on one or both sides of the face is occasionally seen. The syndrome consists of a subacute onset of boring facial pain, followed by paralysis of motor cranial nerves. The clinical features overlap those of Tolosa-Hunt syndrome and appear to be due to idiopathic inflammation of the dura mater, which may be visualized by MRI. The syndrome is usually responsive to glucocorticoids. ■ ■FURTHER READING Abad S et al: IgG4-related disease in patients with idiopathic orbital inflammation syndrome: Data from the French SIOI prospective cohort. Acta Ophthalmol 97:e648, 2019. Bendsten L et al: European Academy of Neurology guideline on tri geminal neuralgia. Eur J Neurol 26:831, 2019. Gagyor I et al: Antiviral treatment of Bell’s palsy (idiopathic facial paralysis). Cochrane Database Syst Rev 9:CD001869, 2019.

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Diseases of the

Spinal Cord CHAPTER 453 Diseases of the Spinal Cord Diseases of the spinal cord are frequently devastating. They produce quadriplegia, paraplegia, and sensory deficits far beyond the damage they would inflict elsewhere in the nervous system because the spinal cord contains, in a small cross-sectional area, almost the entire motor output and sensory input of the trunk and limbs. Many spinal cord diseases are reversible if recognized and treated at an early stage (Table 453-1); thus, they are among the most critical of neurologic emergencies. Proper management requires the efficient use of diag nostic procedures, guided by knowledge of the anatomy and clinical features of spinal cord diseases. APPROACH TO THE PATIENT Spinal Cord Disease SPINAL CORD ANATOMY RELEVANT TO CLINICAL SIGNS The spinal cord is a thin, tubular extension of the central nervous system contained within the bony spinal canal. It originates at the medulla and continues caudally to the conus medullaris at the lumbar level; its fibrous extension, the filum terminale, terminates at the coccyx. The adult spinal cord is ~46 cm (18 in.) long, oval in shape, and enlarged in the cervical and lumbar regions, where neu rons that innervate the upper and lower extremities, respectively, are located. The white matter tracts containing ascending sensory and descending motor pathways are located peripherally, whereas nerve cell bodies are clustered in an inner region of gray matter shaped like a four-leaf clover that surrounds the central canal (ana tomically an extension of the fourth ventricle). The membranes that cover the spinal cord—the pia, arachnoid, and dura—are continu ous with those of the brain, and the cerebrospinal fluid is contained within the subarachnoid space between the pia and arachnoid. The spinal cord has 31 segments, each defined by an exit ing ventral motor root and entering dorsal sensory root. During embryologic development, growth of the cord lags behind that of the vertebral column, and the

mature spinal cord ends at approxi mately the first lumbar vertebral body. The lower spinal nerves take an increasingly downward course to exit via intervertebral foramina. The first seven pairs of cervical spinal nerves exit above the same-numbered vertebral bodies, whereas all the subsequent nerves exit below the same-numbered vertebral bodies; this is because there are eight cervical spinal cord segments but only seven cervical vertebrae. The relationship between spinal cord segments and the corresponding vertebral bodies is shown in Table 453-2. These relationships assume particular importance for localization of lesions that cause spinal cord compression. Sensory loss below

TABLE 453-1 Treatable Spinal Cord Disorders Compressive Epidural, intradural, or intramedullary neoplasm Epidural abscess Epidural hemorrhage Cervical spondylosis Herniated disk Posttraumatic compression by fractured or displaced vertebra or hemorrhage Vascular Arteriovenous malformation and dural fistula Antiphospholipid syndrome and other hypercoagulable states Inflammatory Multiple sclerosis Neuromyelitis optica Sarcoidosis PART 13 Neurologic Disorders Systemic immune-mediated disorders: SLE, Sjögren’s, Behcet’s disease, APL antibody syndrome, others vasculitis Other CNS disorders: anti-MOG, anti-GFAP, paraneoplastic,a CLIPPERS, Erdheim-Chester Infectious Viral: VZV, HSV-1 and -2, CMV, HIV, HTLV-1, others Bacterial and mycobacterial: Borrelia, Listeria, syphilis, others Mycoplasma pneumoniae Parasitic: schistosomiasis, toxoplasmosis, cysticercosis Developmental Syringomyelia Meningomyelocele Tethered cord syndrome Metabolic Vitamin B12 deficiency (subacute combined degeneration) Folate deficiency Copper deficiency aIncluding anti-amphiphysin, CRMP-5, Hu. Abbreviations: CLIPPERS, chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids; CMV, cytomegalovirus; CNS, central nervous system; CRMP5, collapsin response mediator 5-IgG; GFAP, glial fibrillary acidic protein; HSV, herpes simplex virus; HTLV, human T-cell lymphotropic virus; MOG, myelin oligodendrocyte glycoprotein; SLE, systemic lupus erythematosus; VZV, varicella-zoster virus. the level of the umbilicus, for example, corresponds to pathology at the T10 cord segment, which is located adjacent to the seventh or eighth thoracic vertebral body (see Figs. 27-2 and 27-3). In addition, at every level, the main ascending and descending tracts are somatotopically organized with a laminated distribution that reflects the origin or destination of nerve fibers. Determining the Level of the Lesion The presence of a horizon tally defined level below which sensory, motor, and autonomic function is impaired is the hallmark of a spinal cord lesion. This sensory level is sought by asking the patient to identify a pinprick or cold stimulus applied to the proximal legs and lower trunk and successively moved up toward the neck on each side. Sensory loss below this level is the result of damage to the spinothalamic tract on the opposite side, one to two segments higher in the case of a TABLE 453-2 Spinal Cord Levels Relative to the Vertebral Bodies SPINAL CORD LEVEL CORRESPONDING VERTEBRAL BODY Upper cervical Same as cord level Lower cervical 1 level higher Upper thoracic 2 levels higher Lower thoracic 2–3 levels higher Lumbar T10–T12 Sacral T12–L1

unilateral spinal cord lesion, and at the level of a bilateral lesion. The discrepancy in the level of a unilateral lesion is the result of the course of the second-order sensory fibers, which originate in the dorsal horn and ascend for one or two levels as they cross ante rior to the central canal to join the opposite spinothalamic tract. Lesions that transect the descending corticospinal and other motor tracts cause paraplegia or quadriplegia with heightened deep ten don reflexes, Babinski signs, and eventual spasticity (upper motor neuron syndrome). Transverse damage to the cord also produces autonomic disturbances consisting of absent sweating below the implicated cord level and bladder,

bowel, and sexual dysfunction. The uppermost level of a spinal cord lesion can also be local ized by attention to the segmental signs corresponding to disturbed motor or sensory innervation by an individual cord segment. A band of altered sensation (hyperalgesia or hyperpathia) at the upper end of the sensory disturbance, fasciculations or atrophy in muscles innervated by one or several segments, or a muted or absent deep tendon reflex may be noted at this level. These signs also can occur with focal root or peripheral nerve disorders; thus, they are most useful when they occur together with signs of long-tract damage. With severe and acute transverse lesions, the limbs initially may be flaccid rather than spastic. This state of “spinal shock” lasts for several days, rarely for weeks, and may be mistaken for extensive damage to the anterior horn cells over many segments of the cord or for an acute polyneuropathy. The main features of transverse damage at each level of the spinal cord are summarized below. Cervical Cord Upper cervical cord lesions produce quadriplegia and weakness of the diaphragm. The uppermost level of weakness and reflex loss with lesions at C5–C6 is in the biceps; at C7, in finger and wrist extensors and triceps; and at C8, finger and wrist flexion. Horner’s syndrome (miosis, ptosis, and facial hypohidrosis) may accompany a cervical cord lesion at any level. Thoracic Cord Lesions here are localized by the sensory level on the trunk and, if present, by the site of midline back pain. Useful markers of the sensory level on the trunk are the nipples (T4) and umbilicus (T10). Leg weakness and disturbances of bladder and bowel function accompany the paralysis. Lesions at T9–T10 para lyze the lower—but not the upper—abdominal muscles, resulting in upward movement of the umbilicus when the abdominal wall contracts (Beevor’s sign). Lumbar Cord Lesions at the L2–L4 spinal cord levels paralyze flexion and adduction of the thigh, weaken leg extension at the knee, and abolish the patellar reflex. Lesions at L5–S1 paralyze only movements of the foot and ankle, flexion at the knee, and extension of the thigh, and abolish the ankle jerks (S1). Sacral Cord/Conus Medullaris The conus medullaris is the tapered caudal termination of the spinal cord, comprising the sacral and single coccygeal segments. The distinctive conus syndrome consists of bilateral saddle anesthesia (S3–S5), prominent bladder and bowel dysfunction (urinary retention and incontinence with lax anal tone), and impotence. The bulbocavernosus (S2–S4) and anal (S4–S5) reflexes are absent (Chap. 433). Muscle strength is largely preserved. By contrast, lesions of the cauda equina, the nerve roots derived from the lower cord, are characterized by low back and radicular pain, asymmetric leg weakness and sensory loss, variable areflexia in the lower extremities, and relative sparing of bowel and bladder function. Mass lesions in the lower spinal canal often produce a mixed clinical picture with elements of both cauda equina and conus medullaris syndromes. Special Patterns of Spinal Cord Disease The location of the major ascending and descending pathways of the spinal cord are shown in Fig. 453-1. Most fiber tracts—including the posterior col umns and the spinocerebellar and pyramidal tracts—are situated on the side of the body they innervate. However, afferent fibers medi ating pain and temperature sensation ascend in the spinothalamic

Posterior Columns (Joint Position, Vibration, Pressure) Fasciculus gracilis Fasciculus cuneatus Dorsal root Dorsal spinocerebellar tract C T L S Ventral spinocerebellar tract L/ S L/ S S L T C Lateral spinothalamic tract S L T C Pain, temperature Ventral reticulospinal tract Ventral root Ventral spinothalamic tract Pressure, touch (minor role) FIGURE 453-1 Transverse section through the spinal cord, composite representation, illustrating the principal ascending (left) and descending (right) pathways. The lateral and ventral spinothalamic tracts ascend contralateral to the side of the body that is innervated. In humans, the lateral corticospinal (pyramidal) tract is thought to lack strict somatotopic organization in the spinal cord. C, cervical; D, distal; E, extensors; F, flexors; L, lumbar; P, proximal; S, sacral; T, thoracic. tract contralateral to the side they supply. The anatomic

configura tions of these tracts produce characteristic syndromes that provide clues to the underlying disease process. Brown-Sequard Hemicord Syndrome This consists of ipsi lateral weakness (corticospinal tract) and loss of joint position and vibratory sense (posterior column), with contralateral loss of pain and temperature sense (spinothalamic tract) one or two levels below the lesion. Segmental signs, such as radicular pain, muscle atrophy, or loss of a deep tendon reflex, are unilateral. Partial forms are more common than the fully developed syndrome. Central Cord Syndrome This syndrome results from selective damage to the gray matter nerve cells and crossing spinothalamic tracts surrounding the central canal. In the cervical cord, the central cord syndrome produces arm weakness out of proportion to leg weakness and a “dissociated” sensory loss, meaning loss of pain and temperature sensations over the shoulders, lower neck, and upper trunk (cape distribution), in contrast to preservation of light touch, joint position, and vibration sense in these regions. Spinal trauma, syringomyelia, and intrinsic cord tumors are the main causes. Anterior Cord Syndrome Infarction of the cord is generally the result of occlusion or diminished flow in the anterior spinal artery. The result is bilateral tissue destruction at several contiguous levels that spares the posterior columns. All spinal cord functions—motor, sensory, and autonomic—are lost below the level of the lesion, with the striking exception of retained vibration and position sensation. Foramen Magnum Syndrome Lesions in this area interrupt decussating pyramidal tract fibers destined for the legs, which cross caudal to those of the arms, resulting in weakness of the legs (cru ral paresis). Compressive lesions near the foramen magnum may produce weakness of the ipsilateral shoulder and arm followed by weakness of the ipsilateral leg, then the contralateral leg, and finally the contralateral arm, an “around-the-clock” pattern that may begin

Anterior horn (motor neurons) Lateral corticospinal (pyramidal) tract Distal limb movements Rubrospinal tract Lateral reticulospinal tract P E D F CHAPTER 453 Vestibulospinal tract Axial and proximal limb movements Diseases of the Spinal Cord Tectospinal tract Ventral (uncrossed) corticospinal tract Distal limb movements (minor role) in any of the four limbs. There is typically suboccipital pain spread ing to the neck and shoulders. Intramedullary and Extramedullary Syndromes It is useful to differentiate intramedullary processes, arising within the sub stance of the cord, from extramedullary ones that lie outside the cord and compress the spinal cord or its vascular supply. The differ entiating features are only relative and serve as clinical guides. With extramedullary lesions, radicular pain is often prominent, and there is early sacral sensory loss and spastic weakness in the legs with incontinence due to injury to the corresponding sensory and motor fibers in the spinothalamic and corticospinal tracts (Fig. 453-1). Intramedullary lesions tend to produce poorly localized burn ing pain rather than radicular pain and to spare sensation in the perineal and sacral areas (“sacral sparing”), reflecting the laminated configuration of the spinothalamic tract with sacral fibers outer most; corticospinal tract signs appear later. Regarding extramedul lary lesions, a further distinction is made between extradural and intradural masses, as the former are generally malignant and the latter benign (neurofibroma being a common cause). Consequently, a long duration of symptoms favors an intradural origin. ACUTE AND SUBACUTE SPINAL

CORD DISEASES Symptoms of the cord diseases that evolve over days or weeks typically present as focal neck or back pain, followed by various combinations of paresthesias, sensory loss, motor weakness, and sphincter disturbance. There may be mild sensory symptoms only or a devastating functional transection of the cord. When paresthesias begin in the feet and then ascend, a

polyneuropathy is often considered, and in such cases, the presence of bladder disturbances and a sharply demarcated spinal cord level provide important clues to the spinal cord origin of the disease. In severe and abrupt cases, areflexia reflecting spinal shock may be present, but hyperreflexia supervenes over days or weeks; persistent

areflexic paralysis with a sensory level usually indicates necrosis over multiple segments of the spinal cord.

APPROACH TO THE PATIENT Compressive and Noncompressive Myelopathy DISTINGUISHING COMPRESSIVE FROM NONCOMPRESSIVE MYELOPATHY The first priority is to exclude treatable compression of the cord by a mass lesion. The common causes are tumor, epidural abscess or hematoma, herniated disk, and spondylitic vertebral pathology. Epi dural compression due to malignancy or abscess often causes warn ing signs of neck or back pain, bladder disturbances, and sensory symptoms that precede the development of paralysis. Spinal sublux ation, hemorrhage, and noncompressive etiologies such as infarc tion are more likely to produce myelopathy without antecedent symptoms. Magnetic resonance imaging (MRI) with gadolinium, centered on the clinically suspected level, is the initial diagnostic procedure if it is available; it is often appropriate to image the entire spine (cervical through sacral regions) to search for additional clini cally silent lesions. Once compressive lesions have been excluded, noncompressive causes of acute myelopathy that are intrinsic to the cord are considered, primarily vascular, inflammatory, and infec tious etiologies. PART 13 Neurologic Disorders ■ ■COMPRESSIVE MYELOPATHIES Neoplastic Spinal Cord Compression In adults, most neo plasms are epidural in origin, resulting from metastases to the adjacent vertebral column. The propensity of solid tumors to metastasize to the vertebral column probably reflects the high proportion of bone marrow located in the axial skeleton. Almost any malignant tumor can metasta size to the spinal column, with breast, lung, prostate, kidney, lymphoma, and myeloma being particularly frequent. The thoracic spinal column is most commonly involved; exceptions are metastases from prostate and ovarian cancer, which occur disproportionately in the sacral and lumbar vertebrae, probably from spread through Batson’s plexus, a network of veins along the anterior epidural space. Retroperitoneal neoplasms (especially lymphomas or sarcomas) enter the spinal canal laterally through the intervertebral foramina and produce radicular pain with signs of weakness that corresponds to the level of involved nerve roots. Pain is usually the initial symptom of spinal metastasis; it may be aching and localized or sharp and radiating in quality and typically worsens with movement, coughing, or sneezing and characteristi cally awakens patients at night. A recent onset of persistent back pain, particularly if in the thoracic spine (which is uncommonly involved by spondylosis), should prompt consideration of vertebral metasta sis. Rarely, pain is mild or absent. Plain radiographs of the spine and radionuclide bone scans have a limited role in diagnosis because they do not identify 15–20% of metastatic vertebral lesions and fail to detect paravertebral masses that reach the epidural space through the inter vertebral foramina. MRI provides excellent anatomic resolution of the extent of spinal tumors (Fig. 453-2) and is able to distinguish between malignant lesions and other masses—epidural abscess, tuberculoma, lipoma, or epidural hemorrhage, among others—that present in a simi lar fashion. Vertebral metastases are usually hypointense relative to a normal bone marrow signal on T1-weighted MRI; after the administra tion of gadolinium, contrast enhancement may deceptively “normalize” the appearance of the tumor by increasing its intensity to that of nor mal bone marrow. Infections of the spinal column (osteomyelitis and related disorders) are distinctive in that, unlike tumor, they often cross the disk space to involve the

adjacent vertebral body. If spinal cord compression is suspected, imaging should be obtained promptly. If there are radicular symptoms but no evidence of myelopa thy, it may be safe to defer imaging for 24–48 h. Up to 40% of patients who present with cord compression at one level are found to have asymptomatic epidural metastases elsewhere; thus, imaging of the entire length of the spine is important to define the extent of disease.

A B FIGURE 453-2 Epidural spinal cord compression due to breast carcinoma. Sagittal T1-weighted (A) and T2-weighted (B) magnetic resonance imaging scans through the cervicothoracic junction reveal an infiltrated and collapsed second thoracic vertebral body with posterior displacement and compression of the upper thoracic spinal cord. The low-intensity bone marrow signal in A signifies replacement by tumor. TREATMENT Neoplastic Spinal Cord Compression Proper management is based on multiple considerations, includ ing radiosensitivity of the primary tumor, extent of compression, prior therapy to the site, and stability of the spine. Treatment includes glucocorticoids to reduce cord edema, surgery and/or local radiotherapy (initiated as early as possible) to the symptomatic lesion, and specific therapy for the underlying tumor type. Gluco corticoids (typically dexamethasone, 10 mg intravenously) can be administered before an imaging study if there is clinical suspicion of cord compression and continued at a lower dose (4 mg every 6 h orally) until definitive treatment with radiotherapy and/or surgi cal decompression is completed. In one trial, initial management with surgery followed by radiotherapy was more effective than radiotherapy alone for patients with a single area of spinal cord compression by extradural tumor; however, patients with recur rent cord compression, brain metastases, radiosensitive tumors, or severe motor symptoms of >48 h in duration were excluded from this study. Stereotactic body radiotherapy, which delivers high doses of focused radiation, is preferred for radioresistant tumor types and for patients requiring re-irradiation. Biopsy of the epidural mass is unnecessary in patients with known primary cancer, but it is indicated if a history of underly ing cancer is lacking. Surgical treatment, either decompression by laminectomy or a spinal fixation procedure, is also indicated when signs of cord compression worsen despite radiotherapy; the maximum-tolerated dose of radiotherapy has been delivered previ ously to the site; a vertebral compression fracture or spinal instabil ity contributes to cord compression; or in cases of high-grade spinal cord compression from a radioresistant tumor. A good response to therapy can be expected in individuals who are ambulatory at presentation. Treatment usually prevents new weakness, and some recovery of motor function occurs in up to one-third of patients. Motor deficits (paraplegia or quadriplegia), once established for >12 h, do not usually improve, and beyond 48 h, the prognosis for substantial motor recovery is poor. Although most patients do not experience recurrences in the months fol lowing radiotherapy, with survival beyond 2 years, recurrence becomes increasingly likely and can be managed with additional radiotherapy.

FIGURE 453-3 Magnetic resonance imaging of a thoracic meningioma. Coronal T1-weighted postcontrast image through the thoracic spinal cord demonstrates intense and uniform enhancement of a well-circumscribed extramedullary mass (arrows) that displaces the spinal cord to the left. In contrast to tumors of the epidural space, most intradural mass lesions are slow-growing and benign. Meningiomas and neurofibromas account for most of these, with occasional cases caused by chordoma, lipoma, dermoid, or sarcoma. Meningiomas (Fig. 453-3) are often located posterior to the thoracic cord or near the foramen magnum, although they can arise from the meninges anywhere along the spinal canal. Neurofibromas are benign tumors of the nerve sheath that typi cally arise from the posterior root; when multiple, neurofibromatosis is the likely

etiology. Symptoms usually begin with radicular sensory symptoms followed by an asymmetric, progressive spinal cord syn drome. Therapy is surgical resection. Primary intramedullary tumors of the spinal cord are uncommon. They present as central cord or hemicord syndromes, often in the cervical region. There may be poorly localized burning pain in the extremities and sparing of sacral sensation. In adults, these lesions are ependymomas, hemangioblastomas, or low-grade astrocytomas (Fig. 453-4). Complete resection of an intramedullary ependymoma is often possible with microsurgical techniques. Debulking of an intra medullary astrocytoma can also be helpful, as these are often slowly growing lesions; the value of adjunctive radiotherapy and chemother apy is uncertain. Secondary (metastatic) intramedullary tumors also occur, especially in patients with advanced metastatic disease (Chap. 95), although these are not nearly as frequent as brain metastases. Spinal Epidural Abscess Spinal epidural abscess presents with midline back or neck pain, fever, and progressive limb weakness. Prompt recognition of this distinctive process may prevent permanent sequelae. Aching pain is almost always present, either over the spine or in a radicular pattern. The duration of pain prior to presentation is generally ≤2 weeks but may on occasion be several months or longer. Fever is typically but not invariably present, accompanied by elevated white blood cell count, sedimentation rate, and C-reactive protein. As the abscess expands, further spinal cord damage results from venous congestion and thrombosis. Once weakness and other signs of myelopathy appear, progression may be rapid and irreversible. A more chronic sterile granulomatous form of abscess is also known, usually after treatment of an acute epidural infection. Risk factors include an impaired immune status (HIV, diabetes mel litus, renal failure, alcoholism, malignancy), intravenous drug abuse,

CHAPTER 453 FIGURE 453-4 Magnetic resonance imaging of an intramedullary astrocytoma. Sagittal T1-weighted postcontrast image through the cervical spine demonstrates expansion of the upper cervical spine by a mass lesion emanating from within the spinal cord at the cervicomedullary junction. Irregular peripheral enhancement occurs within the mass (arrows). Diseases of the Spinal Cord and infections of the skin or other tissues. Two-thirds of epidural infections result from hematogenous spread of bacteria from the skin (furunculosis), soft tissue (pharyngeal or dental abscesses; sinusitis), or deep viscera (bacterial endocarditis). The remainder arises from direct extension of a local infection to the subdural space; examples of local predisposing conditions are vertebral osteomyelitis, decubitus ulcers, lumbar puncture, epidural anesthesia, or spinal surgery. Most cases are due to Staphylococcus aureus; gram-negative bacilli, Streptococcus, anaerobes, and fungi can also cause epidural abscesses. Methicillinresistant Staphylococcus aureus (MRSA) is an important consideration, and therapy should be tailored to this possibility. Tuberculosis from an adjacent vertebral source (Pott’s disease) remains an important cause in the developing world. MRI (Fig. 453-5) localizes the abscess and excludes other causes of myelopathy. Blood cultures are positive in more than half of cases, but direct aspiration of the abscess at surgery is often required for a A B FIGURE 453-5 Magnetic resonance (MR) imaging of a spinal epidural abscess due to tuberculosis. A. Sagittal T2-weighted free spin-echo MR sequence. A hypointense mass replaces the posterior elements of C3 and extends epidurally to compress the spinal cord (arrows). B. Sagittal T1-weighted image after contrast administration reveals a diffuse enhancement of the epidural process (arrows) with extension into the epidural space.

microbiologic diagnosis. Lumbar puncture is only required if encepha lopathy or other clinical signs raise the question of associated menin gitis, a feature that is found in <25% of cases. The level of the puncture should be planned to minimize the risk of meningitis due to passage of the needle

through infected tissue. A high cervical tap is sometimes the safest approach. Cerebrospinal fluid (CSF) abnormalities in epidural and subdural abscesses consist of pleocytosis with a preponderance of polymorphonuclear cells, an elevated protein level, and a reduced glucose level, but the responsible organism is not cultured unless there is associated meningitis.

TREATMENT Spinal Epidural Abscess Treatment is by decompressive laminectomy with debridement combined with long-term antibiotic treatment. Surgical evacua tion prevents development of paralysis and may improve or reverse paralysis in evolution, but it is unlikely to improve fixed deficits more than several days in duration. Broad-spectrum antibiotics, typically vancomycin 15–20 mg/kg q12h (Staphylococcus including MRSA, Streptococcus), ceftriaxone 2 g q12h (gram-negative bacilli), and when indicated, metronidazole 30 mg/kg per day divided into q6h intervals (anaerobes), should be started empirically before sur gery and then modified on the basis of culture results; medication is generally continued for 6–8 weeks. If surgery is contraindicated or if there is a fixed paraplegia or quadriplegia that is unlikely to improve following surgery, long-term administration of systemic and oral antibiotics can be used; in such cases, the choice of antibiotics may be guided by results of blood cultures. Surgical management remains the treatment of choice unless the abscess is limited in size and causes few or no neurologic signs. PART 13 Neurologic Disorders With prompt diagnosis and treatment, up to two-thirds of patients experience significant recovery. Spinal Epidural Hematoma Hemorrhage into the epidural (or subdural) space causes acute focal or radicular pain followed by vari able signs of a spinal cord or conus medullaris disorder. Therapeutic anticoagulation, trauma, tumor, or blood dyscrasias are predisposing conditions. Rare cases complicate lumbar puncture or epidural anes thesia. MRI and computed tomography (CT) confirm the clinical sus picion and can delineate the extent of the bleeding. Treatment consists of prompt reversal of any underlying clotting disorder and surgical decompression. Surgery may be followed by substantial recovery, espe cially in patients with some preservation of motor function preopera tively. Because of the risk of hemorrhage, lumbar puncture should be avoided whenever possible in patients with severe thrombocytopenia or other coagulopathies. Hematomyelia Hemorrhage into the substance of the spinal cord is a rare result of trauma, intraparenchymal vascular malformation (see below), vasculitis due to polyarteritis nodosa or systemic lupus erythematosus (SLE), bleeding disorders, or a spinal cord neoplasm. Hematomyelia presents as an acute painful transverse myelopathy. With large lesions, extension into the subarachnoid space results in subarachnoid hemorrhage (Chap. 440). Diagnosis is by MRI or CT. Therapy is supportive, and surgical intervention is generally not useful. An exception is hematomyelia due to an underlying vascular malfor mation, for which spinal angiography and endovascular occlusion may be indicated, or surgery to evacuate the clot and remove the underlying vascular lesion. Acute Spondylytic Myelopathy Of particular concern are hyperextension injuries in patients with underlying degenerative cervi cal spine disease (Chap. 19). The provoking stimulus may be obvious, such as a forward fall, or occur after seemingly innocuous low-impact movements of the neck. A preexisting stenotic spinal canal is often present, and “buckling” of the posterior ligamentum flavum (less com monly acute disk herniation or subluxation) is believed to produce the cord compression, sometimes with a central cord syndrome (see above)

and involvement of the upper, more than lower, limbs. Deficits can be transient, resulting in a “concussion” of the spinal cord, or permanent. The more common syndrome of chronic spondylitic myelopathy is dis cussed below. ■ ■NONCOMPRESSIVE MYELOPATHIES Once a compressive etiology has been excluded as the cause of an acute myelopathy, the principal challenge is to

distinguish vascular/ischemic from inflammatory/infectious causes. This is often not straightforward because clinical presentations can overlap. Moreover, findings that usually point to an inflammatory etiology—such as focal gadolinium enhancement on MRI scans or pleocytosis in the CSF—can also occur with spinal cord ischemia. Ischemia is likely in hyperacute presenta tions with back or neck pain and when an anterior pattern of spinal cord injury is identified on clinical examination or by MRI. By contrast, inflammation is more likely in cases that develop subacutely or when systemic symptoms, CSF oligoclonal bands, or multiple discrete spinal cord MRI lesions are present. The most frequent inflammatory causes of acute myelopathy are multiple sclerosis (MS); neuromyelitis optica (NMO); sarcoidosis; systemic inflammatory diseases such as SLE and Behcet's disease; postinfectious or idiopathic transverse myelitis, which is presumed to be an immune condition related to acute disseminated encephalomyelitis (Chap. 456); and infectious (primarily viral) causes. The evaluation generally requires a lumbar puncture and a search for underlying systemic disease (Table 453-3). Spinal Cord Infarction The cord is supplied by three arteries that course vertically over its surface: a single anterior spinal artery and paired posterior spinal arteries. The anterior spinal artery originates in paired branches of the vertebral arteries at the craniocervical junction and is fed by additional radicular vessels that arise at C6, at an upper thoracic level, and, most consistently, at T11–L2 (artery of Adamkie wicz). At each spinal cord segment, paired penetrating vessels branch from the anterior spinal artery to supply the anterior two-thirds of the TABLE 453-3 Considerations in the Evaluation of Myelopathy

1. MRI of spinal cord with and without contrast (exclude compressive causes).
2. CSF studies: Cell count, protein, glucose, IgG index/synthesis rate, oligoclonal bands, VDRL; Gram's stain, acid-fast bacilli, and India ink stains; PCR for VZV, HSV-2, HSV-1, EBV, CMV, HHV-6, enteroviruses, HIV; antibody for HTLV-1, Borrelia burgdorferi, Mycoplasma pneumoniae, and Chlamydia pneumoniae; viral, bacterial, mycobacterial, and fungal cultures.
3. Blood studies for infection: HIV; RPR; IgG and IgM enterovirus antibody; IgM WNV, group B arbovirus, mumps, measles, rubella, Brucella melitensis, Chlamydia psittaci, Bartonella henselae, schistosomal antibody; PCR and antigen tests for SARS-CoV-2; cultures for B. melitensis. Also consider nasal/ pharyngeal/anal cultures for enteroviruses; stool O&P for Schistosoma ova.
4. Vascular causes: MRI, CT myelogram; spinal angiogram.
5. Multiple sclerosis: Brain MRI scan; evoked potentials.
6. Neuromyelitis optica and related disorders: Serum anti-aquaporin-4 antibody, anti-MOG antibody, anti-GFAP antibody.
7. Sarcoidosis: Serum angiotensin-converting enzyme; serum Ca; 24-h urine Ca; chest x-ray; chest CT; slit-lamp eye examination; total-body gallium scan; lymph node biopsy.
8. Systemic immune-mediated disorders: ESR; ANA; ENA; dsDNA; rheumatoid factor; anti-SSA; anti-SSB, complement levels; antiphospholipid and anticardiolipin antibodies; pANCA; antimicrosomal and antithyroglobulin antibodies; if Sjögren's syndrome suspected, Schirmer test, salivary gland scintigraphy, and salivary/lacrimal gland biopsy.
9. Paraneoplastic disorders: Antibody for amphiphysin, CRMP5, Hu, others.
10. Other: vitamin B12, copper, zinc. Abbreviations: ANA, antinuclear antibodies; Ca, calcium; CMV, cytomegalovirus; CRMP5, collapsin response mediator 5-IgG; CSF, cerebrospinal fluid; CT, computed tomography; EBV, Epstein-Barr virus; ENA, epithelial neutrophil-activating peptide; ESR, erythrocyte sedimentation rate; GFAP, glial fibrillary acidic

protein; HHV, human herpes virus; HSV, herpes simplex virus; HTLV, human T-cell leukemia/lymphoma virus; MOG, myelin oligodendrocyte glycoprotein; MRI, magnetic resonance imaging; O&P, ova and parasites; pANCA, perinuclear antineutrophilic cytoplasmic antibodies; PCR, polymerase chain reaction; RPR, rapid plasma reagin (test); VDRL, Venereal Disease Research Laboratory; VZV, varicella-zoster virus; WNV West Nile virus.

cord; the posterior spinal arteries, which often become less distinct below the midthoracic level, supply the posterior columns. Spinal cord ischemia can occur at any level; however, the presence of the artery of Adamkiewicz below, and the anterior spinal artery circula tion above, creates a region of marginal blood flow in the upper tho racic segments. With hypotension or cross-clamping of the aorta, cord infarction typically occurs at the level of T3–T4 and also at boundary zones between the anterior and posterior spinal artery territories. The latter may result in a rapidly progressive syndrome over hours of weak ness and spasticity with little sensory change. Acute infarction in the territory of the anterior spinal artery pro duces paraplegia or quadriplegia, dissociated sensory loss affecting pain and temperature sense but sparing vibration and position sense, and loss of sphincter control (anterior cord syndrome). Onset may be sudden but more typically is progressive over minutes or a few hours, unlike stroke in the cerebral hemispheres. Sharp midline or radiating back pain localized to the area of ischemia is frequent. Areflexia due to spinal shock is often present initially; with time, hyperreflexia and spasticity appear. Less common is infarction in the territory of the posterior spinal arteries, resulting in loss of posterior column function either on one side or bilaterally. Causes of spinal cord infarction include aortic atherosclerosis, dis secting aortic aneurysm, vertebral artery occlusion or dissection in the neck, aortic surgery, or profound hypotension from any cause. Car diogenic emboli, vasculitis (Chap. 375), and collagen vascular disease (particularly SLE [Chap. 368], Sjögren’s syndrome [Chap. 373], and the antiphospholipid antibody syndrome [Chap. 369]) are other etiologies. Occasional cases develop from embolism of nucleus pulposus material into spinal vessels, usually from local spine trauma. A surfer’s myelopa thy, usually in the thoracic region, has been associated with prolonged back extension due to lifting the upper body off the board while wait ing for waves; it typically manifests as back pain followed by an anterior cord syndrome with progressive paralysis and loss of sphincter control and is likely vascular in origin. A few reports have also been associated with cocaine use, as well as with heroin. In a substantial number of cases, no cause can be found, and thromboembolism in arterial feeders is suspected. MRI may fail to demonstrate infarctions of the cord, especially in the first day, but often the imaging becomes abnormal at the affected level. MRI features suggestive of cord infarction include diffusionweighted restriction; longitudinally extensive anterior T2 signal bright ness on sagittal images (“pencil-like sign”); focal enhancement in the anterior horns; and paired areas of focal T2 hyperintensity in the anterior medial cord on axial images (“owl’s eyes”). When present, infarction of a vertebral body adjacent to the area of cord involvement is diagnostically helpful. With cord infarction due to presumed thromboembolism, acute anticoagulation is not indicated, with the possible exception of the unusual transient ischemic attack or incomplete infarction with a stut tering or progressive course. The antiphospholipid antibody syndrome is treated with anticoagulation (Chap. 369). Increasing systemic blood pressure to a mean arterial pressure of >90 mmHg, or lumbar drainage of spinal fluid, was reportedly helpful in a few published cases of cord infarction, but neither of these approaches has been studied system atically. Prognosis following spinal cord infarction is influenced by the severity of the deficits at presentation; patients with severe motor weakness and

those with persistent areflexia usually do poorly, but in one large series, some improvement over time occurred in many patients, with more than half ultimately regaining some ambulation. Inflammatory and Immune Myelopathies (Myelitis) This broad category includes MS, NMO, and postinfectious myelitis, as well as sarcoidosis, systemic autoimmune disease, and infections. In approximately one-quarter of cases of myelitis, no underlying cause can be identified. Some will later manifest additional symptoms of an immune-mediated disease. Transverse myelitis refers to a pattern of extensive spinal cord injury due to inflammation, clinically manifest as bilateral sensory symptoms, unilateral or bilateral weakness, and bladder and/or bowel disturbance. In most of the developed world,

MS is the most common inflammatory cause of an acute myelitis, but involvement is usually partial and not transverse. Recurrent episodes of myelitis are usually due to one of the immune-mediated diseases or to infection with herpes simplex virus (HSV) type 2 (below).

MULTIPLE SCLEROSIS MS may present with acute myelitis, particu larly in individuals of Asian or African ancestry. In whites, MS attacks rarely cause a transverse myelopathy (i.e., attacks of bilateral sensory disturbances, unilateral or bilateral weakness, and bladder or bowel symptoms), but MS is among the most common causes of a partial cord syndrome. MRI findings in MS-associated myelitis typically consist of mild swelling of the cord and diffuse or multifocal “shoddy” areas of abnormal signal on T2-weighted sequences. Contrast enhance ment, indicating disruption in the blood-brain barrier associated with inflammation, is present in many acute cases. In one study 68% of patients presenting with partial myelitis developed MS after a mean follow-up of 4 years; risk factors for conversion to MS included age <40 years, inflammatory CSF, and more than three periventricular lesions on brain MRI. CHAPTER 453 Treatment of acute episodes of MS-associated myelitis consists of intravenous methylprednisolone (500 mg qd for 3 days) followed by oral prednisone (1 mg/kg per day for several weeks, then a gradual taper). A course of plasma exchange may be indicated for severe cases if glucocorticoids are ineffective. MS is discussed in Chap. 455. Diseases of the Spinal Cord NEUROMYELITIS OPTICA NMO is an immune-mediated disorder consisting of a severe myelopathy that is typically longitudinally extensive, meaning that the lesion typically spans three or more ver tebral segments. NMO is associated with optic neuritis that is often bilateral and may precede or follow myelitis by weeks or months and also by brainstem and, in some cases, hypothalamic or focal cerebral white matter involvement. Recurrent myelitis without optic nerve or other involvement can also occur in NMO. CSF studies reveal a variable mononuclear pleocytosis of up to several hundred cells per microliter (higher than in typical MS) with occasional cases show ing polymorphonuclear predominant pattern; oligoclonal bands are present in <20% of NMO cases. Diagnostic serum autoantibodies against the water channel protein aquaporin-4 (AQP-4) are present in 90% of patients with NMO; in some AQP-4-negative cases, auto antibodies against the central nervous system (CNS) myelin protein myelin oligodendrocyte glycoprotein (MOG) are found. NMO is also associated with SLE (see below) as well as with other systemic autoim mune diseases; rare cases are paraneoplastic. Acute relapses of NMO are treated with glucocorticoids and, for severe or refractory cases, plasma exchange. Three monoclonal antibodies are now available for prophylactic treatment: eculizumab, a terminal complement inhibitor; inebilizumab, a B-cell depleter; and satralizumab, an interleukin (IL) 6 receptor blocker. Other options include off-label use of azathioprine, mycophenolate, or rituximab. Treatment for 5 years or longer is gener ally recommended. NMO is discussed in Chap. 456. SARCOIDOSIS Sarcoid myelopathy may present as a slowly progressive or relapsing disorder.

Clinically, sensory involvement often predomi nates. MRI may show edematous swelling of the spinal cord mimicking tumor and in some cases longitudinally extensive involvement resem bling NMO. Subpial gadolinium enhancement of active lesions, which may appear nodular, are typically located along the dorsal surface of the cord; on axial images, these dorsal lesions combined with enhance ment of the central canal can produce a characteristic “trident sign.” The typical CSF profile consists of a mild lymphocyte-predominant pleocytosis and elevated protein level; in a minority of cases, reduced glucose and oligoclonal bands are found. When present, the hypogly corrhachia can be helpful in distinguishing neurosarcoid from other noninfectious causes of myelitis. The diagnosis is particularly difficult when systemic manifestations of sarcoid are minor or absent (nearly 50% of cases) or when other typical neurologic manifestations of the disease, such as cranial neuropathy, hypothalamic involvement, or meningeal enhancement visualized by MRI, are lacking. A slit-lamp examination of the eye to search for uveitis, chest x-ray and CT to assess pulmonary involvement and mediastinal lymphadenopathy, serum or CSF angiotensin-converting enzyme (ACE; lacks specificity

and values are elevated in only a minority of cases), serum calcium, and a gallium scan may assist in the diagnosis. Initial treatment is with high doses of glucocorticoids, which need to be administered long term and tapered slowly while monitoring resolution of clinical and MRI signs of active disease; relapses are managed with high-dose glucocorticoids plus a steroid-sparing immunosuppressant drug (typically mycopheno late mofetil, azathioprine, or methotrexate) or with the tumor necrosis factor α-inhibitor infliximab. Sarcoidosis is discussed in Chap. 379.

SYSTEMIC IMMUNE-MEDIATED DISORDERS Myelitis occurs in a small number of patients with SLE, many cases of which are associated with antibodies to AQP-4 and satisfy diagnostic criteria for NMO (discussed above). These patients are at high risk of developing future episodes of myelitis and/or optic neuritis. In others, the etiology of SLE-associated myelitis is uncertain. Antiphospholipid antibodies have been sug gested to play a role; however, the frequency of these antibodies is similar in SLE patients with and without myelitis. NMO-associated myelitis typically produces severe clinical disease, CSF pleocytosis with polymorphonuclear leukocytes, and an MRI pattern of central gray matter spinal cord involvement; in cases not due to NMO, less severe and more subacutely evolving clinical findings are often present, with milder CSF lymphocytic pleocytosis and MRI changes consistent with white matter involvement of the cord. In both forms, CSF oligoclonal bands are variable findings. There are no systematic trials of therapy for SLE myelitis, but based on limited data, patients with AQP-4 antibodies should be treated as for NMO (above), and in others, high-dose glu cocorticoids followed by cyclophosphamide have been recommended. Severe episodes that do not initially respond to glucocorticoids are often treated with a course of plasma exchange. Sjögren’s syndrome (Chap. 373) can also be associated with NMO and also with cases of chronic progressive myelopathy. Other immune-mediated myelitides include Behçet’s disease (Chap. 376), antiphospholipid antibody syn drome (Chap. 369), mixed connective tissue disease (Chap. 372), and vasculitis related to polyarteritis nodosa, perinuclear antineutrophilic cytoplasmic (pANCA) antibodies, or primary CNS vasculitis (Chap. 375). Occasional cases of myelitis, often accompanied by other manifestations that can include encephalitis or optic neuritis, have been associated with autoantibodies against glial fibrillary acidic pro tein (GFAP) (Chap. 456). Other rare etiologies are chronic lympho cytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) and Erdheim-Chester disease producing inflammatory mass-like lesions that can be intramedullary or extra axial and compressive. PART 13

Neurologic Disorders POSTINFECTIOUS MYELITIS Many cases of myelitis, termed postinfec tious or postvaccinal, follow an infection or vaccination. Numerous organisms have been implicated, including Epstein-Barr virus (EBV), cytomegalovirus (CMV), and mycoplasma most frequently, with many others including influenza, measles, varicella, mumps, and yellow fever also described. Recently, vaccination (or active infection) with SARS-CoV-2 virus has been associated with a small number of cases of myelitis and NMO. As in the related disorder acute disseminated encephalomyelitis (Chap. 456), postinfectious myelitis often begins as the patient appears to be recovering from an acute febrile infection or in the subsequent days or weeks, but an infectious agent cannot be isolated from the nervous system or CSF. Serum anti-MOG antibodies are present acutely in some cases, especially in children. The presump tion is that the myelitis represents an autoimmune disorder triggered by infection and is not due to direct infection of the spinal cord. No randomized controlled trials of therapy exist; treatment is usually with glucocorticoids or, in fulminant cases, plasma exchange. ACUTE INFECTIOUS MYELITIS Many viruses have been associated with an acute myelitis that is infectious in nature rather than postinfec tious. Nonetheless, the two processes are often difficult to distinguish. Herpes zoster is a well characterized agent of viral myelitis, with direct spread to the spinal cord from dorsal root ganglia, and HSV types 1 and 2, EBV, CMV, and rabies virus are other well-described causes. Zika virus has also been recognized as a cause of infectious myelitis, as has a rare association with monkeypox. HSV-2 (and less commonly HSV-1) produces a distinctive syndrome of recurrent sacral and

cauda equina neuritis in association with outbreaks of genital herpes (Elsberg’s syndrome). Poliomyelitis is a prototypic viral myelitis that is more or less restricted to the anterior gray matter of the cord contain ing the spinal motoneurons. A polio-like syndrome can also be caused by a large number of enteroviruses (including enterovirus A-71 and coxsackie) and, importantly, by West Nile virus and other flaviviruses such as Japanese encephalitis. Beginning in 2012, cases of acute flaccid paralysis in children and adolescents have appeared associated with enterovirus A-71 and D-68 infection. Chronic viral myelitic infections, such as those due to HIV or human T-cell lymphotropic virus type 1 (HTLV-1), are discussed below. Bacterial and mycobacterial myelitis (most are essentially abscesses) are less common than viral causes and much less frequent than cerebral bacterial abscess. Almost any pathogenic species may be responsible, including Borrelia burgdorferi (Lyme disease), Listeria monocytogenes, Mycobacterium tuberculosis, and Treponema pallidum (syphilis). Myco plasma pneumoniae may be a cause of myelitis, but its status is uncer tain because many cases are more properly classified as postinfectious. Schistosomiasis (Chap. 241) is an important cause of parasitic myelitis in endemic areas. The process is intensely inflammatory and granulomatous, caused by a local response to tissue-digesting enzymes from the ova of the parasite, typically Schistosoma haematobium or Schistosoma mansoni. Toxoplasmosis (Chap. 235) can occasionally cause a focal myelopathy, and this diagnosis should especially be con sidered in patients with AIDS (Chap. 208). Cysticercosis (Chap. 242) is another consideration, although myelitis from this helminth is far less common than parenchymal brain or meningeal involvement. In cases of suspected viral myelitis, it may be appropriate to begin specific therapy pending laboratory confirmation. Herpes zoster, HSV, and EBV myelitis are treated with intravenous acyclovir (10 mg/kg q8h) or oral valacyclovir (2 g tid) for 10–14 days; CMV is treated with ganciclovir (5 mg/kg IV bid) plus foscarnet (60 mg/kg IV tid) or cido fovir (5 mg/kg per week for 2 weeks, then biweekly for two additional doses). High-Voltage Electrical Injury Spinal cord injuries are promi nent following electrocution from lightning strikes or other accidental electrical exposures. The syndrome consists of transient weakness acutely (often with an altered sensorium

and focal cerebral distur bances), sometimes followed several days or even weeks later by a myelopathy that can be severe and permanent. This is a rare injury type, and limited data incriminate a vascular pathology involving the anterior spinal artery and its branches in some cases. Therapy is supportive. CHRONIC MYELOPATHIES ■ ■SPONDYLOTIC MYELOPATHY Spondylotic myelopathy is the most common cause of myelopathy and of gait difficulty in the elderly, accounting for more than half of non traumatic spinal cord injuries in some series. Neck and shoulder pain with stiffness are early symptoms; impingement of bone and soft tissue overgrowth on nerve roots results in radicular arm pain, most often in a C5 or C6 distribution. Compression of the cervical cord, which occurs in fewer than one-third of cases, produces a slowly progressive spastic paraparesis, at times asymmetric and often accompanied by paresthesias in the feet and hands. Vibratory sense is diminished in the legs, there is a Romberg sign, and occasionally there is a sensory level for vibration or pinprick on the upper thorax. In some cases, cough ing or straining produces leg weakness or radiating arm or shoulder pain. Dermatomal sensory loss in the arms, atrophy of intrinsic hand muscles, increased deep-tendon reflexes in the legs, and extensor plan tar responses are common. Urinary urgency or incontinence occurs in advanced cases, but there are many alternative causes of these problems in older individuals. A tendon reflex in the arms is often diminished at some level, most often at the biceps (C5–C6). In individual cases, radicular, myelopathic, or combined signs may predominate. The diagnosis should always be considered in cases of progressive cervical myelopathy, paresthesias of the feet and hands, or wasting of the hands.

Diagnosis is usually made by MRI and may be suspected from CT images; plain x-rays are less helpful. Extrinsic cord compression and deformation are appreciated on axial MRI views, and T2-weighted sequences may reveal areas of high signal intensity within the cord adjacent to the site of compression. A cervical collar may be helpful in milder cases, but the likelihood of progression of medically treated myelopathy is high, estimated at 8% over 1 year. Definitive therapy consists of surgical decompression, either posterior laminectomy or an anterior approach with resection of the protruded disk and bony material. Cervical spondylosis and related degenerative diseases of the upper spine are discussed in Chap. 19. ■ ■VASCULAR MALFORMATIONS OF THE

CORD AND DURA Vascular malformations, comprising ~4% of all mass lesions of the cord and overlying dura, are treatable causes of progressive myelopathy. Most common are fistulas located within the dura or posteriorly along the surface of the cord. Most dural arteriovenous (AV) fistulas are located at or below the midthoracic level, usually consisting of a direct connection between a radicular feeding artery in the nerve root sleeve with dural veins. The typical presentation is a middle-aged man with a progressive myelopathy that worsens slowly or intermittently and may have periods of remission, sometimes mimicking MS. Acute deteriora tion due to hemorrhage into the spinal cord (hematomyelia) or sub arachnoid space may also occur but is rare. In many cases, progression results from local ischemia and edema due to venous congestion. Most patients have incomplete sensory, motor, and bladder disturbances. The motor disorder may predominate and produce a mixture of upper and restricted lower motor neuron signs, simulating amyotrophic lateral sclerosis (ALS). Pain over the dorsal spine, dysesthesias, or radicular pain may be present. Other symptoms suggestive of AV mal formation (AVM) or dural fistula include intermittent claudication; symptoms that change with posture, exertion, Valsalva maneuver, or menses; and fever. Less commonly, AVM disorders are intramedullary rather than dural. One unusual disorder is a progressive thoracic myelopathy with paraparesis developing over weeks or months,

characterized pathologi cally by abnormally thick, hyalinized vessels within the cord (subacute necrotic myelopathy or Foix-Alajouanine syndrome). Spinal bruits are infrequent but may be sought at rest and after exercise in suspected cases. A vascular nevus on the overlying skin may indicate an underlying vascular malformation as occurs with KlippelTrenaunay-Weber syndrome. MR angiography and CT angiography can detect the draining vessels of many AVMs (Fig. 453-6). Definitive diagnosis requires selective spinal angiography, which defines the feed ing vessels and the extent of the malformation. Treatment is tailored to the anatomy and location of the lesion and generally consists of microsurgical resection, endovascular embolization of the major feed ing vessels, or a combination of the two approaches. ■ ■RETROVIRUS-ASSOCIATED MYELOPATHIES The myelopathy associated with HTLV-1, formerly called tropical spas tic paraparesis, is a slowly progressive spastic syndrome with variable sensory and bladder disturbance. Approximately half of patients have mild back or leg pain. The neurologic signs may be asymmetric, often lacking a well-defined sensory level; the only sign in the arms may be hyperreflexia after several years of illness. The onset is usually insidi ous, and the tempo of clinical progression occurs at a variable rate; in one study, median time for progression to cane-, walker-, or wheel chair-dependent state was 6, 13, and 21 years, respectively. Progres sion appears to be more rapid in older patients and those with higher viral loads. Diagnosis is made by demonstration of HTLV-1-specific antibody in serum by enzyme-linked immunosorbent assay (ELISA), confirmed by radioimmunoprecipitation or Western blot analysis. Especially in endemic areas, a finding of HTLV-1 seropositivity in a patient with myelopathy does not necessarily prove that HTLV-1 is causative. The CSF/serum antibody index may provide support by establishing intrathecal synthesis of antibodies, including oligoclonal antibodies, favoring HTVL-1 myelopathy over asymptomatic carriage.

CHAPTER 453 FIGURE 453-6 Arteriovenous malformation. Sagittal magnetic resonance scans of the thoracic spinal cord: T2 fast spin-echo technique (left) and T1 postcontrast image (right). On the T2-weighted image (left), abnormally high signal intensity is noted in the central aspect of the spinal cord (arrowheads). Numerous punctate flow voids indent the dorsal and ventral spinal cord (arrow). These represent the abnormally dilated venous plexus supplied by a dural arteriovenous fistula. After contrast administration (right), multiple, serpentine, enhancing veins (arrows) on the ventral and dorsal aspect of the thoracic spinal cord are visualized, diagnostic of arteriovenous malformation. This patient was a 54-year-old man with a 4-year history of progressive paraparesis. Diseases of the Spinal Cord Measuring proviral DNA by polymerase chain reaction (PCR) in peripheral blood and CSF cells can be useful as an ancillary part of diagnosis. The pathogenesis of the myelopathy is uncertain. It could result from an immune response directed against HTLV-1 antigens in the nervous system or, alternatively, to secondary autoimmunity trig gered by the viral infection. There is no proven effective treatment. Based on limited evidence, systemic glucocorticoids, pulsed high-dose induction followed by low-dose chronic maintenance, can be tried, and mogamulizumab, a monoclonal antibody directed against CCR4, has been reported in one preliminary trial to slow progression and reduce neurologic disability in some recipients. A progressive myelopathy can also result from HIV infection (Chap. 208). It is characterized by vacuolar degeneration of the pos terior and lateral tracts, resembling subacute combined degeneration (see below). SYRINGOMYELIA Syringomyelia is a developmental cavity in the cervical cord that may enlarge and produce progressive myelopathy or may remain asymptomatic. Symptoms begin insidiously in adolescence or early adulthood, progress irregularly, and may undergo spontaneous arrest for several years. Many young patients acquire a cervical-thoracic scoliosis. More than half of all cases are associated with Chiari type 1 malformations in which the

cerebellar tonsils protrude through the foramen magnum and into the cervical spinal canal. The pathophysi ology of syrinx expansion is controversial, but some interference with the normal flow of CSF seems likely, perhaps by the Chiari malfor mation. Acquired cavitations of the cord in areas of necrosis are also termed syrinx cavities; these follow trauma, myelitis, necrotic spinal cord tumors, and chronic arachnoiditis due to tuberculosis and other etiologies. The presentation is a central cord syndrome consisting of a regional dissociated sensory loss (loss of pain and temperature sensation with sparing of touch and vibration) and areflexic weakness in the upper limbs. The sensory deficit has a distribution that is “suspended” over the nape of the neck, shoulders, and upper arms (cape distribution) or in the hands. Most cases begin asymmetrically with unilateral sensory loss in the hands that leads to injuries and burns that are not

PART 13 Neurologic Disorders FIGURE 453-7 Magnetic resonance imaging of syringomyelia associated with a Chiari malformation. Sagittal T1-weighted image through the cervical and upper thoracic spine demonstrates descent of the cerebellar tonsils below the level of the foramen magnum (black arrows). Within the substance of the cervical and thoracic spinal cord, a cerebrospinal fluid collection dilates the central canal (white arrows). appreciated by the patient. Muscle wasting in the lower neck, shoul ders, arms, and hands with asymmetric or absent reflexes in the arms reflects expansion of the cavity in the gray matter of the cord. As the cavity enlarges and compresses the long tracts, spasticity and weakness of the legs, bladder and bowel dysfunction, and Horner’s syndrome appear. Some patients develop facial numbness and sensory loss from damage to the descending tract of the trigeminal nerve (C2 level or above). In cases with Chiari malformations, cough-induced headache and neck, arm, or facial pain may be reported. Extension of the syrinx into the medulla, syringobulbia, causes palatal or vocal cord paralysis, dysarthria, horizontal or vertical nystagmus, episodic dizziness or ver tigo, and tongue weakness with atrophy. MRI accurately identifies developmental and acquired syrinx cavi ties and their associated spinal cord enlargement (Fig. 453-7). Images of the brain and the entire spinal cord should be obtained to delineate the full longitudinal extent of the syrinx, assess posterior fossa struc tures for the Chiari malformation, and determine whether hydro cephalus is present. TREATMENT Syringomyelia Surgical decompression is the treatment of choice, with mixed results reported in most series. The Chiari tonsillar herniation may be decompressed, generally by suboccipital craniectomy, upper cer vical laminectomy, and placement of a dural graft. Fourth ventricular outflow is reestablished by this procedure. If the syrinx cavity is large, some surgeons recommend direct decompression or drainage, but an added benefit of this procedure has not been demonstrated, and complications are common. Shunting of hydrocephalus, when pres ent, generally precedes any attempt to correct the syrinx. Surgery may stabilize the neurologic deficit, and some patients improve. Patients with few symptoms and signs from the syrinx do not require surgery and are followed by serial clinical and imaging examinations. Syrinx cavities secondary to trauma or infection, if symptomatic, can be treated with a decompression and drainage procedure in which a small shunt is inserted between the cavity and subarach noid space; alternatively, the cavity can be fenestrated. Cases due to intramedullary spinal cord tumor are generally managed by resec tion of the tumor.

■ ■CHRONIC MYELOPATHY OF MULTIPLE SCLEROSIS A chronic progressive myelopathy is the most frequent cause of dis ability in both primary progressive and secondary progressive forms of MS. Involvement is typically bilateral but asymmetric and produces motor, sensory, and bladder/bowel disturbances. Fixed motor disabil ity appears to result from extensive loss of axons in the

corticospinal tracts. Diagnosis is facilitated by identification of earlier attacks such as optic neuritis. MRI, CSF, and evoked-response testing are confirma tory. Treatment with ocrelizumab, an anti-CD20 B-cell monoclonal antibody, is effective in patients with primary progressive MS, and disease-modifying therapy is also indicated in patients with secondary progressive MS who have clinical or MRI evidence of active disease. MS is discussed in Chap. 455. ■ ■SUBACUTE COMBINED DEGENERATION (VITAMIN B12 DEFICIENCY) This treatable myelopathy presents with subacute paresthesias in the hands and feet, loss of vibration and position sensation, and a progres sive spastic and ataxic weakness. Loss of reflexes due to an associated peripheral neuropathy in a patient who also has Babinski signs is a helpful diagnostic clue. Optic atrophy and irritability or other cogni tive changes may be prominent in advanced cases and are occasion ally the presenting symptoms. The myelopathy of subacute combined degeneration tends to be diffuse rather than focal; signs are generally symmetric and reflect predominant involvement of the posterior and lateral tracts, including Romberg sign. Causes include dietary defi ciency, especially in vegans, and gastric malabsorption syndromes including pernicious anemia (Chap. 104). The diagnosis is confirmed by the finding of macrocytic red blood cells, a low serum B12 concen tration, and elevated serum levels of homocysteine and methylmalonic acid. Treatment is by replacement therapy, beginning with 1000 µg of intramuscular vitamin B12 daily for 5–7 days and then continued as a once-weekly dose for 4–8 weeks and then as a monthly maintenance dose; oral maintenance with high doses of cyanocobalamin (1–2 mg daily) can also be used for maintenance, as small amounts of vitamin B12 are absorbed passively by the gut even in pernicious anemia. Two closely related conditions deserve mention here. The first is folate deficiency–associated myelopathy, now only rarely seen since widespread programs of dietary fortification with folate have been implemented. A second is due to inhalation with nitrous oxide (laugh ing gas), an irreversible inhibitor of vitamin B12, which also produces a myelopathy identical to subacute combined degeneration. Exposure to nitrous oxide may occur during dental or surgical procedures or from recreational inhalation (“doing whippets”). ■ ■HYPOCUPRIC MYELOPATHY This myelopathy is similar to subacute combined degeneration, except serum levels of B12 are normal. Low levels of serum copper are found, and often there is also a low level of serum ceruloplasmin. Some cases follow gastrointestinal procedures, particularly bariatric surgery, that result in impaired copper absorption; others have been associated with excess zinc from health food supplements or, in the past, zinccontaining denture creams, all of which impair copper absorption via induction of metallothionein, a copper-binding protein. Many cases are idiopathic. There is often a coexisting anemia. Improvement or at least stabilization may be expected with reconstitution of copper stores by oral supplementation (2 mg/d). ■ ■TABES DORSALIS The classic syphilitic syndromes of tabes dorsalis and meningovascular inflammation of the spinal cord are now less frequent than in the past but must be considered in the differential diagnosis of spinal cord dis orders. The characteristic symptoms of tabes are fleeting and repetitive lancinating pains, primarily in the legs or less often in the back, thorax, abdomen, arms, and face. Ataxia of the legs and gait due to loss of position sense occurs in half of patients. Paresthesias, bladder distur bances, and acute abdominal pain with vomiting (visceral crisis) occur in 15–30% of patients. The cardinal signs of tabes are loss of reflexes in the legs; impaired position and vibratory sense; Romberg sign; and,

in almost all cases, bilateral Argyll Robertson pupils, which fail to constrict to light but accommodate. Diabetic polyradiculopathy may simulate this condition. Treatment of tabes dorsalis and other forms of neurosyphilis consists of penicillin G administered intravenously, or intramuscularly in combination with oral probenecid (Chap. 187). ■ ■HEREDITARY SPASTIC

PARAPLEGIA Many cases of slowly progressive myelopathy are genetic in origin (Chap. 448). More than 90 different causative loci have been identi fied, including autosomal dominant, autosomal recessive, and X-linked forms. Especially for the recessive and X-linked forms, a family his tory of myelopathy may be lacking. Most patients present with almost imperceptibly progressive spasticity and weakness in the legs, usually but not always symmetrical. Sensory symptoms and signs are absent or mild, but sphincter disturbances may be present. In some families, additional neurologic signs are prominent, including nystagmus, ataxia, or optic atrophy. The onset may be as early as the first year of life or as late as middle adulthood. Only symptomatic therapies are available. PRIMARY LATERAL SCLEROSIS This is a mid- to late-life-onset degenerative disorder characterized by progressive spasticity with weakness, eventually accompanied by dysarthria and dysphonia; bladder symptoms occur in approximately half of patients. Sensory function is spared. The disorder resembles ALS and is considered a variant of the motor neuron degenerations, but without the characteristic lower motor neuron disturbance and with typically a slower progression. Some cases may represent late-onset cases of hereditary spastic paraplegia, particularly autosomal recessive or X-linked varieties in which a family history may be absent. (See also Chap. 448.) ■ ■ADRENOMYELONEUROPATHY This X-linked peroxisomal disorder is a variant of adrenoleukodystro phy (ALD). Most affected males have a history of adrenal insufficiency and then develop a progressive spastic (or ataxic) paraparesis begin ning in early or sometimes middle adulthood; some patients also have cerebral involvement and/or a mild peripheral neuropathy. Female heterozygotes may develop a slower, insidiously progressive spastic myelopathy beginning later in adulthood and without adrenal insuffi ciency. Diagnosis is usually made by demonstration of elevated levels of very-long-chain fatty acids in plasma and in cultured fibroblasts. The responsible gene encodes the adrenoleukodystrophy protein (ALDP), a peroxisomal membrane transporter involved in carrying long-chain fatty acids to peroxisomes for degradation. Corticosteroid replacement is indicated if hypoadrenalism is present. Allogeneic bone marrow transplantation has been successful in slowing progression of cogni tive decline in some patients with ALD treated early in their disease but appears to be ineffective for the myelopathy. A preliminary study of leriglitazone, a peroxisome proliferator-activated receptor gamma (PPARγ) agonist, reported suggestive slowing of myelopathic signs in some patients, but the primary endpoint was not met. Nutritional supplements (Lorenzo’s oil) have also been attempted for this condition without evidence of efficacy. ■ ■CANCER-RELATED SYNDROMES Cancer-related causes of chronic myelopathy, besides the common neoplastic compressive myelopathy discussed earlier, include radia tion injury (Chap. 95) and a myelopathy resembling subacute com bined degeneration that can follow intrathecal administration of TABLE 453-4 Expected Neurologic Function Following Complete Cord Lesions LEVEL SELF-CARE TRANSFERS MAXIMUM MOBILITY High quadriplegia (C1–C4) Dependent on others; requires respiratory support Dependent on others Motorized wheelchair Low quadriplegia (C5–C8) Partially independent with adaptive equipment May be dependent or independent May use manual wheelchair, drive an automobile with adaptive equipment Paraplegia (below T1) Independent Independent Ambulates short distances with aids Source: Adapted from JF Ditunno, CS Formal: Chronic spinal cord injury. N Engl J Med 330:550, 1994.

methotrexate (a folate antagonist). Rare paraneoplastic myelopathies are most often associated with lung cancer and anti-amphiphysin (also breast), anti-collapsin response mediator 5 (CRMP5) (also lymphoma), or anti-Hu antibodies (Chap. 99). Another uncommon lymphomaassociated paraneoplastic syndrome is a progressive flaccid paresis with destruction of anterior horn cells.

NMO with AQP-4 antibodies (Chap. 456) can also rarely be paraneoplastic in origin. Several series have reported cases of myelopathy associated with use of checkpoint inhibitors in cancer treatment; some are associated with development of paraneoplastic or NMO antibodies. Metastases to the cord are prob ably more common than any of these disorders in patients with cancer.

■ ■OTHER CHRONIC MYELOPATHIES Tethered cord syndrome is a developmental disorder of the lower spinal cord and nerve roots that rarely presents in adulthood as low back pain accompanied by a progressive lower spinal cord and/or nerve root syndrome. Some patients have a leg or foot deformity indicating a longstanding process, and in others, a dimple, patch of hair, or sinus tract on the skin overlying the lower back is the clue to a congenital lesion. Diagnosis is made by MRI, which demonstrates a low-lying conus medullaris and thickened filum terminale. The MRI may also reveal diastematomyelia (division of the lower spinal cord into two halves), lipomas, cysts, or other congenital abnormalities of the lower spine coexisting with the tethered cord. Treatment is with surgical release. CHAPTER 453 Diseases of the Spinal Cord There are a number of rare toxic causes of spastic myelopathy, including lathyrism due to ingestion of chickpeas containing the exci totoxin β-N-oxalylamino-L-alanine (BOAA), seen primarily in the developing world or during famines, and Konzo due to ingestion of the cyanogen-containing casava plant found in sub-Saharan Africa. Often, a cause of intrinsic myelopathy can be identified only through periodic reassessment. REHABILITATION OF SPINAL CORD DISORDERS The prospects for recovery from an acute destructive spinal cord lesion fade after ~6 months. There are currently no effective means to promote repair of injured spinal cord tissue; promising but entirely experimental approaches include the use of factors that influence rein nervation by axons of the corticospinal tract, nerve and neural sheath graft bridges, forms of electrical stimulation at the site of injury, and the local introduction of stem cells. The disability associated with irreversible spinal cord damage is determined primarily by the level of the lesion and by whether the disturbance in function is complete or incomplete (Table 453-4). Even a complete high cervical cord lesion may be compatible with a productive life. The primary goals are devel opment of a rehabilitation plan framed by realistic expectations and attention to the neurologic, medical, and psychological complications that commonly arise. Many of the usual symptoms associated with medical illnesses, especially somatic and visceral pain, may be lacking because of the destruction of afferent pain pathways. Unexplained fever, worsening of spasticity, or deterioration in neurologic function should prompt a search for infection, thrombophlebitis, or an intraabdominal pathol ogy. The loss of normal thermoregulation and inability to maintain normal body temperature can produce recurrent fever (quadriplegic fever), although most episodes of fever are due to infection of the uri nary tract, lung, skin, or bone. Bladder dysfunction generally results from loss of supraspinal innervation of the detrusor muscle of the bladder wall and the

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