Chapter 14

Meningitic Disorders and Myelopathies

E.M.R. Critchley

The spinal cord is that part of the central nervous system lying within the vertebral canal. It extends as an oval tube from the medulla oblongata at the foramen magnum to the L1–2 interspace or the upper part of the L2 vertebra. Its enveloping membranes are confluent with those covering the surface of the brain. The pia mater is intimately adherent to the cord with fine septa penetrating into the parenchyma. The arachnoid mater covers the cord more loosely, extending laterally over the dorsal ganglia and emergent roots, and downwards over the nerves of the cauda equina where it is attached to the sacrum at S2. CSF, secreted in the main by the choroid plexuses within the ventricular system of the brain, is contained within the transparent arachnoid membrane. Externally, the dura mater forms a tougher, opaque membrane over the surface of the brain and spinal cord. At spinal level it is tethered laterally by the dentate ligaments and ensheathes the arachnoid, pia, spinal cord and upper part of the cauda equina before ending at S2–3.

Any inflammatory, irritative or infiltrative disorder of the leptomeninges (pia mater and arachnoid) will cause a meningitic reaction – meningitis – with thickening of the meninges and exudation of cells and protein into the CSF of the subarachnoid space. Almost invariably, the meningeal reaction also involves the dura and spreads into the substance of the brain and spinal cord producing local inflammatory, infiltrative or arteritic changes. Viral diseases, predominantly but not invariably, invade the brain producing an encephalitis. Some secondary changes occur elsewhere but the pyogenic reaction is minimal. Where a bacterial infection clearly involves the substance of the brain, terms such as encephalomyelitis or myeloencephalitis are used; but even where there has been little encephalitic reaction, a bacterial meningitic infection will result in systemic changes such as pyrexia and leucocytosis; cerebral irritation with headache, epilepsy, cranial nerve palsies or photophobia; as well as cerebrospinal and spinal manifestations. There are two valid reasons that explain the undue emphasis usually given to the spinal component of meningitis: the clinical recognition of its presence by means of tests which depend essentially upon the presence of muscle spasm over the irritated meninges, and the use of a lumbar puncture needle, penetrating the lower subarachnoid space, in diagnosis, and sometimes therapeutically, in the management of meningitis.

Most spinal infections result from haematogenous spread. The meninges may be invaded directly as happens with disseminated miliary tuberculosis, via the choroid plexus with bacteria entering the CSF directly, or as a result of septic

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emboli lodging in the smaller arteries causing mycotic aneurysms to develop and rupture. Ascending vascular spread via the venous plexuses of blood vessels around the cord is a rare but well-documented cause of infection. Next most common after blood-borne infection is direct spread from local sites of infection such as bone, the sinuses and middle ear. In the case of certain viral infections neural spread from the nasopharynx and other infected tissues may also occur. Lastly, direct penetration of the meninges can occur aided by dysraphism, fractures or the introduction of contaminants – bacteria, chemicals, or the development of dermoids – via a lumbar puncture needle. Repeated episodes of meningitis raise questions of additional factors such as dural tears with CSF leakage, dermal sinuses, unhealed fractures, midline deformities and immunodeficient states.

An acute epidural abscess is likely to be the result of a blood-borne infection but at least 50% of chronic abscesses and granulomas develop from contiguous infection from neighbouring bones. Most epidural abscesses are caused by staphylococci but brucella, typhoid and gram-negative infections due to *E. coli*, pseudomonas or proteus may also present with the formation of an epidural abscess. Such abscesses are mostly seen over several segments of the thoracic spine. Partial compression of the cord may result, accompanied by excessive secretion of protein into the CSF to give Froin's syndrome with a thick, yellow, gelatinous and proteinaceous spinal fluid; but such classical signs suggest delayed diagnosis.

Subdural infection usually arises via the paranasal sinuses where the adherent dura becomes infected and the infection spreads on to its inner more vascular layer. Once the dura has been penetrated, the leptomeninges offer little resistance and fungal infections in particular spread locally to produce a combination of chronic meningitis, thrombophlebitis, microabscesses and granulomata.

The CSF offers an excellent culture medium for many organisms but the innate vascularity of the meninges enables a rapid blood-borne cellular response to develop. Where the infection is bacterial, the resultant pyogenic exudation shows a predominantly polymorphonuclear pleocytosis; if the infection is viral a lymphocytic pleocytosis is more usual. These cellular changes are accompanied by a seepage of protein into the CSF rendering it more sticky and eventually impeding flow. If the meningitis becomes chronic, as may happen with subacute or partially treated infections, fibroblasts proliferate and adhesions develop blocking the basal cisterns, sealing off the foramina of Lushka and Magendie, or matting together the roots of the cauda equina. Later complications include the development of hydrocephalus, arachnoid cysts at various levels, and a progressive spinal arachnoiditis. Spinal arachnoiditis occurs particularly as a response to the injection of toxic chemicals. Radio-opaque contrast media have been especially inculpated in the past but the combination of aetiological factors required is far from clear with the suggestion that there should be some evidence of infection as well as irritation. Thus certain non-infective causes of chronic meningitis such as neoplasia, sarcoidosis, Behçet's and chronic benign lymphocytic meningitis (Mollaret's meningitis), are associated with a low incidence of arachnoiditis whereas chronic infections with tuberculosis, brucellosis and fungi frequently cause widespread arachnoid reactions.

Meningitis may be overlooked and obscured by other disease manifestations in the very young and very old. At the extremes of life the differential diagnosis of unexplained pyrexia, failure to thrive or inanition require an

examination of the CSF. Chronic infections may present insidiously in all age groups, but especially in the immunocompromised individual. Nonetheless, most forms of meningitis present with a tetrad of headache, fever, increasing drowsiness and meningeal irritation. Headache is almost invariable and usually severe, continuous and increasing in intensity, especially at the back of the head and neck. Its presence may be indicated in young children and in those too ill to complain by other accompanying features such as photophobia, vomiting and papilloedema. Even taking these characteristics into account it is a lesser diagnostic feature than meningeal irritability.

The neck is the most mobile part of the spinal column and any muscular spasm in response to irritation due to meningitis, raised intracranial pressure or blood in the CSF is best seen as nuchal rigidity developing within a few hours. In its extreme form, nuchal rigidity encompasses the whole length of the spine with opisthotonus due to extreme hyperextension of the back. However, nuchal rigidity can be missed in the early stages, with overwhelming infection, or in the presence of disc pathology. Neck rigidity essentially occurs in the sagittal plane and can be elicited by placing a hand behind the head and trying to flex the neck passively. The presence of rigidity primarily in the sagittal plane is helpful in separating meningeal irritation from limited movements due to cervical spondylosis or to meningism occurring as a result of swollen neck glands or throat infections in children. A useful test in a child or young person is to see whether they can flex their head to touch their knees, or to "kiss the knees".

There are more formal tests. Kernig's test is useful in children and young adults. Extension of the knee with the hip flexed produces spasm and pain in the hamstrings. In the elderly, Brudzinski's set of signs of meningeal irritation is obtained more readily. Firstly, there may be spontaneous flexion of the knees and hips with attempted flexion of the neck, and secondly, extension of the knee with the hip flexed results in flexion of the other knee, or occasionally in extension.

Investigation of Acute Meningitis

Whenever possible a CT or ultrasound scan should be performed before a lumbar puncture. If the patient is drowsy, has had fits, or there is any suspicion of raised intracranial pressure a CT scan is mandatory. Even so, unless the meningitis is part of a septicaemia and the diagnosis can be obtained by blood culture, or in the course of an endemic a pathognomonic rash of meningococcal meningitis has been observed, examination of the CSF is required in order to make an accurate diagnosis and enable the clinician to contend with an unusual organism, an unusual strain, antibiotic resistance or antibiotic hypersensitivity necessitating a change in treatment as the meningitis progresses (Addy 1987). A CT scan should alert the clinician to the presence of a cerebral abscess, which may have ruptured to produce meningitis, to raised intracranial pressure from cerebral oedema complicating purulent bacterial infections or in the later stages to hydrocephalus, arachnoid cysts or secondary abscess formation. Drowsiness and coma, altered conscious levels due to fits, shock and disseminated intravascular coagulation may all develop and require urgent action.

It is accepted practice to start therapy with broad spectrum antibiotics whilst awaiting the outcome of CSF examination and to modify the treatment once the organism is known. The problem is how to minimize the risks of obtaining CSF in the presence of the complications mentioned. If there is any suspicion of raised intracranial pressure, the clinician may either elect to give a bolus of mannitol 2 g/kg intravenously before the CSF is examined or to obtain CSF from the cerebral ventricles. In the event of hydrocephalus a needle or catheter can be introduced into the ventricles via an open or bulging fontanelle or, in older children and adults, via burr holes. The catheter can then be used to withdraw CSF for examination, to relieve the increase in intracranial pressure and to continue to monitor intracranial pressure. If there is raised intracranial pressure but slit-like ventricles the clinician will have to decide between treating empirically with antibiotics or inserting a subarachnoid screw to monitor intracranial pressure before beginning treatment (Brown and Steer 1986; Newton 1987).

Neonatal meningitis, resulting from intrapartum infection with *E. coli*, group B streptococci or *Listeria*, carries a mortality of 20%–50%. Later infections up to three months after delivery are usually from exogenous contaminants such as *Staphylococcus aureus*, pseudomonas and *Klebsiella* with a lesser mortality of 10%–20%. In childhood the prevalent organisms are *Neisseria meningitis* and *Haemophilus influenzae* and in the elderly, *Streptococcus pneumoniae* and *E. coli*. A detailed discussion of the management of meningitis is outside the scope of this book and can be found in Critchley (1988) or Wood and Anderson (1988).

Tuberculous Infections

Tuberculous (TB) infection of the CNS may take on many protean forms but it is essential to recognize that the onset of TB meningitis may be as acute as any other type of bacterial or viral infection. The difference often lies in the subsequent progress. Instead of reaching a plateau or showing regression, the infection may fulminate and the patient becomes increasingly stuporose. Meningeal involvement is always secondary to TB infection elsewhere and may develop on a background of myalgia, anorexia, generalized malaise, low grade fever and intermittent headache. The onset of meningeal signs can be accompanied by headache, nerve palsies and drowsiness. If unsuccessfully treated a third phase follows with progressive neurological defects, coma and decerebration. Infants can present with full fontanelles and vomiting, children with abdominal pain and fits, and adults with focal features – an apparent stroke, a painful or paralysed eye, acute hydrocephalus or acute cerebral oedema (Tandon and Pathak 1973). Acute TB meningitis used to be the scourge of children under six years of age in developing countries. Even after the introduction of effective antibiotics, there was a 35% mortality with much attendant morbidity. Despite a perceptible shift from younger children to older children and young adults as the major risk group the mortality still remains unacceptably high.

Inflammation, exudation, giant cell proliferation and caseation are features of a fully developed TB meningitis; but many patients begin with a serous

meningitis related to the haematogenous dissemination of miliary tuberculosis secondary to the breakdown of a silent Ghon focus in the lungs or gastrointestinal tract. In about 75% of these patients the chest X-ray will show miliary tubercles with enlarged mediastinal lymph nodes. Very occasionally tubercles may be seen with the ophthalmoscope in the choroidal layer of the eye appearing as rounded, white patches about half the size of the optic disc. Miliary tubercles are secreted via the choroid plexus and become scattered over the leptomeninges. At first the CSF is clear and in all respects normal, but changes rapidly within one or two days into an opalescent fluid capable of forming a fine, fibrinous clot on standing. The white cell count rises to 100–200/mm^3, initially with a slight preponderance of polymorphs over lymphocytes but the ratio is soon reversed. The protein content may exceed 15 g/l and the sugar fall below 40% of the blood sugar level. The cornerstone of successful management is early diagnosis: any delay in the onset of treatment weighs on the prognosis. Rather than await the identification of acid-fast bacilli or the outcome of cultures and guinea-pig inoculation tests, therapy should be started on clinical suspicion and backed up by a thorough search for organisms in the lumbar CSF and even ventricular fluid.

Meningitis may be associated with any form of underlying systemic tuberculosis (Rich 1952) and its various forms described with reference to the main pathological characteristics e.g. focal plaques with caseation, acute inflammatory caseous meningitis or proliferative meningitis. TB as a disease is highly dependent upon the state of resistance of the host, the presence of infection elsewhere, the state of nutrition, and the immune responses. The onset of meningitis may be protracted over several months. The patient may have no discernible fever but complain of malaise, apathy, listlessness, anorexia, weight loss, occasional vomiting and focal symptoms. The complications of a chronic, slowly progressive meningitis include the development of arachnoiditis, subdural empyemata, and perivascular arteritic inflammatory changes involving infarction and granuloma formation within the spinal cord.

Caseous changes may remain focal at any site within the nervous system with the production of tuberculomata. A further breakdown in resistance may present with meningitis after a long latent period. Similarly, tuberculous spinal osteomyelitis secondary to haematogenous spread may involve one or more vertebral bodies and discs with minimal symptoms until an acute paraplegia develops secondary to vertebral collapse or direct extension leads to epidural granuloma or abscess formation, or even to meningitis. The differential diagnosis of a progressive paraplegia in the presence of TB includes: (1) vertebral collapse, (2) cord compression secondary to an epidural abscess or granuloma, (3) cord ischaemia and infarction secondary to arteritis or thrombophlebitis in the neighbourhood of a tuberculous infection, (4) an expanding subdural empyema, or (5) arachnoiditis or a high CSF protein resulting in a spinal block.

Neurobrucellosis

The intraspinal manifestations of brucellosis mimic closely those of TB and fungal infections. Systemic brucellosis primarily involves the whole of the reticuloendothelial system with secondary involvement of bone. Organisms

enter and proliferate within the cytoplasm of macrophages, thus the acute stage may be followed by a protracted, subclinical or relapsing illness. Non-specific symptoms such as headache, back pain and low grade fever can persist for months or years. In the acute stages meningism can arise from tender, enlarged cervical lymph nodes and occasionally there may be an acute serous meningitis which responds readily to tetracycline.

Four main intraspinal manifestations of brucellosis can occur with chronic infection, often presenting in combination.

Spinal Brucellosis or Spondylitis

Infection of a disc is most liable to occur in the lumbosacral or lower thoracic spine with spread to the adjacent vertebral bodies. Local tenderness and pain are common and the spine may become deformed with sciatica and radicular pains resulting from root compression. Vertebral erosion may lead to collapse with compression of the cord or cauda equina and the development of paraplegia. Alternatively, local spread can affect the meninges with epidural abscess formation also producing compression.

Chronic Lymphocytic Meningitis

The lymphocytic meningitis closely resembles that of TB with normal or reduced sugar levels and a greatly raised protein. Chronic meningitis may also affect the brain – meningoencephalitis, or the cord – meningomyelitis. Cerebral oedema or basal adhesions may result in a raised intracranial pressure with papilloedema and headache. Similarly, the high protein and arachnoid adhesions may result in a spinal block with paraplegia.

Radiculopathy

A Guillain-Barré like syndrome is described with radiculopathy, peripheral neuropathy and autonomic manifestations.

Myelopathy

The cord itself may be involved with demyelination, e.g. progressive ataxic quadriparesis (Al Deeb et al. 1989), acute transverse myelopathy, infarction or other vascular manifestations. In AIDS or other immune-deficient states, brucellosis may appear as an opportunistic infection.

The presence of chronic infection may be confirmed by a raised ESR and standard brucella agglutination tests. Identification of the organism can be difficult but may be achieved from blood or marrow culture or CSF. The accepted treatment of neurobrucellosis is one or more six-week course of oral tetracycline 2–3 g daily or co-trimoxazole b.d. with intramuscular streptomycin 1 g daily, gentamicin 6 mg/kg or rifampicin, but eradication cannot be guaranteed.

Sarcoidosis

About 5% of patients with sarcoidosis develop symptomatic nervous system disease, sometimes in isolation and sometimes in a setting of extraneural sarcoidosis. The percentage is higher if ocular manifestations – uveitis, conjunctivitis, scleral scarring and choroidoretinitis – are also included. The majority of neurological manifestations, amounting to 75% of the total, are peripheral, typically involving the facial nerve, singly, bilaterally or in Heerfordt's triad of uveoparotid fever. Other cranial nerves may be affected singly or as a cranial polyneuritis. Peripheral manifestations may develop unevenly with the evolution of mononeuritis multiplex or produce a combination of neuropathy and radiculopathy as in the Guillain-Barré syndrome.

Twenty-five per cent of neurosarcoidosis involves the CNS. Disease manifestations are seen relatively early in the course of the systemic illness, notably with the development of diabetes insipidus or other neuroendocrine dysfunction. The predominant lesion is a basal granulomatous meningitis blocking the basal cisterns and invading the parenchyma, infiltrating and compressing structures at the base of the brain. Leptomeningeal granulomata may be patchy rather than continuous. Their presence may account for the development of cranial nerve palsies and for symptomatic spinal cord sarcoidosis. Thus brain stem and spinal neurosarcoidosis can frequently masquerade as multiple sclerosis or transient ischaemic attacks in vertebrobasilar territory. A low grade or subclinical lymphocytic meningitis possibly occurs more frequently than a granulomatous meningitis; thus at least 75% of patients with neurosarcoidosis, perhaps presenting with a hypothalamic granuloma, will be shown to have a raised spinal fluid protein and a lymphocytic pleocytosis.

The pathology of the spinal lesions is little different from that of the more overt lesions at the base of the brain, but if they arise in isolation they can present much diagnostic difficulty. Isolated intra- or extramedullary granulomas in the cervical cord, or less commonly in the thoracic and lumbar cord, can present similarly to ependymomas or gliomas at the same site. Compression of the cord can develop from within, from without or from multiple parenchymatous granulomata associated with adhesive arachnoiditis. Granulomatous vasculitis and local infiltration can produce primary segmental demyelination, axonal degeneration, multiple small infarcts and, ultimately, necrosis of the cord. A common clinical presentation is of progressive paraplegia, especially at the thoracic level. The myelographic appearance is that of cord compression, but unless the diagnosis appears certain from the presence of other systemic manifestations it is advisable to confirm the sarcoid lesion by biopsy before treating with high-dose steroids. An improvement may be confirmed radiographically but a careful follow-up is required to exclude yeast, tubercle or fungal infection which may mimic neurosarcoidosis or be alighted as opportunistic infections by prolonged treatment with corticosteroids.

Neurosyphilis

Early Presentations

Spirochaetal invasion of the meninges can occur in the primary and secondary stages and at any time before the onset of the tertiary stage. The result is usually a clinically silent lymphocytic meningeal reaction in which a positive diagnosis from the CSF is only possible in 10%–15% of cases. Subsequently the lymphocytosis disappears and the fluid returns to normal. Later however, a brisk symptomatic meningeal reaction can occur, occasionally associated with optic neuritis, or cranial and spinal nerve lesions. The CSF is abnormal with positive treponemal reactions, a raised protein and a prolific cytosis with up to 1000/μl lymphocytes, polymorphs and plasma cells. A reduction of the CSF sugar content can make the differential diagnosis from TB meningitis dependent on the treponemal tests. If untreated at this stage the meningitis may continue to develop with granulomatous involvement of the meninges, adhesions and endarteritis.

Congenital Syphilis

Before two years of age, neurological signs are rare. However, hydrocephalus can develop secondarily to an acute or subacute meningitis. Later onset congenital syphilis has the same spectrum as the adult variety of the disease. A high proportion of meningeal and vascular forms are noted, cervical pachymeningitis is described but congenital tabes is extremely rare.

Meningovascular Syphilis

Meningovascular syphilis assaults the brain or spinal cord or both together. The essential lesion is an arteritis, sometimes with intermittent symptoms as in so-called cerebral congestive attacks. Fits and hemiplegia may be more permanent or there can be a relentless progression of symptoms. Arteritis of the meninges causes widespread, diffuse thickening of the pia arachnoid. Pachymeningitis cervicalis hypertrophica differs from cervical spondylosis in that the brunt of the thickening involves the pia arachnoid rather than dura and ligamentum flavum. A painful radiculopathy of the upper limbs may develop from root compression with a less marked spastic weakness of the legs. In addition, meningovascular syphilis involving the cervical region may produce tabetic amyotrophy or amyotrophic meningomyelitis resembling motor neurone disease (ALS). The features in common are an asymmetric wasting of the shoulder girdles and upper limbs with spasticity of the lower limbs, but distinct differences exist in that an appreciable proportion of patients have Argyll-Robertson pupils, impaired vibration sense in the lower limbs and loss of sphincter control.

In meningovascular syphilis the cellular and protein changes in the CSF are less marked than in the earlier acute symptomatic meningitis but there is infiltration of the Virchow-Robin spaces by lymphocytes and plasma cells, an

obliterative endarteritis and spinal arachnoiditis. The end result of a diffuse syphilitic spinal arachnoiditis can be: root symptoms with small gummata along the nerve roots, arachnoid cysts, vascular occlusion, and a slow strangulation of the cord under a swollen pia arachnoid with obliteration of small penetrating arteries thereby producing a concentric peripheral rim of demyelination and infarction – a syphilitic halo (Hughes 1978).

At the beginning of the century, spinal meningovascular syphilis was a major cause of transverse myelitis. The syndromes tended to be subacute or chronically progressive and invariably involved a combination of leptomeningeal exudation with granulomata, and a pan- or endarteritis. Erb's syphilitic paraplegia is a progressive form of meningomyelitis of the thoracic region with radicular pains, intense spasticity, some loss of vibration and position sense and severe sphincter impairment. Other manifestations may be thrombosis of major arteries such as the anterior spinal artery, infarction of a lateral branch of the anterior spinal artery causing a hemitransection akin to the Brown-Séquard syndrome, or multiple scattered lesions that bear a macroscopic resemblance to multiple sclerosis – so-called syphilitic sclerosis.

Tabes Dorsalis

Two to five per cent of patients with syphilis ultimately develop tabes or taboparesis 10, 15, 20 or more years after the primary infection. Tabes dorsalis is regarded as a parenchymatous affliction of the cord but this is not strictly true. There is a meningeal cellular reaction and vascular changes are rarely absent. Concentric lesions occur round the dorsal roots which appear pinkish and gelatinous. As a result, retrograde degeneration affects Lissauer's tracts and the posterior columns of the spinal cord. The cord shrinks and appears flattened in its antero–posterior diameter.

Most clinical manifestations which develop slowly in the fullness of time depend on this insidious sensory degeneration. Irritative sensory changes account for: (1) lightening pains or "screws" in the legs and trunk occurring as clusters of lancinating agony which can respond to carbamazepine 100 mg t.d.s., (2) laryngeal, gastric, rectal or bladder crises with pain concentrated upon a viscus, (3) areas of skin hyperaesthesia which gradually become hypoanaesthetic. These involve the nose and upper lip (Duchenne's tabetic mask), the breast plate area of the trunk, ulnar borders of the forearms and the fronts of the shins. Sensory loss mainly affects the lower limbs with (1) Romberg's sign of ataxia dependent on eye closure, (2) hyporeflexia, areflexia, and sluggish or absent plantar responses, (3) muscle hypotonia, (4) a sensation of walking on cotton wool, (5) impaired and delayed responses to Achilles tendon pressure, (6) neuropathic arthropathies producing Charcot's joints, and (7) trophic skin ulceration over pressure points.

Visceral sensory impairment can result in constipation, impotence, paralytic ileus or bladder retention, cysts and overflow. Clumsiness and pseudoathetosis may be present in the upper limbs. Involvement of sympathetic afferents may account for bilateral ptosis with compensatory puckering of the brows and synechial degeneration of the iris with adhesions causing the irregularity of the Argyll-Robertson pupil. Ependymitis and gliosis, affecting the oculomotor fibres in the pretectal region dorsal to the Edinger Westphal nucleus, prevent

the response to light but spare the ventral fibres which subserve accommodation (Harriman 1976). Treatment of tabes dorsalis is essentially symptomatic and does not affect the progression of the disease.

Neoplastic Meningomyelitis

The comparative frequency of neoplastic meningitis contrasts with the occasional finding of solitary leukaemic or lymphomatous deposits lodged within the meninges and with the exceedingly rare event of haematogenous metastases thriving within the spinal cord. Diffuse or multifocal infiltration of the leptomeninges by tumour cells can envelop the whole spinal cord, nerve roots and basal cisterns of the brain, with or without associated intraparenchymal lesions (Olsen et al. 1974). Apart from primary neuroectodermal tumours and haematopoietic malignancies, the other tumours that commonly lead to meningeal spread include primary lesions in the lung, breast, gastrointestinal tract and malignant melanoma (Moseley et al. 1989). In a series of 216 patients with malignant melanoma, leptomeningeal infiltration was seen in 24% of cases, thus occurring in 44% of patients with CNS metastatic disease (Patel et al. 1978). In a separate clinicopathological study, leptomeningeal metastases were seen at necropsy in 70% of those with CNS disease (Amer et al. 1978). Although the proportion of patients developing neoplastic meningitis from primary lesions elsewhere is much smaller than with malignant melanoma, the generalization can be made that neoplastic meningitis develops insidiously and some patients remain asymptomatic. Others develop root pains, sensory loss or paraparesis, and the progression can be potentially lethal, compressing, strangling or necrosing the cord.

Neoplastic meningitis may be apparent from myelography, CT scanning or MRI, and the CSF findings may mimic those of TB meningitis. Examination for mitotic cells in the CSF can be most helpful in the diagnosis and management of malignant disease even in the absence of a definite neoplastic meningitis. Unfortunately, conventional CSF cytological methods are frequently unsatisfactory with a reported rate of detection as low as 20% in some series (Bigner and Johston 1981). A frequent fault is to report malignant cells as lymphocytes. However, with the addition of monoclonal antibody immunocytology to conventional techniques, cytological accuracy is enhanced and the type of malignant cell can also be determined (Moseley et al. 1989).

Cord lesions secondary to neoplasia are uncommon. Intraparenchymal infiltration by leukaemic cells leading to a myelopathy and radiculopathy is recorded (Norris 1979) but of greater interest is the possibility of changes due to the remote effects of carcinoma. Acute or subacute necrotizing myelopathies with progressive glial involvement, a reactive astrocytosis and eventual necrosis may cause death from respiratory insufficiency. The other condition believed to be a remote effect of carcinoma is amyotrophic myelopathy. The neurological effects of this syndrome are usually indistinguishable from motor neurone disease (ALS) but in some patients fewer anterior horn cells are destroyed and there appears to be a cellular reaction verging on frank infiltration of the spared ventral horns and CNS ganglia (suggesting a definite similarity to

poliomyelitis). The course is relatively benign (Norris 1979). Historically, the first association between malignancy and ALS involved gastric neoplasms but of the recorded cases over 80% arise from bronchial endothelium and reticuloendothelial tissue. Some improvement in the amyotrophy can follow successful removal of the neoplasm.

Tropical Myeloneuropathies

Slow viruses, treponemal infections, plant toxins and nutritional factors have long featured in the presumed aetiology of tropical myelopathies. The homogeneity of the various subtypes has been questioned and there may be several aetiopathologies.

Lathyrism is perhaps the best understood. The disease is endemic in Central India and has occurred in outbreaks throughout the Mediterranean littoral. Flour, made by grinding the chickling pea (*Lathyrus sativus*), contains a toxin -B,N-oxalylaminoalanine (BOAA) which causes marked spasticity in the legs with cramps and secondary wasting (Spencer et al. 1986). Extensive corticospinal degeneration of both ventral and lateral tracts occurs with lesser involvement of the dorsal columns.

Tropical ataxic neuropathy (TAN) is a sensory ataxia due to symmetrical dorsal column lesions often associated with optic atrophy, deafness and a polyneuropathy. Outbreaks occur in Mozambique during periods of drought when the usual process of detoxicating the cyanogenic glycosides contained in cassava roots by soaking thoroughly then sun-drying, cannot be performed. The children at risk are those with malnutrition or malabsorption of methionine and other sulphur-containing aminoacids as the excess dietary cyanide is inadequately converted to thiocyanate (Cliff et al. 1985).

A neurotropic retrovirus, identical with or cross-reacting with human T-lymphotropic virus type 1 (HTLV-1), may explain the aetiology of at least 60%–75% of cases of tropical spastic paraparesis (TSP) found in the Caribbean and sub-Saharan Africa and of patients with Japanese myelopathy (HAM). Positive but low titres of HTLV-1 antigens have also been identified in patients diagnosed as having clinically definite multiple sclerosis (MS) in both Florida and Japan but not in MS patients elsewhere.

Tropical spastic paraparesis (TSP) usually affects women more than men, commonly begins in the fourth decade (30–40 years) and is slowly progressive over a decade. No race is immune. Early cases are often asymptomatic with increased reflexes and a spastic gait. Low back pain, constipation and bladder symptoms become noticed, with impotence in men. Eventually there is a frank paraplegia with some weakness of the arms. The spinal lesions bear a resemblance to AIDS myelopathy and to the degenerative changes of subacute combined degeneration of the cord but do not respond to vitamin B12. Axonal degeneration and myelin loss are best seen in the lumbar region but extend upwards to the brain stem involving predominantly the pyramidal tracts with lesser changes in other spinal tracts and peripheral nerves, mild gliosis and scattered spongiform changes. Somatosensory and visual evoked potentials are abnormal in about 50%. The CSF is usually normal though there can be a

chronic meningomyelitis with perivascular infiltration and hyaline arteriolar thickening. Where this is so, oligoclonal bands and lymphoctyes containing HTLV-1 virions can be identified. Whereas the incidence of TSP and HTLV-1 antigenicity have not fallen, the proportion with treponemal seropositivity has declined with the eradication of yaws (Rodgers-Johnson et al. 1986).

Japanese HTLV-1 associated myelopathy (HAM) shows more obvious sensory loss with extensive demyelination of both the corticospinal tracts and dorsal columns. The meningovascular changes are more prominent with up to 2000 lymphocytes/μl. Although no overt case of adult T-cell leukaemia has been identified with HAM, 39% in some series have had blood transfusions and adult T-cell leukaemic cells have been found in the peripheral blood and CSF (Roman 1987). A further complication has been the finding of an altered antibody response to Epstein-Barr associated antigens (Itoyama et al. 1988).

AIDS-related Myelopathies

AIDS-related myelopathies (ARDS myelopathies) are fairly common. They start insidiously and may remain asymptomatic for some time. However, Denning et al. (1987) reported the occurrence of a symptomatic transient myelopathy developing at the time of seroconversion, presumably associated with primary HIV infection. The myelopathy improved over six weeks with some residual signs. The more typical AIDS myelopathy is a vacuolar myelopathy, pathologically resembling subacute combined degeneration of the spinal cord and found post mortem in 20 out of 89 patients dying from AIDS (Petito et al. 1985). The vacuoles are surrounded by a thin myelin sheath and appear to arise from swelling within myelin sheaths. The lower thoracic cord appears grey, slightly expanded and shows particular involvement of the posterior and lateral columns. One-third of the patients are asymptomatic but others develop a monoparesis or paraparesis with spasticity, ataxia and incontinence. Spinal cord dysfunction occurring as a complication of HIV infection may occur during latent HIV infection (Jakobsen et al. 1989) and has distinctive features. The most common complaints are of weakness of the legs and incontinence. Ambulation is often difficult, and the weakness is frequently attributed inappropriately to general debility from supervening infections or malnutrition rather than to spinal cord dysfunction (Berger 1987). Physical examination reveals spastic paraparesis with hyperreflexia and extensor plantar responses. The gait is typically spastic-ataxic. Sensory examination often displays greater impairment of the sensations of position and vibration than of light touch, temperature and pin-prick, but this is not invariable. There may be a concomitant peripheral neuropathy. These clinical findings are important as they rule out potentially treatable disorders that may result in myelopathy, including other viral infections associated with AIDS. Myelopathies caused by these viruses often assume a more fulminant tempo than the subacute course of HIV myelopathy (Berger 1987).

AIDS patients secondarily infected by herpes simplex type 2 viruses may develop a progressive thoracic myelopathy (Britton et al. 1985) or an acute ascending necrotizing myelopathy (Wiley et al. 1987). The patients initially

complain of radicular and back pain and HSV type 2 viruses have been isolated from spinal root ganglia and spinal cord, suggesting a direct invasion of the cord by the virus from spinal ganglia. Likewise cytomegalovirus infection in AIDS has lead to progressive segmental thoracic myelopathy with necrosis of the anterior spinal artery (Tyler et al. 1986).

In the presence of AIDS, syphilitic infections may realight and take on a new form unique to AIDS; thus Lowenstein et al. (1987) have described acute syphilitic transverse myelitis with lesions shown by angiography, CT and MRI.

Acute Transverse Myelopathy

Myelopathy refers to pathology of the substance of the cord. The term, acute transverse myelopathy, is a useful anatomical formulation for disease syndromes involving the cord bilaterally, at or up to a horizontal segmental level which may lie in the sacral, lumbar, thoracic or cervical portion of the cord. The term also implies a monophasic illness with the onset of symptoms and signs developing over a period of 2 hours to 14 days and resulting in a diagnostic triad of: complete sensory loss below the level of involvement, an initially flaccid paraparesis or quadriparesis, and severe impairment of sphincter function.

Myelopathies may occur as part of a more widespread disease process. Where this is so, spinal cord involvement may accompany or be overshadowed by other manifestations such as encephalitis, peripheral neuropathy or polyradiculopathy. However, rapidly developing transverse lesions of the spinal cord, occurring as the sole manifestation of a disease process, often present a difficult diagnostic and therapeutic problem.

The probable diagnosis of acute transverse myelopathy is made more likely if there is a preceding history of an exanthema, vaccination or an upper respiratory tract infection. The alternative diagnosis of MS may be suggested if the patient has had previous neurological symptoms. With recurrent episodes, recurring at exactly the same level each time, a third diagnosis, namely a spinal arteriovenous malformation, is also possible. However, the immediate differential diagnosis is the exclusion of cord compression either from an intrinsic tumour or from an extradural tumour or abscess. Unless these conditions can be excluded beyond reasonable doubt, the definitive test is lumbar myelography. Unfortunately, examination of the spinal fluid without myelography provides little useful information.

Initially the cord lesion is limited longitudinally to a few segments and the full thickness of the cord is not usually involved. The lesion is not necessarily stable but may progress rostrally spreading as an ascending myelitis. Radiographic support for the diagnosis of acute transverse myelitis comes from the finding of a spinal cord of normal calibre; but this is not invariably so. With the rapid development of transverse myelopathy, oedematous swelling of the cord may trap and compress radicular veins within the cord causing further congestion so that the clinical level in effect marks the upper boundary of this drainage. Where swelling has occurred an attempt may be made to establish the nature of the lesions by MR imaging. But if this is not possible or the

findings remain uncertain, surgical decompression and biopsy may be the only way to exclude other intrinsic lesions. Decompression rarely has an adverse effect on the course of the disease and has been used in the past to establish whether the disease has progressed to necrosis or if recovery is still possible.

Acute transverse myelopathy as an isolated event remains a relatively rare but probably underdiagnosed condition. Berman et al. (1981) found 62 patients who fulfilled the necessary diagnostic criteria in Israel over a 20-year period from 1955–1975; thus giving an incidence of 1.34 per million. Transverse myelitis (or myelopathy) is often classified as a demyelinative condition developing as a result of secondary non-specific hypersensitivity phenomena similar pathologically to the lesions of acute disseminated encephalomyopathy. In this form it may be indistinguishable from spinal mutliple sclerosis; thus Lipton and Teasdall in 1973 reported a follow-up study of 34 patients: 7 of whom were diagnosed 5 to 42 years later as having multiple sclerosis. Nowadays the proportion developing multiple sclerosis can be further reduced by means of visual, auditory and upper limb somatosensory evoked potentials, by MR imaging or CT scanning of the brain or by MR imaging of the spinal cord.

Viral Aetiology

In recognizing that acute transverse myelography is essentially an anatomical formulation we recognize that there may be many disparate causes and that the natural history of one form may not coincide with another. Between 20%–40% of cases have a probable viral origin (Tyler et al. 1986) and represent the most typical picture of transverse myelitis. The diagnosis of a viral infection is never straightforward. In a classical paper (Wells 1971) investigated 19 patients from the Cardiff area of South Wales who had developed an acute neurological disorder with predominant spinal and radicular symptoms following an upper respiratory infection during the winter of 1969–1970. Serological tests showed that the infection was probably due to influenza A virus in 8 cases and to other viruses (including adenovirus and herpes zoster) in 6, while in 5 cases the studies were negative. It was not possible to isolate a virus or to culture it from the blood in any case. The interval between the onset of the febrile illness and the development of neurological complications varied from 1 to 112 days, and it was indeed so variable that it was difficult to draw any valid conclusions whether the neurological state resulted from direct viral invasion or from an autoimmune or hypersensitivity process, though the latter seemed more probable. It is also possible that some symbiosis between viruses can occur; thus Boiardi et al. (1986) reported the recurrence of herpes zoster myelitis in combination with a Coxsackie infection; and cases of transverse myelitis have been reported in the past during epidemics of poliomyelitis (Foley and Beresford 1974).

Transverse myelitis can develop over hours or days. The sequence of events is usually similar. Both sexes are equally affected and there is little variation with age. The most common site of affliction is the upper or mid-thoracic cord. There may be an acute pyrexia and radiculopathy or back pain localized over a few spinal segments, soon followed by symptoms of spinal cord transection. A low grade temperature may persist for several days. Bilateral paraesthesiae start in the feet and ascend with numbness and sensory impairment until a

discrete sensory level is reached. Sphincter dysfunction occurs with urinary retention and loss of bowel control. There follows a progressive flaccid weakness of the lower limbs and abdominal muscles. With high dorsal lesions assisted ventilation is required. The paresis may remain flaccid if the spinal cord starts to necrose. More often the initial flaccid weakness gives way to an increasingly spastic paraplegia.

The CSF can be normal, or mildly abnormal with a pleocytosis and a slightly raised protein. Occasionally it is frankly xanthochromic with high levels of protein often exceeding 10 g/l and up to 200 lymphocytes. Such abnormal findings usually occur when the onset is apoplectic. A clinical state of spinal shock develops, as seen after traumatic transection, and the cord becomes oedematous. The presence of an acute spinal block may be confirmed by myelography, with or without CT, but the differential diagnosis is more clearly revealed by MRI which may give an abnormal signal over the full extent of the lesion.

With milder degrees of myelopathy, not affecting the full thickness of the cord, various patterns of sensory loss may be seen. Thus vibration and joint position sensation may be spared suggesting that there has been segmental occlusion of the anterior spinal artery. Occlusion of the anterior spinal artery mainly involves anterior horn cells and corticospinal tracts; spinothalamic sensation is lost at the beginning but tends to recover and dorsal column sensation is spared. It may also be difficult to differentiate transverse myelopathy from an acute ascending polyradiculopathy unless an ascending sensory level is present on the trunk thereby indicating that the spinal cord is affected. As with acute disseminated encephalomyelitis, the pathology of the cord can vary from patchy perivenous demyelination to a severe necrotizing, haemorrhagic form. The cord may appear oedematous and hyperaemic with perivascular cuffing, arteritis and yet more extensive vascular involvement, and there may be an inflammatory cellular exudation involving the leptomeninges.

There is a tendency to compare the natural history of acute transverse myelopathy with that of an isolated spinal plaque of MS with recovery within approximately six weeks. Such a supposition can be very misleading. Full recovery is not invariable: Lipton and Teasdall (1973) reported a mortality of 14.5%, a reasonable recovery may occur in just over 33% often spread over three or more months, with residual deficits in about 25% (Berman et al. 1981; Lancet 1986); 23% progress to the Foix-Alajouanine syndrome (Foix and Alajouanine 1926) of subacute necrosis of the spinal cord (Berman et al. 1981).

After the initial stage the majority of patients pass to a stable plateau phase lasting days or weeks before proceeding imperceptibly into a phase of recovery. Improvement may take place over several months, often with a mild residual disability which fails to clear. Those who fail to make a good recovery may develop osteomalacia with necrotic softening and cavitation of the whole extent of the cord below the lesion. Once this occurs further recovery is unlikely. A small number of patients make a delayed but complete functional recovery apart from the persistence of hyperreflexia and extensor plantar responses.

Three mechanisms have been postulated to explain the viral pathogenesis of acute transverse myelopathy:

1. Viral invasion of the spinal cord – the mechanism which most probably explains myelopathy in AIDS

Table 14.1. Viruses which cause myelitis in humans

DNA viruses	
Enveloped:	Herpes viruses (simplex, simiae, varicella-zoster), Epstein-Barr and cytomegalovirus
	Pox viruses: vaccinia and variola
Non-enveloped:	Hepatitis B
RNA viruses	
Non-enveloped:	Picornaviruses: Coxsackie, ECHO, polio
	Other enteroviruses: hepatitis A, encephalomyocarditis virus
Enveloped:	Togaviruses: arborviruses, tick-borne encephalitis, rubella
	Retroviruses: HTLV-1, HTLV-111 (HIV)
	Orthomyxoviruses: influenza
	Paramyxoviruses: measles, mumps
	Bunyaviruses: Californian encephalitis
	Arenaviruses: lymphocytic choriomeningitis
	Rhabdoviruses: rabies

(After Tyler et al. 1986.)

2. A toxic myelopathy – extremely hard to prove or disprove
3. A delayed hypersensitivity reaction – this is the most probable explanation of myelopathy following vaccination (Bitzen 1987)

Of the neurotropic viruses, the DNA viruses are more prone to cause myelopathy than the RNA viruses. Table 14.1 shows those included in causing myelitis in humans.

Herpes Viruses

These are most commonly incriminated in sporadic cases. Broadbent (1866) described muscle wasting with zoster infections. As the intercostal muscles are most frequently involved, wasting may be difficult to quantify clinically. Zoster myelopathy can lead to dysfunction of the bladder and anus (Jellinek and Tulloch 1976). The authors emphasize that severe sphincter disturbances, e.g. retention, loss of sensation, or incontinence are the result of bilateral lesions; thus hemisection of the spinal cord does not cause sphincter problems. Recovery is usually complete and the segmental distribution of any rash does not necessarily coincide with the level of myelopathy. Retention may occur with thoracic or lumbar lesions, and sacral involvement may be accompanied by sensory loss and a flaccid detrusor paralysis. Herpes zoster infections can be unpredictable, remaining dormant until another viral infection reduces the body's resistance; and myelopathy can be a feature of symptomatic herpes zoster infections, e.g. developing at the site of trauma, a metastatic deposit or a prolapsed intervertebral disc.

Acute necrotizing myelitis has been a frequent complication of herpes simiae infection in laboratory workers, less commonly with herpes simplex infection. It is particularly prone to occur in immune-compromised individuals. Clinically a rapidly progressive myelitis with necrotizing arteritis is found with Cowdray

type A inclusions or HSV 2 antigens within the spinal cord (Wiley et al. 1987). Some cases have followed a viraemia provoking a severe inflammatory response to the viral infection and in others there is evidence of virus dissemination from intra-axonal spread into the spinal cord from the dorsal root ganglia.

Other Viruses

Immunosuppression in the recipients of renal transplants can lead to disseminated cytomegalovirus infection with acute transverse myelopathy (Spitzer et al. 1987). Rubella myelitis has been reported in conjunction with encephalitis in children and confirmed by MR imaging (Bitzen 1987). Rubella virus specific IgM has been detected in serum and spinal fluid using ELISA Rubazyme M. Likewise the Epstein-Barr virus has been identified by the direct fluorescent antibody test.

A syndrome primarily involving the bladder with acute but transient urinary retention can arise from sacral myeloradiculitis (Vanneste et al. 1980; Herbaut et al. 1987). It may be associated with anogenital herpes simplex infections, but non-herpetic causes include ECHO, cytomegaloviruses and Epstein-Barr viral infections. The differential diagnosis includes multiple sclerosis and disc protrusions.

Following Vaccination

Myelopathy may complicate smallpox vaccination (Shyamalan and Singh 1964), pertussis immunization, and rabies vaccination. The incidence of postvaccinal encephalomyelitis was between 1 in 5000 and 1 in 2 000 000 vaccinations. Postvaccinal encephalomyelitis was rare in infancy but more liable to occur with primary vaccination between the ages of 4–16 than with secondary vaccination. After an incubation period of 8–15 days the onset is abrupt or explosive with encephalitic symptoms. A flaccid paralysis from transverse myelitis was more frequently observed than hemiplegia. Survivors are said to make a complete recovery but Miller (1953) recognized numerous mild residual deficits.

Neuroparalytic accidents used to occur in 1 in 1000 to 1 in 4000 patients treated with anti-rabies vaccines. An acute disseminated encephalomyelitic reaction would occur because all three anti-rabies vaccines – Pasteur, Semple and even duck embryo vaccines – contain myelin (Behan and Currie 1978). Until vaccines were grown on duck embryos or tissue culture, patients received a lengthy course of repeated inoculations with an emulsion of animal nervous tissues containing dead or attenuated rabies virus. A monophasic illness would develop suddenly after an incubation period of 1–3 months and run a downhill course with a mortality of 30%. The condition could be almost indistinguishable from MS with dense plaques of demyelination scattered asymmetrically throughout the neuraxis (Matthews and Miller 1972). At other times the

clinical picture resembled the Guillain-Barré syndrome with an ascending myelitis, transverse myelitis usually in the thoracic or lumbar segments, or a polyradiculitis with facial nerve involvement (Adaros and Held 1971; Toro et al. 1977). In no case are Negri bodies present.

Parasitic Infections

Schistosomiasis has been the most frequently reported cause of an acute tropical myelopathy (Kerr et al. 1987; Suchet et al. 1987) The eggs of *S. haematobium* and *S. mansoni* may lodge as emboli in the blood vessels of the cord and in infested areas there is probably much asymptomatic or unrecognized spinal cord involvement. However, symptoms may result from:

1. Vascular syndromes, e.g. anterior spinal artery occlusion
2. Granulomata around spinal roots or the cauda equina
3. Multiple small granulomata within the cord surrounding one or more eggs
4. Larger granulomata microscopically resembling gliomata

The lower lumbar and sacral regions of the spinal cord are most likely to be infected and widening of the conus has been reported radiologically (Kerr et al. 1987). Patients may present with wasting, fasciculation, back pain and distal weakness. The condition has been successfully treated with praziquantel, either given with steroids or in conjunction with oxamniquine and niridazole.

Another reported tropical cause of myelopathy is larva migrans (Weng et al. 1987). The diagnosis can be made on the clinical course of the disease and the finding of eosinophilia, serum IgE, raised CSF IgG and IgA and the presence of larvae in the CSF.

Collagen Vascular Disease

Spinal cord damage in collagen vascular diseases can occur as a result of thrombosed arteries or veins, or from microscopic haemorrhages. A true myelopathy can also result from a vasculopathy with proliferative changes involving small blood vessels. Transverse myelitis can occur in mixed connective tissue disease in the presence of antibodies to ribonucleoprotein (anti-RNP) (Pedersen et al. 1987) or, more commonly, in systemic lupus erythematosus (SLE). In SLE the vascular changes may be associated with demyelination or with areas of gliosis with associated perivascular collections of mononuclear cells and deposits of immune complexes and reactive (antineuronal) antibodies, also present in the CSF and plasma (Siebold et al. 1982; Kaye et al. 1987). Some cases, particularly in childhood, may be related to immune deficiency syndromes (Kaye et al. 1987).

Transverse myelitis may occasionally be the first manifestation of lupus erythematosus (Siekert and Clark 1955; Granger 1960) but the total number of reported cases does not exceed 40. The spinal cord is most vulnerable to

damage in the event of an exacerbation of the underlying disease (Andrews et al. 1970). The most common neurological level is mid-thoracic in 60% (Hachen and Chantraine 1979–1980) and an abnormal signal may be obtained over a wide area by MR imaging (Kenik et al. 1987). In the vast majority of patients the paraplegia is complete and irreversible and multiple zones of myelomalacia in both grey and white matter with fibrinoid degeneration of arterioles may be present post mortem. Myelopathy at cervical (20%) or lumbar (20%) levels tends to be less severe with only partial motor and sensory loss (Piper 1953; Andrianakos et al. 1975).

In 3 of the 40 patients reported in the literature (April and VanSonnenberg 1976), systemic lupus sclerosis was combined with Devic's syndrome of neuromyelitis optica. Demyelination of white matter in SLE is a relatively rare finding. However, demyelinating plaques in MS display an outer ring of immune complexes and the overlapping condition of lupus sclerosis is well described where the levels of immunoglobulins in the CSF are particularly high.

The results of treatment of SLE myelopathy with high dosage corticosteroids have been disappointing. A slow recovery occurred in only 3 paraplegic patients and in 1 quadriplegic patient from a total of 26 (Andrianakos et al. 1975). Anecdotally, chloroquine has been successful in the treatment of one patient (Granger 1960). Slovick (1986) advocated the use of plasma exchange and immunosuppression and reported the successful treatment of one patient.

Transverse Myelopathy Related to Acute Disseminated Encephalomyelitis

Myelopathy occurring in conjunction with the Guillain-Barré syndrome of allergic, postinfective peripheral neuropathy or polyradiculopathy, confirms the hypothesis that many forms of transverse myelopathy can arise as a result of a cell-mediated response. The violence of this response may vary from perivenous demyelination to a severe necrotizing myelopathy. The clinical diagnosis of an accompanying myelopathy may not be easy but is suggested by the development of extensor plantar responses and severe sphincter disturbances.

In Devic's disease bilateral retrobulbar or optic neuritis with massive demyelination of the optic nerves may be followed after a few months by similar massive demyelination of the spinal cord. Thereafter the disease may be self-limiting or run a progressive downward course (Walton 1977). Demyelinating lesions, often with destruction of axis cylinders, are seen elsewhere in the neuraxis and there is a distinct tendency to necrosis and cavity formation within the spinal cord. Many remain unconvinced that Devic's disease is a distinct pathological entity (Hughes 1978).

In subacute myelo-optico-neuropathy (SMON) diarrhoea and abdominal pain are followed by the acute or subacute onset of an ascending sensory neuropathy spreading over the lower half of the body, accompanied in two-thirds of those affected by an ataxic gait. Half the patients also develop motor weakness in the lower limbs. Myelopathy or neuropathy with or without optic atrophy occurs in 26.2% of non-Japanese patients (Thomas 1984). The disease was originally thought to be a viral disorder but clioquinol toxicity is now

incriminated as the causal agent. Yagi et al. (1978) found that the neurotoxicity of clioquinol depends on decomposition of the conjugated form and chelation with iron and other metals. When a concentration of free clioquinol in serum of 20 μg/ml has been maintained for several days (Tamura 1975) the drug is taken up in chelated form by neural tissue where it produces destructive peroxidases (Yagi et al. 1978). The simultaneous ingestion of drugs containing aluminium, calcium, magnesium, copper and bismuth will produce different chelates. Different combinations can affect the clinical severity of the disorder (Okada et al. 1984).

Myelopathy can also result from toxicity from other drugs: heavy metal poisoning, arsphenamine, paraquin, orthocresyl phosphate; drugs injected into the subarachnoid space, e.g. penicillin; or contrast agents used in aortography.

An allergic myelopathy can develop from scorpion stings, hymenoptera stings and spider bites (Rosenberg and Coull 1982). The venom of some scorpion species contains powerful neurotoxins capable of producing paralysis of the hind limbs and respiratory muscles of laboratory animals. Such findings fuel speculation that myelopathy in man may result from a direct neurotoxic effect as an alternative to a secondary immune-mediated response.

Ischaemic myelopathy is a recognized complication of anterior spinal artery occlusion, circulatory arrest as from clamping of the aorta, or Stokes-Adams attacks. Myelopathy following burns, heat stroke or trauma could be due to similar anoxic changes as a consequence of ischaemia, disseminated intravascular coagulopathy or electrolyte imbalance (Delgado et al. 1985). Alternatively, there may be an allergic response to the release of altered proteins into the circulation producing an autoimmune reaction within the spinal cord.

Opiates

Myelopathy has been described among heroin addicts. The circumstances of drug addiction, particularly when intravenous drugs are taken, favour both sepsis and thromboembolism. These factors require exclusion before a direct toxic effect on the spinal cord is accepted (Hughes 1978). Ell et al. (1981) list hypotension, toxic or hypersensitivity reactions, reactions to contaminants or to the heroin itself, vasculitis, embolism and hyperextension injury among the factors which may be involved and suggest that the most usual causative factor is an adulterant taken with the heroin. In favour of a hypersensitivity reaction is the fact that some cases have occurred after a period of abstinence (Ell et al. 1981). The chances of recovery are uniformly poor.

Treatment of Myelopathies

In many ways the least satisfactory aspect of acute transverse myelopathy is its treatment and the prevention of complications. A proportion of all types of myelopathy can improve spontaneously but an attempt should be made to

determine the underlying pathology and treat accordingly. Where specific agents can be given, e.g. acyclovir for herpes simplex or zoster, or praziquantel for myelopathy following schistosomiasis, there can be a reasonable expectation of improvement. Corticosteroids are potentially indicated where the cause of the myelopathy is unknown, where there is a possibility of a collagen disease, or an allergic reactive state (i.e. a hypersensitivity reaction). The results of steroid therapy remain uncertain and their efficacy has yet to be established. Early treatment with methylprednisolone has not been evaluated and should be tried as early as possible in the disease unless there is a clear alternative form of treatment available.

If the cord appears swollen it is advisable to perform a diagnostic decompression and biopsy and to follow this with dexamethasone. Acyclovir and similar drugs may be used in AIDS myelopathies where viruses other than HIV are implicated. Antibiotics, if necessary covered by steroids, should be used in myelopathy with meningovascular syphilis. In other situations, as with collagen vascular disease, Slovick's suggestion (1986) of a combination of plasma exchange and immunosuppression should be considered.

Spinal Multiple Sclerosis

Multiple sclerosis is a disease of the CNS and lesions are characteristically distributed in time and space. In established disease it is rare for the spinal cord not to be involved. Among the manifestations recorded in patients with MS examined at autopsy, 98% will have developed paresis of the lower limbs, spasticity and hyperreflexia, 82% will have had urinary disturbances and 65% paraesthesiae such as episodes of numbness or a positive Lhermitte's phenomenon. The occurrence of MS limited to the spinal cord is probably rare but plaques seen only in the spinal cord are found occasionally in patients at autopsy. However, lesions of the spinal cord are the presenting feature in at least one-third of patients with MS (Shibasaki et al. 1981). In many it may be possible to confirm the diagnosis by finding evidence of silent lesions elsewhere, e.g. by visual evoked potentials or MR imaging. The finding of a lesion elsewhere merely increases the probability that the spinal cord manifestation is due to MS; it never constitutes absolute proof. The diagnosis of spinal MS depends upon the clinical presentation, the finding of confirmatory evidence and exclusion of alternative diagnoses, and increasingly upon supportive evidence from oligoclonal banding in the CSF, somatosensory evoked potentials and MR imaging of the cervical cord. At present none of these sophisticated investigations provide absolute proof of the diagnosis.

Among the highly characteristic presenting manifestations are:

1. Intermittent weakness of a leg occurring either on exertion with dragging of the foot after prolonged activity or as a paroxysmal symptom with sudden loss of power causing unexpected falls, locking of the knees or collapse of the legs.

2. About 10% of patients presenting with acute transverse myelopathy are found to have MS (Poser 1984). This may take one of three characteristic

forms: as a partial Brown-Séquard syndrome, as a spastic paraplegia with negative myelography, or as numbness below the waist with sphincter disturbance and loss of vaginal sensation often improving spontaneously before myelography is possible.

3. As a chronic myelopathy or progressive spastic paraparesis. This may be the presenting form of the condition in middle age and in the elderly (Noseworthy et al. 1983). The differential diagnosis may include cord compression, cervical spondylosis or familial or sporadic forms of spastic paraparesis.

4. Paroxysmal phenomena such as Lhermitte's sign or unilateral spasms of limbs which are often painful with the limb "kicking out" or adopting a brief tetanic posture.

5. Isolated bladder disturbances, e.g. retention, urgency, or hesitancy of micturition; impairment of sex functions or, rarely, bowel dysfunction. Usually MS can only be diagnosed by exclusion.

6. Uncertain or bizarre paraesthesiae, hemianaesthesia or intermittent weakness or clumsiness. Some of these symptoms may have an allergic basis or even suggest hysteria. It is often wiser to regard them as due to an allergic neuritis unless there is positive proof of MS.

MR imaging of the cervical spinal cord to identify plaques is possible but difficult. Longitudinal (sagittal or coronal) cuts are more likely to be of value than axial cuts because of the longitudinal arrangement of plaques as seen post mortem. The cervical spinal cord is small compared to the brain stem or cerebrum and requires high imaging resolution but the signal to noise ratio can be improved by the use of surface coils (Maravilla et al. 1984). The thoracic and lumbar cord is almost impossible to image because of its smaller size and the presence of respiratory and cardiac movement artefact.

The differentiation of progressive spastic paraplegia due to MS from familial spastic paraparesis depends upon finding lesions at MR imaging, or delayed visual evoked potentials. A relative lymphocytosis in the CSF with a raised IgG, oligoclonal bands, or the presence of HLA DR2 antigen increases the likelihood of MS. Somatosensory evoked potentials from upper or lower limbs can be abnormal with either condition and although it is often worth trying the response to steroids over 4–6 weeks, this is an unreliable factor in making a differential diagnosis.

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