



Disorders affecting the spinal cord

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INTRODUCTION

Pathologies that affect the spinal cord are diverse. In addition to trauma, common etiologies of myelopathy include autoimmune, infectious, neoplastic, vascular, and hereditary-degenerative diseases. The relative incidence of each of these entities depends in large part upon the clinical setting. In a regional neuroscience center in the United Kingdom, the most common cause of spastic paraparesis or quadriparesis among 585 patients was cervical spondylotic myelopathy (24 percent), followed by tumor (16 percent), multiple sclerosis (MS; 18 percent), and motor neuron disease (4 percent) [1].

This topic will review some of the more common and important causes of nontraumatic spinal cord dysfunction. Clinical features of the more common of these disorders are summarized in the table ([table 1](#)). Traumatic spinal cord injury and the anatomy and clinical localization of spinal cord disease are discussed separately. (See "[Acute traumatic spinal cord injury](#)" and "[Anatomy and localization of spinal cord disorders](#)".)

DIAGNOSTIC APPROACH

The differential diagnosis of myelopathy is wide but can be significantly narrowed by the clinical syndrome, which is defined by features on examination. These are summarized in the table ([table 2](#)) and described in detail separately. (See "[Anatomy and localization of spinal cord disorders](#)", section on 'Spinal cord syndromes'.)

Other features in the examination and history can also limit the differential diagnosis and tailor the diagnostic workup. Clinical features of some of the more common causes of myelopathy are outlined in the table ([table 1](#)). These are described in detail in the sections below.

For patients with a clinical syndrome that suggests a localized process within the spinal cord (eg, transection syndrome, central cord syndrome, ventral cord syndrome, etc), an imaging study, usually magnetic resonance imaging (MRI), of the relevant section of the spinal cord is usually required [2,3]. Administration of gadolinium contrast is often helpful. When an infectious or inflammatory disorder is suspected, cerebrospinal fluid (CSF) examination may be helpful [4]. The role of positron emission tomography in evaluating patients with myelopathy is under investigation; it appears to be particularly sensitive for neoplastic disease [5].

In general, the pace at which spinal cord deficits appear dictates the urgency of the neurologic evaluation. Even when the deficits are not severe, acute myelopathic signs need to be evaluated urgently because neurologic deterioration can occur abruptly, and the clinical deficit at the time of intervention often dictates the chances of recovery. This is true particularly for compressive etiologies such as spinal cord metastases and epidural spinal abscess.

INFLAMMATORY DISEASES

Transverse myelitis — Transverse myelitis (TM) is a segmental spinal cord injury caused by acute inflammation [6-8]. TM is uncommon, with an approximate incidence of between one to five cases per million population annually [9].

Most cases of TM are idiopathic and presumably result from an autoimmune process; up to half of these patients have a preceding infection [10-12]. TM can also occur as part of other inflammatory demyelinating diseases, including multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), and acute disseminated encephalomyelitis (ADEM) [13]. (See "[Transverse myelitis: Etiology, clinical features, and diagnosis](#)", section on 'CNS demyelinating disorders'.)

TM is also associated with connective tissue diseases, including systemic lupus erythematosus, Sjögren's disease, antiphospholipid antibody syndrome, ankylosing spondylitis, and others. (See "[Transverse myelitis: Etiology, clinical features, and diagnosis](#)", section on 'Systemic autoimmune disorders'.)

The inflammation of TM is generally restricted to one or two segments, usually in the thoracic cord. Symptoms typically develop rapidly over several hours; approximately 37 percent of patients worsen maximally within 24 hours [14]. Occasionally patients worsen more slowly, over

several weeks. Typically the inflammation is bilateral, producing weakness and multimodality sensory disturbance below the level of the lesion [9,11]. Unilateral syndromes (eg, Brown-Séquard) have been described as well. Almost all patients develop leg weakness of varying severity. Arm weakness also occurs if the lesion is in the cervical cord. In addition to diminished sensation, pain and tingling are common and frequently include a tight banding or girdle-like sensation around the trunk, which may be very sensitive to touch. Back and radicular pain are also common. Bowel and bladder dysfunction, reflective of autonomic involvement, also occur. (See "[Transverse myelitis: Etiology, clinical features, and diagnosis](#)", section on 'Clinical features'.)

MRI of the involved section of the spinal cord shows gadolinium-enhancing signal abnormality, usually extending over one or more cord segments ([image 1](#)) [9,12,15,16]. The cord often appears swollen at these levels. Cerebrospinal fluid (CSF) is abnormal in half of patients, with elevated protein level (usually 100 to 120 mg/100 mL) and moderate lymphocytosis (usually <100/mm³). Glucose levels are normal. Oligoclonal bands are usually not present in isolated TM, and when present suggest a higher risk of subsequent MS [9,17]. Other studies can help delineate the underlying cause ([table 3](#)). (See "[Transverse myelitis: Etiology, clinical features, and diagnosis](#)", section on 'Determining the cause of TM'.)

Patients presenting with acute transverse myelitis are typically treated with glucocorticoids and other immunosuppressive therapies. Most patients have at least a partial recovery. Long-term outcomes vary by the underlying condition. (See "[Transverse myelitis: Treatment and prognosis](#)".)

Sarcoidosis — The granulomatous inflammation of sarcoidosis can affect the spinal cord and produce an acute or subacute segmental myelopathy [10,18-20]. The lesions can be extramedullary or intramedullary, and can involve the cauda equina as well as the cord. MRI signal abnormalities are not specific; neurosarcoid lesions can appear similar to TM or can resemble a tumor. CSF evaluation usually shows elevated protein and/or pleocytosis. Hilar lymphadenopathy may suggest the diagnosis; however, serum and CSF angiotensin converting enzyme levels are neither sensitive nor specific for neurosarcoidosis. Patients with neurologic sarcoidosis are generally treated with corticosteroids and other immunomodulatory agents and can improve. (See "[Neurologic sarcoidosis](#)".)

Paraneoplastic syndromes — A number of distinct paraneoplastic syndromes involving the spinal cord have been described. These rare syndromes include:

- **Motor neuron syndrome** – A subacute, progressive, painless, and often asymmetric lower motor neuron weakness, most often associated with lymphoma [21].

- Acute necrotizing myelopathy – A rapidly ascending syndrome of sensory deficits, sphincter dysfunction, and flaccid or spastic paraplegia or quadriplegia [22].
- Subacute sensory neuronopathy – An inflammatory disorder affecting the dorsal root ganglia, producing progressive loss of sensory modalities, leading to prominent ataxia [23]. This is most often associated with small cell lung cancer and anti-Hu antibodies.
- Encephalomyelitis – A diffuse involvement of brain and spinal cord regions in which cerebral manifestations frequently overshadow the myelopathy. Several syndromes are described.

These are described separately. (See "[Paraneoplastic syndromes affecting spinal cord, peripheral nerve, and muscle](#)".)

INFECTIONS

Epidural abscess — Spinal epidural abscess is a rare disease, occurring in only 1 patient per 10,000 admitted to the hospital [24]. The infection can originate via contiguous spread from infections of skin and soft tissues or as a complication of spinal surgery and other invasive procedures, including indwelling epidural catheters. Other cases of epidural abscess arise from a remote site via the bloodstream. Diabetes, alcoholism, and human immunodeficiency virus (HIV) infection are risk factors.

The most common pathogen is *Staphylococcus aureus*, which accounts for approximately two-thirds of cases [24]. Damage to the spinal cord can be caused by direct compression of neural elements or arterial blood supply, thrombosis and thrombophlebitis of nearby veins, focal vasculitis, and/or bacterial toxins and mediators of inflammation. The classic clinical triad consists of fever, spinal pain, and neurologic deficits. However, only a few patients have all three components at presentation [25]. The rate of neurologic progression is highly variable.

Imaging of the spinal column is imperative on first suspicion of the disorder [25]. MRI is the preferred test and is highly sensitive for this diagnosis. Blood cultures and/or aspirate of abscess contents are ordered to identify the etiologic organism. Surgical decompression and drainage with systemic antibiotic therapy is the treatment of choice for most patients. Because the preoperative neurologic deficit is an important predictor of final neurologic outcome, early diagnosis and treatment are imperative.

This topic is discussed in detail separately. (See "[Spinal epidural abscess](#)".)

Acute viral myelitis — Two distinct syndromes of spinal cord involvement are associated with acute viral disease. In the first, the virus targets the gray matter of the spinal cord, producing

acute lower motor neuron disease [26]. These viruses include:

- Enteroviruses, such as poliovirus, coxsackie virus, and enterovirus 71 [27]
- Flaviviruses, such as West Nile virus and Japanese encephalitis virus [28-30]

Viral invasion of the anterior horn cells occurs as part of an acute viral illness, usually with fever, headache, and meningismus, and produces asymmetrical flaccid weakness with reduced or absent reflexes and few sensory symptoms or signs. MRI often shows hyperintensities in the anterior horns of the spinal cord on T2-weighted imaging [27,31]. Cerebrospinal fluid (CSF) analysis demonstrates a moderate pleocytosis. These features help to distinguish this form of viral myelitis from Guillain-Barré syndrome, which usually produces symmetric deficits, with no MRI abnormalities, and is associated with elevated CSF protein levels without pleocytosis. (See ["Guillain-Barré syndrome in adults: Pathogenesis, clinical features, and diagnosis"](#).)

Focal or segmental depletion of spinal motor neurons has been described at autopsy, reflecting the observed pattern of neurologic deficits [32,33]. The prognosis for recovery is variable. Treatment is supportive. (See ["Clinical manifestations and diagnosis of West Nile virus infection"](#), section on 'Neuroinvasive disease' and ["Enterovirus and parechovirus infections: Clinical features, laboratory diagnosis, treatment, and prevention"](#), section on 'Acute paralysis and brainstem encephalitis'.)

A second form of viral myelitis has clinical and diagnostic test features that are similar to transverse myelitis. Associated viruses include cytomegalovirus, varicella zoster, herpes simplex virus, hepatitis C, and Epstein Barr virus [34-40]. The association between the myelitis and the virus is not always clear. In some cases, these may represent a postinfectious transverse myelitis. In others, a positive polymerase chain reaction (PCR) test in the CSF suggests that the myelitis is directly related to the viral infection. These patients are often treated with antiviral agents and corticosteroids.

AIDS myelopathy — HIV infection produces a vacuolar myelopathy, which is found in up to half of patients with acquired immunodeficiency syndrome (AIDS) at autopsy [25,41]. However, clinical manifestations occur when the pathology is advanced, and only approximately one-fourth of patients demonstrating vacuolar myelopathy at autopsy have symptoms during life [42]. AIDS myelopathy most often occurs in late stages of AIDS; most patients die within six months of developing symptoms of myelopathy. HIV-related dementia is present in more than half of patients and, with other disease complications, may obscure the myelopathy.

In typical cases, a slowly progressive spastic paraparesis is accompanied by loss of vibration and position sense and urinary frequency, urgency, and incontinence [43]. Upper-extremity function

is usually normal. MRI of the spine is usually normal. CSF examination may show nonspecific abnormalities, such as protein elevation. Abnormal sensory evoked potentials may precede clinical symptoms of myelopathy. Aggressive antiretroviral therapy can lead to improvement of symptoms [44]. In one case series, the use of intravenous immunoglobulin appeared to be associated with neurologic improvement [45].

The pathogenesis of vacuolar myelopathy is unknown but may be related to abnormal transmethylation mechanisms induced by the virus and/or cytokines. In one series of 16 patients, there was no correlation between the viral load in the CSF and the presence or severity of myelopathy [46]. Pathologic descriptions include demyelination of the dorsal columns and the dorsal half of the lateral columns, with prominent vacuoles within the myelin sheaths. This pathologic appearance is similar to the changes seen in the subacute combined degeneration of the cord.

HTLV-I myelopathy — Human T-lymphotropic virus type I (HTLV-I) causes a progressive neurologic disease, which is called either HTLV-1-associated myelopathy (HAM) or tropical spastic paraparesis (TSP) [47,48]. This disorder is endemic in southern Japan, the Caribbean, South America, the Melanesian islands, Papua New Guinea, the Middle East, and central and southern Africa, with seroprevalences as high as 30 percent in southern Japan [49-51]. By contrast, it is quite rare in the United States and Europe. It is more common in women than men.

Primarily involving the thoracic cord, HAM/TSP is characterized by a slowly progressive spastic paraparesis and urinary disturbance. Pathologic studies demonstrate inflammation of the lateral corticospinal, spinocerebellar, and spinothalamic tracts, with relative sparing of the posterior columns [52]. HAM/TSP has also been associated with other nervous system pathology that results in less frequent symptoms, suggesting cerebral, cerebellar, cranial nerve, and peripheral nerve involvement [47,51].

MRI of the spinal cord may show spinal atrophy, particularly of the thoracic cord [48,53]. A brain MRI often shows subcortical, periventricular white matter lesions. CSF examination reveals a mild lymphocytosis and/or elevated protein concentration in some patients. Anti-HTLV-I antibodies are detected in the CSF with a high CSF:serum ratio. The virus can be cultured from CSF lymphocytes and proviral deoxyribonucleic acid (DNA) detected by PCR.

In general, neurologic deficits continue to progress slowly; steroids and other immunomodulatory treatment may slow progression, but this is not proven. This topic is discussed separately. (See "[Human T-lymphotropic virus type I: Disease associations, diagnosis,](#)

and treatment" and ["Human T-lymphotropic virus type I: Virology, pathogenesis, and epidemiology".](#))

Syphilis — Tabes dorsalis is a form of tertiary neurosyphilis in which the dorsal or posterior columns of the spinal cord are primarily affected. Patients present with a sensory ataxia and lancinating pains reflecting dorsal column and dorsal nerve root involvement. CSF examination may be normal or demonstrate elevated protein level, lymphocytosis, and/or a reactive Venereal Disease Research Laboratory (VDRL). Antibiotic treatment may reverse symptoms. (See ["Neurosyphilis", section on 'Tabes dorsalis'.](#))

Syphilitic meningomyelitis and meningovascular myelitis represent an earlier form of syphilis infection in which focal inflammation of the meninges secondarily affects the adjacent spinal cord and/or the anterior spinal artery. In the former situation, a subacute progressive myelopathy develops [54]. In the latter, the clinical presentation may be one of a spinal cord infarction. (See ["Neurosyphilis", section on 'Meningovascular syphilis'](#) and ["Spinal cord infarction: Epidemiology and etiologies".](#))

Tuberculosis — Tuberculosis can produce a myelopathy by different mechanisms. Infection of the vertebral body leads to tuberculous spondylitis or Pott's disease, which can lead to secondary cord compression. These patients present with back pain over the affected vertebra, low-grade fever, and weight loss, followed by a secondary compressive myelopathy [55]. Tuberculomas within the intramedullary, intradural, and extradural space can also produce myelopathy [56,57]. (See ["Bone and joint tuberculosis"](#) and ["Central nervous system tuberculosis: An overview".](#))

Parasite infection — The parasites *Schistosoma mansoni* and *Schistosoma haematobium* typically infect the spinal cord, producing rapidly progressing symptoms of TM, including lower limb pain, weakness, and bowel and bladder dysfunction [58,59]. The lower thoracic region of the spinal cord is most frequently involved, followed by the lumbar and sacral regions. Spinal cord involvement can lead to permanent paralysis. CSF evaluation reveals pleocytosis and elevated protein; eosinophilia occurs in almost half of patients. MRI demonstrates signal change and swelling within the cord. Most patients are treated with glucocorticoids and [praziquantel](#) and achieve at least partial recovery. (See ["Schistosomiasis: Epidemiology, clinical manifestations, and diagnosis"](#) and ["Schistosomiasis: Management and prevention".](#))

Cysticercosis has been reported to cause a cyst within the spinal cord [60].

Others — Bacterial meningitis may be complicated by a myelopathy due to formation of an epidural abscess, myelitis, or vasculitic infarction [55,61,62].

Lyme disease rarely affects the spinal cord. However, cases have been described in which clinical and MRI features resembling acute TM have been attributed to Lyme disease [63,64]. CSF in these cases typically demonstrates a lymphocytic pleocytosis and elevated protein. (See ["Clinical manifestations of Lyme disease in adults"](#).)

VASCULAR DISEASE

Spinal cord infarction — Infarction of the spinal cord is rare compared with cerebral infarction. Spinal cord infarction is most frequently caused by surgical procedures and pathologies affecting the aorta [65]. Other causes of spinal cord infarction are diverse and include any etiology that also produces brain infarction (eg, atherosclerosis, embolism, and hypercoagulable and vasculitic disorders) [65-69]. Spinal cord infarction can also occur in the setting of severe systemic hypotension or cardiac arrest.

Symptoms are consistent with the functional loss within the anterior spinal artery territory and include paralysis, loss of bladder function, and loss of pain and temperature sensation below the level of the lesion. Position and vibratory sensation are spared. The onset of symptoms is sudden and is frequently associated with back pain.

MRI will demonstrate a T2 signal change consistent with cord ischemia, but may be normal in the first 24 hours [70,71]. Diffusion-weighted imaging (DWI) is more sensitive [72-74]. Cerebrospinal fluid (CSF) protein level may be elevated, but pleocytosis is rare.

Less than half of patients show substantial motor recovery following spinal cord infarction [65,75]. Treatment is generally supportive and focused on the underlying aortic pathology and/or secondary stroke prevention.

Spinal cord infarction is discussed in detail separately. (See ["Spinal cord infarction: Epidemiology and etiologies"](#) and ["Spinal cord infarction: Treatment and prognosis"](#).)

Vascular malformations — Vascular malformations of the spinal cord are classified into types according to their location and vascular pathology [76,77].

- **Dural arteriovenous fistula** – Dural arteriovenous fistula is the most common type, making up approximately 70 percent of all lesions [69,78]. These exist on the dural surface and drain intradurally by retrograde flow through a single medullary vein to the anterior or posterior median vein, resulting in engorgement of the coronal venous plexus.

They usually present after the fifth decade of life and are more common in men. The most common clinical presentation is that of progressive, often stepwise myeloradiculopathy,

probably related to venous hypertension. Some patients present with neurogenic claudication [79]. Symptoms may initially fluctuate, but eventually a permanent and progressive paraparesis with sensory disturbances and sphincter dysfunction occurs.

MRI with contrast-enhanced magnetic resonance angiography (MRA) can identify a dural arteriovenous fistula but has imperfect sensitivity [79-84]. The most common finding is a nonspecific hyperintense signal lesion on T2-weighted images. The more specific findings of intradural flow voids on T2-weighted images, and/or serpentine enhancement on MRA and T1 images, are seen in 85 to 100 percent or more of patients. If MRI/MRA cannot be performed, myelography with supine and prone images may demonstrate the serpentine vessels within the intradural space. When positive, MRA and/or myelography can help guide the performance of the spinal angiogram, which remains the gold-standard test, and is required prior to therapeutic intervention. Spinal angiography can be a difficult diagnostic procedure in this setting, often requiring multiple injections of segmental arteries in order to identify the feeding artery, especially when MRA does not provide specific guiding information. However, at least one observational study found that in experienced hands, the complication rate is low (1 to 2 percent) and did not (at least in this series) involve any neurologic morbidity [85].

Occlusion of the fistula by surgery or endovascular embolization can be helpful in stabilizing, even ameliorating, the neurologic deficits [83,86-88].

- **Intramedullary spinal arteriovenous malformations** – Spinal arteriovenous malformations (AVMs) within the spinal cord are supplied by medullary arteries and drain through medullary veins [89,90].

The mean age at clinical presentation is the mid-20s, but close to 20 percent of the lesions are diagnosed in children under 16 years of age [89]. A myelopathy is produced by the mass effect of the lesion or by ischemia or hemorrhage into the cord. Some patients present instead with subarachnoid hemorrhage.

MRI is sensitive for intramedullary AVM, showing a cluster of low-intensity signal foci [77]. Contrast-enhanced MRA also helps localize the nidus and identify arterial supply and venous drainage.

These lesions are treated by endovascular occlusion, surgical resection, or both [91].

- **Intramedullary cavernous malformations** – Spinal cord cavernous malformations may be isolated lesions; however, approximately 25 percent will have an intracranial cavernous malformation as well [69]. Ten percent of patients have a family history; in these patients, multiple cavernous malformations are more common.

Patients typically present with hemorrhage within the spinal cord (hematomyelia); recurrent hemorrhage rates may be as high as 10 percent per year [69]. Cavernous malformations that are discovered incidentally have a lower rate of hemorrhage (<1 percent per year).

These lesions are best visualized on MRI [69]. The lesions are typically well defined with heterogeneous T1- and T2-weighted signal intensity, giving a so-called "popcorn" appearance; a low signal intense rim on T2 images represents hemosiderin deposition.

Asymptomatic lesions are often observed, while surgical or other interventions are considered for those that have bled [69].

Spinal epidural hematoma — Spinal epidural hematoma can complicate procedures that involve a spinal dural puncture, usually in patients with thrombocytopenia or bleeding diathesis, including anticoagulant therapy [92]. Rarely, this occurs spontaneously; a predisposition to bleeding is a risk factor in these patients as well [93-95]. Some occur in the setting of minor trauma.

Patients typically present with local and/or radicular pain, followed by loss of sensory, motor, and bladder and bowel function [93-95]. The source of bleeding is usually venous rather than arterial, and symptoms typically present over days, although more abrupt presentations are also described.

MRI is a sensitive imaging modality for these lesions [94,96]. MRI findings vary according to the age of the clot. In the first 24 hours the hematoma is usually isointense on T1- and hyperintense on T2-weighted images; after 24 hours, it becomes mostly hyperintense on T1 and on T2.

The appropriate treatment for patients with significant and/or progressing neurologic deficits is prompt surgical intervention, usually a laminectomy, and evacuation of the blood. Timely decompression of the hematoma is essential to avoid permanent loss of neurologic function [97,98]. Many individuals with minor, stable neurologic deficits can be managed by observation and have a good prognosis for complete recovery [93,95].

TOXIC, METABOLIC DISORDERS

Subacute combined degeneration — Deficiency in [vitamin B12](#) (cobalamin) leads to degeneration of the dorsal and lateral white matter of the spinal cord, producing a slowly progressive weakness, sensory ataxia, and paresthesias, and ultimately spasticity, paraplegia, and incontinence [99]. Not all patients with neurologic abnormalities will have anemia or macrocytosis [100]. Supplemental treatment with vitamin B12 can stop progression and will

produce neurologic improvement in most patients [101]. (See "[Clinical manifestations and diagnosis of vitamin B12 and folate deficiencies](#)" and "[Clinical manifestations and diagnosis of vitamin B12 and folate deficiencies](#)", section on 'Clinical presentation'.)

[Nitrous oxide](#) abuse can also lead to subacute combined degeneration, by inactivation of [vitamin B12](#) [102-105]. (See "[Inhalant misuse in children and adolescents](#)".)

Copper deficiency myeloneuropathy — A syndrome similar to the subacute combined degeneration of [vitamin B12](#) deficiency can occur with acquired copper deficiency, which may be the result of gastrointestinal surgery, excessive zinc ingestion (eg, overuse of denture cream), and other causes [106-108]. Most patients also have hematologic abnormalities. Treatment can prevent progression, but patients with significant neurologic deficits at presentation often remain disabled. (See "[Copper deficiency myeloneuropathy](#)".)

Radiation myelopathy — Myelopathy is a serious complication of radiation therapy to the spinal cord [109,110]. White matter tracts in the lateral aspects of the cord are preferentially affected [111,112]. Two distinct clinical presentations are described:

- A transient myelopathy occurring two to six months after irradiation is usually mild and resolves spontaneously over several months.
- A late progressive myelopathy begins 6 to 12 months after irradiation. This begins insidiously and generally progresses inexorably, although some cases stabilize. MRI is important to exclude other etiologies and will typically show hyperintensity on T2 and fluid-attenuated inversion recovery (FLAIR) sequences. A high radiation dose is a risk factor [113]. Fractionation size, concomitant chemotherapy, and other comorbidities may play a role. There is no effective treatment.

This topic is discussed in detail separately. (See "[Complications of spinal cord irradiation](#)".)

Intrathecal chemotherapy — Myelopathy can occur as a complication of intrathecal chemotherapy, particularly [methotrexate](#) and [cytarabine](#) [114-117]. This appears to be an idiosyncratic reaction, as a wide range of dose and timing with respect to the administration of intrathecal chemotherapy has been reported. The clinical syndrome resembles subacute combined degeneration, and MRI frequently shows abnormalities in the dorsal columns on T2-weighted images. (See "[Overview of neurologic complications of conventional non-platinum cancer chemotherapy](#)", section on 'Transverse myelopathy' and "[Overview of neurologic complications of conventional non-platinum cancer chemotherapy](#)", section on 'Intrathecal cytarabine'.)

Individual cases of myelopathy with treatment with antitumor necrosis factors as well as intravenous administration of [cisplatin](#), [cladribine](#), and [carmustine](#) have also been reported, but these appear to be rare [114,118].

Electrical injury — High-voltage electrical injury can be associated with a variety of neurologic complications, including spinal cord injury. (See "[Electrical injuries and lightning strikes: Evaluation and management](#)".)

Different syndromes have been described:

- A transient flaccid paralysis, called keraunoparalysis, is apparent immediately following the injury, affects the legs more than the arms, and typically resolves within the first 24 hours [119,120]. This is most often described in association with lightning strike. Peripheral vasoconstriction and sensory disturbances are commonly associated. The pathophysiology is uncertain.
- Other patients develop a more enduring and sometimes permanent spinal cord injury after electrical injury [121-124]. In this situation, clinical signs of myelopathy may be present at the time of injury, or may develop after several days or weeks. Motor deficits are more prominent than sensory findings. Bladder and other sphincter dysfunction can occur. Spine MRI is typically normal. The clinical course and prognosis are not well characterized. Direct heat and electrical injury to neural elements, as well as a delayed microvascular disease, are proposed mechanisms.

Hepatic myelopathy — Progressive myelopathy is a rare neurologic complication of chronic liver disease with portal hypertension; the mechanism is unknown [125-129]. The myelopathy is predominantly or entirely motor in manifestation, reflected as a spastic paraparesis that progresses over months to paraplegia [130]. Deficits are limited to the lower extremities; sensory and bladder function is often unaffected. MRI and cerebrospinal fluid (CSF) studies are normal. Neuropathologic studies have demonstrated demyelination of the lateral corticospinal tracts with various degrees of axonal loss [127].

In contrast to hepatic encephalopathy, ammonia-lowering treatments have little or no effect on the myelopathy, but patients with early manifestations of spinal cord impairment may improve with liver transplantation [130].

Decompression sickness myelopathy — Impairment of spinal cord function can be a manifestation of decompression sickness, a complication of deep sea diving [131-135]. Symptoms usually develop during or immediately after ascent but may be delayed for several hours or a few days. The thoracic cord is most commonly involved, producing paraparesis of

varying severity and a sensory level in the mid or low thoracic region. Lesions at higher spinal cord levels producing quadriplegia have also been described [134].

Early therapeutic recompression frequently reverses symptoms and signs [132]. Residual corticospinal and minor sensory signs may remain for months or indefinitely [135]. Both MRI and pathologic studies have shown multifocal white matter degeneration in the posterior and lateral columns of the spinal cord with secondary ascending and descending tract degeneration [128,134]. Gaseous occlusion of venous plexi within the spinal cord is one postulated mechanism of injury. (See "[Complications of SCUBA diving](#)", section on '[Decompression sickness](#)'.)

Lathyrism and konzo — Two disorders of spastic paraparesis have been described, which occur in association with increased dietary intake of food plants with neurotoxic potential, as occurs in certain geographic regions during times of famine [136,137].

- Neurolathyrism is associated with prolonged consumption of the grass or chickling pea (*Lathyrus sativus*) [138]. Exposed persons develop a slowly developing spastic paraparesis with cramps, paresthesias, and numbness, accompanied by bladder symptoms and impotence. Some patients have tremors and other involuntary movements in their arms. Pathologic studies have demonstrated a loss of myelinated fibers in the corticospinal and spinocerebellar tracts. The toxin appears to be the neuroexcitatory amino acid, beta-N-oxalylaminoalanine. There is no treatment.
- Konzo, a disorder characterized by acute spastic paraparesis or quadriparesis, is linked to high exposure to cyanogenic compounds in diets containing insufficiently processed bitter cassava (*Manihot esculenta*) [139,140]. This disorder is less well characterized than lathyrism, and it may reflect a disorder of intracranial rather than intraspinal motor pathways.

NEOPLASMS

Both benign and malignant tumors can produce a myelopathy as a result of external compression or intramedullary growth.

- **Neoplastic epidural spinal cord compression** – The most common syndrome is that of extradural spinal cord compression, as produced by metastases to the extradural space. Patients present with a progressive weakness below the level of the lesion with accompanying sensory loss and bladder dysfunction [141]. Pain at the site of involvement is typical. Progression to paraplegia can occur abruptly, as a result of vascular compression.

Because the prognosis for neurologic recovery depends on the severity of the deficit at the time of intervention (high-dose corticosteroids with radiation therapy and/or surgical decompression), diagnostic evaluation (with gadolinium-enhanced spinal MRI) must proceed promptly when this diagnosis is considered [142]. This topic is discussed in detail separately. (See ["Clinical features and diagnosis of neoplastic epidural spinal cord compression"](#) and ["Treatment and prognosis of neoplastic epidural spinal cord compression"](#).)

- **Intramedullary tumors** – Intramedullary spinal cord tumors are typically primary central nervous system tumors (ependymoma, astrocytoma); metastases are less likely [143,144]. These produce a progressive myelopathy, often with central cord features. MRI with gadolinium will show the tumor [145]; biopsy with histologic examination is usually required for diagnosis. Because of their intramedullary location, management of these lesions is difficult. (See ["Spinal cord tumors"](#).)
- **Other causes of myelopathy in patients with cancer** – Myelopathy can occur as a complication of radiation therapy (see ["Radiation myelopathy"](#) above); as a complication of intrathecal chemotherapy, particularly [methotrexate](#) and [cytarabine](#) (see ["Overview of neurologic complications of conventional non-platinum cancer chemotherapy"](#), section on ["Transverse myelopathy"](#) and ["Overview of neurologic complications of conventional non-platinum cancer chemotherapy"](#), section on ["Intrathecal cytarabine"](#)); and as a paraneoplastic syndrome. (See ["Paraneoplastic syndromes"](#) above and ["Paraneoplastic syndromes affecting spinal cord, peripheral nerve, and muscle"](#), section on ["Myelopathy"](#).)

INHERITED AND DEGENERATIVE CONDITIONS

Amyotrophic lateral sclerosis — Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder that produces progressive weakness, usually with mixed upper and motor neuron signs [146,147]. Symptoms begin insidiously in older adults (usually >60 years) and progress inexorably. In typical patients, there is asymmetric limb weakness with a mixture of upper and lower motor neuron features. Sensory and sphincter disturbances are usually absent. MRI is normal. Electromyography typically shows denervation in clinically affected muscles. (See ["Clinical features of amyotrophic lateral sclerosis and other forms of motor neuron disease"](#) and ["Diagnosis of amyotrophic lateral sclerosis and other forms of motor neuron disease"](#).)

Unusual variants of ALS with atypical symptoms can present a diagnostic challenge. Primary lateral sclerosis is a rare variant of ALS with primarily upper motor neuron features [148]. Muscle stiffness leading to overt and progressive spasticity without associated muscle weakness or atrophy typifies the disorder. In approximately two-thirds of patients, there is an

ascending pattern with spasticity spreading in a rather stereotyped fashion from the legs to the arms and finally to involve the bulbar musculature [149]. Without positive test findings, this is a diagnosis of exclusion. There is no treatment. (See "[Clinical features of amyotrophic lateral sclerosis and other forms of motor neuron disease](#)", section on 'Primary lateral sclerosis'.)

One familial form of ALS, the recessively inherited D90A mutation, can also present with atypical features, including a long preparetic phase of lower extremity discomfort, followed by a slowly ascending asymmetric paresis that is often accompanied by bladder symptoms [150-153]. (See "[Familial amyotrophic lateral sclerosis](#)".)

Hereditary spastic paraplegias — Hereditary spastic paraplegia (HSP) is a large group of inherited neurologic disorders, in which the prominent feature is a progressive spastic paraparesis [154]. HSP is classified according to the mode of inheritance, the genetic locus when known, and whether the spastic paraplegia syndrome occurs alone or is accompanied by additional neurologic or systemic abnormalities ("pure" versus "complicated") [155-159]. There have been no recent epidemiologic studies, but previously the incidence has been reported to be between 1 in 10,000 and 1 in 100,000.

Genetically diverse, with at least 28 genetic loci for HSP identified, the final common pathway for these disorders is a degeneration of the corticospinal tracts [155]. Inheritance is usually autosomal dominant, but recessive and X-linked variants (eg, Pelizaeus-Merzbacher disease) are known.

The typical patient with pure HSP will have a slowly progressive spastic paraparesis [155]. The age of onset can vary from infancy to the eighth decade. The first symptoms are often gait disturbance or urinary urgency. Examination reveals spasticity, hyperreflexia, extensor plantar responses, and impaired vibration and/or joint position sense. Weakness may be demonstrated but is rarely the major cause of disability. Upper limb involvement is generally limited to hyperreflexia.

HSP is a clinical diagnosis, based in large part on the family history [155]. MRI may be normal or may show atrophy in the spinal cord. Thinning of the corpus callosum on brain MRI is seen in half of patients with the autosomal recessive form of HSP [160]. Otherwise, the diagnosis is based on careful exclusion of other etiologies. Treatment for HSP is limited to symptomatic management [155].

HSP is discussed in more detail separately. (See "[Hereditary spastic paraplegia](#)".)

Adrenoleukodystrophy — Adrenomyeloneuropathy, a variant of adrenoleukodystrophy, an X-linked recessive disorder, is characterized by a slowly progressive spastic paraparesis and mild

polyneuropathy [161,162]. As opposed to the more common and severe phenotype of adrenoleukodystrophy, adrenomyeloneuropathy generally presents in adult men or in female carriers of the mutation. Sensory and sphincter disturbances are typically absent. There may be mild adrenal insufficiency. MRI is typically normal. In the absence of a family history, the finding of a neuropathy on electrophysiologic testing may be a clue to the disorder. The diagnosis is made by the finding of increased very long chain fatty acids in plasma, red blood cells, or cultured skin fibroblasts. (See "[Clinical features, evaluation, and diagnosis of X-linked adrenoleukodystrophy](#)".)

Friedreich ataxia — Friedreich ataxia is an autosomal recessive degenerative disorder of uncertain pathogenesis that typically presents in adolescence [163]. The neuropathologic changes in Friedreich ataxia include degeneration of the posterior columns and the spinocerebellar tracts of the spinal cord and loss of the larger sensory cells of the dorsal root ganglia. These findings correspond to the clinical manifestations of progressive ataxia of all four limbs and gait, weakness, absent reflexes with extensor plantar responses, loss of position and vibration sense, and sparing of pain and temperature. Cardiomyopathy and diabetes mellitus are part of the syndrome. Patients with late-onset disease are more likely to have retained reflexes, spasticity, and no cardiomyopathy [164]. MRI may show atrophy of the cervical cord. Disease severity and rate of progression are highly variable. There is no treatment. This topic is discussed separately. (See "[Friedreich ataxia](#)".)

OTHERS

Syringomyelia — Syringomyelia is a fluid-filled, gliosis-lined cavity within the spinal cord. Most lesions are between C2 and T9; however, they can descend further down or extend upward into the brainstem (syringobulbia). A syrinx can represent a focal dilation of the central canal, or it may lie separately, within the spinal cord parenchyma [165].

Syringomyelia most commonly occurs in the setting of the Chiari malformation type I [166]. (See "[Chiari malformations](#)".)

Other causes of syringomyelia are [165-169]:

- Other congenital malformations (eg, Klippel-Feil syndrome, and tethered spinal cord) (see "[Approach to neck stiffness in children](#)", section on 'Congenital')
- Postinfectious
- Postinflammatory (transverse myelitis [TM] and multiple sclerosis [MS])

- Spinal neoplasms (especially ependymoma and hemangioblastoma) (see ["Spinal cord tumors"](#))
- Post-traumatic (see ["Chronic complications of spinal cord injury and disease"](#), section on 'Syringomyelia')

A syrinx can be asymptomatic and discovered incidentally on spinal cord imaging. Other patients present with progressive central cord deficits that can include a prominent central pain syndrome in a segmental distribution [170]. (See ["Anatomy and localization of spinal cord disorders"](#).)

MRI will typically identify the intramedullary cavity; gadolinium administration will increase the sensitivity of finding an associated tumor. Surgical decompression with fenestration and/or shunt placement is recommended for patients with neurologic deterioration or intractable central pain [168-170]. Neurologic deficits usually stabilize after intervention and sometimes improve.

Cervical spondylotic myelopathy — In many case series, cervical spondylotic myelopathy is the most common cause of myelopathy, particularly in older adults [1]. Degenerative changes in the vertebral bodies, discs, and connecting ligaments encroach on the cervical canal, producing a progressive myelopathy [171]. Symptoms begin insidiously, usually with a spastic gait. Sensory loss, muscle weakness, and atrophy in the hands also cause functional impairment over time. Some patients may develop or present with an acute myelopathy characterized by a central cord syndrome, often in the setting of mild neck trauma.

The diagnosis is made by correlating clinical features with evidence of cervical spondylosis and cord compression on MRI [172]. Treatment options include cervical immobilization and surgical decompression. When and if to operate remains controversial. This topic is discussed separately. (See ["Cervical spondylotic myelopathy"](#).)

Ossification of the posterior longitudinal ligament — Ossification of the posterior longitudinal ligament (OPLL) is a condition of abnormal calcification of the posterior longitudinal ligament, usually in the cervical spine [173-178]. Its pathogenesis is not known, but it is more common in individuals in East Asia, including Japan, and in males (roughly 2:1 male:female ratio) [179]. OPLL can be associated with idiopathic skeletal hyperostosis, ankylosing spondylitis, and other spondyloarthropathies, or may occur as an isolated condition. (See ["Diffuse idiopathic skeletal hyperostosis \(DISH\)"](#), section on 'Differential diagnosis'.)

Symptomatic patients typically present in the fifth to sixth decades of life with progressive myelopathic symptoms, but they are also at risk for and can present with acute spinal cord

injury [180]. It is diagnosed by characteristic findings on imaging findings (computed tomography [CT] or MRI); significant compressive symptoms typically require surgical decompression.

Surfers' myelopathy — A syndrome of acute low back pain followed by progressive lower extremity numbness and weakness has been described in at least 26 patients while surfing [181-186]. Patients are generally young (ages 15 to 46 years), mostly male, are often surfing for the first time, and have suffered no apparent trauma. MRI shows restricted diffusion in the lower thoracic spinal cord to the conus medullaris. The pathogenesis is unclear; however, the MRI findings along with reports of individuals lying prone on the surfboard with possible lumbar hyperextension for prolonged periods of time suggest that vascular compression may play a role. The severity of the neurologic deficits and degree of recovery is variable.

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "[Patient education: Paraplegia and quadriplegia \(The Basics\)](#)" and "[Patient education: Friedreich ataxia \(The Basics\)](#)")

SUMMARY

- **Causes of myelopathy** – Pathologies that affect the spinal cord are diverse. Common etiologies of myelopathy include autoimmune, infectious, neoplastic, vascular, and hereditary-degenerative diseases. (See '[Inflammatory diseases](#)' above and '[Infections](#)' above and '[Vascular disease](#)' above and '[Toxic, metabolic disorders](#)' above and '[Neoplasms](#)' above and '[Inherited and degenerative conditions](#)' above.)

- **Clinical localization** – The neurologic examination will elicit the deficits and define a specific spinal cord syndrome ([table 2](#)). The approach to localization and the features of specific spinal cord syndromes are described separately. (See "[Anatomy and localization of spinal cord disorders](#)", section on 'Clinical localization' and "[Anatomy and localization of spinal cord disorders](#)", section on 'Spinal cord syndromes'.)
- **Diagnostic approach** – The spinal cord syndrome, along with the clinical setting, course of presentation, and findings on a neuroimaging study (usually MRI), will identify the likely pathogenesis in most cases ([table 1](#)). (See '[Diagnostic approach](#)' above.)

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