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24.13 Disorders of the spinal cord CONTENTS 24.13.1 Diseases of the spinal cord 6127 Anu Jacob and Andrew J. Larner 24.13.2 Spinal cord injury and its management 6135 Wagih El Masri(y) and Michael Barnes 24.13.1 Diseases of the spinal cord Anu Jacob and Andrew J. Larner ESSENTIALS The spinal cord is subject to numerous pathological processes which may be intrinsic (intramedullary) and/or extrinsic (extramedullary) to the cord. Clinical features Symptoms and signs suggestive of spinal cord disease include (1) motor—weakness and alteration in tone; acute cord lesions produce flaccidity ('spinal shock') whereas chronic processes pro- duce spasticity, with hyperreflexia, clonus, and upgoing (extensor) plantar responses; pathological processes affecting lower motor neurons in the anterior horns typically produce early muscle wasting and fasciculation; (2) sensory—including numbness, loss of sensation, tingling, sensory ataxia; the demonstration of a sen- sory level and analysis of specific sensory deficit patterns are of particular importance in localizing the site, and therefore the likely cause, of a spinal cord lesion; and
(3) autonomic—sphincter dysfunction, most commonly affecting bladder function. Other clinical features may give clues to the cause of spinal cord dis- ease (e.g. multiple sclerosis, systemic lupus erythematosus, neurofibromatosis). Investigation Intramedullary and extramedullary pathologies may produce distin- guishable symptom profiles, but the clinical distinction can only ever be probabilistic. If there is acute onset of myelopathy, and/or struc- tural disease is suspected, imaging of the cord is mandatory, with MRI the investigation of choice. Once structural lesions are excluded, further investigation depends on suspected cause (e.g. neurogenetic testing for some hereditary spastic paraplegias and spinocerebellar ataxias), and on geographical location or travel history (e.g. schisto some ova in faeces). Examination of the cerebrospinal fluid may

be required. Particular conditions affecting the spinal cord Many diseases can affect the spinal cord. Those of particular note include (1) spondylotic myelopathy—the most common cause of progressive myelopathy due to cord compression; (2) mul- tiple sclerosis—may present as an isolated cord syndrome, usually partial rather than complete; (3) transverse myelitis—most com- monly affects the thoracic cord; there may be a preceding his- tory of infection, and cerebrospinal fluid analysis may disclose an infective agent; (4) subacute combined degeneration of the cord—demyelination of the posterior and lateral columns due to vitamin B12 deficiency; neurological features may occur in the absence of haematological abnormality; (5) genetic disorders— hereditary spastic paraplegia is usually an autosomal dominant disorder; causative mutations have been described in several genes; (6) vascular disorders—anterior spinal artery occlusion can infarct whole or part of the anterior two-thirds of the cord; (7) syr- ingomyelia; (8) injury/trauma—see Chapter 24.13.2; (9) motor neuron disease—see Chapter 24.15; (10) cancer—most common spinal cord tumours are metastasis, astrocytoma, ependymoma, lymphoma. Treatment and prognosis Specific medical and surgical treatments are determined by the particular cause of myelopathy. These may arrest progression, but function that has been lost may not recover fully. Prognosis of acute cord compression is directly related to the time delay between symptom onset and relief of compression. Chronic dis- ability as a consequence of spinal cord disease requires intensive neurorehabilitation. Introduction Disease within the substance of the spinal cord, intramedullary myelopathy, may result from a wide variety of pathological causes. Myelopathy may also result from pathology located outside the spinal cord (extramedullary) but within structures

 immediately adjacent to the cord, either intradural or extradural, affecting normal cord function. Clinical features may some- times give clues to both the pathological nature and anatomical location of disease, but these have been greatly augmented with the development of magnetic resonance imaging studies of the spinal cord. Aetiology and pathogenesis The spinal cord and its addenda may be affected by structural, inflammatory, demyelinating, metabolic, infective, neoplastic, and paraneoplastic, genetic, vascular, and iatrogenic disorders (Table 24.13.1.1). Chronic progressive myelopathy should al- ways prompt consideration of a structural lesion such as a tu- mour, intrinsic or extrinsic, but cervical spondylotic change with osteophyte formation, with or without concurrent interverte- bral disc degeneration and prolapse, is the most common cause of progressive cord compression. Hyperacute cord syndromes (evolving over minutes) may result from trauma or vascular path- ology, and infective or inflammatory disorders (myelitis) may develop acutely (hours to days) or subacutely (days to weeks), although sometimes present in a chronic progressive fashion (over months).

Table 24.13.1.1 Overview of causes of myelopathy

Pathological process (NB not necessarily mutually exclusive)	Intramedullary	Extramedullary
Structural: developmental	Syringomyelia related to Chiari malformation	Spina bifida, spinal dysraphism, diastematomyelia Chiari malformation Tethered cord syndrome Platybasia/basilar invagination
	Arteriovenous malformations (AVM)	Arachnoid cysts (e.g. in Marfan syndrome) Achondroplasia
Structural: acquired/ traumatic	Cord transection Contusion/haematoma Haematomyelia Central cord syndrome (hyperextension injury)	Whiplash (hyperextension/flexion injury) Spinal cord injury without radiologic abnormality (SCIWORA) Intervertebral disc prolapse +/- osteophytes +/- spinal stenosis Vertebral fracture (e.g. wedge fracture with vertebral metastasis) Atlanto-axial subluxation (e.g. rheumatoid arthritis) Ossification of the posterior longitudinal ligament Dural herniation of the spinal cord (e.g. neuroenteric cyst) Epidural lipomatosis
Structural: neoplastic	Astrocytoma/glioma	

Ependymoma Lymphoma Medulloblastoma Metastases Intradural: meningioma; neurofibroma; lipoma (+/- spina bifida) Extradural: myeloma, lymphoma, sarcoma, haemangioblastoma, chordoma Metastases Leukaemic meningeal infiltration Demyelinating disease Multiple sclerosis Acute disseminated encephalomyelitis (ADEM) Neuromyelitis optica (NMO) and NMO spectrum disease Solitary sclerosis (Not applicable) Inflammatory and/or immunological Transverse myelitis (idiopathic > clinically isolated syndrome) Sarcoidosis Systemic lupus erythematosus (SLE) Sjögren's syndrome Behçet's disease Giant cell arteritis Paraneoplastic myelitis Necrotizing myelitis (Foix–Alajouanine syndrome) Eales' myelopathy Arachnoiditis (e.g. related to radiological contrast media, ankylosing spondylitis) Discitis Infection Viral (e.g. poliomyelitis, HIV, HTLV-1 [tropical spastic paraparesis], enterovirus, herpes simplex 1 and 2, herpes zoster, EBV, CMV, HHV6, HHV7) Spirochaetal: neurosyphilis (tabes dorsalis) Bacterial (e.g. brucellosis, tuberculoma) Parasitic (e.g. schistosomiasis) 'Atypicals' (e.g. mycoplasma) Spinal abscess: epidural, subdural Empyema Osteomyelitis (e.g. staphylococcal) Osteitis (e.g. tuberculosis [Pott's disease], syphilis) Parasitic cysts (e.g. echinococcus) Metabolic and nutritional disorders Vitamin B12 deficiency (subacute combined degeneration of the cord) Copper deficiency associated myelopathy 'Hepatic myelopathy' Adrenomyeloneuropathy Vitamin E deficiency Lathyrism Konzo Krabbe's globoid cell leukodystrophy Paget's disease ('osteitis deformans') (continued)

24.13.1 Diseases of the spinal cord 6129 Clinical features The clinical features of spinal cord disease, the symptoms and signs, and their temporal progression, may give clues to disease localiza- tion (Tables 24.13.1.2 and 24.13.1.3) and pathogenesis. Symptoms and signs suggestive of spinal cord disease may be motor (weakness, spasticity), sensory (numbness, loss of sensation, tingling, sensory ataxia), and autonomic (sphincter and sexual dys- function). Acute and chronic pathologies may result in differing pat- terns of symptoms and signs, the former sometimes evolving to the latter. Involvement of specific spinal cord pathways may be inferred from the clinical features. Motor symptoms Weakness may affect all limbs (quadriparesis) or only the legs (paraparesis). The most severe presentation, for example, after traumatic cord transection, is with complete absence of power (quadriplegia, paraplegia). Exceptionally with extramedullary cer- vical cord lesions a triparesis may be seen, sometimes evolving in a sequential ('round the clock') pattern: arm, then ipsilateral leg, then contralateral leg. Alterations in tone often accompany weakness: in acute lesions flaccidity ('spinal shock') but with more chronic processes spasti- city with clonus, along with pathological accentuation of myotatic (tendon, phasic) reflexes (hyperreflexia), loss of cutaneous reflexes, and upgoing (extensor) plantar responses (Babinski's sign). Tonic spasms, abrupt and painful spasm of limbs on one side that last seconds to less than a minute, and often occurring multiple times in a day, are often seen in neuromyelitis optica. They respond exceptionally well to carbamazepine. Muscle wasting is a late sign with upper motor neurone path- ology. Concurrent radiculopathy or neuropathy may however modulate the typical upper motor neurone signs, for example the absent ankle jerks with upgoing plantars sometimes seen in sub- acute combined degeneration of the cord in which there is concur- rent neuropathy, or in motor neuron disease with both upper and lower motor neurone involvement, or the segmental reflex depres- sion in a compressive cervical myeloradiculopathy. Inversion of re- flexes (i.e. movement opposite to that usually seen, such as elbow Pathological process (NB not necessarily mutually exclusive) Intramedullary Extramedullary Neuronal degeneration and hereditary disorders Motor neuron disease Other motor neuron diseases: spinal muscular atrophies, Hirayama disease Hereditary spastic paraplegias (HSP) Spinocerebellar ataxias Familial Alzheimer's disease with presenilin-1 gene deletion Familial British dementia (Worster–Drought syndrome) (Not

applicable) Vascular Cord infarction (e.g. anterior spinal artery syndrome) Cord ischaemia (e.g. ‘surfer’s myelopathy’) Aortic aneurysm Fibrocartilaginous embolism Decompression sickness Haematomyelia/haematoma: into metastasis or vascular malformation, primary coagulation disorder Vascular malformations: dural arteriovenous fistula, arteriovenous malformations, cavernous angioma Iatrogenic Surgery of aortic aneurysm: anterior spinal artery syndrome Lumbar puncture: direct trauma to cord Radiation myelopathy (acute, delayed) Vaccination-related myelopathy Drugs: anticoagulants (bleed into cord); heroin; subacute myelo- optic neuropathy with clioquinol Lumbar puncture: spinal subdural haematoma Medically unexplained ‘Hysterical paraplegia’ Table 24.13.1.2 Clinical clues to differentiation of intramedullary from extramedullary myelopathy Symptoms/Signs Intramedullary Extramedullary Sensory Central (funicular) distribution of pain may occur. Patterns of sensory loss may be: dissociated (spinothalamic > dorsal column modalities, or vice versa) including classic Brown–Séquard syndrome; suspended (cape-like, cuirasse); sacral sparing. Vibratory sensibility more often affected than proprioception. Pain may be radicular or vertebral in distribution. Sensory signs not usually marked until the later stages and all modalities often involved. Brown–Séquard syndrome may be more common with extrinsic than intrinsic pathologies. Motor Lower motor neurone signs at the level of the lesion(s) may be prominent and diffuse; upper motor neurone signs of spastic paraparesis below the level of the lesion tend to occur late. Combination of upper and lower motor neurone signs more likely to reflect intrinsic than extrinsic pathology. Sequential spastic paraparesis below the level of the lesion. Upper motor neurone signs occur early; lower motor neurone signs unusual and if present typically have segmental (radicular) distribution. Autonomic Bladder involvement common, often early symptom; slow to recover. Later involvement than in intramedullary lesions.

section 24 Neurological disorders 6130 extension when eliciting the supinator reflex) may occur when pathology affects both the local reflex arc and segments higher in the cord. High spinal cord lesions may affect segments innerv- ating the diaphragm (C3–5) with subsequent respiratory com- promise, particularly acute lesions, hence the need for respiratory monitoring in these circumstances. The root values of abnormal myotatic and cutaneous reflexes help to localize the lesion. Pathological processes targeting lower motor neurones in the an- terior horns of the spinal cord typically produce early muscle wasting and fasciculation. Motor neuron disease is the most common cause of these signs, sometimes in isolation (‘progressive muscular at- rophy’), but they may also occur following certain viral infections (poliomyelitis, enterovirus 71, flaviviruses such as Japanese enceph- alitis virus). A subacute motor neuronopathy is also described in association with underlying lymphoma. Sensory symptoms Spinal cord pathologies are often accompanied by a localizing sensory level, which may be defined clinically as the spinal seg- ment below which sensation is altered and above which it is in- tact. Because pain fibres forming the spinothalamic tracts ascend in the posterior horns for two or three segments prior to decussa- tion through the ventral commissure, contralateral loss or reduction of pain and temperature sensation may be associated with a level two or three segments above the site of pathology. The deficit asso- ciated with a sensory level may be complete, affecting all modalities, for example in cord transection (‘sawn off’) or complete transverse myelopathies, but more often is partial. Specific patterns of sensory deficit have particular localizing im- plications (Table 24.13.1.3). Because of the anatomical separation within the cord of the pathways subserving the sensory modal- ities of pain and temperature (spinothalamic) and proprioception (dorsal column), dissociated sensory loss may occur. Central cord pathologies such as syringomyelia selectively involve decussating spinothalamic pathways within the ventral commissure resulting in impaired pain and temperature

sensation, often in a suspended (‘cape-like’, cuirasse, ‘bathing suit’) distribution, dependent on the exact level of the syrinx. Osteoarthropathy (Charcot joints) due to loss of pain fibres may also occur in syringomyelia. Anterior spinal artery syndrome also spares the dorsal (posterior) columns. Conversely, the dorsal columns are preferentially affected in dis- orders such as subacute combined degeneration of the cord. Focal cervical cord pathology, most typically demyelination, may be ac- companied by Lhermitte’s sign, tingling paraesthesia radiating like an electric shock into the arms and legs on neck flexion; rarely there may be a motor equivalent, increased limb weakness on neck flexion (McArdle’s sign). Both signs reflect mechanosensitivity and impaired impulse transmission in demyelinated axons. Preservation of pain and temperature sensation in sacral dermatomes (‘sacral sparing’) below a sensory level may be seen with intramedullary lesions as a result of the topographical lamination of fibres in the spinothalamic tracts, the ventrolateral fibres of sacral origin being most external and hence later involved with expanding intramedullary lesions. Although ataxia is sometimes thought of as a motor symptom, it may also be a consequence of sensory dysfunction, specific- ally when afferent proprioceptive information is degraded or lost. Sensory ataxia, as distinct from cerebellar or optic ataxia, results in falling or markedly increased sway when standing with the eyes closed (Romberg’s sign) and impaired heel-toe (tandem) walking (‘dynamic Romberg’s sign’). Pseudoathetosis, involuntary move- ments in the outstretched hands (‘piano-playing fingers’), may also be seen. Dorsal column pathologies are particularly associated with sensory ataxia, classically the tabes dorsalis form of neurosyphilis, also sometimes known as locomotor ataxia. Table 24.13.1.3 Clinical presentations of intramedullary myelopathies Lesion type Tracts involved Clinical signs Examples Complete All Motor, sensory, and autonomic dysfunction below lesion Traumatic cord transection, acute necrotizing viral myelitis Brown–Séquard (hemicord) syndrome Ipsilateral corticospinal and dorsal columns, contralateral spinothalamic columns Ipsilateral pyramidal weakens and dorsal cord sensory loss, contralateral spinothalamic loss Multiple sclerosis Anterior cord syndrome Bilateral anterior horn cells, corticospinal tracts, spinothalamic and autonomic Acute bilateral flaccid weakness, loss of pain/temperature, sphincter/autonomic dysfunction, preserved dorsal column function Anterior spinal artery occlusion Dorsal (posterior) cord syndrome Bilateral dorsal columns Bilateral loss of proprioception, vibration sensation Vitamin B12 deficiency, copper deficiency, tabes dorsalis, AIDS-associated vacuolar myelopathy Central cord Crossing spinothalamic, corticospinal, and autonomic fibres Dissociated sensory loss: pain and temperature impaired with preserved vibration and proprioception. May have pyramidal weakness and autonomic dysfunction below lesion Syringomyelia Conus medullaris Autonomic outflow and sacral spinal cord segments Early sphincter dysfunction, sacral sensory loss; mild (proximal) leg weakness L1 central disc prolapse, postviral myelitis Cauda equina syndrome Spinal nerve roots of the cauda equina Early flaccid leg weakness, often asymmetric, sensory loss in root distribution, followed by autonomic dysfunction Compression, acute cytomegalovirus polyradiculitis Tractopathies Selective tract involvement Selective pyramidal or dorsal column involvement Vitamin B12 deficiency, paraneoplastic myelopathy

 Autonomic symptoms Autonomic symptoms associated with spinal cord pathology are most typically those related to sphincter, particularly bladder, func- tion. Acute spinal cord lesions may result in urinary retention, for example cauda equina compression with central L1 disc prolapse, although sometimes the pathology may be many segments rostral to the clinical signs. Inflammatory and chronic lesions, for example multiple sclerosis, may be associated with urinary frequency, ur- gency and urge incontinence with

urodynamic evidence of detrusor muscle hyperreflexia and detrusor sphincter dyssynergia (i.e. inability of the sphincter to relax while the detrusor contracts). Loss of awareness of bladder fullness with urinary retention and overflow (atonic bladder) may result from direct damage to the sacral cord. Cord damage may also result in constipation or faecal urgency or incontinence, and sexual (e.g. erectile) dysfunction. Loss of or ex- cessive sweating may be observed in syringomyelia. Horner's syn- drome may be associated with cord pathology since the sympathetic afferents originate there, for example, isolated Horner's syndrome has been reported with syringomyelia. Autonomic dysreflexia is a life-threatening situation when sympa- thetic overactivity below the lesion, which cannot be countered by descending inhibitory spinal cord pathways due to the cord lesion, leads to severe hypertension. It occurs typically in complete trans- verse myelitis above T6 level and is triggered by visceral stimuli like a full bladder. Intramedullary versus extramedullary myelopathy Intramedullary and extramedullary pathologies may produce dis- tinguishable symptom profiles (Table 24.13.1.2) but the clinical dis- tinction can only ever be probabilistic, and further investigation by means of spinal cord imaging, ideally with MRI, is indicated. The syndrome originally described by Brown–Séquard in the context of traumatic cord hemisection consists of ipsilateral spastic weakness with or without segmental lower motor neurone signs at the level of the lesion, with dissociated sensory loss comprising ipsilateral pro- prioceptive loss and contralateral pain and temperature loss below the level of the lesion. This pattern may occur with various patholo- gies including prolapsed disc, intra- and extramedullary tumours, and multiple sclerosis. Other clinical features may give clues to the aetiological diag- nosis of myelopathy. A history of hindbrain headache may indi- cate a Chiari malformation. Likewise, other clinical signs may be informative: a segmental rash may be seen acutely with varicella zoster, and clinical stigmata may point to diagnoses such as systemic lupus erythematosus (SLE), neurofibromatosis, Paget's disease, and rheumatoid arthritis. False localizing signs Although the 2–3 segment mismatch between a clinically defined pain sensory level and the location of cord pathology is easily ex- plicable based on the known anatomy of spinal cord connections, other clinical signs distant from pathology are less easy to explain. Such false localizing signs in the cord include the association of for- amen magnum or upper cervical cord lesions with paraesthesia in the hands, intrinsic hand muscle wasting ('remote atrophy') and distal upper limb areflexia, a gestalt more suggestive of lower cer- vical myeloradiculopathy. Similarly, a midthoracic sensory level (described as a tight band, squeeze, or 'girdle sensation') with spastic paraparesis may occur with lower cervical or upper thoracic com- pressive pathology. Differential diagnosis The particular pattern of symptoms and signs may allow differenti- ation of myelopathy from disorders of nerve roots (radiculopathy), although because of their close proximity to the cord simultaneous segmental involvement is not uncommon (radiculomyelopathy) particularly with cervical spinal lesions; likewise, peripheral nerves (neuropathy), although certain disease processes may simultan- eously affect both (myeloneuropathy, e.g. subacute combined de- generation). Isolated lesions of the conus typically present with numbness in the lowest dermatomes (perianal) with bladdder and bowel involvement without weakness, but may soon progress to in- volve higher levels of cord causing motor symptoms. It may however be difficult to differentiate it from the cauda equina syndrome of multiple radiculopathies, although often both are present. Clinical investigations If there is acute onset of myelopathy, and/or structural disease is sus- pected, imaging of the cord is mandatory and MRI the investigation of choice, usually requiring axial and sagittal sequences with T1- and T2-weighting, with or without gadolinium contrast. Appearances may diagnose structural abnormalities such as spondylotic compres- sion, disc prolapse, intrinsic or extrinsic tumours, syringomyelia, Chiari malformations, abscess, or haematoma. Arteriovenous mal- formations may

be seen, although it remains the case that on occa- sion myelography will reveal vascular anomalies not seen on MRI. Further definition of these vascular lesions with selective spinal angiography or magnetic resonance angiography may be helpful in planning appropriate treatment. Neurosurgical biopsy of mass le- sions may on occasion be required. Intrinsic cord disease may have characteristic appearances on MR imaging. Typical demyelinating lesions of multiple sclerosis usually extend for no more than two vertebral segments and may be mul- tiple, whereas more extensive lesions ('longitudinal myelitis') sug- gest neuromyelitis optica (NMO), or other infective, postinfectious, or vascular disease. These lesions may be associated with enhance- ment on postcontrast scans. Certain viral myelitides, such as polio- myelitis or enterovirus 71, may produce signal change confined to the anterior horns, consistent with a purely motor syndrome. T2-weighted hyperintensity in the grey matter of the anterior horns ('snake-eyes') may also be seen in Hirayama disease/O'Sullivan- McLeod syndrome, or paraneoplasia. Magnetic resonance spectros- copy of cord lesions may prove difficult because of partial volume effects in selected voxels. Once structural lesions are excluded, further investigation of myel- opathy will depend on the suspected cause. Blood tests may include haematological parameters such as full blood count and film, ESR, and vitamin B12 level. Biochemical analyses are seldom helpful other than for specific entities, such as angiotensin converting enzyme for sarcoidosis, and very long chain fatty acids for adrenoleukodystrophy which may be associated with the typical electrolyte changes of Addison's disease. Raised alkaline phosphatase may alert to a possible

section 24 Neurological disorders 6132 diagnosis of Paget's disease. Serology for the venereal diseases re- search laboratory, autoantibodies including double-stranded DNA, antiphospholipid antibodies, and gastric parietal cell antibodies may be required if specific diseases are suspected. NMO is associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG). Serology for infective agents may encompass viral (HIV, HTLV-1, enterovirus 71, EBV, CMV, varicella zoster, coxsackievirus, polio- virus), bacterial (brucella, tuberculosis), spirochaetal (syphilis) and parasitic (schistosomiasis) causes of myelopathy. In the appropriate geographical distribution or with positive travel history, a search for schistosome ova in faeces may be undertaken. Neurogenetic testing, following appropriate genetic counselling, is available for some of the many genetic loci which have been de- fined for the hereditary spastic paraplegias and spinocerebellar ataxias. Adrenoleukodystrophy has been linked to over 500 different mutations in the ATP-binding cassette ABCD1 gene. Examination of the cerebrospinal fluid may be required. Depending on the clinical scenario, this may require analysis for cell count, protein, glucose, xanthochromia, oligoclonal bands, serology, cytology, angiotensin converting enzyme and polymerase chain reaction for infective agents such as viruses and tuberculosis (see Chapter 24.3.1). Neurophysiological investigations (electromyography, nerve con- duction studies) have little direct role in the diagnosis of cord syn- dromes, although electromyography may be diagnostic for motor neuron disease, but may help to define concurrent radiculopathies or neuropathies which may focus differential diagnostic consider- ations. Somatosensory evoked potential studies may confirm a clin- ically defined spinal cord lesion, or provide evidence of a subclinical lesion, for example in multiple sclerosis, as may visual evoked poten- tial studies. However, MRI is more sensitive in this regard. Central motor conduction times to muscles in lower (e.g. tibialis anterior) or upper limb (e.g. abductor digiti minimi) may indicate cord path- ology, often being abnormal in transverse myelopathies, but this in- vestigation is not widely available. Criteria for diagnosis Clinical features of some of the more common causes of myelopathy (Table 24.13.1.1) are briefly presented. Structural disorders A syrinx is a fluid-filled cavity within the spinal cord (syringomyelia) or

brainstem (syringobulbia) which may be connected to a dilated central canal or separate from it. Most are associated with Chiari type hindbrain anomalies, sometimes with concurrent hydrocephalus, but there are also associations with spinal trauma, spinal tu- mours, arachnoiditis, and inflammatory/demyelinating disorders of the spinal cord such as multiple sclerosis and NMO. Demyelinating diseases The spinal cord is one the sites of predilection for demyelinating diseases. Multiple sclerosis (MS; see Chapter 24.10.2) may present as an isolated cord syndrome, usually partial rather than complete. Clues to the diagnosis may be typical MRI features in the cord, concurrent demyelination on brain MRI, and cerebrospinal fluid (CSF) with oligoclonal bands. Distinct from this acute presentation is a progressive myelopathy, either following (secondary progressive MS) or without prior relapsing episodes (primary progressive MS). Neuromyelitis optica (NMO), also known as Devic's syndrome, is an inflammatory disorder, an autoimmune astrocytopathy, with a predilection for optic nerves and spinal cord, causing typic- ally a long myelitis usually greater than three vertebral segments, associated with AQP4-IgG. The phenotype has broadened with increasing availability of serological testing, with classification now encompassing NMO spectrum disorder (NMOSD). Further anti- bodies have been described in NMO (e.g. myelin oligodendrocyte), but as yet lack the specificity of AQP4-IgG. Solitary sclerosis is a progressive neurological syndrome resulting from a single demyelinating lesion in the lower brainstem or upper cervical spinal cord, but not fulfilling diagnostic criteria for MS or NMOSD. Some patients have CSF oligoclonal bands suggesting that in some instances solitary sclerosis might be a spatially isolated, forme fruste, of MS. Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory disorder of brain and spinal cord, more commonly seen in children than adults, and sometimes following infection or vaccination. Acute haemorrhagic leukoencephalitis (or Hurst's disease) is probably related. The clinical picture is heterogeneous, with encephalopathy, focal neurological signs, and even psychosis being the presenting features. Multiphasic and recurrent variants have occasionally been described, and it may be difficult to differ- entiate ADEM from a first episode of MS. Clinical and radiological findings said to be more common in ADEM than MS include pre- ceding infectious disease, polysymptomatic presentation, pyram- idal signs, encephalopathy, bilateral optic neuritis, and epileptic seizures. Inflammatory and infective diseases Transverse myelitis most commonly affects the thoracic cord. If complete, there is paralysis, sensory loss, and incontinence, often with an acute flaccid paraparesis or paraplegia. There may be a preceding history of infection. MR imaging often reveals exten- sive longitudinal abnormal signal over several contiguous spinal segments, unlike the pattern typical of MS. Differential diag- nosis of such 'longitudinal myelitis' includes NMOSD, infective (viral), postinfectious, and postvaccination myelitides, and col- lagen vascular diseases. CSF analysis may disclose an infective agent, including coxsackieviruses, polioviruses, enterovirus 71, flaviviruses (Japanese encephalitis, West Nile virus), some of which have a predilection for the anterior horn cells producing a largely or exclusively motor picture and MR signal change confined to the anterior horns. HTLV-1 more typically produces a chronic spastic paraparesis, also known as HTLV-1-associated myelopathy (HAM), and was probably the agent responsible for 'tropical spastic parapar- esis'. The vacuolar myelopathy associated with HIV infection may be overlooked clinically because of other neurological involvement and is often defined only at post-mortem. Postinfectious myelitis may be a variant of ADEM, hence the term 'acute postinfectious encephalomyelitis' has been suggested. Collagen vascular dis- eases such as SLE, with or without antiphospholipid antibodies, may be associated, and sometimes presents, with an acute myelitis which, as in the case of postinfectious myelitis, is associated with raised CSF cell count and protein but without oligoclonal bands.
A depressed CSF glucose level has sometimes been reported in

24.13.1 Diseases of the spinal cord 6133 SLE transverse myelitis. However, much of the literature on SLE, Sjögren's syndrome, or other connective tissue associated mye- litis predates the discovery of aquaporin-4 IgG, which has been increasingly identified in such myelitides, suggesting that NMO rather than the connective tissue disease was responsible for the myelitis. Other multisystem inflammatory disorders like sarcoidosis and Behçet's disease can affect the spinal cord and present typically as intramedullary single or multiple, short or long, contrast-enhancing lesions that respond to steroids. Careful history, systemic examin- ation, and noninvasive tests will avoid misdiagnosis and spinal cord biopsy. A syndrome of acute necrotizing myelitis, sometimes known as Foix–Alajouanine syndrome, may merge with the severe end of the transverse myelitis spectrum. This condition may be asso- ciated with vascular pathologies (see next), or haematological or lung neoplasms, and hence represent a paraneoplastic syndrome, although more usually these latter manifest as an encephalomy- elitis. A progressive encephalomyelitis with rigidity and myo- clonus may occur as a paraneoplastic syndrome associated with antibodies directed against glutamic acid decarboxylase or gly- cine receptors. Some episodes of transverse myelitis resist all diagnostic efforts to define their aetiology and hence by a process of exclusion may be classified as idiopathic transverse myelitis. Metabolic and nutritional disorders In subacute combined degeneration of the cord due to vitamin B12 (cobalamin) deficiency, myelopathy is due to demyelination of spinal cord white matter tracts, specifically the posterior and lat- eral columns. MRI of the cervical spinal cord may show evidence of posterior column high signal intensity extending over several segments, unlike the appearances of MS, which may resolve or im- prove with vitamin B12 repletion. Although vitamin B12 deficiency may occur in the context of pernicious anaemia, myelopathy may also occur in the absence of haematological abnormality. A Schilling test to examine B12 absorption may be required. Elevated serum levels of homocysteine and methylmalonic acid, the substrates for cobalamin-dependent enzymes, may be helpful when there is diag- nostic uncertainty and vitamin B12 levels are borderline. A concur- rent peripheral neuropathy, usually of axonal type, may be clinically and/or neurophysiologically evident. Overuse of nitrous oxide analgesia may produce a similar clinical syndrome, due to functional B12 deficiency, as may acquired copper deficiency, often in the context of intestinal resection or dietary zinc excess. This disorder is associated with low serum copper and caeruloplasmin levels and increased signal in the dorsal columns on MRI. It may be the human equivalent of swayback disease seen in ruminants with copper deficiency. Vitamin E deficiency may be acquired, in the context of intestinal fat malabsorption, including patients with cystic fibrosis, or result from an autosomal recessive genetic disorder due to mutations in the α-tocopherol gene. Ataxia is both cerebellar and spinal in these disorders and may respond to vitamin E supplements. Hepatic myelopathy has been described, in association with chronic liver disease and portal hypertension, without cord imaging abnormalities. This diagnosis of exclusion should be evident from the clinical context. Hereditary disorders Hereditary spastic paraplegia is a heterogeneous group of motor system disorders typified by lower limb spasticity which greatly predominates over weakness. There may, in addition, be mild dim- inution of lower limb vibration and proprioception, and in compli- cated cases there may be additional clinical features such as epileptic seizures, cognitive impairment or frank dementia, peripheral neur- opathy, amyotrophy, or extrapyramidal features. Most instances are inherited as autosomal dominant disorders although recessive and X-linked variants are described, with over 70 genetic loci (heredi- tary spastic paraplegias) defined and over 50 genes harbouring de- terministic mutations, encoding proteins such as spastin, atlastin, paraplegin, spartin, and strumpellin. Adrenoleukodystrophy is an X-linked recessive peroxisomal disorder with variable clinical phenotype related to age. Whereas children and adolescents have a

cerebral presentation with per- sonality and intellectual changes leading to dementia, young adult males often present with a progressive spastic paraparesis with a mild distal polyneuropathy, adrenomyeloneuropathy, with de- layed cerebral involvement. There may be additional adrenal in- sufficiency. Positive family history may alert clinicians to the diagnosis. Some female heterozygotes (carriers) may manifest an adrenomyeloneuropathy-like syndrome with mild spastic parapar- esis. Cord imaging in adrenomyeloneuropathy may show atrophy but no signal abnormality. Friedreich's ataxia, the most common autosomal recessive cere- bellar ataxia, may present with a spastic paraparesis with extensor plantars, accompanied by absent ankle jerks due to the concur- rent axonal sensory polyneuropathy. The autosomal dominant spinocerebellar ataxias form a heterogeneous group, linked to over 30 different genetic loci, many associated with trinucleotide repeat expansions. The phenotype is of a progressive cerebellar syndrome with or without additional neurological features which may include spastic paraparesis. Although typically an exclusively cognitive disorder, variants of Alzheimer's disease with spastic paraparesis have been described in association with mutations in the presenilin-1 gene, most par- ticularly the exon 9 deletion. These patients also manifest a patho- logical phenotype, cotton wool plaques of amyloid protein, which although not absolutely specific are seldom seen in other cases. Familial British dementia, originally described as Worster–Drought syndrome and now characterized as one of the hereditary cerebral amyloid angiopathies, resulting from stop codon mutations in the A-Bri gene, typically presents with presenile dementia which is later complicated by cerebellar ataxia and spastic paraparesis. Vascular disorders of the spinal cord Vascular disorders of the spinal cord encompass both arterial infarction and haemorrhage or venous hypertension; venous in- farction is uncommon. Cord ischaemia has been postulated to contribute to spondylotic myelopathy and delayed radiation myelopathy. Arterial infarction is most commonly due to anterior spinal ar- tery occlusion; for example, during thoraco-abdominal aneurysm repair. In this syndrome, because of the respective watersheds of an- terior and posterior spinal arteries, the whole or part of the anterior two-thirds of the cord may be infarcted with loss of descending

 motor and ascending sensory pathway integrity but with preserva- tion of dorsal column function. Hypoperfusion of the cord may be responsible for the myelopathies associated with fibrocartilaginous embolism, often associated with back injury, and with air embolism in decompression sickness (Caisson disease). A syndrome in novice surfers of low back pain, bilateral leg numbness and paralysis for 10–60 min in association with restricted diffusion on MR imaging ('surfer's myelopathy'), may reflect cord ischaemia. Haemorrhage and/or venous hypertension may occur with spinal vascular malformations, which may broadly be divided into dural arteriovenous fistulas, usually acquired, and arteriovenous malfor- mations, usually of developmental origin. Spinal dural arteriovenous fistulas typically present in middle age and beyond, most commonly in men, with a progressive myelopathy. Venous hypertension re- sults in cord hypoxia which may progress to irreversible necrosis (Foix–Alajouanine syndrome; subacute necrotizing myelopathy). Stepwise progression may occur. In contrast, spinal arteriovenous malformations tend to present at a younger age than arteriovenous fistulas, with a mean age at onset in the third decade but sometimes in childhood. Arteriovenous malformations may be at any cord level, on the surface, within the parenchyma, or both. High flow lesions may also have arterial aneurysms on the supplying vessels. Spinal haemorrhage is the typical clinical manifestation, presenting with acute painful paraplegia, back pain, sciatica, with or without meningism and disturbance of consciousness; blood may track intracranially and simulate subarachnoid haemorrhage. Progressive neurological dysfunction is less often seen with arteriovenous mal- formations than with arteriovenous fistulas. The presence of a spinal bruit and/or segmentally

related cutaneous malformations may give a clue to the presence of an intradural arteriovenous malforma- tion. Spinal vascular malformations may occur in association with similar lesions in other organs or cutaneous angiomas; for example, in neurofibromatosis, with haemangioblastomas or cerebral aneur- ysms, and in specific syndromes (Cobb, Klippel-Trénaunay-Weber). Cavernous malformations may also occur in the spinal cord. Treatment and prognosis Treatment of myelopathy is, of course, dependent on establishing the precise aetiology. Structural lesions may require neurosurgical inter- vention, sometimes acutely to save or salvage cord function. With acute compressive lesions, prognosis is directly related to the time delay between symptom onset and relief of compression. Infective mass lesions may require debridement and systemic antibiotics. Foramen magnum decompression may be undertaken for syringo- myelia associated with Chiari malformation. Certain spinal cord vascular malformations may be amenable to endovascular treat- ment, or targeted (stereotactic) radiotherapy to shrink lesion size and reduce haemorrhagic risk. Radiotherapy of vertebral metastases causing malignant spinal cord compression is often undertaken. Specific treatment is sometimes available. Vitamin B12 myelop- athy may remit with vitamin repletion, although it is well recognized that there is an inverse relationship between duration of deficiency and extent of recovery following repletion. Dysaesthesia and pro- prioceptive deficits often persist, although these may be related in part to concurrent peripheral nerve involvement. Likewise with copper deficiency myelopathy, neurological decline is halted but seldom reversed by copper repletion. Cord compression with Paget’s disease may respond to specific treatment (bisphosphonates). Steroids are often prescribed for noninfectious inflammatory and necrotizing myelitides, sometimes with clinical improvement, al- though this may simply be a hastening of recovery which would have occurred anyway. Severe steroid unresponsive cases often improve following plasma exchange, which may be effective even many weeks after reaching clinical nadir. More specific immunosuppressive re- gimes (azathioprine, mycophenolate, rituximab) may be required in relapsing disorders such as NMOSD and SLE. Anticoagulation is in- dicated in the antiphospholipid antibody syndrome. Multiple scler- osis now has many effective disease-modifying agents that reduce relapse rates and slow the accumulation of disability. Residual or progressive deficits in sensorimotor and sphincter function resulting from myelopathy may benefit from targeted symptomatic and neurorehabilitation strategies, including physio- therapy and occupational therapy. Symptom management may in- clude agents for spasticity (oral baclofen, tizanidine, dantrolene; focal injections of botulinum toxin; intrathecal baclofen), pain (antineuropathic pain medications such as pregabalin, gabapentin; duloxetine; spinal cord stimulators), bladder dysfunction (anti- cholinergic medications, clean intermittent self-catheterization, suprapubic catheterization), and erectile dysfunction (sildenafil). FURTHER READING Jacob A, Weinshenker BG (2008). An approach to the diagnosis of acute transverse myelitis. Semin Neurol, 28, 105–20. Jaiser SR, Winston GP (2010). Copper deficiency myelopathy. J Neurol, 257, 869–81. Krupp LB, et al. (2013). International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis and immune- mediated central nervous system demyelinating disorders: revisions to the 2007 definitions. Mult Scler, 19, 1261–7. Larner AJ (2016). A dictionary of neurological signs, 4th edition. Springer, London. Lo Giudice T, et al. (2014). Hereditary spastic paraplegia: clinical- genetic characteristics and evolving molecular mechanisms. Exp Neurol, 261, 518–39. Lohre ET, et al. (2012). Radiation therapy in malignant spinal cord com- pression: what is the current knowledge on fractionation schedules? A systematic literature review. BMJ Support Palliat Care, 2, 51–6. Mariano R, et al. (2018). A practical approach to the diagnosis of spinal cord lesions. Pract Neurol, 18, 187–200. Polman CH, et al. (2011). Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol, 69, 292–302. Rathnasabapathi D, et al. (2015). Solitary sclerosis: progressive neuro- logical deficit from a

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