CHRONIC MYELOPATHY OF MULTIPLE SCLEROSIS

A chronic progressive myelopathy is the most frequent cause of disability 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 disability 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 confirmatory. Disease-modifying therapy is indicated for patients with progressive myelopathy who also have coexisting MS relapses. Therapy is sometimes offered to patients who have a progressive course without relapses but with "active" MRI scans (e.g., the presence of new focal demyelinating lesions) despite the lack of evidence supporting the value of treatment in this setting. **MS is discussed in Chap. 458.**

SUBACUTE COMBINED DEGENERATION (VITAMIN B_{12} DEFICIENCY)

This treatable myelopathy presents with subacute paresthesias in the hands and feet, loss of vibration and position sensation, and a progressive spastic and ataxic weakness. Loss of reflexes due to an associated peripheral neuropathy in a patient who also has Babinski signs is an important diagnostic clue. Optic atrophy and irritability or other cognitive changes may be prominent in advanced cases and are occasionally 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's sign. The diagnosis is confirmed by the finding of macrocytic red blood cells, a low serum B_{12} concentration, elevated serum levels of homocysteine and methylmalonic acid, and in uncertain cases, testing for anti–parietal cell antibodies and a Schilling test. Treatment is by replacement therapy, beginning with 1000 μg of intramuscular vitamin B_{12} repeated at regular intervals or by subsequent oral treatment **(Chap. 128)**.

HYPOCUPRIC MYELOPATHY

This myelopathy is similar to subacute combined degeneration (described above), except there is no neuropathy, and explains cases with normal serum levels of B_{12}. 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, until recently, zinc-containing denture creams, all of which impair copper absorption via induction of metallothionein, a copper-binding protein. Many cases are idiopathic. Improvement or at least stabilization may be expected with reconstitution of copper stores by oral supplementation. There is microcytic or macrocytic anemia. The pathophysiology and pathology of the idiopathic form are not known.

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 disorders. 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 disturbances, 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's sign; and, in almost all cases, bilateral Argyll Robertson pupils, which fail to constrict to light but accommodate. Diabetic polyradiculopathy may simulate tabes.

FAMILIAL SPASTIC PARAPLEGIA

Many cases of slowly progressive myelopathy are genetic in origin **(Chap. 452)**. More than 30 different causative loci have been identified, including autosomal dominant, autosomal recessive, and X-linked forms. Especially for the recessive and X-linked forms, a family history 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.

ADRENOMYELONEUROPATHY

This X-linked disorder is a variant of adrenoleukodystrophy. Most affected males have a history of adrenal insufficiency and then develop a progressive spastic (or ataxic) paraparesis beginning in early or sometimes middle adulthood; some patients also have a mild peripheral neuropathy. Female heterozygotes may develop a slower, insidiously progressive spastic myelopathy beginning later in adulthood and without adrenal insufficiency. 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 (ADLP), a peroxisomal membrane transporter involved in carrying long-chain fatty acids to peroxisomes for degradation. Corticosteroid replacement is indicated if hypoadrenalism is present, and bone marrow transplantation and nutritional supplements have been attempted for this condition without clear evidence of efficacy.

OTHER CHRONIC MYELOPATHIES

Primary lateral sclerosis **(Chap. 452)** is a 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. Some cases may represent familial spastic paraplegia, particularly autosomal recessive or X-linked varieties in which a family history may be absent.

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 small leg or foot deformity indicating a long-standing 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.

There are a number of rare toxic causes of spastic myelopathy, including lathyrism due to ingestion of chickpeas containing the excitotoxin β-*N*-oxalylamino-L-alanine (BOAA), seen primarily in the developing world, and nitrous oxide inhalation producing a myelopathy identical to subacute combined degeneration. SLE, Sjögren's syndrome, and sarcoidosis may each cause a myelopathy without overt evidence of systemic disease. Cancer-related causes of chronic myelopathy, besides the common neoplastic compressive myelopathy discussed earlier, include radiation injury **(Chap. 118)** and rare paraneoplastic myelopathies. The last of these are most often associated with lung or breast cancer and anti-Hu antibodies **(Chap. 122)** or with lymphoma that causes a syndrome of destruction of anterior horn cells; NMO **(Chap. 458)** can also rarely be paraneoplastic in origin. Metastases to the cord are probably more common than either of these in patients with cancer. 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