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Transverse Myelitis

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KEYWORDS

• Transverse myelitis • Longitudinally-extensive transverse myelitis • Multiple sclerosis • Lupus myelopathy • Sjogren's myelopathy • Idiopathic transverse myelitis

KEY POINTS

- Transverse myelitis (TM) constitutes a pathobiologically heterogeneous syndrome that has significant neurologic implications and requires urgent attention.
- Magnetic resonance imaging (MRI) evaluation of the entire spinal cord axis is mandatory in all myelopathic patients.
- The length of the spinal cord lesion on MRI is an important discriminator with etiologic and prognostic significance; longitudinally extensive transverse myelitis (LETM) refers to lesions that extend over 3 or more vertebral segments.
- Early and timely identification and immunotherapy are critical to minimize, or even prevent, future disability.
- The long-term management should focus on neurorehabilitation and a multidisciplinary approach aimed at managing the various complications of spinal cord damage.

INTRODUCTION

Acute noncompressive myelopathies have been recognized since the nineteenth century.[1] The terms myelitis and myelopathy are often used interchangeably, but have different connotations. Both suggest a lesion affecting the spinal cord. Whereas myelopathy is a broad, generic term (much like neuropathy or encephalopathy) that

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does not imply any particular etiology, myelitis refers to an inflammatory disease process.

Transverse myelitis (TM) includes a pathobiologically heterogeneous syndrome characterized by acute or subacute spinal cord dysfunction resulting in paresis, a sensory level, and autonomic (bladder, bowel, and sexual) impairment below the level of the lesion.[2,3] Etiologies for TM can be broadly classified as parainfectious, paraneoplastic, drug/toxin-induced, systemic autoimmune disorders (SAIDs), and acquired demyelinating diseases like multiple sclerosis (MS) or neuromyelitis optica (NMO).[3–6] Patients with isolated TM present a diagnostic dilemma, as it is common in both MS and NMO, but may also be the initial manifestation of SAIDs. Also, there are noninflammatory etiologies (eg, vascular, metabolic) that may mimic the clinical and radiologic appearance of TM. Further complicating the diagnostic process is the frequent coexistence of systemic autoantibodies in NMO and, sometimes, MS. The implications of an incorrect diagnosis can be severe, as treatment may not only be ineffective, but may exacerbate the underlying disease process. The cause of TM remains unknown despite an extensive workup in about 15% to 30%[4] of patients and is therefore referred to as "idiopathic" according to set criteria.[7] **Box 1** explains important terms related to TM.

The annual incidence of TM ranges from 1.34 to 4.60 cases per million,[8–10] but increases to 24.6 cases per million if acquired demyelinating diseases like MS are included.[11] TM can occur at any age, although a bimodal peak in incidence occurs in the second and fourth decades of life.[8–10,12] Half of patients have an antecedent infection.[10]

Case report

A 30-year-old white woman presents with 3 days of progressive paraparesis, constipation, and urinary incontinence. In addition, she reports a feeling a circumferential tightness around her abdomen (as though she was wearing a corset). Examination revealed spasticity, hyperreflexia with up-going plantar reflexes, and muscle strength of 3 in her lower extremities. Anal tone was decreased. A T8 sensory level was detected. Spine MRI revealed a T2/fluid-attenuated inversion recovery (FLAIR) hyperintense signal with associated contrast enhancement and cord swelling from T2 to 7 vertebral segments. What are the next steps in managing this patient?

CLINICAL PRESENTATION

It is important to consider the age and gender of the patient when evaluating myelopathic patients. Older patients (older than 50 years) are more likely to suffer spinal cord infarction. Female patients are at higher risk of having TM. Demographic features are otherwise not particularly useful in distinguishing the etiologic causes of myelopathy.[13]

The temporal profile of the myelopathic features must be elucidated. TM typically has an acute to subacute onset, with neurologic deficits reaching a nadir within a few weeks. An apoplectic onset with deficits reaching the nadir in less than 4 hours indicates a vascular event. An insidious, progressive course in which the deficits continue to worsen beyond 4 weeks is uncharacteristic of TM. Clinically, TM may present as one of several syndromes of the spinal cord. Acute complete TM (ACTM) manifests as paresis/plegia, sensory dysfunction (characterized by numbness, paresthesias, or other manifestations in conjunction with a sensory level), and autonomic impairment below the level of the lesion. Acute partial TM (APTM) results in asymmetric manifestations or deficits specific to particular anatomic tracts; manifestations include the

Box 1
Nosology of transverse myelitis

Myelopathy: a broad, generic term referring to a lesion affecting the spinal cord

Myelitis: refers to an inflammatory disease of the spinal cord

Transverse myelitis (TM): classically describes a pathobiologically heterogeneous syndrome characterized by acute or subacute spinal cord dysfunction resulting in paresis, a sensory level, and autonomic impairment below the level of the lesion

Acute Complete TM (ACTM): TM causing paresis of the lower and/or upper extremities, sensory dysfunction (characterized by a sensory level), and autonomic impairment below the level of the lesion. On magnetic resonance imaging (MRI), there is typically a single lesion spanning 1 or 2 vertebral segments; on axial sections, there is either full-thickness involvement, or the central portion of the spinal cord is maximally affected.

Acute Partial TM (APTM): TM causing asymmetric neurologic impairment (localizable to the spinal cord) or deficits attributable to a specific anatomic tract. On MRI, it spans 1 or 2 vertebral segments; there is involvement of a small portion of the spinal cord on axial sections.

Longitudinally-Extensive TM (LETM): a spinal cord lesion that extends over 3 or more vertebral segments on MRI. On axial sections, it typically involves the center of the cord over more than two-thirds of the spinal cord area.

Secondary TM: TM related to a systemic inflammatory autoimmune disorder (eg, lupus, Sjögren syndrome, sarcoidosis). It is typically an ACTM.

Idiopathic TM: TM without any clear etiology despite a thorough investigation. It should meet the criteria listed in **Table 8**.

hemi-cord (Brown-Sequard), central cord, or posterior column syndrome, as well as selective tract impairment. **Table 1** describes these syndromes. Distinguishing ACTM and APTM has etiologic and prognostic significance, as discussed later.

Acutely, limb tone and muscle stretch reflexes may be diminished and even absent ("spinal shock syndrome") leading to possible diagnostic confusion with Guillain-Barre syndrome (GBS). Clinically, spinal shock may persist for days to weeks, with a mean duration of 4 to 6 weeks following an insult.[14] Over time, spasticity, hyper-reflexia, and extensor plantar responses (ie, classic features of the upper motor neuron [UMN] syndrome) become evident.

Sensory symptoms (both positive and negative) are common in TM. Some patients report a circumferential band of dysesthesia, attributable to the dermatomes just rostral to the sensory level, around their trunk. In some cases, this may be associated with a constricting sensation (colloquially referred to as the "MS hug") that ranges from mild discomfort to a severe spasmodic or burning pain. In the authors' experience, this symptom may be so distressing that it may be more appropriately called the "anaconda squeeze"! TM-related pain may be a central, deep aching pain or radicular in nature.[3] Exacerbation of spinal pain with recumbency may indicate a neoplastic lesion involving the spinal cord.[15] Phantom limb phenomenon has been observed.[16] Lhermitte phenomenon (paresthesia traveling down the limbs and trunk with neck flexion) suggests an intrinsic cervical spinal cord lesion, typically affecting the dorsal columns. A reverse Lhermitte phenomenon (paresthesia with neck extension) usually indicates a compressive extra-axial cervical lesion.[17] Inverse Lhermitte phenomenon (paresthesia traveling upward) is another reported variation.[18]

Autonomic dysfunction is almost always present in the form of perturbations of bladder, sexual, gastrointestinal, cardiovascular, and thermoregulatory functions. Priapism is a rare acute manifestation.[19,20] These features are discussed later.

Table 1
Spinal cord syndromes

Syndrome	Tracts Involved	Clinical Manifestations
Complete transverse myelitis	All	Paresis, sensory loss, and autonomic impairment below the level of the lesion
Hemicord (Brown-Sequard)	Ipsilateral corticospinal; Ipsilateral dorsal columns; contralateral spinothalamic	Ipsilateral paresis and impaired dorsal column sensation; contralateral pain and temperature loss
Dorsal column	Bilateral dorsal columns	Bilateral loss of vibratory and proprioceptive sensation; Lhermitte phenomenon
Subacute Combined Degeneration	Bilateral dorsal columns and corticospinal tracts	Bilateral dorsal column dysfunction; paresis and upper motor neuron signs below the level of the lesion
Central cord	Crossing spinothalamic fibers, and corticospinal tracts	Dissociated sensory loss (diminished pain and temperature with normal dorsal column function) in a shawl-like pattern. Saddle-sparing sensory loss. Upper motor neuron weakness below the level of the lesion.
Conus medullaris	Sacral autonomic fibers	Early and prominent sphincter and sexual impairment; saddle pattern sensory loss; mild weakness
Tract-specific dysfunction		Depending on involved tract

Certain clinical signs can aid in localizing the level of the lesion and are described in **Table 2**.

The list of differential diagnoses of TM is long; hence, a meticulous history and detailed physical examination are indispensible. A systematic and careful history may help exclude other mimics of TM (these are discussed in **Box 2**). An antecedent infection or prior vaccination may implicate acute disseminated encephalomyelitis (ADEM) or parainfectious TM. Travel abroad may indicate more exotic infectious causes of TM, such as schistosomiasis. Risk factors for or concomitant existence of malignancy may implicate a paraneoplastic etiology.

Women of reproductive age are at higher risk of acquired demyelinating diseases and SAIDs with the exception of Behcet disease (BD) and ankylosing spondylitis (AS). A history of relapsing-remitting attacks of neurologic deficits, eg, acute optic neuritis (AON) or internuclear ophthalmoparesis (INO), would suggest MS. Uhthoff phenomenon (discussed later) may be present in demyelinating diseases. A thorough neurologic examination may reveal evidence of prior neurologic impairments suggestive of MS exacerbations disseminated in time and space. NMO usually causes attacks of severe AON (sometimes bilateral) and brainstem lesions resulting in intractable nausea, vomiting, or hiccups.[21–24] Although the manifestations of NMO may be similar to MS, attacks are typically more devastating.[25] In cases of NMO mistakenly diagnosed as MS, treatment with interferon beta-1a would dramatically increase attacks.[26]

Autoimmune disorders, in particular systemic lupus erythematosus (SLE), BD, AS, Sjögren's syndrome (SS), and antiphospholipid syndrome (APS), are known causes of TM. In some, TM may be the initial clinical manifestation of such a disorder. Fatigue

Table 2
Clinical signs with useful localizing value in myelopathic patients

Clinical Sign	Description	References
Beevor sign	Describes the upward migration of the umbilicus during the act of sitting up from supine position owing to weakness of the lower half of the rectus abdominis (because the upper rectus segments pull in a direction opposite of the lower segments, the movement of the abdomen is upward). In some cases, downward migration of the umbilicus may be observed. This sign indicates a lesion at the level of the T10–12 spinal cord and/or roots.	[22]
Superficial abdominal reflexes	A lesion above T6 segmental cord level will abolish all superficial abdominal reflexes. A lesion at or below T10 spares the upper and middle abdominal reflexes. All the reflexes are present with a lesion below T12.	[23]
Cremasteric reflex	Lost in lesions at or above L2 segmental cord level.	[23]
Bulbocavernous reflex	Mediated by S2–4 nerve roots; hence, is abolished in lesions above S2 segmental cord level.	[24]
Anal wink reflex	Mediated by S2–4 nerve roots; hence, is abolished in lesions above S2 segmental cord level	[24]

Box 2
Red flags arguing against TM in myelopathic patients

1. Apoplectic onset (reaching the nadir less than 4 hours from onset).
2. Insidious progressive course.
3. Older age of onset.
4. Preceding trauma, pain, and/or vertebral tenderness would suggest traumatic myelopathy.
5. Vascular instrumentation (in particular, aortic and cardiac surgery) or maneuvers that increase intra-abdominal pressure (eg, weight-lifting or straining) before the acute/subacute appearance of myelopathic features may implicate spinal cord infarction.
6. Prior bariatric surgical procedures, malabsorption syndromes, dietary restrictions, malnutrition, use of zinc supplements, excessive use of zinc-containing denture cream, alcoholism, and/or drug/toxin exposure may implicate a metabolic or toxic etiology.
7. Prior radiation therapy.
8. Immunocompromised state (HIV/AIDS or immunosuppressive therapy).
9. Features of infection: fever, meningismus, rash, leukocytosis, burning dermatomal pain.
10. Paralysis with dissociated sensory loss (loss of pinprick and temperature but preserved dorsal column function) indicates an anterior spinal artery infarction.
11. The exacerbation of spinal pain with recumbency suggests malignancy.
12. Foix-Alajouanine syndrome (congestive venous myelopathy) is characterized by exacerbation of myelopathic features with exercise and relief with rest.

and constitutional complaints are common in patients with autoimmune disorders. A thorough integumentary examination may offer valuable clinical signs. Systemic (eg, renal, cardiac) and nonmyelopathic neurologic manifestations (eg, mononeuritis multiplex, myositis, cerebellar ataxia) may occur in some SAIDs. The presence of peripheral nervous system deficits rules out MS and NMO, unless there are concomitant disorders in the same patient (eg, diabetic peripheral neuropathy). **Table 3** describes some salient manifestations of selected systemic autoimmune disorders.

EVALUATION AND DIAGNOSIS

Magnetic resonance imaging (MRI) of the complete spinal axis is mandatory in any patient with myelopathic features to exclude structural lesions, particularly those amenable to emergent neurosurgical intervention. The spinal cord cephalad to the suspected level of the lesion should always be imaged owing to possibly misleading signs, eg, paraparesis attributable to cervical lesions. The most sensitive MRI sequence for detecting spinal cord lesions (especially MS plaques) are short-tau inversion recovery (STIR) fast spin-echo and T2-weighted fast spin-echo sequences.[27,28]

The location and length of the cord lesion on MRI may also provide clues about the underlying disease. Based on clinical and radiologic data, TM can first be dichotomized into longitudinally limited and longitudinally extensive TM (LETM). Longitudinally limited TM can be further classified as ACTM or APTM. ACTM and APTM span 1 or 2 vertebral segments. ACTM causes a complete spinal cord syndrome; on axial sections, there is either full-thickness involvement, or the central portion of the spinal cord is maximally affected.[29] APTM results in asymmetric spinal cord involvement or neurologic deficits attributable to a specific anatomic tract; on axial sections, there is involvement of a portion of the spinal cord. Patients with APTM are at increased risk of recurrence and transition to MS.[13,29,30] Conversely, ACTM carries a lower risk of transition to clinically definite multiple sclerosis (CDMS) and is usually related to other

Table 3
Systemic manifestations of autoimmune disorders

Disorder	Clinical Sign/Symptom
Sjögren syndrome	Xerophthalmia, xerostomia, parotid gland enlargement, Raynaud phenomenon, dysphagia, and dry cough (owing to xerotrachea). A positive Schirmer test detects deficient tear production.
Systemic lupus erythematosus	Joint pains, morning stiffness, myalgias, and integumentary manifestations (alopecia, unguium mutilans, perniotic lesions, leuconychia, splinter hemorrhages, nail-fold hyperkeratosis, ragged cuticles, malar rash, Raynaud phenomenon, photosensitivity, and/or discoid lupus).
Antiphospholipid syndrome	History of deep vein thromboses, pulmonary embolism, multiple miscarriages, and/or young-onset stroke.
Behcet disease	Classic triad of recurrent aphthous ulcers, genital ulcers, and uveitis. Other manifestations: ophthalmic (hypopyon and retinal vasculitis) and cutaneous (pseudofolliculitis, erythema nodosumlike lesions, or acneiform lesions). Positive pathergy test.
Ankylosing spondylitis	Back pain, enthesitis, and limited spinal flexion.

causes (eg, SAIDs). LETM refers to lesions that extend over 3 or more vertebral segments; on axial sections, it typically involves more than two-thirds of the spinal cord thickness (maximally affecting the central portion).[3,29] **Box 3** summarizes the differential diagnoses of LETM. The unique radiologic features of different etiologies are explored later.

A brain MRI with and without gadolinium administration should also be obtained on all patients to look for evidence of concomitant or prior lesions that may provide clues about the etiology. The presence of MS-like brain lesions in patients with partial TM portends an 80% risk of transition to clinically definite MS at 3 to 5 years.[13]

Serum vitamin B12 level, thyroid function tests, syphilis, and HIV serologies *always* should be obtained to evaluate for potentially treatable causes of myelopathy. Vitamin E, serum copper, and ceruloplasmin levels are checked in those at risk of deficiency (see later in this article for further details). Serum aquaporin-4–specific autoantibodies (NMO-immunoglobulin [Ig]G) should be checked on all patients with TM because of its high specificity for NMO or NMO spectrum disorders (NMOSD).[31,32] NMO-IgG seropositivity is rarely found in patients with APTM[30] but its presence would have profound implications on treatment. Inflammatory markers (please see **Box 4**) should be checked if SAID is suspected. In suspected parainfectious TM, serologic evidence of recent infection (eg, *Mycoplasma* antibody titers) should be sought. Serum paraneoplastic profiles should be performed in suspected cases of paraneoplastic TM; additionally, in such cases, appropriate investigations should be undertaken to search for the occult malignancy, the identification of which can have profound ramifications for the patient; even a cure if a malignancy can be confirmed and eradicated before pathologic dissemination.

Cerebrospinal fluid (CSF) analysis is essential in the evaluation of TM. CSF cell count, differential, protein, glucose, oligoclonal bands (OCBs) and IgG index should be checked on all patients with TM. Isoelectric focusing is the superior method for the detection of OCBs, providing a much higher yield and specificity.[33] OCBs are useful in predicting conversion to MS, as OCBs are present in 85% to 90% of patients

Box 3
Differential diagnosis of LETM

1. Neuromyelitis optica (NMO) or NMO-spectrum disorders
2. Acute disseminated encephalomyelitis (ADEM)
3. Systemic autoimmune disorders: systemic lupus erythematosus (SLE), Sjögren syndrome (SS), neurosarcoidosis, neuro-Behcet disease
4. Parainfectious TM: *Borrelia burgdorferi*, *Chlamydia psittaci*, mumps virus, cytomegalovirus, coxsackie virus, *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, enterovirus 71, hepatitis C virus, *Brucella melitensis*, Epstein-Barr virus, echovirus type 30, *Ascaris suum*, *Toxocara canis*, and *Schistosoma* species.
5. Paraneoplastic TM (in particular, anti-collapsin response-mediator protein [CRMP]-5 antibodies)
6. Mimics of TM
   a. Neoplasms: primary intramedullary spinal cord tumors, metastatic intramedullary tumors, lymphoma
   b. Radiation myelitis
   c. Metabolic myelopathies: B12 deficiency, copper deficiency, nitrous oxide toxicity
   d. Vascular myelopathies: anterior spinal artery infarction, spinal dural arteriovenous fistula

Box 4
Investigations into suspected TM

Must be obtained on all patients:

1. Magnetic resonance image (MRI) of the spine
2. Brain MRI
3. Cerebrospinal fluid (CSF): cells, differential, protein, glucose, Venereal Disease Research Laboratory (VDRL), immunoglobulin (Ig)G index, oligoclonal bands, cytologic analysis
4. Serum: B12, methylmalonic acid, HIV antibodies, syphilis serologies, thyroid stimulating hormone (TSH), Free T4, 25-hydroxyvitamin D

Must be obtained on all patients with LETM:

1. Serum NMO-IgG
2. Serum erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies, antibodies to extractable nuclear antigen, rheumatoid factor, antiphospholipid antibodies, and anti-neutrophil cytoplasmic antibodies (ANCA)
3. Visual-evoked potentials

May need to be obtained:

1. Neuro-ophthalmological evaluation
2. Paraneoplastic panel
3. Infectious serologies and CSF studies (cultures and viral polymerase chain reaction)
4. Serum copper and ceruloplasmin
5. Serum vitamin E level
6. Computed tomography of the chest
7. Nerve conduction studies and electromyography
8. Minor salivary gland biopsy

with MS, in 20% to 30% of patients with NMO or SAIDs, and rarely in other causes of TM.[13] Bear in mind that their mere presence clearly does not militate against being reflective of a myriad of inflammatory, infectious, and neoplastic or paraneoplastic processes.

A neuro-ophthalmological evaluation is warranted to look for ophthalmic manifestations that may provide valuable diagnostic clues, especially when radiologic and laboratory investigations are unremarkable. For example, different subtypes of uveitis are associated with unique etiologic underpinnings.[34] Demyelinating diseases affecting the brainstem and/or cerebellum commonly cause ocular motor manifestations.[35]

Electrophysiologic tests may be very useful in assessing patients with TM. Nerve conduction studies and electromyography (EMG) may reveal and help characterize any peripheral nervous pathology, the exclusion of which would lend compelling support for a spinal cord process. This latter principle is especially salient in that acute TM can present as a spinal shock variant, one that may mimic a polyneuropathic process like GBS. In early TM, F-waves may be absent,[36] an observation that can serve to misguide even the most experienced neurologic consultant (especially when the MRI is unremarkable) to localize the disease process to the peripheral nervous system. EMG-evidence of anterior horn cell dysfunction may portend a poor prognosis for recovery.[37] Somatosensory evoked potentials may offer evidence of a myelopathy in the presence of a normal spinal cord MRI. In addition,

conventional and multifocal visual-evoked potentials (VEP) may provide evidence of subclinical demyelination along the afferent visual pathways not clearly identified on imaging. Evidence of such disruption may support the diagnosis of MS or NMO but are by no means specific for these disease entities (discussed in greater detail later).

A list of investigations into TM is provided in **Box 4**.

CAUSES OF TM

Box 5 summarizes the causes of TM.

Multiple Sclerosis

MS is a disabling progressive neurologic disorder affecting approximately 400,000 people in the United States.[38] First attacks of MS, called clinically isolated syndrome (CIS), usually consist of AON, brainstem syndromes, or APTM. The probability for APTM to transition to CDMS ranges from 10% to 62%.[30,39–43] APTM may be a CIS with a higher risk of conversion to MS.[43]

TM in MS most commonly presents with sensory phenomena. Spine MRI typically reveals an asymmetrically placed lesion (usually occurring in the posterolateral or lateral portion of the spinal cord) less than 2 segments in length (ie, APTM) with a predilection for the cervicothoracic cord.[3,30,39,42,43]

The most important investigation that helps determine the risk of conversion to CDMS is the brain MRI. If it is normal, only 10% of patients with APTM will develop CDMS at 61 months[30]; this increases to 21% risk of progression at 20 years follow-up according to another study of CIS.[44] White matter lesions predict higher risk of conversion to MS (with rates of up to 88% reported).[43,44] If the lesions meet at least 3 of the Barkhof criteria[45] this risk is increased substantially.[43]

Another important factor that helps predict the risk of transition to CDMS is CSF OCBs. In the setting of TM, OCBs have been shown to have a robust predictive value of for predicting conversion to MS.[43,46–48] In patients with TM with normal brain MRIs, the presence of OCBs and/or an elevated IgG index portends a higher risk of developing MS.[49] The risk of developing MS is less than 10% with a normal brain MRI and CSF findings.[43]

Longitudinally extensive lesions in the context of TM is actually quite rare in MS and, when present, is significantly shorter than those seen in NMO. When MS is confirmed, spinal lesions tend to favor a cervical localization, and tend to have less cord swelling and gadolinium-enhancement.[50] In general, patients with LETM have been shown to have a conspicuously low risk of developing MS.[30]

Neuromyelitis Optica

NMO is diagnosed on the basis of the revised Wingerchuk criteria[51] requiring the presence of optic neuritis and TM as well as 2 of 3 of the following: NMO antibodies, LETM, and/or brain MRI lesions inconsistent with MS. NMOSDs include Asian optic-spinal MS, recurrent LETM, recurrent AON, and AON or TM in the context of certain organ-specific and non–organ-specific autoimmune disease. The article on NMO by Sahraian, MA, elsewhere in this issue discusses this disease in detail. Here, we underscore the important features of NMO that give rise to diagnostic confusion.

Diagnostic confusion may arise with SAIDs, as patients with NMO/NMOSD often have accompanying autoimmune diseases and multiple non–organ-specific autoantibodies. Autoimmune diseases observed to coexist with NMO include SS, SLE, autoimmune thyroid disease, type 1 diabetes mellitus, ulcerative colitis, idiopathic

Box 5
Summary of reported causes of TM

1. Acquired demyelinating disorders
   a. Multiple sclerosis
   b. NMO
   c. ADEM
2. Systemic inflammatory autoimmune disorders
   a. SLE
   b. SS
   c. Antiphospholipid syndrome
   d. Behcet disease
   e. Vogt-Koyanagi Harada disease
   f. Ankylosing spondylitis
   g. Mixed connective tissue disease
   h. Others: systemic sclerosis, anti-Jo-1 antibody, urticarial vasculitis, psoriatic arthritis, perinuclear ANCA systemic vasculitis, graft-versus-host disease, common variable immunodeficiency, celiac disease
3. Neurosarcoidosis
4. Parainfectious TM
   a. Viral: hepatitis A, hepatitis B, hepatitis C, hepatitis E, measles, mumps, rubella, varicella zoster, Epstein-Barr, cytomegalovirus, herpes simplex, influenza A/B, lymphocytic choriomeningitis virus, chikungunya, Hanta virus, HIV, human T-cell lymphotropic virus, human herpes virus 6, Japanese encephalitis, Murray Valley encephalitis, St Louis encephalitis, tick-borne encephalitis, vaccinia, Rocky Mountain spotted fever, dengue virus, enterovirus 71, coxsackievirus A and B, West Nile virus, parvovirus B19, human corona virus, and echovirus
   b. Bacterial: *Mycoplasma pneumoniae, Campylobacter jejuni, Borrelia burgdorferi, Acinetobacter baumanii, Coxiella burnetii, Bartonella henselae, Chlamydia psittaci, Leptospira, Chlamydia pneumoniae*, *Legionella pneumonia, Orientia tsutsugamushi* (scrub typhus), *Salmonella* paratyphi B, *Mycobacterium tuberculosis, Treponema pallidum, Brucellosis melitensis*, and groups A and B streptococci
   c. Fungal: *Actinomyces, Blastomyces, Coccidioides, Aspergillus, Cryptococcus*, and *Cladophialophora bantiana*
   d. Parasitic: *Toxocara* species, *Schistosoma* species, *Gnasthostoma spinigerum, Echinococcus granulosus, Taenia solium, Toxoplasma gondii, Acanthamoeba* species, *Paragonimus westermani*, and *Trypanosoma brucei*
5. Paraneoplastic syndromes
   a. Anti-Ri (ANNA-2) antibody
   b. CRMP-5-IgG antibody
   c. Anti-amphiphysin IgG antibody
   d. Anti-GAD65 antibody
   e. NMDAR antibody
6. Atopic myelitis
7. Drugs and toxins
   a. Tumor necrosis factor-alpha inhibitors

b. Sulfasalazine
c. Epidural anesthesia
d. Chemotherapeutic agents: gemcitabine, cytarabine, cisplatin
e. Heroin
f. Benzene
g. Brown recluse spider toxin
8. Idiopathic TM

thrombocytopenic purpura, myasthenia gravis, rheumatoid arthritis, polymyositis, celiac disease, and Raynaud phenomenon.[52,53]

We propose that all patients with a known SAID (eg, SS or SLE) who present with TM undergo serologic testing for NMO-IgG. The high specificity of NMO-IgG seropositivity[31,54] will establish the additional diagnosis of NMO coexisting with the systemic autoimmune disorder. In patients with NMO or TM, the isolated presence of systemic non–organ-specific antibodies should not be used to make a diagnosis of any particular rheumatic disease; instead, these assays can lend support in corroborating such conditions, when the established clinical criteria for each respective disorder has been fulfilled.

Sjögren Syndrome

SS is a chronic, protean, progressive, systemic autoimmune disorder characterized by mononuclear infiltration and destruction of the salivary and lacrimal glands, leading to keratoconjunctivitis sicca, typically affecting middle-aged to elderly women. SS may appear alone (primary SS) or exist with another autoimmune disease (secondary SS).[55–57]

A wide range of central nervous system (CNS) manifestations may occur, including AON and TM.[56,58,59] The precise prevalence of neurologic manifestations in SS is unclear, and has been reported to range from 8.5% to 70.0%[57]; this large discrepancy may be related to the inclusion or exclusion of psychiatric and cognitive impairment. Neurologic deficits may be the initial presentation in as many as 57% of patients with SS.[57] Spinal cord involvement (either acute TM or progressive myelopathy) may occur in 20% to 35% of patients with SS and may constitute the initial presentation of the disease in up to about 20%.[55,57] The lesions tend to affect the cervical cord and may be longitudinally extensive.[57,60]

CSF typically reveals pleocytosis, mildly increased protein, and a mildly elevated IgG index.[56,60] Cytologic analysis may reveal small round lymphocytes, reactive lymphoid cells, plasma cells, and atypical mononuclear cells.[56] OCBs have been reported in about 30% of patients with SS.[57] SS-A or SS-B antibody seropositivity is not mandatory for the diagnosis of SS, because only 21% of patients with primary SS and neurologic manifestations demonstrate such seropositivity.[57]

Although other CNS manifestations of SS are corticosteroid-responsive,[56] spinal cord involvement is often refractory to steroids.[60] Intravenous (IV) cyclophosphamide is effective[56,57]; there is anecdotal evidence supporting the use of plasmapheresis[61] and IV gammaglobulin.[62] Maintenance immunosuppressive therapy with monthly pulse IV cyclophosphamide may be considered.[56] Rituximab is another promising agent[63] and may be a suitable agent for patients with coexisting NMO or MS, or where there is diagnostic confusion with these diseases.

Careful longitudinal follow-up is important in SS, as recurrent attacks of TM or AON can culminate in substantial disability, and may ultimately lead to a confirmed diagnosis of NMO or MS.

Systemic Lupus Erythematosus

SLE is a chronic, systemic, autoimmune disease. The diagnosis of SLE requires at least 4 of 11 features, as outlined by the American College of Rheumatology.[64] Although neuropsychiatric manifestations of SLE are common, TM accounts for only 1% to 2% of patients,[65] but constitutes the most devastating complication of SLE and one that often portends a poor prognosis.[66] SLE-related TM tends to occur within the first 5 years from diagnosis, is the initial clinical manifestation in almost half of patients, and recurs in 21% to 55% of cases.[67–69] AON and brainstem manifestations may accompany TM in SLE,[70,71] mimicking MS and representing a significant source of diagnostic confusion.

A short period of prodromal symptoms (eg, headache, fever, nausea) typically heralds the onset of thoracic myelopathy with prominent bladder dysfunction.[69,71] In a large series of SLE-related TM, 2 different clinical patterns at presentation were observed: gray and white matter myelitis. Gray matter myelitis demonstrated lower motor neuron (LMN) features, urinary retention, and a more devastating but monophasic course. White matter myelitis demonstrated UMN features and a more indolent but recurrent course.[72] An earlier study suggested that EMG evidence of anterior horn cell dysfunction in patients with TM predicts a poor prognosis for recovery.[37] The features of gray and white matter myelitis are summarized in **Table 4**.

Although low-titer positive antinuclear antibodies (ANA) in idiopathic TM (ITM) cases are similar to that of the general population, much higher serum ANA titers, anti–double-stranded DNA antibodies, and hypocomplementemia are found in SLE-related TM.[68,71] The presence of antiphospholipid antibodies (APLA) in SLE has been suggested to increase the risk of developing TM[73] but this association has been challenged.[67,69] CSF pleocytosis with elevated protein and intrathecal IgG synthesis are typically detected, particularly in LETM[68,69,71,74]; interestingly, OCBs, although unusual, have been observed in APLA-seropositive patients.[69]

The most common MRI finding in SLE-related TM is a longitudinally extensive, T2-hyperintense lesion (accompanied by cord swelling).[68,69,71,74–78] In severe cases, the lesion involves the entire spinal cord and extends into the medulla.[79,80] Radiologic findings may not correlate with the clinical course.[68] Almost a third of patients with SLE-related TM do not have any detectable MRI abnormalities at presentation.[67] On brain MRI, subcortical lesions predominate in APS and SLE, whereas periventricular and callosal lesions are more common in MS.[81]

In a randomized controlled trial, IV cyclophosphamide was found to be more efficacious in treating neuropsychiatric manifestations of SLE compared with IV methylprednisolone.[82] The combination of high-dose IV methylprednisolone and IV cyclophosphamide may be effective in SLE-related TM if instituted promptly, resulting in improvement in a few days to 3 weeks.[67,70,83,84] Relapses are common (50%–60%) during corticosteroid dose taper, emphasizing the need for maintenance immunosuppression.[70] Plasmapheresis has been used in severe cases.[67,71,85,86] There is anecdotal evidence for using intravenous immunoglobulin and rituximab.[71,87,88] Anticoagulation therapy is indicated only in those with a history of thrombotic phenomena.[69,71,73,74] Long-term aspirin use has anecdotal support.[74]

Factors associated with severe neurologic deficits include extensive cord MRI lesions, LMN features and sphincteric dysfunction at onset, APLA, and delayed (>2 weeks) initiation of therapy.[67,72,89]

Table 4
The differences between gray and white matter myelitis in SLE

	Gray Matter Myelitis	White Matter Myelitis
Presentation	Lower motor neuron features with urinary retention (urinary retention always heralds paraplegia)	Upper motor neuron features
Prodrome (fever, nausea, vomiting)	Very frequent	Infrequent
Clinical course	More rapid deterioration; more severe weakness at nadir. Lower motor neuron features persist beyond the time expected for spinal shock. More aggressive immunosuppression needed.	Less severe clinical deterioration; longer time to reach nadir; less severe weakness at nadir.
Long-term Disability	Greater	Less
CSF	Neutrophilic pleocytosis; higher protein; hypoglycorrachia	Mild pleocytosis; mildly elevated protein; normal glucose
MRI	Cord swelling; frequent LETM; less frequent gadolinium-enhancement	Infrequent cord swelling; less frequent LETM; More frequent gadolinium-enhancement
Recurrence	Very rare	More than 70% of patients
Prior optic neuritis	Absent	Frequent
Coexisting NMO and/or NMO-IgG seropositivity	None	Frequent
Higher SLE disease activity	Frequent	Infrequent

Abbreviations: CSF, cerebrospinal fluid; LETM, longitudinally extensive transverse myelitis; NMO, neuromyelitis optica; NMO-IgG, aquaporin-4-antibody; SLE, systemic lupus erythematosus.
Data from Birnbaum J, Petri M, Thompson R, et al. Distinct subtypes of myelitis in systemic lupus erythematosus. Arthritis Rheum 2009;60(11):3378–87.

Antiphospholipid Syndrome

APS is a systemic, autoimmune disorder characterized by recurrent thrombotic events and/or miscarriages, as well as APLA seropositivity (2 or more occasions at least 6 weeks apart) (ie, anticardiolipin, lupus anticoagulant, and anti-beta-2-glycoprotein I antibodies).[90] In secondary APS, the disease coexists with another autoimmune disorder.

TM is an unusual complication of APS, with a prevalence of less than 1%.[91–93] Although typically monophasic, recurrent corticosteroid-responsive LETM has also been observed.[92] Characteristically, acute thoracic cord dysfunction occurs with sphincter involvement.[93] Spine MRI may be normal on presentation in up to 40% of patients, underscoring the importance of repeat imaging in suspected cases.[94] It is hypothesized that interactions between APLA and spinal cord phospholipids are responsible for APS-related TM,[95] explaining the efficacy of and justifying the use of early high-dose corticosteroid therapy.[93] In corticosteroid-refractory patients, cyclophosphamide, plasmapheresis, and rituximab may be needed.[93]

A higher prevalence of APLA seropositivity has been reported in patients with MS and appears to rise with disease duration.[96–100] Although diagnostic confusion may

arise in APLA-positive patients with TM, the presence of CSF OCBs and the absence of prior miscarriages or thrombotic phenomena would favor MS rather than APS.

Behcet Disease

BD is a relapsing multisystem inflammatory disorder of unclear etiology resulting in oral aphthous ulcers, genital ulcers, uveitis, cutaneous manifestations, and involvement of other organ systems.[101]

Neurologic involvement in BD (neuro-BD) may follow or precede the onset of systemic manifestations.[102] Neuro-BD typically occurs in the third to fourth decade of life, is more common in men, and is usually associated with ocular involvement.[102–104] The frequency of neuro-BD varies greatly, from 1.3% to 59.0%, with a pooled average of 9.4%.[102,104] Neuro-BD can be classified as parenchymal or nonparenchymal (vascular). Parenchymal neuro-BD commonly manifests as a meningoencephalitic syndrome with headaches and focal neurologic deficits.[102] The manifestations of vascular BD stem from cerebral venous thrombosis (often with subsequent increased intracranial hypertension) and/or rarely, arterial infarctions.[105] Spinal cord involvement ranges between 2.5% and 30.0%, with a predilection for the cervical and thoracic cord segments (in particular the posterolateral cord), and carries a poor prognosis.[102,103,106–109] Isolated TM in neuro-BD is distinctly unusual.[102,105]

Spinal cord lesions are usually longitudinally extensive and involve multiple noncontiguous segments, or even involve the entire cord. Cord swelling and T2-hyperintense, nonenhancing lesions are present in the acute or subacute phase.[106,107,109–114] An unusual report of TM (extending from T9 to the conus) following CT-guided L2 nerve root injection, may be a florid demonstration of the pathergic reaction in the spinal cord.[115]

Brain MRI may reveal T1-hypo/isointense and T2-hyperintense lesions that may or may not show gadolinium enhancement acutely. Characteristically, an upper pontomesencephalic lesion with thalamic, hypothalamic, and basal ganglial extension on one side is seen.[102,105,107,109,116,117] Interestingly, the red nucleus is almost always spared.[107,109] Striking brainstem atrophy, as well as the rarity of periventricular lesions, optic neuropathy, cortical atrophy, and gray matter lesions in neuro-BD,[102,109,117,118] distinguish it from MS.

CSF typically reveals normal glucose, increased protein, and neutrophilic pleocytosis; the IgG index may be elevated, and OCBs are rare.[103–106,108,117]

Acutely, administration of high-dose corticosteroids results in improvement in most patients[103,104,108,110,111,113,119]; corticosteroid therapy also improved pleocytosis.[117] Infliximab, cyclophosphamide, and intravenous immunoglobulin have been used with some success.[104,120]

No randomized controlled trials have been conducted into the treatment of neuro-BD. Azathioprine, mycophenolate mofetil, and methotrexate have been used as initial immunosuppressive therapy. In more aggressive disease, tumor necrosis factor-antagonists or monthly infusions of cyclophosphamide have been used. Colchicine, thalidomide, and pentoxifylline may be used for mucocutaneous lesions.[102–104] Cyclosporin A has been used to treat ophthalmic manifestations but may be neurotoxic and worsen neurologic manifestations.[121–124]

TM in Other Rheumatologic Diseases

TM has been reported in AS, psoriatic arthritis, mixed connective tissue disease, and systemic sclerosis (please refer to **Table 5**).

Table 5
Other dysimmune disorders associated with TM

Disorder	Comment	References
Ankylosing spondylitis	Neurologic involvement is rare and is almost always attributable to compressive myelopathy. Noncompressive myelopathy is exceptionally rare with only 2 clearly documented cases of TM.	368–370
Psoriatic arthritis		371
Mixed connective tissue disease	Female preponderance; predilection for the thoracic cord.	372–377
Systemic sclerosis	Rare and typically compressive in etiology. Progressive myelopathy, subacute TM, and NMO-IgG positive LETM have been reported.	378–381
Anti-Jo-1 antibody	A single report of TM preceding the development of polymyositis and pulmonary fibrosis in a patient with anti-Jo-1 antibody.	382
Urticarial vasculitis	Urticarial vasculitis may be primary disorder or coexist with other autoimmune diseases.	383
pANCA seropositivity	Perinuclear antineutrophil cytoplasmic antibody (pANCA) seropositivity has been reported to cause TM associated with CSF pleocytosis and increased protein with typically absent OCBs.	384,385
Celiac disease	Celiac disease is an immune-mediated disorder characterized by intolerance to dietary gluten.	386
Thymic follicular hyperplasia	Recurrent multifocal TM associated with thymic follicular hyperplasia that resolved following thymectomy.	387
Graft-vs-host disease	TM may be a rare manifestation of graft-vs-host disease following hematopoietic cell transplantation.	388–390
Common variable immunodeficiency	A primary immune deficiency disorder characterized by hypogammaglobulinemia, antibody deficiency, and recurrent infections.	391,392

Abbreviations: CSF, cerebrospinal fluid; LETM, longitudinally extensive transverse myelitis; NMO-IgG, aquaporin-4-antibody; OCB, oligoclonal bands; SLE, systemic lupus erythematosus.

Neurosarcoidosis

Sarcoidosis is a multisystem granulomatous disease with protean manifestations that may affect any organ. Neurologic involvement (neurosarcoidosis) is reported in 5% to 13% of patients with sarcoidosis[125–128] but may be as high as 26%.[129] The usual age of onset is the fourth decade.[127,130] Spinal cord neurosarcoidosis appears to be more common in men.[131,132]

CNS features are the initial manifestation of neurosarcoidosis in up to 70% of patients.[130] Although unusual, spinal cord involvement portends a poor outcome, and may be related to intramedullary, intradural extramedullary, or extradural lesions; cauda equina syndrome; or arachnoiditis.[130,131,133] Although isolated myelopathy has been observed, half of patients with spinal cord neurosarcoidosis demonstrate systemic manifestations.[129,133,134]

Neurosarcoidosis has a predilection for the cervical and thoracic cord[131,132,135–137] and is frequently associated with back pain and radicular symptoms.[131,138–140]

Intramedullary disease typically appears as a longitudinally extensive, T1-hypointense, T2-hyperintense, heterogeneously enhancing lesion with fusiform cord enlargement or myelomalacia.[131,141] Spinal cord lesions may be multifocal; gadolinium enhancement may be nodular or predominate at the periphery of the lesion.[129,131,132] Neurosarcoidosis should be suspected in any infiltrating intramedullary cord lesion with leptomeningeal enhancement. Half of patients with spinal neurosarcoidosis have concomitant intracranial lesions.[131,141]

The diagnosis of spinal cord neurosarcoidosis is challenging, particularly if systemic manifestations are absent. When clinical suspicion is high, even in the absence of systemic symptoms, it is worthwhile performing a high-resolution chest CT, positron emission tomography, ophthalmic examination, or a gallium-67 scan to identify extraneural granulomas that may be amenable to biopsy.[66,140,142]

CSF findings reveal elevated protein, lymphocytic pleocytosis, occasional hypoglycorrachia, and infrequent OCBs. CSF angiotensin-converting enzyme levels are normal in more than half of patients. Hypoglycorrachia is specific and can distinguish neurosarcoidosis from other inflammatory etiologies.[130,131,140,143]

Early corticosteroid therapy results in remarkable recovery but delayed treatment leads to only partial resolution of myelopathic manifestations.[132] A high index of suspicion for the diagnosis is required because early intervention is associated with a favorable outcome.

Vogt-Koyanagi-Harada Syndrome

Vogt-Koyanagi-Harada syndrome (VKH), also known as uveomeningoencephalitis, is a systemic inflammatory disorder affecting the melanin-forming cells in different organs.[144] TM is an infrequent complication of VKH,[145,146] and bilateral AON with papilitis has been reported.[147] These manifestations may mimic MS or NMO. CSF pleocytosis can provide early evidence of disease activity, therefore allowing early treatment with corticosteroids.[148,149]

Acute Disseminated Encephalomyelitis

ADEM is a monophasic disorder that occurs following infections or vaccinations, is associated with multifocal demyelinating lesions, and may include encephalopathy, coma, and/or seizures.[150] TM occurs in about 24% of patients[151] and, in unusual cases, may be the sole manifestation of ADEM.[152] It is possible that some cases of TM represent limited forms of ADEM.[29] Unlike MS and NMO, ADEM may be associated with demyelinating peripheral neuropathies.[153]

ADEM may occur at any age but is most common in the pediatric population (mean age of onset of 5.7 years).[154] Postvaccination ADEM incidence is variable, and the most frequently implicated vaccine is the non-neural measles, mumps, and rubella vaccine.[66,155] An initial attack consistent with a demyelinating event with acute or subacute onset, a stable to stuttering course (evolving over 1 week to 3 months), characteristic MRI features, and concomitant encephalopathy and meningismus, suggests a diagnosis of ADEM.[66]

Radiologically, acute, multiple, symmetric, supratentorial and infratentorial lesions, with one at least 1 cm in diameter are observed; symmetric basal ganglial and thalamic involvement is common.[66,151] The lesions should be of the same age and demonstrate homogeneous gadolinium enhancement, as ADEM is typically monophasic.[156,157] The typical spinal cord lesion is swollen, enhances variably, and predominantly affects the thoracic cord.[151] It may take up to 14 days from the onset of symptoms for the MRI to show abnormalities.[158] CSF in ADEM typically reveals marked pleocytosis, elevated protein, normal IgG index, and no OCBs.[155,159,160]

Treatment with high-dose IV corticosteroid therapy may help diminish inflammation and restore the blood-brain barrier integrity. Early initiation of plasmapheresis (within 15 days of onset) has been shown to result in clinical improvement and should be offered to those who fail steroid therapy.[161–165]

Parainfectious TM

Parainfectious TM (PITM) refers to TM associated with an antecedent infection. It is unclear if it shares the same pathophysiological underpinnings as ADEM (and represents different ends of a spectrum) or if they are separate entities. Both are preceded by typically monophasic, steroid-responsive events preceded by infections. It is difficult to determine if PITM is caused by direct microbial invasion (causing myelitis by either the direct pathogenic destruction, or from the pathogen-triggered immune reaction), or a consequence of immune-mediated, inflammatory mechanisms induced by a remote infection. The antecedent infection has typically resolved before the onset of TM and it is difficult to demonstrate the offending organism in the spinal cord parenchyma.

The hepatitis viruses may cause TM via postinfectious, immune-mediated, inflammatory mechanisms.[166] Hepatitis A virus and Hepatitis B virus infection have been associated with immune-mediated TM.[166] Hepatitis C virus (HCV) is the most commonly implicated hepatitis virus in TM. HCV has been associated with recurrent, corticosteroid-responsive, demyelinating TM (even without hepatic involvement).[166–171] There is a single report of hepatitis E–virus associated TM.[172]

Viruses associated with PITM[155,173–186] are listed in **Box 5**.

CNS manifestations are the most common extrapulmonary complication of *Mycoplasma pneumoniae* infection.[155,187–189] Although encephalitis is the most frequent complication,[189] TM is the most severe and debilitating manifestation.[190] Acute to subacute thoracic myelopathy typically arise 2 to 4 weeks after the antecedent respiratory infection and progress to a nadir in about 3 days; it may be accompanied by meningoencephalitis and/or polyradiculopathy.[190] LETM has been reported.[191–193] A predominantly mononuclear pleocytosis with increased protein and normal glucose levels are frequently found.[190] Serologic detection of anti-*Mycoplasma* antibodies supports the diagnosis. Positive *M pneumoniae* CSF polymerase chain reaction provides reliable diagnostic evidence of preceding infection.

Antecedent *Campylobacter jejuni* infection has been classically associated with GBS, presumably because of molecular mimicry between bacterial lipopolysaccharides and human gangliosides. It has been associated with TM,[194–196] ADEM,[197–199] and 1 case of biopsy-proven CNS vasculitis.[200] In patients with TM with a recent diarrheal illness, stool cultures for *C jejuni* and serologic studies for antiganglioside antibodies should be considered.

Bacteria reported to cause PITM[155,195,201–214] are listed in **Box 5**.

Fungal and parasitic causes of PITM[5,215–223] are rare; these are listed in **Box 5**. These microbes most likely cause myelopathy by direct pathogenic effects. One noteworthy parasite is the pinworm (*Enterobius vermicularis*), which has been reported to cause TM associated with anti-GM1 antibodies (which are also seen in *C jejuni* infection) via molecular mimicry.[224]

Pathogens associated with parainfectious LETM[167–170,186,192,193,201,209,212,213,225–239] are listed in **Box 3**.

It is imperative to remember that the occurrence of TM following an infection does not automatically implicate ADEM or a parainfectious autoimmune response. Longitudinal follow-up is needed and further evaluation may be warranted because infections may trigger TM that heralds the diagnosis MS or NMO. Diagnostic confusion may arise

in cases in which concomitant parainfectious AON[240,241] and TM may mimic the appearance of a demyelinating disease. As such, longitudinal follow-up is required to ascertain the nature of the disease.

Paraneoplastic TM

Collapsin response-mediator protein-5 (CRMP-5-IgG) antibodies, observed in small-cell lung cancer, is the paraneoplastic antibody most commonly associated with TM; LETM has also been observed. CRMP-5-IgG–related AON is a recognized manifestation of this paraneoplastic syndrome. A clinical picture resembling MS or NMO may arise.[242,243] Patients demonstrate a subacute, progressive, predominantly motor myelopathy as well as increased CSF protein, elevated IgG index, and mild pleocytosis.[242,244] MRI demonstrates T2-hyperintense lesions with occasional gadolinium enhancement. In more than 40% of patients, LETM may be demonstrated.[242] Other paraneoplastic antibodies associated with TM are listed in **Table 6**.

Atopic Myelitis

Atopic myelitis (AM) demonstrates a chronic persistent or fluctuating course of predominantly cervical myelitis, associated with marked hyper-IgEemia, allergen-specific IgE (most commonly to dust mites), and occasional coexistent atopic diseases (eg, atopic dermatitis, atopic rhinitis, asthma).[245] The vast majority of reported cases occur in Japanese patients, but a there are a few reports of AM in White patients.[246,247] Sensory deficits are the predominant symptom, with infrequent motor and bladder involvement.[248]

On MRI, the lesions are T2-hyperintense with variable gadolinium enhancement, appear to favor the posterior columns of the cervical cord, and are limited to 1 to 2 vertebral bodies.[248,249] Because the clinical and radiologic picture resembles MS, it is imperative to obtain a brain MRI to look for lesions that would be suggestive of MS.[250] CSF cell count and protein are typically normal and OCBs are not seen.[249,250] VEP may be abnormal in more than 20% of patients with AM (and therefore may not help distinguish it from MS), as atopic AON has been reported to occur as well.[250,251]

TM in Other Dysimmune Disorders

Table 5 lists various dysimmune disorders that have been associated with TM.

Table 6
Paraneoplastic antibodies associated with TM aside from collapsin response-mediator protein 5 Ig antibodies

Paraneoplastic Antibody	Comment	References
Anti-Ri (ANNA-2)	Anti-Ri antibodies are usually associated with lung or breast carcinoma	393,394
Anti-amphiphysin IgG	Classically associated with breast cancer and stiff man syndrome	395,396
Anti-glutamic acid decarboxylase (GAD65)	Classically associated with stiff person syndrome, cerebellar ataxia, diabetes mellitus type 1, and limbic encephalitis	244,397
N-methyl-d-aspartate receptor (NMDAR)	Classically associated with limbic encephalitis, and related to ovarian teratomas.	398–400

Drug-induced and Toxin-related TM

Drugs and toxins associated with TM are listed in **Table 7**.

Idiopathic TM

The Transverse Myelitis Consortium Working Group has proposed a set of strict criteria for the diagnosis of ITM,[7] which are summarized in **Table 8**. To make the diagnosis, all inclusion and no exclusion criteria should be present. The application of these criteria has resulted in a fairly homogeneous group of patients in terms of clinical and radiologic data.[252] The reported proportion of patients with TM with ITM varies widely, from 16%[252] to approximately 60%.[253,254]

The overall mean age of disease onset appears to be between 35 and 40 years, with a female preponderance.[252,254] The MRI typically demonstrates a centromedullary lesion, extending over 2 vertebral segments and involving more than two-thirds of the cross-sectional area of the spinal cord, with a predilection for the thoracic cord.[41,252,253,255–259] Cord swelling is seen in half of cases. Gadolinium enhancement (which may be nodular, peripheral, heterogeneous, or moderately diffuse) occurs in approximately one-third to one-half of cases.[41,252,253,255] CSF shows increased protein in most patients; pleocytosis and OCBs are sometimes seen.[41,252,258] Interestingly, unlike other causes of TM, negative OCBs is correlated with recurrence.[252]

ITM is typically monophasic but recurs in about one-quarter to one-third of cases (recurrence of initial insult, expansion of prior lesion, or a new lesion).[8,12,66,252,259] Risk factors for recurrence seem to be the following: (1) male gender; (2) age older than 50 years; (3) severe motor weakness and sphincteric dysfunction; and (4) negative CSF OCBs, normal IgG index, and NMO-IgG seronegativity.[252,258,259] Recurrences are associated with a poor outcome.[259] Interestingly, Kim and colleagues[258] and Alvarenga and colleagues[254] both reported recurrences exceeding 60% in their respective studies despite the low rate of NMO-IgG seropositivity. There are several serologic, CSF, and radiologic differences among the patients with recurrent ITM in these studies and may represent distinct clinical entities that have yet to be characterized. A Korean study of 15 patients with recurrent ITM lends support to the hypothesis that recurrent ITM may represent a unique entity.[260] More longitudinal studies are needed to clearly elucidate the characteristics of recurrent ITM.

Table 7
Drugs and toxins associated with TM

Drug/Toxin	Comment	Reference
TNF-alpha inhibitors	Reported to cause CNS demyelination and TM.	401,402
Sulfasalazine		403
Chemotherapeutic agents	Gemcitabine, cytarabine (cytosine arabinoside), and cisplatin.	404–408
General and epidural anesthesia	The association between TM and general anesthesia is debatable.	409–415
Heroin	Although most of cases of myelopathy in heroin addicts result from anterior spinal artery infarction, there are reports of TM.	416–419
Benzene		420
Brown recluse spider bite	Incomplete TM (anterior spinal syndrome), responsive to corticosteroid therapy.	421

Abbreviations: CNS, central nervous system; TM, transverse myelitis; TNF, tumor necrosis factor.

Table 8
Transverse Myelitis Consortium Working group criteria for the idiopathic transverse myelitis

Inclusion Criteria	Exclusion Criteria
Neurologic impairment attributable to the spinal cord	History of radiation to the spine within 10 y
Bilateral signs or symptoms (may be asymmetric)	Anterior spinal artery distribution of deficits
Clearly defined sensory level	Abnormal flow voids on the spinal cord
Exclusion of extra-axial compressive etiology by neuroimaging	Serologic or clinical evidence of systemic autoimmune disease
Evidence of inflammation in the spinal cord (CSF cells or IgG index, or MRI gadolinium enhancement) seen at onset or within 7 d	CNS manifestations of infectious etiology (eg, syphilis, Lyme, HIV, HTLV-1, *Mycoplasma*)
Progressive worsening to a nadir between 4 h to 21 d after onset	Brain MRI lesions suggestive of MS
	History of optic neuritis

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; HTLV, Human T-Lymphotropic Virus; Ig, immunoglobulin; MRI, magnetic resonance imaging; MS, multiple sclerosis.
Data from Transverse Myelitis Consortium Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology 2002;59:499–505.

The response of ITM to corticosteroid therapy is usually disappointing.[41,252] In general, one-third of patients with idiopathic acute transverse myelitis recover with little or no sequelae, one-third are left with a moderate degree of permanent disability, and one-third have severe disabilities.[252] Spinal shock at presentation was highly predictive of a poor outcome.[252] Interestingly, a higher CSF glucose level (related to higher serum levels) may portend a poorer outcome.[41]

Pediatric TM

On the whole, the incidence of TM in children is much lower than that of the adult population. There appears to a bimodal distribution: toddlers younger than age 3, and children between 5 and 17 years. Males and females are equally affected. Antecedent infections (typically respiratory) or preceding vaccinations are common.[10,261,262] Because of the association with respiratory infections, there is a clustering of TM cases in the winter months.[262,263]

Compared with adults, pediatric TM is more frequently postinfectious, thoracic, centromedullary, and longitudinally extensive. The risk of conversion to MS is lower and functional recovery is often better than in the adult population.[261–266] Complete recovery appears to be the rule with poor outcome in only a minority of patients.[264,266,267] The course in pediatric TM has been divided into 3 phases: onset, plateau, and recovery. The plateau may last up to 4 weeks; if recovery has not started by the end of this period, the likelihood of recovery diminishes.[262,264,268] Beyond 6 months, any improvement is very improbable.[264]

CSF analysis frequently reveals pleocytosis and elevated protein; OCBs and increased IgG indices are rare.[261,262,264] Although the proportion of pediatric TM cases with LETM is higher than that of adults, the rate of NMO-IgG seropositivity is much lower.[262,269] This low rate of NMO-IgG seropositivity, with the typically monophasic clinical course and benign outcome in pediatric LETM, suggests that the pathobiological underpinnings of LETM in the pediatric population is different from that in adults.

Age younger than 3 years, requirement for respiratory support, severe impairment at onset, flaccid paralysis at onset, a more rapid progression to the nadir of weakness, CSF pleocytosis, and MRI T1-hypointensity at the time of diagnosis were poor prognostic indicators for recovery.[261,264,267,268] Early treatment with IV methylprednisolone had a significant positive effect on outcome.[264] The most common long-term neurologic complication of TM in children is bladder dysfunction.[261,264,266] As in adults, APTM, CSF OCBs, and the brain MRI lesions portend an increased risk for transition to MS; LETM carries a low risk of developing MS.[262]

Table 9 highlights the important CSF and MRI features of the different causes of TM.

PSEUDOEXACERBATION

Pseudoexacerbation is a phenomenon in which patients experience temporary worsening of previously suffered neurologic deficits. In demyelinating disorders, Uhthoff phenomenon is the most common underlying cause of pseudoexacerbation (authors' personal experience). Any condition that increases the patient's body temperature (eg, febrile illness, exercise, hot weather, hot baths, hot showers, stress, menses, dehydration) can cause a pseudoexacerbation. Any infection, particularly urinary tract infections (UTI) may result in pseudoexacerbation. In fact, any metabolic or physiologic derangements (eg, hyperglycemia, hypertension) has the potential to transiently worsen prior neurologic deficits. In conclusion, worsening of prior myelopathic symptoms in a patient with previous TM does not automatically implicate a recurrence or relapse. Pseudoexacerbation should be considered and investigations into the cause of pseudoexacerbation should be undertaken. Treatment of recurrent TM entails immunosuppressive therapy, but treatment of pseudoexacerbation involves addressing the underlying cause (eg, treating the UTI).

MIMICS OF TRANSVERSE MYELITIS

In making the diagnosis of TM, it is essential to remember that many noninflammatory etiologies may mimic the appearance of TM. Recognizing these entities is important, as the treatment and management strategies would be vastly different.

Entities important to recognize include vascular myelopathy, compressive myelopathy, metabolic/toxic myelopathy, neoplasms, and radiation myelitis. Selected etiologies are described in **Table 10**.

MANAGEMENT

Acute Management

Once the diagnosis of TM is made, immunotherapy should be instituted to stop the inflammatory process and therefore allow recovery to commence. In a small open-label trial, high-dose IV methylprednisolone was shown to improve the outcome in pediatric TM.[264] Despite the lack of randomized controlled studies, administration of high-dose IV corticosteroids (IV methylprednisolone 1 g daily for 3–7 days) should be started as early as possible in all patients with TM.[13]

In patients with poor or no response to corticosteroids, plasmapheresis should be offered,[13] with the rationale of removing humoral factors inciting TM. The benefits of plasmapheresis have been proven in acute attacks of CNS demyelinating diseases.[163–165,270] Early initiation of plasmapheresis (within 15 days of onset) is the best predictor of a favorable acute response and of improvement at 6 months.[164,165] The typical regimen is exchanges of 1.5 plasma volumes for 5 treatments over 10 days.[271] Plasmapheresis also has anecdotal support in various systemic autoimmune disorders (described previously).

Table 9
Highlighted CSF and MRI differences for various causes of TM

	CSF	MRI Features of Spinal Cord Lesion	MRI Features of Brain Lesions	Comments
Multiple sclerosis	OCB Increased IgG index	APTM Cigar-shaped Posterior cord	Periventricular plaques (Dawson fingers) Juxtacortical lesions T1 black holes Cortical atrophy	
Neuromyelitis optica	OCB rare	LETM	Periventricular lesions (not perpendicularly oriented), hypothalamic, lesions around 3rd and 4th ventricles, or brainstem lesions. Clinically silent lesions rare. "Cloudlike" gadolinium enhancement	NMO-IgG seropositivity
Neurosarcoidosis	Lymphocytic pleocytosis OCB rare Low glucose	LETM Favors cervical and thoracic cord Patchy enhancement Leptomeningeal enhancement	Leptomeningeal enhancement	Cranial neuropathies Pulmonary manifestations
Systemic lupus erythematosus	Pleocytosis OCBs infrequent	LETM Cord swelling	Subcortical lesions	Gray and white matter myelitis
Sjögren syndrome	Pleocytosis OCBs in a third of patients	Favors cervical cord LETM	Basal ganglial lesions Corpus callosal lesions rare	Cochlear neuropathy
Behcet disease	Mixed pleocytosis OCBs rare	LETM Posterolateral cord	Unilateral upper brainstem-diencephalic-basal ganglial Brainstem atrophy	
ADEM	Marked pleocytosis Increased protein No OCB IgG index negative	LETM	Acute, multiple, symmetric, supratentorial and infratentorial lesions, with one at least 1 cm in diameter Symmetric basal ganglial and thalamic lesions	Typically monophasic Antecedent infection or vaccination

(*continued on next page*)

Table 9
(*continued*)

	CSF	MRI Features of Spinal Cord Lesion	MRI Features of Brain Lesions	Comments
Atopic Myelitis	Bland CSF No OCB	APTM Cervical cord Posterior columns	No brain lesions	Marked hyperIgEemia
Idiopathic transverse myelitis	Increased protein OCBs may be seen	LETM Involves two-thirds of cross-sectional cord area Predilection for thoracic cord	No brain lesions	Typically monophasic Negative OCBs correlate with recurrence

Abbreviations: ADEM, acute disseminated encephalomyelitis; APTM, acute partial transverse myelitis; CSF, cerebrospinal fluid; LETM, longitudinally extensive transverse myelitis; MRI, magnetic resonance imaging; NMO-IgG, aquaporin-4-antibody; OCB, oligoclonal bands.

Although plasmapheresis may provide benefit beyond that obtained with steroids, patients with American Spinal Injury Association (ASIA) A level of disability may need IV cyclophosphamide as well.[272] IV cyclophosphamide appears to be efficacious in active inflammatory MS[273,274] and other autoimmune conditions. The major concern with cyclophosphamide is the adverse effect profile, which includes nausea, hemorrhagic cystitis, and malignancies.

In high cervical cord lesions extending into the medulla, respiratory failure may be fatal[275]; therefore, in such patients, vital signs and respiratory function should be vigilantly monitored. Other acute issues that may arise include immobility (and the complications thereof), urinary retention, constipation, and gastroparesis. These are discussed later in this article.

In cases of TM attributable to systemic autoimmune disease or acquired demyelinating disease, commencement of long-term immunomodulatory therapies would help prevent future attacks.[3] A discussion of these therapies is beyond the scope of this article.

The Importance of a Multidisciplinary Approach to Neurorehabilitation

A very important aspect of managing TM focuses on the multiple complications arising from the disease. The main thrust of long-term management is neurorehabilitation, the active process by which those disabled by injury or disease achieve a full recovery or, if full recovery is not possible, realize their optimal physical, mental, and social potential and are integrated into their most appropriate environment.[276] Successful neurorehabilitation is dependent on a multidisciplinary assessment that can develop goal-oriented programs tailored for the patient's specific needs; therefore, early consultation with the physical medicine and rehabilitation physician, physical therapist, occupational therapist, and psychologist/psychiatrist is vital. In fact, there is evidence that a multidisciplinary comprehensive care center is a highly efficient and cost-effective care delivery system that minimizes adverse events, lowers rehospitalization rate, and improves patients' perception.[277]

Mobility and Gait Impairment

Acute immobility

In the acute phase of TM, weakness may be severe and care should be taken to avoid the complications of prolonged immobility. Low molecular weight heparin or

Table 10
Mimics of TM

Etiology	Description	References
Vitamin B12 deficiency	May present as an isolated myelopathy or in combination with neuropathy, encephalopathy, and/or behavioral changes. Dorsal column impairment is the most common manifestation, followed by pyramidal dysfunction (the classic subacute combined degeneration of the cord). Hematologic manifestations may be absent up to 30% of patients with neurologic manifestations. MRI reveals T2-hyperintense signal in the posterior columns (the "inverted V" or "inverted rabbit ear" sign on axial views). In severe cases, MRI shows the "anchor" sign (because of involvement of the posterior, anterior, and pyramidal tracts).	422–425
Vitamin E deficiency	May cause a predominantly dorsal column syndrome associated with a peripheral neuropathy because of axonal degeneration. Preferentially affects the cervical cord. Clinically and radiologically similar to B12 deficiency.	426–428
Copper deficiency	May cause both myelopathy and optic neuropathy. Causes of acquired copper deficiency include malnutrition, zinc toxicity, Menke disease, bariatric surgery, gastrectomy, malabsorption syndromes, and use of copper chelating agents. Clinically and radiologically indistinguishable from B12 deficiency.	429–433
Nitrous oxide (N_2O) toxicity	Analgesic gas commonly abused because of euphoric effects. N_2O inactivates vitamin B12 by irreversible oxidation of the cobalt center of methylcobalamine, thereby inhibiting the methionine synthesis pathway. In healthy subjects, this does not cause clinical manifestations. In subclinically B12-deficient individuals, N_2O exhausts residual stocks of vitamin B12, leading to neurologic manifestations.	434–436
Neurolathyrism and neurocassivism	Neurolathyrism is caused by consumption of grass pea. Neurocassavism (konzo) is caused by bitter cassava root consumption. Both are found in malnourished populations, and are characterized by subacute paraparesis with prominent UMN features.	437

Intramedullary primary spinal cord tumors	May be ependymomas, astrocytomas, or hemangioblastomas. Typically cause an insidious, progressive myelopathy. Hemorrhage or infarction of the tumor may result in an acute presentation and radiologic appearance mimicking TM.	5
Primary CNS lymphoma	May give rise to a clinical and radiologic picture mimicking TM compounded by its corticosteroid-responsiveness. Congenital or acquired immunodeficiency is the only established risk factor. More common in middle-aged and older men. Insidious onset of myelopathy with back pain and constitutional symptoms. Serum lactate dehydrogenase may be elevated. CSF: lymphocytic pleocytosis, markedly elevated protein, and hypoglycorrachia. OCBs and IgG index are absent. Cytologic analysis may demonstrate malignant cells (large-volume CSF examination can increase the diagnostic yield). MRI: T2-hyperintensity, gadolinium enhancement, cord swelling, conus medullaris involvement, and concomittant brain lesions.	438–440
Intravascular lymphoma	Predominantly affects vessels in the skin and neurologic system. May mimic TM and even LETM. CSF: lymphocytic pleocytosis and increased protein, but no malignant cells. MRI: affects the conus medullaris (unlike TM).	441–446
Radiation myelitis	Early radiation myelopathy: begins 10–16 weeks after starting radiotherapy with predominantly sensory phenomena (including Lhermitte) and typically resolves spontaneously. Delayed radiation myelopathy: begins months or years following radiation exposure and manifests as a subacute or insidious myelopathy. Concurrent use of chemotherapeutic agents may cause widespread white matter necrosis owing to synergistic toxicity. Preexisting myelopathy from any cause may be risk factors for radiation myelitis. MRI: cord swelling on T1-weighted images, intramedullary T2-hyperintensity, ring-like gadolinium enhancement.	447–450

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; Ig, immunoglobulin; LETM, longitudinally extensive transverse myelitis; MRI, magnetic resonance imaging; OCB, oligoclonal bands; TM, transverse myelitis; UMN, upper motor neuron.

fondaparinux can be used to prevent venous thromboembolism.[278] Respiratory therapy may prevent atelectasis. In severely weak patients, pressure sores are a serious complication. Addressing risk factors (eg, malnutrition, impaired circulation), conscientious use of pressure-reducing measures (eg, frequent and regular turning, pressure-distributing positioning aids, sheepskins), and early mobilization are critical.[279]

Long-term mobility

Decreased mobility is a factor associated with diminished quality of life (QOL) following spinal cord injury (SC)I.[280] Improving mobility in an energy-efficient manner may thus improve health-related QOL following TM and should be a priority of rehabilitation.[281]

Bipedal locomotion is a complex phenomenon that requires intricate interactions between central pattern generators and peripheral reflexes that involve multiple neural networks, including the visual, vestibular, proprioceptive, and corticospinal systems.[282] Walking parameters can be affected by age, weight, spasticity, lower limb strength, balance, pain, duration of rehabilitation, cord lesion level, and the presence of other comorbidities. Functional walking has several requisites, including safety (which dictates the need for walking aids), speed, comfort, and distance.[283]

Velocity is one of the most important parameters in determining functional ambulation, particularly community ambulation[283]; SCI patients have tremendous difficulty achieving the speed needed to cross an intersection safely.[284] Following nontraumatic SCI, although inpatient rehabilitation may improve walking abilities, gait speed often remains impaired and insufficient to safely negotiate community environments.[285] **Table 11** describes concepts and strategies in managing mobility following TM.

The benefits of physical exercise extend beyond improvements in strength and functional capacity; mood, fatigue, balance, and QOL can also improve.[286] Exercise also carries anti-inflammatory benefits.[287]

Spasticity

Spasticity is the velocity-dependent increase in muscle tone owing to disruption of the descending corticospinal, vestibulospinal, and reticulospinal pathways. It often affects the patient by causing muscle stiffness, spasms, pain, and clonus. Paroxysmal tonic spasms are sudden, episodic, brief, painful, stereotypic, dystonic contractions that may occur following TM.[3,288] Spasticity may result in pain, interrupted sleep, and impaired ambulation.[288]

Although some degree of spasticity may protect against osteoporosis,[289] and is needed for weight bearing to allow ambulation, excessive spasticity can disrupt activities of daily living (eg, transferring, hygiene, sexual activity). Successful treatment of spasticity can be attained with an integrated multidisciplinary approach. **Table 12** summarizes management options for spasticity.

Movement Disorders

Movement disorders that may be complicate TM include propriospinal myoclonus (PSM), periodic limb movement disorder (PLMS) and restless leg syndrome (RLS). PSM is an unusual movement disorder, sometimes seen after spinal cord lesions, characterized by myoclonic jerks arising in muscles corresponding to a myelomere (myoclonic generator) and spreading rostrally and caudally to the other myotomes.[290] Drug therapy of PSM is disappointing but there are reports of treatment with benzodiazepines, zonisamide, and valproate.

Table 11
Management options for addressing long term mobility issues following transverse myelitis

Therapy/Device/ Concept	Description	References
Conventional therapy	Focuses on compensatory strategies for nonremediable neurologic deficits. Focuses on strengthening muscles above the level of the lesion, and unaffected muscles below the level of the lesion.	
Activity-based therapy	Interventions that provide activation of the neuromuscular system below the level of lesion with the goal of retraining the nervous system to recover a specific motor task.	[451]
Ankle-foot orthoses (AFOs)	AFOs can support the weakened musculature around the ankle. AFOs address excess plantar flexion during initial contact, stabilize the ankle for effective push-off during late stance, and prevent toe-drag during swing.	[452]
Functional electrical stimulator devices	Can reduce toe drag, circumduction, pelvic obliquity, and genu recurvatum, improving energy efficiency and facilitating safety and walking duration. Long-term use results in stable improvements of walking performance that persist even when the device is turned off. Adherent use of a dorsiflexion assist device may enhance the fidelity of activation of motor cortical regions and the descending corticospinal connections that control the swing phase of ambulation.	[286,453,454]
Robot-assisted gait training	Different systems are commercially available, including the "Lokomat," the "LokoHelp," and the "Gait trainer."	[455]
Neuromuscular electrical stimulation (NMES)	Helpful in improving interlimb coordination during locomotion	[456]
Dalframpridine	Dalframpridine is the extended-release, oral form of 4-aminopyridine approved by the Food and Drug Administration that has been shown to improve the walking ability in patients with multiple sclerosis by improving conduction along demyelinated axons.	[457]

PLMS and RLS have been reported as a consequence of spinal cord pathologies, including TM, and may be related to the emergence of spasticity.[291] These disorders may impair sleep quality and, as such, should be treated. Serum ferritin levels should be ascertained, as iron-deficiency anemia is a common and treatable cause of RLS.[291] Caffeine, alcohol, nicotine, and medications that may aggravate RLS should be avoided. The first-line choice for pharmacologic therapy is a dopaminergic agonist (eg, ropinorole, pramipexole). Other options include levodopa, opiates, gabapentin, lamotrigine, or clonazepam.[292]

Bladder Dysfunction

Bladder dysfunction remains one of the most common and disabling consequences of TM[293]; UTI is the most common medical complication in myelopathic patients.[294]

Table 12
Management options for spasticity in patients with transverse myelitis

Management Strategy	Comment
Nonpharmacologic measures	Physical therapy, stretching exercises, orthotics, and aquatic therapy Useful for mild cases.
Pharmacologic therapy	Baclofen Tizanadine Dantrolene (must monitor liver function tests) Anticonvulsants Benzodiazepines Anticonvulsants and benzodiazepines are useful for paroxysmal tonic spasms. Sedation may limit the use of the above-mentioned drugs.
Botolinum neurotoxin	Particularly useful for nonambulatory patients with severe adductor spasms that complicate adequate perineal hygiene.
Intrathecal baclofen (ITB)	May be used when oral medications cause too much sedation. Patients must be carefully evaluated before ITB use because of serious risks associated with baclofen withdrawal.

Despite complete motor recovery following TM, bladder dysfunction often persists.[295] In general, 3 forms of bladder dysfunction may be present: detrusor overactivity (failure to store), detrusor-sphincter dyssynergia (DSD), and detrusor hypocontractility (failure to empty).

In acute TM, urinary retention from a hypocontractile "shocked" bladder (detrusor areflexia or hyporeflexia) often necessitates placement of a urinary catheter.[293,295] Similar to how UMN signs appear following spinal shock, detrusor hyperreflexia typically develops, characterized by frequency, urgency, urge incontinence, and the sensation of bladder spasms[295,296]; in fact, the resolution of spinal shock and subsequent emergence of UMN signs may parallel similar changes in the bladder.[293] Some patients experience DSD, where insufficient external urinary sphincter relaxation during detrusor contraction results in urinary retention, increasing the risk for vesicoureteral reflux, infection, and nephrolithiasis.[296] Patients with DSD can also report urgency, frequency, incontinence, urinary hesitancy, and a sensation of incomplete bladder emptying after voiding.[297] More infrequently, a hypotonic, overly compliant bladder (failure to empty) may present with frequency, overflow incontinence, and signs of incomplete emptying.[297,298] Urinary symptoms are unreliable in differentiating poor bladder compliance from urinary retention.[3]

Although ultrasonographic assessment of postvoid residual urine volume is useful, urodynamic studies (and hence, urologic consultation) and renal ultrasound are often required to properly characterize the nature of bladder dysfunction, plan management, and identify those at risk for future complications.[295,298] **Table 13** summarizes the various problems of bladder dysfunction and management options.

Gastrointestinal Dysfunction

TM may result in gastrointestinal dysfunction following perturbation of the autonomic pathways of the spinal cord. In the setting of spinal shock, there is an increased risk for gastroduodenal ulceration and hemorrhage, paralytic ileus, acute gastric dilatation, and atypical presentations of acute abdominal pathology.[299]

Table 13
Managing the urinary dysfunction following transverse myelitis

	Treatment Options	Comments
Detrusor hyperreflexia (failure to store)	• Anticholinergic agents (eg, trospium, fesoterodine, oxybutynin, tolterodine) • Selective M2- and M3-antimuscarinics (darifenacin and solifenacin) • Intravesical atropine, oxybutinin, capsaicin, or resiniferatoxin • Detrusor muscle botulinum toxin A injection • Suprapubic vibration ("Queen Square bladder stimulator")	Common side effects include dry mouth and constipation. Contraindicated in patients with angle-closure glaucoma and mechanical bladder outlet obstruction. Nonselective agents should be used cautiously, if at all, in patients with cognitive dysfunction.
Detrusor-sphincter dyssynergia	• Alpha-1 adrenergic antagonists (eg, tamsulosin) • Clean intermittent catheterization (CIC) • Suprapubic vibration ("Queen Square bladder stimulator") • Neuromodulation (InterStim) • Intrasphincteric botulinum toxin • Indwelling Foley catheter • Suprapubic catheter	Alpha antagonists may cause hypotension, tachycardia, and bladder incontinence, particularly in those patients with coincident bladder spasms. CIC should be considered if postvoid residual volume exceeds 100 mL. Patients with sacral nerve stimulators cannot undergo MRIs. Indwelling Foley catheters are contraindicated in females.
Frequent urinary tract infections	Appropriate antibiotics Prophylactic antibiotic therapy Cranberry preparations Vitamin C supplementation	Cystoscopic evaluation may be needed to look for bladder trabeculations that serve as a nidus for infections.
Painful bladder spasms	Pharmacotherapy Timed voiding Neuromodulation	Pharmacotherapy: baclofen, benzodiazepines, hyoscine butylbromide, gabapentin and cannabinoids.
Nocturia	Behavioral measures Pelvic floor exercises Imipramine Desmopressin (DDAVP) Bladder rehabilitation	Avoid alcoholic and caffeinated beverages after 5 PM, to limit fluid intake in the evening, to avoid any fluids 2 h before bedtime and to void before going to bed.

Data from Refs.[3,297,298,458–465]

Gastroparesis

Gastroparesis (presenting with nausea, vomiting, pain, bloating, and/or early satiety) increases the risk of reflux and aspiration of gastric contents. It has been reported following cervical cord, thoracic cord, and cervico-medullary junction lesions.[300–303]

Gastroparesis may occur in the acute and chronic phases of TM. **Table 14** summarizes the management of gastroparesis.

Neurogenic bowel dysfunction

Bowel dysfunction is a source of considerable psychosocial disability, limiting the ability to work and affecting patients' QOL.[304] It may manifest as either constipation or fecal incontinence. The exact pathophysiology of bowel dysfunction in TM is unclear, but may because of disruption of the extrinsic neurologic control of gut and sphincter function, pelvic floor musculature, autonomic dysfunction, and/or impaired anorectal sensation.[304] Psychiatric disorders and medications also contribute to bowel dysfunction. For example, although opioid narcotics and anticholinergic drugs cause constipation, baclofen can theoretically alter the response to rectal distension and the threshold of conscious rectal sensation and cause fecal incontinence.[304] Management strategies for neurogenic bowel dysfunction are summarized in **Table 14**.Transanal irrigation (TAI) can be carried out using either a rectal balloon catheter or a cone-shaped colostomy tip. In a retrospective study of 348 patients (either constipation or fecal incontinence) during a 10-year period, TAI showed benefit in treating neurogenic bowel dysfunction.[305]

Miscellaneous gastrointestinal disorders

Hemorrhoids (and hemorrhage) are more frequent in patients with bowel dysfunction and is likely a consequence of straining and the use of suppositories and enemas.[299]

Gallbladder disease is also more prevalent following SCI.[299]

Superior mesenteric artery syndrome (where the third part of the duodenum is intermittently compressed by the vessel) causes vomiting when supine. Rapid weight loss, prolonged supine positioning, and the use of spinal orthosis are predisposing factors.[299]

Sexual Dysfunction

Sexuality is a fundamental aspect of health at the core of individual identity and influences a person's well-being.[306] Sexual dysfunction is a frequent complication of spinal cord lesions and has been shown to increase the risk of suicide.[307] As the incidence of TM is higher in the second and fourth decades of life, it affects adolescents or young adults who are sexually active.

Sexual dysfunction may be a direct consequence of damage to the autonomic and sensory pathways in the spinal cord following TM. Indirectly, complications of TM, including the psychological response to disability, spasticity, immobility, pressure ulcers, pain, and sphincter dysfunction, affect sexual function. Psychological dysfunction contributes more to sexual dysfunction than the actual physical disabilities.[308] Comorbidities (eg, mood disorders, diabetes) and medications are other important contributors to sexual dysfunction.

An open, frank, and nonjudgmental discussion about sexual function, expectations, beliefs, preferences, and the potential complications from TM should be undertaken with the patient. Including the patient's partner in such discussions is often helpful. A medical assessment of the reproductive system should be conducted as part of the multidisciplinary approach to TM.[306] Skin, bladder, and bowel care before sexual activity is important.[306] Autonomic dysreflexia (see later in this article) is a potentially dangerous consequence of sexual activity. Because of diminished or absent sensation, skin breakdown may occur from excessive friction, and in men, there is an increased risk of penile trauma.

Following spinal cord damage, most men can have some form of erection (psychogenic or reflexogenic) but these are often insufficiently predictable, rigid, or long

Table 14
Management of gastrointestinal dysfunction in patients with transverse myelitis

Problem	Management Strategies
Gastroparesis	Stop drugs that inhibit gastrointestinal motility (eg, narcotics, calcium channel blockers, anticholinergics). Consultation with a gastroenterologist for endoscopy, gastric emptying studies, and investigations to characterize the nature of dysmotility. Gastric decompression with a nasogastric tube, bowel rest, intravenous fluids, and proton-pump inhibitors or gastric H2-receptor blockers should be considered. Prokinetic agents (eg, metoclopramide, macrolide antibiotics, bethanecol or pyridostigmine) may be used. Tardive dyskinesia is a risk of metoclopramide use. Gastric electrical stimulation (Enterra therapy) and endoscopic injection of botulinum neurotoxin may be of potential benefit. In refractory cases, surgical interventions like pyloroplasty may be needed.
Constipation	*General measures*: high-fiber diet, bulking agents, increased fluid intake (at least 2 L daily), physical exercise, and establishing a regular toileting routine (best accomplished after breakfast to take advantage of the gastrocolic response, which peaks about 30 minutes after eating). Stimulant or osmotic laxatives (senna and bisacodyl) can be titrated to produce a satisfactory response (without producing liquid stool). Osmotic laxatives, although effective, can produce liquid stool with subsequent incontinence. Rectal stimulants have a predictable time of response. Begin with a glycerine suppository, progressing to bisacodyl, sodium citrate micro-enema, and ultimately a phosphate enema. Biofeedback may help, particularly in pelvic floor incoordination. Neostigmine in combination with glycopyrrolate has been shown to be effective. 4-aminopyridine may improve constipation. Digital stimulation of the anal canal serves to manually disimpact the rectum. Abdominal massage may be helpful. For refractory cases: colostomy, neuromodulation, Malone Antegrade Continence Enema. Transanal irrigation (TAI).
Fecal incontinence	Mild and infrequent: loperamide, codeine phosphate. Antidiarrheal drugs should be used with caution if incontinence and constipation coexist, and periodic checks for impaction may be required. Fecal impaction is a common complication and patients experience anorexia, nausea, and spurious diarrhea (liquid stool passing around the blockage). Biofeedback is another useful tool. Anal plugs or pads may be needed. Severe cases: surgical intervention (eg, dynamic graciloplasty, artificial bowel sphincter, and sacral nerve stimulation). TAI

Data from Refs.[299,304,305,466,467]

lasting to allow sexual intercourse.[309–311] Only 25% of men with SCI have erections adequate for sexual intercourse[312]; erectile dysfunction is a great source of distress in men with SCI, even more so than the loss of functional independence or sphincter dysfunction.[313] A precise coordination of sympathetic, parasympathetic, and somatic

divisions of the nervous system is essential for normal antegrade ejaculation. This intricate neural network is easily disrupted following spinal cord damage, leading to ejaculatory dysfunction and, hence, infertility. Intact genital sensation is the most important positive predictive factor of male sexual function, whereas an important negative predictor of sexuality is the presence of spasticity.[314]

The effects of spinal cord lesions on female sexuality is much less studied than in males, mainly because of the preponderance of male patients with traumatic SCI and partly because female fertility is not affected.[308,315] Manifestations include decreased libido, lack of arousal, vaginal dryness, dyspareunia, and decreased genital sensation.[316]

An important point to emphasize to all patients is that although genital sensation is diminished, individuals are more likely to develop new erotogenous areas above the level of the lesion, or with time, learn to interpret altered autonomic input from genitoperineal stimulation[317,318]; it is, therefore, important to explore new methods of sexual expression. Also, access to programs for sexual rehabilitation that include a multidisciplinary spinal cord team, as well as support groups, may be a pivotal part of treatment. **Table 15** summarizes some management strategies for sexual dysfunction.

Autonomic Dysregulation

Autonomic dysfunction may occur in the acute or chronic phases of TM and appears to be present in lesions above the upper thoracic segments.

Acute spinal cord lesions may cause neurogenic shock. In addition, cardiac dysrhythmias (eg, bradycardia and arrest) may occur.[319] Initial management may require hemodynamic monitoring and management in an intensive care setting.

Orthostatic hypotension

Orthostatic hypotension (OH) may occur in both the acute and chronic phases of TM. OH is defined as a decrease in systolic blood pressure of 20 mm Hg or more or a decrease in diastolic blood pressure of 10 mm Hg or more when the subject moves from an upright to supine posture, regardless of whether symptoms occur.[320] Clinical manifestations include pallor, diaphoresis, light-headed dizziness, syncope, anxiety, and nausea.

It is more common with lesions above the upper thoracic spinal segments.[321] Loss of sympathetic nervous activity and reflex vasoconstriction lead to pooling of venous blood in the abdominal organs and lower limbs; ultimately, cardiac output (and arterial pressure) drops. The reflex tachycardia that occurs often cannot adequately compensate for this. Cerebral hypoperfusion from reduced cardiac output is responsible for its manifestations.

Thermodysregulation

Although classically reported following traumatic SCI, thermodysregulation is another potential complication of TM with lesions at T6 and above; it can be classified as poikilothermia, "quad fever," and exercise-induced hyperthermia.[319]

Disruption of the interomediolateral columns of the spinal cord and hypothalamic lesions likely contribute to thermodysregulation following TM.[322] Perturbed heat dissipation mechanisms, in particular defective sweating (possibly owing to disruption of the descending sudomotor pathways), is believed to be a major contributor to thermodysregulation. Urinary dysfunction following TM often leads to voluntary restriction of fluid intake; further exacerbating thermodysregulation.[323]

"Quad fever" can occur in the acute phase and patients often present with fever.[319] Needless to say, a thorough workup should be undertaken to rule out infection, thromboembolism, inflammation, and atelectasis before attributing pyrexia to "quad fever."

Table 15
Management strategies for sexual dysfunction in patients with transverse myelitis

Problem	Management Strategies
Reduced libido	Stop any offending medication (particularly selective serotonin reuptake inhibitors). Consider using bupropion. Check free testosterone levels (in both men and women) - testosterone replacement therapy for deficient states.
Erectile dysfunction	Phosphodiesterase 5 inhibitors (sildenafil, tadalafil, and vardenafil). If unresponsive to oral agents, intracavernosal alprostadil injection, intraurethral alprostadil pellet, penile tension rings, vacuum devices, implantable penile prostheses, and sacral neuromodulation (Sacral Anterior Root Stimulator Implants) may be considered.
Ejaculatory dysfunction (affecting fertility)	Strong afferent stimulation and intense activation of the autonomic nervous system is needed to trigger the ejaculatory reflex. Penile vibratory stimulation (PVS) is the first line of treatment. Midodrine may be used as an adjunct to PVS in men who failed PVS alone. Rectal probe electro-ejaculation may be used but frequently results in retrograde ejaculation and may cause significant discomfort. Surgical techniques for sperm retrieval (eg, Brindley reservoir, microsurgical aspiration of spermatozoa from the vas deferens, or testicular biopsy) may also be considered if other measures fail.
Female orgasmic dysfunction	Manual and vibratory clitoral stimulation (eg, Eroscillator). Clitoral vacuum suction device (Eros) is approved by the Food and Drug Administration for female orgasmic dysfunction.
Lubrication dysfunction	Lubricants Topical estrogen Clitoral vacuum suction device (Eros) Estrogen replacement therapy

A description of the various considerations and measures to improve sexual activity and function in patients with spinal cord lesions is beyond the scope of this article. An excellent resource is the clinical practice guideline published by the Consortium for Spinal Cord Medicine.[306]
Data from Refs.[306,317,465,468–472]

Exercise-induced hyperthermia as a result of Uhthoff phenomenon and heat-induced fatigue is important to recognize.[323] Approximately 60% to 80% of patients with MS experience transient worsening of neurologic symptoms as a result of elevated body temperature (ie, Uhthoff phenomenon).[323]

In addition to defective sweating (hypohidrosis), profuse sweating (hyperhidrosis) can occur above the level of the lesion with little or no sweating below it. Episodic hyperhidrosis may be associated with episodes of autonomic dysreflexia.[319]

Autonomic dysreflexia

Autonomic dysreflexia (AD) is a well-recognized chronic complication of SCI and may occur following TM. It usually occurs in subjects with lesions above the outflow to the splanchnic and renal vascular beds (T5-6). AD is characterized by paroxysms of excessive, uninhibited sympathetic output leading to hypertension, bradycardia

(although tachycardia may occur), pounding headache, piloerection, nasal congestion, anxiety, nausea, chills and shivering, flushing, and profuse sweating above the level of the lesion[319,324–326]; severe cases may result in myocardial ischemia, seizures, retinal detachment, intracranial hemorrhage, hypertensive emergency, reversible posterior leukoencephalopathy, and even death.[325,327–329]

The higher the level of the lesion, the more severe the cardiovascular dysfunction; complete SCI is associated with a higher incidence of AD compared with incomplete lesions.[325] Any stimuli below the affected spinal level may precipitate AD, including bladder catheterization, manipulation of an indwelling catheter, DSD, UTI, bladder percussion, sexual activity, fecal impaction, pressure sores, ingrown toenails, sacral stress fracture, and use of devices for ejaculation.[319,325,330–332] In most cases, AD is related to bladder distention or bowel impaction.[325,333]

Table 16 summarizes the management strategies for AD.

Pain and Sensory Complaints

Sensory phenomena are a common complication of TM. Early recognition and intervention may prevent chronic pain syndromes.[261] TM-related pain may be classified as nociceptive or neuropathic. Nociceptive pain is related to musculoskeletal and visceral (eg, biliary colic) sources. Neuropathic pain may be related to complex regional pain syndromes, segmental deafferentation, radiculopathy, or cord damage. Two unique types of neuropathic pain are recognized: (1) a segementally distributed radicular pain at the level of the lesion; and (2) a late-onset central dysesthesia syndrome below the level of the lesion, characterized by a stimulus-independent, continuous pain.[334]

Treatments include oral tricyclic antidepressants, anticonvulsants, serotonin-norepinephrine reuptake inhibitors, nonsteroidal anti-inflammatory drugs, or narcotics. Lidocaine patches, topical capsaicin, and botulinum neurotoxin are other options.[3,297] Anticonvulsants may be useful for Lhermitte phenomenon.[335] Biofeedback, physical therapy, acupuncture, and transcutaneous electrical nerve stimulation are nonpharmacologic measures that can be considered. Dorsal root entry zone ablation is useful for radicular pain at the level of the lesion. Consultation with a pain management team may be needed.

A rare complication of TM is neurogenic pruritus, characterized by a dermatomal distribution of pruritus that is often associated with hypoesthesia or hyperesthesia; it responds poorly to medical therapy.[336]

Osteoporosis

Osteoporosis is a known complication of SCI[337,338] and may be a consequence of both the cord lesion, subsequent immobilization, and neuroendocrinological dysfunction.[339,340] The duration of paralysis correlates with the degree of bone loss.[340] The pathobiological underpinnings of bone demineralization are unclear and, interestingly, its pattern differs from that seen in endocrine-related osteoporosis.[339]

Bone loss begins immediately after SCI and is greater below the level of the lesion. In the first months, demineralization occurs exclusively in the sublesional areas and predominantly in weight-bearing skeletal sites.[339,340] The largest decrease in bone mass occurs during the first 6 months after injury and stabilizes after 12 to 16 months, at which point approximately two-thirds of the original bone mass is close to the threshold for pathologic fractures.[341] Hypercalcemia and hypercalciuria resulting from increased bony resorption may increase the risk of nephrolithiasis.[339,340] Women are at greater risk of osteoporosis following SCI.[340]

Supplementation with calcium and vitamin D is a cost-effective and easily implemented method of addressing bone loss. Physical exercise (weight-bearing activities,

Table 16
Management strategies for autonomic dysregulation following transverse myelitis

Problem	Management Strategy
Orthostatic hypotension	*Nonpharmacologic*: increasing fluid intake; a high salt diet (>8 g/d); avoiding a hot environment; avoiding large carbohydrate-rich meals; avoiding prolonged recumbency; application of external counterpressure (eg, abdominal binding, compression stockings); functional electrical stimulator devices (induces intermittent muscle contractions and therefore increasing venous return); exercise training may also induce positive changes in autonomic cardiovascular regulation. *Pharmacologic*: midodrine; L-threo-3,4-dihydroxyphenylserine (L-DOPS); fludrocortisone.
Thermodysregulation	Adequate hydration. Exercising or working during cooler hours of the day. Cold showers. Regional cooling devices. Precooling by immersing the lower extremities in cold water before thermal stress, allows the lower limbs to serve as "heat sinks." Dalframpridine.
Autonomic dysreflexia	*Acute Management* Identify the possible trigger and decrease afferent stimulation. Sit the patient up to cause an orthostatic decrease in the blood pressure. Loosen the clothing and other constrictive devices. Check the blood pressure every 2–5 minutes until the patient is stable. The best antihypertensive medications have a rapid onset and short duration of action (eg, nitrates, hydralazine and immediate-release nifedipine); 10 mg nifedipine may be given using the "bite and swallow" method. Alternatively, 1 inch of 2% nitropaste can be applied above the level of the lesion and wiped off when the hypertensive episode subsides. *Preventive Measures* Preventative measures are the most effective approach. Prevention of pressure sores and addressing urinary and bowel dysfunction are imperative. Individuals should carry a medical emergency card for AD. Pharmacologic prevention: Alpha-1 antagonists (terazosin and prazosin); gabapentin; prostaglandin E2; phenozybenzamine.

Data from Refs.[323,325,473–480]

verticalization, and aided-walking systems) has been shown to have an osteogenic influence in healthy subjects and in those with SCI. Functional electrical stimulator–induced mechanical loading has also been shown to conserve bone density, but this benefit is seen only if it is started as early as possible following spinal cord damage (less than 6 months postinjury). Bisphosphonates and salmon calcitonin are potentially beneficial therapies.[339]

Vitamin D Deficiency

Vitamin D deficiency is commonly found in patients with both acute and chronic SCI.[342] It may lead to elevated parathyroid hormone levels that subsequently increase

bone loss.[343] Aside from its role in osteoporosis, Vitamin D is important in the immunopathogenesis of TM.

Low vitamin D levels have been linked to TM[344] as well as various autoimmune disorders, including MS,[345,346] SLE,[347] and AS.[348] In MS, suboptimal vitamin D levels increase the relapse rate as well as the risk of developing the disease. Interestingly, low vitamin D levels have been shown to correlate with an increased risk for recurrent TM.[349,350] The immunologic role of vitamin D is fascinating but remains unclear. Reductions in proinflammatory agents, such as interleukin (IL)-6, IL-1-beta, gamma-interferon, and IL-17 have been observed with vitamin D supplementation.[351,352] Optimal vitamin D levels have been shown to suppress Th17-mediated autoimmunity[353] and augment T-cell regulatory cell populations, providing a putative mechanism for preventing autoimmunity.[354]

Factors contributing to vitamin D deficiency include inadequate dietary intake and sun exposure. The primary source of vitamin D in humans is sunlight.[355] TM-related complications, including immobility and thermodysregulation, as well as photosensitivity in some autoimmune disorders, limit sunlight exposure. Many patients also harbor the misconception that consuming foods with calcium and vitamin D causes nephrolithiasis.[342] The use of hepatically metabolized anticonvulsants to treat various complications of TM further exacerbates vitamin D deficiency.[356]

The “normal” value of 25-hydroxyvitamin D levels remains 10 to 20 ng/mL in many institutions and commercial laboratories.[342] Unfortunately, recommendations about vitamin D intake from health agencies lags behind developments in the field.[357] An amount of 5000 IU per day has been shown to reduce the number of MS relapses[358] and intakes up to 10,000 IU per day appear safe.[359] Vitamin D3 appears superior to vitamin D2[360] and is available at all retail pharmacies in the United States for a low price. Patients seen at the neuroimmunologic disease clinic at our institution are encouraged to take between 5000 and 10,000 IU of vitamin D3 daily to achieve serum levels of between 60 and 80 ng/mL.

Adequate vitamin D levels have several other notable benefits, including a decreased risk of breast and colon cancer,[361,362] improved muscle strength,[363] decreased frequency of falls,[364] and diminished musculoskeletal pain.[365]

Psychological Considerations

In patients presenting for the first time with TM, consultation with a clinical psychologist or psychiatrist is valuable in addressing its understandably devastating impact on the patient’s QOL. Indeed, a recent study found that almost 90% of parents of children with TM perceive a need for psychiatric care but only a quarter receive it.[277]

The loss of functional independence, along with sphincter and sexual dysfunction, would be expected to negatively affect the patient’s psychological constitution and adversely affect future expectations. Mood disorders and emotional changes following TM may also be a consequence of the pathobiological changes engendered by the underlying disease process. Mood disorders, fatigue, and cognitive impairment are well-recognized sequelae of MS and autoimmune disorders like BD, SS, and SLE.[56,102,103,105,366] Additionally, certain immunomodulatory drugs (eg, interferon-beta) may cause depression.[367]

Recognition of the neuropsychiatric symptoms associated with TM is important because it affects the patient’s QOL. Formal neuropsychological testing may help identify the mood disorder or cognitive domain(s) affected. Consultation with a clinical psychologist and/or psychiatrist is useful is deciding if the patient can be managed with counseling, psychotherapy, group therapy, and/or pharmacotherapy. Cognitive

dysfunction may be treated with memantine or anticholinesterase inhibitors like donepezil.[297]

SUMMARY

TM constitutes a pathobiologically heterogeneous syndrome, with immune-mediated, inflammatory damage of the spinal cord at its core. A detailed history and thorough physical examination are indispensible. The most important investigation to undertake is an MRI of the entire spinal axis and the brain. The location and length of the lesion are important discriminators with etiologic and prognostic significance.

APTM is commonly attributable to MS. Although LETM is characteristic of NMO, longitudinally extensive lesions may occur in other diseases as well. The brain MRI and CSF OCBs are powerful predictors of conversion to MS. NMO-IgG seropositivity has a high specificity for NMO.

The epidemiologic, clinical, radiologic, and longitudinal data seen in pediatric TM suggests that the pathobiological underpinnings are distinct from TM in the adult population. As such, caution should be exercised when applying findings from studies in the adult population to children and vice versa.

Although the application of set criteria for diagnosing ITM has resulted in a fairly homogeneous group of patients (clinically and radiologically), it remains possible that recurrent ITM represents a unique disease entity. More longitudinal studies are needed to elucidate the nature of recurrent ITM.

REFERENCES

1. Oppenheim H. Zum Capitel der Myelitis. Berl Klin Wchnschr 1891;28:761.
2. Cree BA, Wingerchuk DM. Acute transverse myelitis: is the “idiopathic” form vanishing? Neurology 2005;65:1857–8.
3. Frohman EM, Wingerchuk DM. Clinical practice. Transverse myelitis. N Engl J Med 2010;363(6):564–72.
4. de Seze J, Stojkovic T, Breteau G, et al. Acute myelopathies: clinical, laboratory, and outcome profiles in 79 cases. Brain 2001;124:1509–21.
5. Jacob A, Weinshenker BG. An approach to the diagnosis of acute transverse myelitis. Semin Neurol 2008;28:105–20.
6. Wingerchuk DM. Postinfectious encephalomyelitis. Curr Neurol Neurosci Rep 2003;3:256–64.
7. Transverse Myelitis Consortium Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology 2002;59:499–505.
8. Berman M, Feldman S, Alter M, et al. Acute transverse myelitis: incidence and etiologic considerations. Neurology 1981;31:966–71.
9. Jeffrey DR, Mandler RN, Davis LE. Transverse myelitis. Retrospective analysis of 33 cases, with differentiation of cases associated with multiple sclerosis and parainfectious events. Arch Neurol 1993;50:532–5.
10. Bhat A, Naguwa S, Cheema G, et al. The epidemiology of transverse myelitis. Autoimmun Rev 2010;9:A395–9.
11. Debette S, de Seze J, Pruvo JP, et al. Long-term outcome of acute and subacute myelopathies. J Neurol 2009;256:980–8.
12. Christensen PB, Wermuth L, Mulder DW, et al. Clinical course and long-term prognosis of acute transverse myelopathy. Acta Neurol Scand 1990;81:431–5.
13. Scott TF, Frohman EM, de Seze J, et al. Evidence-based guideline: clinical evaluation and treatment of transverse myelitis: report of the Therapeutics and

Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2011;77(24):2128–34.
14. Ditunno JF, Little JW, Tessler A, et al. Spinal shock revisited: a four-phase model. Spinal Cord 2004;42(7):383–95.
15. Fogelson J, Williams K. Compressive and traumatic myelopathies. Continuum (Minneap Minn) 2008;14(3):110–33.
16. Bakheit AM. Phantom limb sensations after complete thoracic transverse myelitis. J Neurol Neurosurg Psychiatry 2000;69(2):275–6.
17. Kempster PA, Rollinson RD. The Lhermitte phenomenon: variant forms and their significance. J Clin Neurosci 2008;15(4):379–81.
18. Layzer RB. Myeloneuropathy after prolonged exposure to nitrous oxide. Lancet 1978;312(8102):1227–30.
19. Todd NV. Priapism in acute spinal cord injury. Spinal Cord 2011;49(10):1033–5.
20. Hammond ER, Kerr DA. Priapism in infantile transverse myelitis. Arch Neurol 2009;66(7):894–7.
21. Kim SM, Go MJ, Sung JJ, et al. Painful tonic spasm in neuromyelitis optica: incidence, diagnostic utility and clinical characteristics. Arch Neurol 2012;69(8): 1026–31.
22. Tashiro K. Charles Edward Beevor. J Neurol 2001;248:635–6.
23. Brazis PW, Masdeu JC, Biller J. Spinal cord. In: Localization in clinical neurology. 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2007. p. 99–123.
24. Blumenfeld H. The neurologic exam as a lesson in neuroanatomy. In: Neuroanatomy through clinical cases. Sunderland (MA): Sinauer Associates, Inc; 2002. p. 49–82.
25. Wingerchuk DM, Hogancamp WF, O'Brien PC, et al. The clinical course of neuromyelitis optica (Devic's syndrome). Neurology 1999;53(5):1107–14.
26. Palace J, Leite MI, Nairne A, et al. Interferon beta treatment in neuromyelitis optica: increase in relapses and aquaporin 4 antibody titers. Arch Neurol 2010;67(8):1016–7.
27. Bot JC, Barkhof F, Lycklama à Nijeholt GJ, et al. Comparison of a conventional cardiac-triggered dual spin-echo and a fast STIR sequence in detection of spinal cord lesions in multiple sclerosis. Eur Radiol 2000;10(5):753–8.
28. Campi A, Pontesilli S, Gerevini S, et al. Comparison of MRI pulse sequences for investigation of lesions of the cervical spinal cord. Neuroradiology 2000;42(9): 669–75.
29. Scott TF. Nosology of idiopathic transverse myelitis syndromes. Acta Neurol Scand 2007;115:371–6.
30. Scott TF, Kassab SL, Singh S. Acute partial transverse myelitis with normal cerebral magnetic resonance imaging: transition rate to clinically definite multiple sclerosis. Mult Scler 2005;11(4):373–7.
31. Lennon VA, Wingerchuk DM, Kryzer TJ, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet 2004;364: 2106–12.
32. Weinshenker BG, Wingerchuk DM, Vukusic S, et al. Neuromyelitis optica IgG predicts relapse after longitudinally extensive transverse myelitis. Ann Neurol 2006;59:566–9.
33. McLean BN, Luxton RW, Thompson EJ. A study of immunoglobulin G in the cerebrospinal fluid of 1007 patients with suspected neurological disease using isoelectric focusing and the log IgG-index. A comparison and diagnostic applications. Brain 1990;113(Pt 5):1269–89.

34. Rodriguez A, Calogne M, Pedroza-Seres M, et al. Referral patterns of uveitis in a tertiary eye care center. Arch Ophthalmol 1996;114(5):593–9.
35. Frohman EM, Frohman TC, Zee DS, et al. The neuro-ophthalmology of multiple sclerosis. Lancet Neurol 2005;4(2):111–21.
36. Syme JA, Kelly JJ. Absent F-waves early in a case of transverse myelitis. Muscle Nerve 1994;17:462–5.
37. Misra UK, Kalita J. Can electromyography predict the prognosis of transverse myelitis? J Neurol 1998;245:741–4.
38. Frohman EM, Racke MK, Raine CS. Multiple sclerosis—the plaque and its pathogenesis. N Engl J Med 2006;354:942–55.
39. Cordonnier C, de Seze J, Breteau G, et al. Prospective study of patients presenting with acute partial transverse myelopathy. J Neurol 2003;250(12):1447–52.
40. Harzheim M, Schlegel U, Urbach H, et al. Discriminatory features of acute transverse myelitis: a retrospective analysis of 45 patients. J Neurol Sci 2004;217: 217–23.
41. Bruna J, Martinez-Yelamos S, Martinez-Yelamos A, et al. Idiopathic acute transverse myelitis: a clinical study and prognostic markers in 45 cases. Mult Scler 2006;12(2):169–73.
42. Sellner J, Luthi N, Buhler R, et al. Acute partial transverse myelitis: risk factors for conversion to multiple sclerosis. Eur J Neurol 2008;15(4):398–405.
43. Bourre B, Zephir H, Ongagna JC, et al. Long-term follow-up of acute partial transverse myelitis. Arch Neurol 2012;69(3):357–62.
44. Fisniku LK, Brex PA, Altmann DR, et al. Disability and T2 MRI lesions: a 20-year follow-up of patients with relapse onset of multiple sclerosis. Brain 2008;131: 808–17.
45. Barkhof F, Filippi M, Miller DH, et al. Comparison of MRI criteria at first presentation to predict conversion to clinically definite multiple sclerosis. Brain 1997; 120(pt 11):2059–69.
46. Bashir K, Whitaker JN. Importance of paraclinical and CSF studies in the diagnosis of MS in patients presenting with partial cervical transverse myelopathy and negative cranial MRI. Mult Scler 2000;6:312–6.
47. O'Riordan JI, Thompson AJ, Kingsley DP, et al. The prognostic value of brain MRI in clinically isolated syndromes of the CNSA 10-year follow up. Brain 1998;121:495–503.
48. Martinelli V, Comi G, Rovaris M, et al. Acute myelopathy of unknown etiology: a clinical, neurophysiological and MRI study of short and long-term prognostic factors. J Neurol 1995;242:497–503.
49. Perumal J, Zabad R, Caon C, et al. Acute transverse myelitis with normal brain MRI: long-term risk of MS. J Neurol 2008;255(1):89–93.
50. Qiu W, Wu JS, Zhang MN, et al. Longitudinally extensive myelopathy in Caucasians: a West Australian study of 26 cases from the Perth Demyelinating Diseases Database. J Neurol Neurosurg Psychiatry 2010;81:209–12.
51. Wingerchuk DM, Lennon VA, Pittock SJ, et al. Revised diagnostic criteria for neuromyelitis optica. Neurology 2006;66:1485–9.
52. Pittock SJ, Lennon VA, de Seze J, et al. Neuromyelitis optica and non organ-specific autoimmunity. Arch Neurol 2008;65:78–83.
53. Wingerchuk DM, Lennon VA, Lucchinetti CF, et al. The spectrum of neuromyelitis optica. Lancet Neurol 2007;6:805–15.
54. Jarius S, Jacobi C, de Seze J, et al. Frequency and specificity of antibodies to aquaporin-4 in neurological patients with rheumatic disorders. Mult Scler 2011; 17(9):1067–73.

55. Vitali C, Bombardieri S, Jonsson R, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002;61:554–8.
56. Govoni M, Padovan M, Rizzo N, et al. CNS involvement in primary Sjogren's syndrome: prevalence, clinical aspects, diagnostic assessment and therapeutic approach. CNS Drugs 2001;15:597–607.
57. Delalande S, de Seze J, Fauchais AL, et al. Neurologic manifestations in primary Sjögren syndrome: a study of 82 patients. Medicine (Baltimore) 2004;83: 280–91.
58. Alexander EL, Provost TT, Stevens MD, et al. Neurologic complications of primary Sjögren's syndrome. Medicine (Baltimore) 1982;61:247–57.
59. Escudero D, Latorre P, Codina M, et al. Central nervous system disease in Sjögren's syndrome. Ann Med Interne (Paris) 1995;146:239–42.
60. Kim SM, Water P, Vincent A, et al. Sjögren's syndrome myelopathy: spinal cord involvement in Sjogren's syndrome might be a manifestation of NMO. Mult Scler 2009;15:1062–8.
61. Konttinen YT, Kinnunen E, Von Bonsdorff M, et al. Acute transverse myelopathy successfully treated with plasmapheresis and prednisone in a patient with primary Sjogren's syndrome. Arthritis Rheum 1987;30:339–44.
62. Canhao H, Fonseca JE, Rosa A. Intravenous gammaglobulin in the treatment of central nervous system vasculitis associated with Sjögren's syndrome. J Rheumatol 2000;27:1102–3.
63. Alcântara C, Gomes MJ, Ferreira C. Rituximab therapy in primary Sjögren's syndrome. Ann N Y Acad Sci 2009;1173:701–5 (Contemporary Challenges in Autoimmunity).
64. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997; 40(9):1725.
65. West SG. Neuropsychiatric lupus. Rheum Dis Clin North Am 1994;20(1):129–58.
66. Eckstein C, Saidha S, Levy M. A differential diagnosis of central nervous system demyelination: beyond multiple sclerosis. J Neurol 2012;259(5):801–16.
67. Kovacs B, LaVerty T, Brent L, et al. Transverse myelopathy in systemic lupus erythematosus: an analysis of 14 cases and review of the literature. Ann Rheum Dis 2000;59:120–4.
68. Schulz SW, Shenin M, Mehta A, et al. Initial presentation of acute transverse myelitis in systemic lupus erythematosus: demographics, diagnosis, management and comparison to idiopathic cases. Rheumatol Int 2012;32(9): 2623–7.
69. Katsiari CG, Giavri I, Mitsikostas DD, et al. Acute transverse myelitis and antiphospholipid antibodies in lupus. No evidence for anticoagulation. Eur J Neurol 2011;18(4):556–63.
70. Bertsias GK, Ioannidis JP, Aringer M, et al. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. Ann Rheum Dis 2010;69(12):2074–82.
71. Espinosa G, Mendizabal A, Minguez S, et al. Transverse myelitis affecting more than 4 spinal segments associated with systemic lupus erythematosus: clinical, immunological, and radiological characteristics of 22 patients. Semin Arthritis Rheum 2010;39(4):246–56.
72. Birnbaum J, Petri M, Thompson R, et al. Distinct subtypes of myelitis in systemic lupus erythematosus. Arthritis Rheum 2009;60(11):3378–87.

73. D'Cruz DP, Mellor-Pita S, Joven B, et al. Transverse myelitis as the first manifestation of systemic lupus erythematosus or lupus-like disease: good functional outcome and relevance of antiphospholipid antibodies. J Rheumatol 2004;31: 280–5.
74. Tellez-Zenteno JF, Remes-Troche JM, Negrete-Pulido RO, et al. Longitudinal myelitis associated with systemic lupus erythematosus: clinical features and magnetic resonance imaging of six cases. Lupus 2001;10:851–6.
75. Provenzale JM, Barboriak DP, Gaensler RL, et al. Lupus-related myelitis: serial MR findings. Am J Neuroradiol 1994;15:1911–7.
76. Salmaggi A, Lamperti E, Eoli M, et al. Spinal cord involvement and systemic lupus erythematosus: clinical and magnetic resonance findings in 5 patients. Clin Exp Rheumatol 1994;12:389–94.
77. Mok CC, Lau CS, Chan EYT, et al. Acute transverse myelopathy in systemic lupus erythematosus: clinical presentation, treatment and outcome. J Rheumatol 1998;25:467–73.
78. Deodhar AA, Hochenedl T, Bennett RM. Longitudinal involvement of the spinal cord in a patient with lupus related transverse myelitis. J Rheumatol 1999;26: 446–9.
79. Neumann-Andersen G, Lindgren S. Involvement of the entire spinal cord and medulla oblongata in acute catastrophic-onset transverse myelitis in SLE. Clin Rheumatol 2000;19:156–60.
80. Katramados AM, Rabah R, Adams MD, et al. Longitudinal myelitis, aseptic meningitis, and conus medullaris infarction as presenting manifestations of pediatric systemic lupus erythematosus. Lupus 2008;17:332–6.
81. Theodoridou A, Settas L. Demyelination in rheumatic diseases. Postgrad Med J 2008;84:127–32.
82. Barile-Fabris L, Ariza-Andraca R, Olguin-Ortega L, et al. Controlled clinical trial of IV cyclophosphamide versus IV methylprenisolone in severe neurological manifestations in systemic lupus erythematous. Ann Rheum Dis 2005;64:620–5.
83. Sherer Y, Hassin S, Shoenfeld Y, et al. Transverse myelitis in patients with antiphospholipid antibodies—the importance of early diagnosis and treatment. Clin Rheumatol 2002;21:207–10.
84. Harisdangkul V, Doorenbos D, Subramony SH. Lupus transverse myelopathy: better outcome with early recognition and aggressive high-dose intravenous corticosteroid pulse treatment. J Neurol 1995;242:326–31.
85. Neuwelt CM. The role of plasmapheresis in the treatment of severe central nervous system neuropsychiatric systemic lupus erythematosus. Ther Apher Dial 2003;7:173–82.
86. Bartolucci P, Bréchignac S, Cohen P, et al. Adjunctive plasma exchanges to treat neuropsychiatric lupus: a retrospective study on 10 patients. Lupus 2007;16:817–22.
87. Armstrong DJ, McCarron MT, Wright GD. SLE-associated transverse myelitis successfully treated with rituximab (anti-CD20 monoclonal antibody). Rheumatol Int 2006;26:771–2.
88. Ye Y, Qian J, Gu Y, et al. Rituximab in the treatment of severe lupus myelopathy. Clin Rheumatol 2011;30(7):981–6.
89. Lu X, Gu Y, Wang Y, et al. Prognostic factors of lupus myelopathy. Lupus 2008; 17:323–8.
90. Wilson WA, Gharavi AE, Koike T, et al. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome: report of an international workshop. Arthritis Rheum 1999;42(7):1309–11.

91. Cervera R, Piette JC, Font J, et al. Antiphospholipid syndrome: clinical and immunologic manifestations and patterns of disease expression in a cohort of 1000 patients. Arthritis Rheum 2002;46:1019–27.
92. Kim JH, Lee SI, Park SI, et al. Recurrent transverse myelitis in primary antiphospholipid syndrome: case report and literature review. Rheumatol Int 2004;24: 244–6.
93. Rodrigues CE, de Carvalho JF. Clinical, radiologic, and therapeutic analysis of 14 patients with transverse myelitis associated with antiphospholipid syndrome: report of 4 cases and review of the literature. Semin Arthritis Rheum 2011;40(4): 349–57.
94. Tristano AG. Acute transverse myelitis as part of the catastrophic antiphospholipid syndrome in a systemic lupus erythematosus patient. Neurologia 2004;19: 774–5.
95. Rodrigues CE, Carvalho JF, Shoenfeld Y. Neurological manifestations of antiphospholipid syndrome. Eur J Clin Invest 2010;40(4):350–9.
96. Tourbah A, Clapin A, Gout O, et al. Systemic autoimmune features and multiple sclerosis. A 5-year follow up. Arch Neurol 1998;55:517–21.
97. Roussel V, Yi F, Jauberteau O, et al. Prevalence and clinical significance of antiphospholipid antibodies in multiple sclerosis: a study of 89 patients. J Autoimmun 2000;14:259–65.
98. Gaarg N, Zivadinov R, Ramanathan M, et al. Clinical and MRI correlates of autoreactive antibodies in multiple sclerosis patients. J Neuroimmunol 2007;187: 159–65.
99. Stosic M, Ambrus J, Garg N, et al. MRI characteristics of patients with antiphospholipid syndrome and multiple sclerosis. J Neurol 2010;257(1):63–71.
100. Szmyrka-Kaczmarek M, Pokryszko-Dragan A, Pawlik B, et al. Antinuclear and antiphospholipid antibodies in patients with multiple sclerosis. Lupus 2012;21: 412–20.
101. The International Study Group for Behcet's disease. Criteria for diagnosis of Behcet's disease. Lancet 1990;335:1078–80.
102. Al-Araji A, Kidd D. Neuro-Behcet's disease: epidemiology, clinical characteristics, and management. Lancet Neurol 2009;8:192–204.
103. Yesilot N, Mutlu M, Gungoer O, et al. Clinical characteristics and course of spinal cord involvement in Behcet's disease. Eur J Neurol 2007;14:729–37.
104. Ideguchi H, Suda A, Takeno M, et al. Neurological manifestations of Behcet's disease in Japan: a study of 54 patients. J Neurol 2010;257(6):1012–20.
105. Akman-Demir G, Serdaroglu P, Tasci B, et al. Clinical patterns of neurological involvement in Behçet's disease: evaluation of 200 patients. Brain 1999;122: 2171–81.
106. Moskau S, Urbach H, Hartmann A, et al. Multifocal myelitis in Behcet's disease. Neurology 2003;60(3):517.
107. Kocer N, Islak C, Siva A, et al. CNS involvement in neuro-Behcet syndrome: an MR study. AJNR Am J Neuroradiol 1999;20:1015–24.
108. Monaco AL, Corte RL, Caniatti L, et al. Neurological involvement in North Italian patients with Behcet's disease. Rheumatol Int 2006;26:1113–9.
109. Lee SH, Yoon PH, Park SJ, et al. MRI findings in neuro-Behcet's disease. Clinical Radiol 2001;56:485–94.
110. Fukae J, Noda K, Fujishima K, et al. Subacute longitudinal myelitis associated with Behcet's disease. Intern Med 2010;49:343–7.
111. Morrissey SP, Miller DH, Hermaszewski R, et al. Magnetic resonance imaging of the central nervous system in Behcet's disease. Eur Neurol 1993;33:287–93.

112. Yoshioka H, Matsubara T, Miyanomae Y, et al. Spinal cord MRI in neuro-Behcet's disease. Neuroradiology 1996;38:661–2.
113. Mascalchi M, Cosottini M, Cellerini M, et al. MRI of spinal cord involvement in Behcet's disease: case report. Neuroradiology 1998;40(4):255–7.
114. Green AL, Mitchell PJ. Spinal cord neuro-Behcet's disease detected on magnetic resonance imaging. Australas Radiol 2000;44(2):201–3.
115. Desphande DM, Krishnan C, Kerr DA. Transverse myelitis after lumbar steroid injection in a patient with Behcet's disease. Spinal Cord 2005;43:735–7.
116. Vuolo L, Bonzano L, Roccatagliata C, et al. Reversibility of brain lesions in a case of neuro-Behcet's disease studied by MR diffusion. Neurol Sci 2010; 31(2):213–5.
117. Kidd D, Steuer A, Denman AM, et al. Neurological complications in Behçet's syndrome. Brain 1999;122:2183–94.
118. Coban O, Bahar S, Akman-Demir G, et al. Masked assessment of MRI findings: is it possible to differentiate neuro-Behcet's disease from other central nervous system. Neuroradiology 1999;41:255–60.
119. Zhao B, He L, Lai XH. A case of neuro-Behcet's disease presenting with lumbar spinal cord involvement. Spinal Cord 2010;48:172–3.
120. Piptone N, Olivieri I, Padula A, et al. Infliximab for the treatment of neuro-Behcet's disease: a case series and review of the literature. Arthritis Rheum 2008; 59:285–90.
121. Serkova NJ, Christians U, Benet LZ. Biochemical mechanisms of cyclosporine neurotoxicity. Mol Interv 2004;4:97–107.
122. Kotake S, Higashi K, Yoshikawa K, et al. Central nervous system symptoms in patients with Behçet disease receiving cyclosporine therapy. Ophthalmology 1999;106:586–9.
123. Kato Y, Numaga J, Kato S, et al. Central nervous system symptoms in a population of Behçet's disease patients with refractory uveitis treated with cyclosporine A. Clin Experiment Ophthalmol 2001;29:335–6.
124. Kötter I, Günaydin I, Batra M, et al. CNS involvement occurs more frequently in patients with Behçet's disease under cyclosporin A (CSA) than under other medications: results of a retrospective analysis of 117 cases. Clin Rheumatol 2006;25:482–6.
125. Lower EE, Broderick JP, Brott TG, et al. Diagnosis and management of neurological sarcoidosis. Arch Intern Med 1997;157(16):1864–8.
126. Chapelon C, Ziza JM, Piette JC, et al. Neurosarcoidosis: signs, course and treatment in 35 confirmed cases. Medicine (Baltimore) 1990;69(5):261–76.
127. Stern BJ, Krumholz A, Johns C, et al. Sarcoidosis and its neurological manifestations. Arch Neurol 1985;42(9):909–17.
128. Delaney P. Neurologic manifestations in sarcoidosis: review of the literature, with a report of 23 cases. Ann Intern Med 1977;87(3):336–45.
129. Saleh S, Saw C, Marzouk K, et al. Sarcoidosis of the spinal cord: literature review and report of eight cases. J Natl Med Assoc 2006;98:965–76.
130. Joseph FG, Scolding NJ. Neurosarcoidosis: a study of 30 new cases. J Neurol Neurosurg Psychiatry 2009;80(3):297–304.
131. Cohen-Aubart F, Galanaud D, Grabli D, et al. Spinal cord sarcoidosis: clinical and laboratory profile and outcome of 31 patients in a case-control study. Medicine (Baltimore) 2010;89(2):133–40.
132. Christoforidis GA, Spickler EM, Recio MV, et al. MR of CNS sarcoidosis: correlation of imaging features to clinical symptoms and response to treatment. AJNR Am J Neuroradiol 1999;20(4):655–69.

133. Bhagavati S, Choi J. Intramedullary cervical spinal cord sarcoidosis. Spinal Cord 2009;47:179–81.
134. Terada T, Shigeno K, Hori M, et al. Isolated spinal neurosarcoidosis: an autopsy case. Spinal Cord 2010;48:776–8.
135. Lidar M, Dori A, Levy Y, et al. Sarcoidosis presenting as "corset-like" myelopathy: a description of six cases and literature review. Clin Rev Allergy Immunol 2010;38(2–3):270–5.
136. Marangoni S, Argentiero V, Tavolato B, Neurosarcoidosis. Clinical description of 7 cases with a proposal for a new diagnostic strategy. J Neurol 2006;253(4): 488–95.
137. Spencer TS, Campellone JV, Maldonado I, et al. Clinical and magnetic resonance imaging manifestations of neurosarcoidosis. Semin Arthritis Rheum 2005;34:649–61.
138. Kumar N, Frohman EM. Spinal neurosarcoidosis mimicking an idiopathic inflammatory demyelinating syndrome. Arch Neurol 2004;61(4):586–9.
139. Sakushima K, Yabe I, Nakano F, et al. Clinical features of spinal cord sarcoidosis: analysis of 17 neurosarcoidosis patients. J Neurol 2011;258(12):2163–7.
140. Zajicek JP, Scolding NJ, Foster O, et al. Central nervous system sarcoidosis—diagnosis and management. QJM 1999;92(2):103–7.
141. Shah R, Roberson GH, Cure JK. Correlation of MR imaging findings and clinical manifestations in neurosarcoidosis. AJNR Am J Neuroradiol 2009;30:953–61.
142. Sulavik SB, Spencer RP, Weed DA, et al. Recognition of distinctive patterns of gallium-67 distribution in sarcoidosis. J Nucl Med 1990;31:1909–14.
143. Dale JC, O'Brien JF. Determination of angiotensin-converting enzyme levels in cerebrospinal fluid is not a useful test for the diagnosis of neurosarcoidosis. Mayo Clin Proc 1999;74(5):535.
144. Read RW, Holland GN, Rao NA, et al. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of the international committee on nomenclature. Am J Ophthalmol 2001;131(5):647–52.
145. Lubin JR, Lowenstein JI, Fredrick AR. VKH syndrome with focal neurological signs. Am J Ophthalmol 1981;91(3):332–41.
146. Dahbour SS. MRI documented acute myelitis in a patient with Vogt-Koyanagi-Harada syndrome: first report. Clin Neurol Neurosurg 2009;111(2):200–2.
147. Rajendram R, Evans M, Khurana RN, et al. Vogt-Koyanagi-Harada disease presenting as optic neuritis. Int Ophthalmol 2007;27(2–3):217–20.
148. Tahara T, Sekitani T. Neurotological evaluation of Harada's disease. Acta Otolaryngol Suppl 1995;519:110–3.
149. Miyanaga M, Kawaguchi T, Shimuzu K, et al. Influence of early cerebrospinal fluid-guided diagnosis and early high-dose corticosteroid therapy on ocular outcomes of Vogt-Koyanagi-Harada disease. Int Ophthalmol 2007;27(2–3): 183–8.
150. Miller DH, Weinshenker BG, Filippi M, et al. Differential diagnosis of suspected multiple sclerosis: a consensus approach. Mult Scler 2008;14(9):1157–74.
151. Tenenbaum S, Chitnis T, Ness J, et al. Acute disseminated encephalomyelitis. Neurology 2007;68(16 Suppl 2):S32–6.
152. Straussberg R, Schonfeld T, Weitz R, et al. Improvement of atypical acute disseminated encephalomyelitis with steroids and intravenous immunoglobulins. Pediatr Neurol 2001;24:139–43.
153. Aimoto Y, Moriwaka F, Matsumoto K, et al. A case of acute disseminated encephalomyelitis (ADEM) associated with demyelinating peripheral neuropathy. No To Shinkei 1996;48:857–60.

154. Torisu H, Kira R, Ishizaki Y, et al. Clinical study of childhood acute disseminated encephalomyelitis, multiple sclerosis, and acute transverse myelitis in Fukuoka Prefecture, Japan. Brain Dev 2010;32(6):454–62.
155. Huynh W, Cordato DJ, Kehdi E, et al. Post-vaccination encephalomyelitis: literature review and illustrative case. J Clin Neurosci 2008;15(12):1315–22.
156. Callen DJ, Shroff MM, Branson HM, et al. Role of MRI in the differentiation of ADEM from MS in children. Neurology 2009;72(11):968–73.
157. Kesselring J, Miller DH, Robb SA, et al. Acute disseminated encephalomyelitis. MRI findings and the distinction from multiple sclerosis. Brain 1990;113: 291–302.
158. Kimura S, Nezu A, Ohtsuki N, et al. Serial magnetic resonance imaging in children with postinfectious encephalitis. Brain Dev 1996;18:461–5.
159. Franciotta D, Columba-Cabezas S, Andreoni L, et al. Oligoclonal IgG band patterns in inflammatory demyelinating human and mouse diseases. J Neuroimmunol 2008;200(1–2):125–8.
160. Stuve O, Nessler S, Hartung HP, et al. Acute disseminated encephalomyelitis: pathogenesis, diagnosis, treatment, and prognosis. Nervenarzt 2005;76(6): 701–7.
161. Straub J, Chofflon M, Delavelle J. Early high-dose intravenous methylprednisolone in acute disseminated encephalomyelitis: a successful recovery. Neurology 1997;49(4):1145–7.
162. Stricker RB, Miller RG, Kiprov DD. Role of plasmapheresis in acute disseminated (post-infectious) encephalomyelitis. J Clin Apher 1992;7(4):173–9.
163. Weinshenker BG, O'Brien PC, Petterson TM, et al. A randomized trial of plasma exchange in acute CNS inflammatory demyelinating disease. Ann Neurol 1999; 46:878–86.
164. Llufriu S, Castillo J, Blanco Y, et al. Plasma exchange for acute attacks of CNS demyelination: predictors of improvement at 6 months. Neurology 2009;73(12): 949–53.
165. Keegan M, Pineda AA, McClelland RL, et al. Plasma exchange for severe attacks of CNS demyelination: predictors of response. Neurology 2002;58: 143–6.
166. Stübgen JP. Immune-mediated myelitis associated with hepatitis virus infections. J Neuroimmunol 2011;239(1–2):21–7.
167. Takahashi-Fujigasaki J, Takagi S, Sakamoto T, et al. Spinal cord biopsy findings of anti-aquaporin-4 antibody-negative recurrent longitudinal myelitis in a patient with sicca symptoms and hepatitis C viral infection. Neuropathology 2009;29(4): 472–9.
168. Aktipi KM, Ravaglia S, Ceroni M, et al. Severe recurrent myelitis in patients with hepatitis C virus infection. Neurology 2007;68:468–9.
169. Pacheco VH, Acharya JN. Recurrent myelopathy and hepatitis C infection. Ann Neurol 2006;60(Suppl 3):S45.
170. Grewal AK, Lopes MB, Berg CL, et al. Recurrent demyelinating myelitis associated with hepatitis C viral infection. J Neurol Sci 2004;224:101–6.
171. Sobukawa E, Sakimura K, Hoshino S, et al. Hepatic myelopathy: an unusual neurological complication of advanced hepatic disease. Intern Med 1994;33: 718–22.
172. Mandal K, Chopra N. Acute transverse myelitis following hepatitis E virus infection. Indian Pediatr 2006;43:365–6.
173. Seet RC, Lim EC, Wilder-Smith EP. Acute transverse myelitis following dengue virus infection. J Clin Virol 2006;35(3):310–2.

174. Kusuhara T, Nakajima M, Inoue H, et al. Parainfectious encephalomyeloradiculitis associated with herpes simplex virus 1 DNA in cerebrospinal fluid. Clin Infect DIs 2002;34(9):1199–205.
175. Larik A, Chiong Y, Lee LC, et al. Longitudinally extensive transverse myelitis associated with dengue fever. BMJ Case Rep 2012. http://dx.doi.org/10.1136/bcr.12.2011.5378. pii: bcr1220115378.
176. Chanthamat N, Sathirapanya P. Acute transverse myelitis associated with dengue viral infection. J Spinal Cord Med 2010;33(4):425–7.
177. Kincaid O, Lipton HL. Viral myelitis: an update. Curr Neurol Neurosci Rep 2006;6(6):469–74.
178. Roos KL. West Nile encephalitis and myelitis. Curr Opin Neurol 2004;17:343–6.
179. Solomon T, Dung NM, Kneen R, et al. Japanese encephalitis. J Neurol Neurosurg Psychiatry 2000;68:405–15.
180. Einsiedel L, Kat E, Ravindran J, et al. MR findings in Murray Valley encephalitis. AJNR Am J Neuroradiol 2003;24:1379–82.
181. Bender A. Severe tick borne encephalitis with simultaneous brain stem, bithalamic, and spinal cord involvement documented by MRI. J Neurol Neurosurg Psychiatry 2005;76:135–7.
182. Scheibe F, Hofmann J, Ruprecht K. Parainfectious myelitis associated with parvovirus B19 infection. J Neurol 2010;257:1557–8.
183. Barton LL, Hyndman NJ. Lymphocytic choriomeningitis virus: reemerging central nervous system pathogen. Pediatrics 2000;105:e35.
184. Arpino C, Curatolo P, Rezza G. Chikungunya and the nervous system: what we do and do not know. Rev Med Virol 2009;19(3):121–9.
185. Huisa BN, Chapin JE, Adair JC. Central nervous system complications following Hanta virus cardiopulmonary syndrome. J Neurovirol 2009;15(2):202–5.
186. Unay B, Kendirli T, Meral C, et al. Transverse myelitis due to echovirus type 30. Acta Paediatr 2005;94(12):1863–4.
187. Ponka A. Central nervous system manifestations associated with serologically verified *Mycoplasma pneumoniae* infection. Scand J Infect Dis 1980;12:175–84.
188. Cassell GH, Cole BC. Mycoplasmas as agents of human disease. N Engl J Med 1981;304:80–9.
189. Koskiniemi M. CNS manifestations associated with *Mycoplasma pneumoniae* infections: summary of cases at the University of Helsinki and review. Clin Infect Dis 1993;17(Suppl 1):S52–7.
190. Tsiodras S, Kelesidis TH, Kelesidis I, et al. *Mycoplasma pneumoniae*-associated myelitis: a comprehensive review. Eur J Neurol 2006;13:112–24.
191. Isoda H, Ramsey R. MR imaging of acute transverse myelitis (myelopathy). Radiat Med 1998;16:179–86.
192. Goebels N, Helmchen C, Abele-Horn M, et al. Extensive myelitis associated with *Mycoplasma pneumoniae* infection: magnetic resonance imaging and clinical long-term follow-up. J Neurol 2001;248:204–8.
193. Csabi G, Komaromy H, Hollody K. Transverse myelitis as a rare, serious complication of *Mycoplasma pneumoniae* infection. Pediatr Neurol 2009;41(4):312–3.
194. Gozzard P, Orr D, Sanderson F, et al. Acute transverse myelitis as a rare manifestation of *Campylobacter* diarrhoea with concomitant disruption of the blood brain barrier. J Clin Neurosci 2012;19:316–8.
195. Baar I, Jacobs BC, Govers N, et al. *Campylobacter jejuni*-induced acute transverse myelitis. Spinal Cord 2007;45:690–4.
196. Aberle J, Kluwe J, Pawlas F, et al. Severe myelitis following infection with *Campylobacter* enteritis. Eur J Clin Microbiol Infect Dis 2004;23:134–5.

197. Huber S, Kappos L, Fuhr P, et al. Combined acute disseminated encephalomyelitis and acute motor axonal neuropathy after vaccination for hepatitis A and infection with *Campylobacter jejuni*. J Neurol 1999;246:1204–6.
198. Orr D, McKendrick MW, Sharrack B. Acute disseminated encephalomyelitis temporally associated with *Campylobacter* gastroenteritis. J Neurol Neurosurg Psychiatry 2004;75:792–3.
199. Gaig C, Valldeoriola F, Saiz A. Acute disseminated encephalomyelitis associated with *Campylobacter jejuni* infection and antiganglioside GM1 IgG antibodies. J Neurol 2005;252:613–4.
200. Nasralla CA, Pay N, Goodpasture HC, et al. Postinfectious encephalopathy in a child following *Campylobacter jejuni* enteritis. AJNR Am J Neuroradiol 1993; 14:444–8.
201. Bigi S, Aebi C, Nauer C, et al. Acute transverse myelitis in Lyme neuroborreliosis. Infection 2010;38(5):413–6.
202. Pourhassan A, Shoja MM, Tubbs RS, et al. Acute transverse myelitis secondary to *Salmonella paratyphi* B infection. Infection 2008;36(2):170–3.
203. Ubogu EE, Lindenberg JR, Werz MA. Transverse myelitis associated with *Acinetobacter baumanii* intrathecal pump catheter-related infection. Reg Anesth Pain Med 2003;28(5):470–4.
204. Waltereit R, Küker W, Jürgens S, et al. Acute transverse myelitis associated with *Coxiella burnetii* infection. J Neurol 2001;249(10):1459–61.
205. Schimmel MS, Schlesinger Y, Berger I, et al. Transverse myelitis: unusual sequelae of neonatal group B streptococcus disease. J Perinatol 2002;22(7): 580–1.
206. Pickerill RG, Milder JE. Transverse myelitis associated with cat-scratch disease in an adult. JAMA 1981;246:2840–1.
207. Salgado CD, Weisse ME. Transverse myelitis associated with probable cat-scratch disease in a previously healthy pediatric patient. Clin Infect Dis 2000; 31(2):609–11.
208. Williams W, Sunderland R. As sick as a pigeon; psittacosis myelitis. Arch Dis Child 1989;64:1626–8.
209. Crook T, Bannister B. Acute transverse myelitis associated with *Chlamydia psittaci* infection. J Infect 1996;32(2):151–2.
210. de Lau LM, Siepman DA, Remmers MJ, et al. Acute disseminating encephalomyelitis following Legionnaires disease. Arch Neurol 2010;67(5):623–6.
211. Lee KL, Lee JK, Yim YM, et al. Acute transverse myelitis associated with scrub typhus: case report and a review of literature. Diagn Microbiol Infect Dis 2008; 60(2):237–9.
212. Feng Y, Guo N, Liu J, et al. Mycobacteria infection in incomplete transverse myelitis is refractory steroids: a pilot study. Clin Dev Immunol 2011;2011: 501369.
213. Krishnan C, Kaplin AI, Graber JS, et al. Recurrent transverse myelitis following neurobrucellosis: immunologic features and beneficial response to immunosuppression. J Neurovirol 2005;11:225–31.
214. Baylor P, Garoufi A, Karpathios T, et al. Transverse myelitis in 2 patients with *Bartonella henselae* infection (cat scratch disease). Clin Infect Dis 2007;45: e42–5.
215. Gumbo T, Hakim JG, Mielke J, et al. Cryptococcus myelitis: atypical presentation of a common infection. Clin Infect Dis 2001;32:1235–6.
216. Shields GS, Castillo M. Myelitis caused by *Cladophialophora bantiana*. AJR Am J Roentgenol 2002;179:278–9.

217. Jabbour RA, Kanj SS, Sawaya RA, et al. *Toxocara canis* myelitis: clinical features, magnetic resonance imaging (MRI) findings, and treatment outcome in 17 patients. Medicine (Baltimore) 2011;90(5):337–43.
218. Dauriac-Le Masson V, Chochon F, Demeret S, et al. *Toxocara canis* meningomyelitis. J Neurol 2005;252(10):1267–8.
219. Marx C, Lin J, Masruha MR, et al. Toxocariasis of the CNS simulating acute disseminated encephalomyelitis. Neurology 2007;69(8):806–7.
220. Helsen G, Vandecasteele SJ, Vanopdenbosch LJ. Toxocariasis presenting as encephalomyelitis. Case Report Med 2011;2011:503913. http://dx.doi.org/10.1155/2011/503913.
221. Ross AG, McManus DP, Farrar J, et al. Neuroschistosomiasis. J Neurol 2012;259:22–32.
222. Bunyaratavej K, Pongpunlert W, Jongwutiwes S, et al. Spinal gnathostomiasis resembling an intrinsic cord tumor/myelitis in a 4-year-old boy. Southeast Asian J Trop Med Public Health 2008;39:800–3.
223. Kibiki GS, Murphy DK. Transverse myelitis due to trypanosomiasis in a middle aged Tanzanian man. J Neurol Neurosurg Psychiatry 2006;77:684–5.
224. Drulovic J, Dujmovic I, Stojsavljevic N. Transverse myelopathy in the antiphospholipid antibody syndrome: pinworm infestation as a trigger? J Neurol Neurosurg Psychiatry 2000;68:246–56.
225. Lesca G, Deschamps R, Lubetzki C, et al. Acute myelitis in early *Borrelia burgdorferi* infection. J Neurol 2002;249:1472–4.
226. Baumann M, Birnbacher R, Koch J, et al. Uncommon manifestations of neuroborreliosis in children. Eur J Paediatr Neurol 2010;14:274–7.
227. Bajaj NPS, Rose P, Clifford-Jones R, et al. Acute transverse myelitis and Guillain-Barre overlap syndrome with serological evidence for mumps viraemia. Acta Neurol Scand 2001;104:239–42.
228. Venketasubramanian N. Transverse myelitis following mumps in an adult—a case report with MRI correlation. Acta Neurol Scand 1997;96:328–31.
229. Rigamonti A, Usai S, Ciusani E, et al. Atypical transverse myelitis due to cytomegalovirus in an immunocompetent patient. Neurol Sci 2005;26:351–4.
230. Ku B, Lee K. Acute transverse myelitis caused by Coxsackie virus B4 infection: a case report. J Korean Med Sci 1998;13:449–53.
231. Minami K, Tsuda Y, Maeda H, et al. Acute transverse myelitis caused by Coxsackie virus B5 infection. J Paediatr Child Health 2004;40:66–8.
232. Chortis P. Study in the therapy of transverse myelitis occurring during tuberculous meningitis. Dis Chest 1958;33:506–12.
233. McMinn P, Stratov I, Nagarajan L, et al. Neurological manifestations of Enterovirus 71 infection in children during an outbreak of hand, foot, and mouth disease in Western Australia. Clin Infect Dis 2001;32(2):236–42.
234. Gruhn B, Meerbach A, Egerer R, et al. Successful treatment of Epstein-Barr virus-induced transverse myelitis with ganciclovir and cytomegalovirus hyperimmune globulin following unrelated bone marrow transplantation. Bone Marrow Transplant 1999;24:1355–8.
235. Caldas C, Bernicker E, Dal Nogare A, et al. Case report: transverse myelitis associated with Epstein-Barr virus infection. Am J Med Sci 1994;307:45–8.
236. Corssmit EP, Leverstein-van Hall M, Portegies P, et al. Severe neurological complications in association with Epstein-Barr virus infection. J Neurovirol 1997;3:460–4.
237. Umehara F, Ookatsu H, Hayashi D, et al. MRI studies of spinal visceral larva migrans syndrome. J Neurol Sci 2006;249:7–12.

238. Lee IH, Kim ST, Oh DK, et al. MRI findings of spinal visceral larva migrans of *Toxocara canis*. Eur J Radiol 2010;75:236–40.
239. Joshi TN, Yamazaki MK, Zhao H, et al. Spinal schistosomiasis: differential diagnosis for acute paraparesis in a U.S. resident. J Spinal Cord Med 2010;33(3): 256–60.
240. Hull TP, Bates JH. Optic neuritis after influenza vaccination. Am J Ophthalmol 1997;124:703–4.
241. Ray CL, Dreizin IJ. Bilateral optic neuropathy associated with influenza vaccination. J Neuroophthalmol 1996;16:182–4.
242. Keegan BM, Pittock SJ, Lennon VA. Autoimmune myelopathy associated with collapsin response-mediator protein-5 immunoglobulin G. Ann Neurol 2008; 63(4):531–4.
243. Cross SA, Salomao DR, Parisi JE, et al. Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5 IgG. Ann Neurol 2003;54:38–50.
244. Pittock SJ, Yoshikawa H, Ahlskog JE, et al. Glutamic acid decarboxylase autoimmunity with brainstem, extrapyramidal, and spinal cord dysfunction. Mayo Clin Proc 2006;81:1207–14.
245. Tanaka M, Matsushita T, Tateishi T, et al. Distinct CSF cytokine/chemokine profiles in atopic myelitis and other causes of myelitis. Neurology 2008;71(13): 974–81.
246. Zoli A, Mariano M, Fusari A, et al. Atopic myelitis: first case report outside Japan? Allergy 2005;60:410–1.
247. Gregoire SM, Mormont E, Laloux P, et al. Atopic myelitis: a clinical, biological, radiological and histopathological diagnosis. J Neurol Sci 2006;247:231–5.
248. Kira J, Kawano Y, Horiuchi I, et al. Clinical, immunological and MRI features of myelitis with atopic dermatitis (atopic myelitis). J Neurol Sci 1999;162(1):56–61.
249. Kira J, Yamasaki K, Kawano Y, et al. Acute myelitis associated with hyperIgEemia and atopic dermatitis. J Neurol Sci 1997;148(2):199–203.
250. Isobe N, Kanamori Y, Yonekawa T, et al. First diagnostic criteria for atopic myelitis with special reference to discrimination from myelitis-onset multiple sclerosis. J Neurol Sci 2012;316:30–5.
251. Constantinescu CS, Thomas M, Zaman AG. Atopic optic neuritis. Ocul Immunol Inflamm 2006;14:125–7.
252. de Seze J, Lanctin C, Lebrun C, et al. Idiopathic acute transverse myelitis: application of the recent diagnostic criteria. Neurology 2005;65(12):1950–3.
253. Krishnan C, Kaplin A, Deshpande D, et al. Transverse myelitis: pathogenesis, diagnosis and treatment. Front Biosci 2004;9:1483–99.
254. Alvarenga MP, Thuler LC, Neto SP, et al. The clinical course of idiopathic acute transverse myelitis in patients from Rio de Janeiro. J Neurol 2010;257(6):992–8.
255. Choi KH, Lee KS, Chung SO, et al. Idiopathic transverse myelitis: MR characteristics. AJNR Am J Neuroradiol 1996;17:1151–60.
256. Alper G, Petropoulou KA, Fitz CR, et al. Idiopathic acute transverse myelitis in children: an analysis and discussion of MRI findings. Mult Scler 2011;17:74–80.
257. Young J, Quinn S, Hurrell M, et al. Clinically isolated acute transverse myelitis: prognostic features and incidence. Mult Scler 2009;15(11):1295–302.
258. Kim SH, Kim SM, Vincent A, et al. Clinical characteristics, prognosis, and seropositivity to the anti-aquaporin-4 antibody in Korean patients with longitudinally extensive transverse myelitis. J Neurol 2010;257(6):920–5.
259. Ravaglia S, Bastianello S, Franciotta D, et al. NMO-IgG-negative relapsing myelitis. Spinal Cord 2009;47:531–7.
260. Kim KK. Idiopathic recurrent transverse myelitis. Arch Neurol 2003;60:1290–4.

261. Pidcock FS, Krishnan C, Crawford TO, et al. Acute transverse myelitis in childhood: center-based analysis of 47 cases. Neurology 2007;68:1474–80.
262. Thomas T, Branson HM, Leonard H, et al. The demographic, clinical and magnetic resonance imaging (MRI) features of transverse myelitis in children. J Child Neurol 2012;27:11–21.
263. Andronikou S, Albuquerque-Jonathan G, Wilmshurst J, et al. MRI findings in acute idiopathic transverse myelopathy in children. Pediatr Radiol 2003;33: 624–9.
264. Defresne P, Hollenberg H, Husson B, et al. Acute transverse myelitis in children: clinical course and prognostic factors. J Child Neurol 2003;18:401–6.
265. Knebusch M, Strassburg HM, Reiners K. Acute transverse myelitis in childhood: nine cases and review of the literature. Dev Med Child Neurol 1998;40:631–9.
266. Dunne K, Hopkins IJ, Shield LK. Acute transverse myelopathy in childhood. Dev Med Child Neurol 1986;28:198–204.
267. Yiu EM, Kornberg AJ, Ryan MM, et al. Acute transverse myelitis and acute disseminated encephalomyelitis in childhood: spectrum or separate entities? J Child Neurol 2009;24:287–96.
268. De Goede CG, Holmes EM, Pike MG. Acquired transverse myelopathy in children in the United Kingdom—a 2 year prospective study. Eur J Paediatr Neurol 2010;14:479–87.
269. Banwell B, Tenembaum S, Lennon VA, et al. Neuromyelitis optica-IgG in childhood inflammatory demyelinating CNS disorders. Neurology 2008;70:344–52.
270. Wang KC, Wang SJ, Lee CL, et al. The rescue effect of plasma exchange for neuromyelitis optica. J Clin Neurosci 2011;18:43–6.
271. Gwathmey K, Balogun RA, Burns T. Neurologic indications for therapeutic plasma exchange: an update. J Clin Apher 2011;26(5):261–8.
272. Greenberg BM, Thomas KP, Krishnan C, et al. Idiopathic transverse myelitis: corticosteroids, plasma exchange, or cyclophosphamide. Neurology 2007; 68(19):1614–7.
273. Khan OA, Zvartau-Hind M, Caon C, et al. Effect of monthly intravenous cyclophosphamide in rapidly deteriorating multiple sclerosis patients resistant to conventional therapy. Mult Scler 2001;7:185–8.
274. Smith D. Preliminary analysis of a trial of pulse cyclophosphamide in IFN-beta-resistant active MS. J Neurol Sci 2004;223:73–9.
275. Borchers AT, Gershwin ME. Transverse myelitis. Autoimmun Rev 2012;11: 231–48.
276. Thompson AJ. Neurorehabilitation in multiple sclerosis: foundations, facts and fiction. Curr Opin Neurol 2005;18:267–71.
277. Trecker CC, Kozubal DE, Quigg M, et al. Quality care in transverse myelitis: a responsive protocol. J Child Neurol 2009;24:577–83.
278. Yavin Y, Cohan AT. Venous thromboembolism prophylaxis for the medical patient: where do we stand? Semin Respir Crit Care Med 2008;29(1):75–82.
279. Anders J, Heinemann A, Carsten L, et al. Decubitus ulcers: pathophysiology and primary prevention. Dtsch Arztebl Int 2010;107(21):371–82.
280. Putzke J, Richards J, Hicken B, et al. Predictors of life satisfaction: a spinal cord injury cohort study. Arch Phys Med Rehabil 2002;83:555–61.
281. Ditunno PL, Patrick M, Stineman M, et al. Who wants to walk? Preferences for recovery after SCI: a longitudinal and cross-sectional study. Spinal Cord 2008;46:500–6.
282. Dietz V. Neurophysiology of gait disorders: present and future applications. Electroencephalogr Clin Neurophysiol 1997;103(3):333–55.

283. Scivoletto G, Romanelli A, Mariotti A, et al. Clinical factors that affect walking level and performance in chronic spinal cord lesion patients. Spine (Phila Pa 1976) 2008;33(3):259–64.
284. Lapointe R, Lajoie Y, Serresse O, et al. Functional community ambulation requirements in incomplete spinal cord injured subjects. Spinal Cord 2001;39: 327–35.
285. Sturt RN, Holland AE, New PW. Walking ability at discharge from inpatient rehabilitation in a cohort of non-traumatic spinal cord injury patients. Spinal Cord 2009;47(10):763–8.
286. Courtney AM, Castro-Borrero W, Davis SL, et al. Functional treatments in multiple sclerosis. Curr Opin Neurol 2011;24(3):250–4.
287. Golzari Z, Shabkhiz F, Soudi S, et al. Combined exercise training reduces IFN-g and IL-17 levels in the plasma and the supernatant of peripheral blood mononuclear cells in women with multiple sclerosis. Int Immunopharmacol 2010;10: 1415–9.
288. Hawker K, Frohman E, Racke M. Levetiracetam for phasic spasticity in multiple sclerosis. Arch Neurol 2003;60:1772–4.
289. Rittweger J, Gerrits K, Altenburg T, et al. Bone adaptation to altered loading after spinal cord injury: a study of bone and muscle strength. J Musculoskelet Neuronal Interact 2006;6:269–76.
290. Roze E, Bounolleau P, Ducreux D, et al. Propriospinal myoclonus revisited: clinical, neurophysiologic, and neuroradiologic findings. Neurology 2009;72(15): 1301–9.
291. Brown LK, Heffner JE, Obbens EA. Tranverse myelitis associated with restless legs syndrome and periodic movements of sleep responsive to an oral dopaminergic agent but not to intrathecal baclofen. Sleep 2000;23(5):1–4.
292. Natarajan R. Review of periodic limb movement and restless leg syndrome. J Postgrad Med 2010;56(2):157–62.
293. Kalita J, Shah S, Kapoor R, et al. Bladder dysfunction in acute transverse myelitis: magnetic resonance imaging and neurophysiological and urodynamic correlations. J Neurol Neurosurg Psychiatry 2002;73(2):154–9.
294. Gupta A, Taly AB, Srivastava A, et al. Non-traumatic spinal cord lesions: epidemiology, complications, neurological and functional outcome of rehabilitation. Spinal Cord 2009;47:307–11.
295. Tanaka ST, Stone AT, Kurzrock EA. Transverse myelitis in children: long-term urological outcomes. J Urol 2006;175(5):1864–8.
296. Lemack GE, Frohman EM, Zimmern PE, et al. Urodynamic distinctions between idiopathic detrusor overactivity and detrusor overactivity secondary to multiple sclerosis. Urology 2006;67:960–4.
297. Samkoff LM, Goodman AD. Symptomatic management in multiple sclerosis. Neurol Clin 2011;29(2):449–63.
298. Fowler CJ, Panicker JN, Drake M, et al. A UK consensus on the management of the bladder in multiple sclerosis. Postgrad Med J 2009;85(1008):552–9.
299. Ebert E. Gastrointestinal involvement in spinal cord injury: a clinical perspective. J Gastrointestin Liver Dis 2012;21(1):75–82.
300. Raghav S, Kipp D, Watson J, et al. Gastroparesis in multiple sclerosis. Mult Scler 2006;12(2):243–4.
301. Reddymasu SC, Bonino J, McCallum RW. Gastroparesis secondary to a demyelinating disease: a case series. BMC Gastroenterol 2007;7:3.
302. Atkinson K, Romano W, Prokopiw I. An unusual cause of gastroparesis: demyelinating disease of the medulla. Dig Dis Sci 1998;43:1430–3.

303. Read SJ, Leggett BA, Pender MP. Gastroparesis with multiple sclerosis. Lancet 1995;346(8984):1228.
304. Wiesel PH, Norton C, Glickman S, et al. Pathophysiology and management of bowel dysfunction in multiple sclerosis. Eur J Gastroenterol Hepatol 2001; 13(4):441–8.
305. Christensen P, Krogh K, Buntzen S, et al. Long-term outcome and safety of transanal irrigation for constipation and fecal incontinence. Dis Colon Rectum 2009;52:286–92.
306. Consortium for Spinal Cord Medicine. Sexuality and reproductive health in adults with spinal cord injury: a clinical practice guideline for health-care professionals. J Spinal Cord Med 2010;33(3):281–336.
307. Lombardi G, Mondaini N, Iazzetta P, et al. Sexuality in patients with spinal cord injuries due to attempted suicide. Spinal Cord 2008;46(1):53–7.
308. Forsythe E, Horsewell JE. Sexual rehabilitation of women with a spinal cord injury. Spinal Cord 2006;44:234–41.
309. Courtois FJ, Charvier KF, Leriche A, et al. Sexual function in spinal cord injury men. Assessing sexual capability. Paraplegia 1993;31:771–84.
310. Courtois FJ, Goulet MC, Charvier KF, et al. Posttraumatic erectile potential of spinal cord injured men: How physiologic recordings supplement subjective reports. Arch Phys Med Rehabil 1999;80:1268–72.
311. Alexander MS, Biering-Sorensen F, Bodner D, et al. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord 2009;47:36–43.
312. Stone AR. The sexual needs of the injured spinal cord patient. Probl Urol 1987;1: 529–36.
313. Barbonetti A, Cavallo F, Felzani G, et al. Erectile dysfunction is the main determinant of psychological distress in men with spinal cord injury. J Sex Med 2012;9(3):830–6.
314. Anderson KD, Borisoff JF, Johnson RD, et al. Long-term effects of spinal cord injury on sexual function in men: implications for neuroplasticity. Spinal Cord 2007;45:338–48.
315. Lombardi G, Del Popolo G, Macchiarella A, et al. Sexual rehabilitation in women with spinal cord injury: a critical review of the literature. Spinal Cord 2010;48(12): 842–9.
316. Lombardi G, Mondaini N, Macchiarella A, et al. Female sexual dysfunction and hormonal status in spinal cord injured (SCI) patients. J Androl 2007;28(5):722–6.
317. Soler JM, Previnaire JG. Ejaculatory dysfunction in spinal cord injury is suggestive of dyssynergic ejaculation. Eur J Phys Rehabil Med 2011;47:677–81.
318. Kreuter M, Taft C, Siösteen A, et al. Women's sexual functioning and sex life after spinal cord injury. Spinal Cord 2011;49(1):154–60.
319. Krassioukov AV, Karlsson AK, Wecht AK, et al. Assessment of autonomic dysfunction following spinal cord injury: rationale for additions to International Standards for Neurological Assessment. J Rehabil Res Dev 2007;44(1):103–12.
320. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. Neurology 1996;46(5):1470.
321. Sidorov EV, Townson AF, Dvorak MF, et al. Orthostatic hypotension in the first month following acute spinal cord injury. Spinal Cord 2008;46(1):65–9.
322. Andersen EB, Nordenbo AM. Sympathetic vasoconstrictor responses in multiple sclerosis with thermo-regulatory dysfunction. Clin Auton Res 1997;7:13–6.

323. Davis SL, Wilson TE, White AT, et al. Thermoregulation in multiple sclerosis. J Appl Physiol 2010;109(5):1531–7.
324. Krassioukov AV, Furlan JC, Fehlings MG. Autonomic dysreflexia in acute spinal cord injury: an under-recognized clinical entity. J Neurotrauma 2003;20(8):707–18.
325. Krassioukov A, Warburton DE, Teasell R, et al. A systematic review of the management of autonomic dysreflexia after spinal cord injury. Arch Phys Med Rehabil 2009;90(4):682–95.
326. Braddom RL, Rocco JF. Autonomic dysreflexia. Am J Phys Med Rehabil 1991; 70:234–41.
327. Ho CP, Krassioukov AV. Autonomic dysreflexia and myocardial ischemia. Spinal Cord 2010;48(9):714–5.
328. Chaves CJ, Lee G. Reversible posterior leukoencephalopathy in a patient with autonomic dysreflexia: a case report. Spinal Cord 2008;46(11):760–1.
329. Dolinak D, Balraj E. Autonomic dysreflexia and sudden death in people with traumatic spinal cord injury. Am J Forensic Med Pathol 2007;28(2):95–8.
330. Beard JP, Wade WH, Barber DB. Sacral insufficiency stress fracture as etiology of positional autonomic dysreflexia: case report. Paraplegia 1996;34(3):173–5.
331. Claydon VE, Elliott SL, Sheel AW, et al. Cardiovascular responses to vibrostimulation for sperm retrieval in men with spinal cord injury. J Spinal Cord Med 2006; 29(3):207–16.
332. Szasz G, Carpenter C. Clinical observations in vibratory stimulation of the penis of men with spinal cord injury. Arch Sex Behav 1989;18(6):461–74.
333. Blackmer J. Rehabilitation medicine: 1. Autonomic dysreflexia. CMAJ 2003; 169(9):931–5.
334. Sjölund BH. Pain and rehabilitation after spinal cord injury: the case of sensory spasticity? Brain Res Brain Res Rev 2002;40:250–6.
335. Pollmann W, Feneberg W. Current management of pain associated with multiple sclerosis. CNS Drugs 2008;22(4):291–324.
336. Bond LD Jr, Keough GC. Neurogenic pruritus: a case of pruritus induced by transverse myelitis. Br J Dermatol 2003;149(1):204–5.
337. Biering-Sorensen F, Bohr H, Schaadt O. Bone mineral content of the lumbar spine and lower extremities years after spinal cord lesion. Paraplegia 1988; 26:293–301.
338. Roberts D, Lee W, Cuneo RC, et al. Longitudinal study of bone turnover after acute spinal cord injury. J Clin Endocrinol Metab 1998;83:415–22.
339. Maïmoun L, Fattal C, Micallef JP, et al. Bone loss in spinal cord-injured patients: from physiopathology to therapy. Spinal Cord 2006;44(4):203–10.
340. Dionyssiotis Y. Spinal cord injury-related bone impairment and fractures: an update on epidemiology and physiopathological mechanisms. J Musculoskelet Neuronal Interact 2011;11(3):257–65.
341. Naftchi NE, Viau AT, Sell GH, et al. Mineral metabolism in spinal cord injury. Arch Phys Med Rehabil 1980;61:139–42.
342. Oleson CV, Patel PH, Wuermser LA. Influence of season, ethnicity, and chronicity on vitamin D deficiency in traumatic spinal cord injury. J Spinal Cord Med 2010;33(3):202–13.
343. Pepe J, Romagnoli E, Nofroni I, et al. Vitamin D status as the major factor determining the circulating levels of parathyroid hormone: a study in normal subjects. Osteoporos Int 2005;16(7):805–12.
344. Hiremath GS, Cettomai D, Baynes M, et al. Vitamin D status and effect of low-dose cholecalciferol and high-dose ergocalciferol supplementation in multiple sclerosis. Mult Scler 2009;15(6):735–40.

345. Asherio A, Munger KL, Simon KC. Vitamin D and multiple sclerosis. Lancet Neurol 2010;9(6):599–612.
346. Munger KL, Levin LI, Hollis BW, et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA 2006;296(23):2832–8.
347. Birmingham DJ, Hebert LA, Song H, et al. Evidence that abnormally large seasonally declines in vitamin D status may trigger SLE flare in non-African Americans. Lupus 2012;21(8):855–64.
348. Braun-Moscovici Y, Toledano K, Markovits D, et al. Vitamin D level: is it related to disease activity in inflammatory joint disease? Rheumatol Int 2011;31(4):493–9.
349. Mealy MA, Newsome S, Greenberg BM, et al. Low vitamin D levels and recurrent inflammatory spinal cord disease. Arch Neurol 2012;69(3):352–6.
350. Gannage-Yared MH, Azoury M, Mansour I, et al. Effects of a short-term calcium and vitamin D treatment on serum cytokines, bone markers, insulin and lipid concentrations in healthy post-menopausal women. J Endocrinol Invest 2003; 26(8):748–53.
351. Dickie LJ, Church LD, Coulthard LR, et al. Vitamin D3 down-regulates intracellular Toll-like receptor 9 expression and Toll-like receptor 9-induced IL-6 production in human monocytes. Rheumatology (Oxford) 2010;49(8):1466–71.
352. Correale J, Ysrraelit MC, Gaitán MI. Immunomodulatory effects of vitamin D in multiple sclerosis. Brain 2009;132(5):1146–60.
353. Tang J, Zhou R, Luger D, et al. Calcitriol suppresses antiretinal autoimmunity through inhibitory effects on the Th17 effector response. J Immunol 2009; 182(8):4624–32.
354. Prietl B, Pilz S, Wolf M, et al. Vitamin D supplementation and regulatory T cells in apparently healthy subjects: vitamin D treatment for autoimmune diseases? Isr Med Assoc J 2010;12(3):136–9.
355. Holick MF. Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. Current Opin Endocrinol Diabetes 2002;9(1): 87–98.
356. Hahn TJ, Hendin BA, Scharp CR, et al. Effect of chronic anticonvulsant therapy on serum 25-hydroxycholecalciferol levels in adults. N Engl J Med 1972; 287(18):900–4.
357. Vieth R. Critique of the considerations for establishing the tolerable upper intake for vitamin D: critical need for revision upwards. J Nutr 2006;136:1117–22.
358. Goldberg P, Flemin MC, Picard EH. Multiple sclerosis: decreased relapse rate through dietary supplementation with calcium, magnesium and vitamin D. Med Hypotheses 1986;21:193–200.
359. Heaney RP, Davies KM, Chen TC, et al. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. Am J Clin Nutr 2003;77: 204–10.
360. Trang HM, Cole DE, Rubin LA, et al. Evidence that vitamin D3 increases serum 25-hydroxyvitamin D more efficiently than does vitamin D2. Am J Clin Nutr 1998; 68(4):854–8.
361. Giovannucci E, Liu Y, Rimm EB, et al. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. J Natl Cancer Inst 2006; 98(7):451–9.
362. Robsahm TE, Tretli S, Dahlback A, et al. Vitamin D3 from sunlight may improve the prognosis of breast, colon, and prostate cancer (Norway). Cancer Causes Control 2004;15(2):149–58.
363. Mowe M, Haug E, Bohmer T. Low serum calcidiol concentration in older adults with reduced muscular function. J Am Geriatr Soc 1999;47(2):220–6.

364. Pfeifer M, Begerow B, Minne HW, et al. Vitamin D status, trunk muscle strength, body sway, falls, and fractures among 237 postmenopausal women with osteoporosis. Exp Clin Endocrinol Diabetes 2001;109(2):87–92.
365. Plotkinoff GA, Quigley BA. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. Mayo Clin Proc 2003; 78(12):1463–70.
366. Patten SB, Beck CA, Williams JV, et al. Major depression in multiple sclerosis: a population-based perspective. Neurology 2003;61:1524–7.
367. Mohr DC, Goodkin DE, Likosky W, et al. Treatment of depression improves adherence to interferon B-1b therapy for multiple sclerosis. Arch Neurol 1997;54:531–3.
368. Edgar MA. Nervous system involvement in ankylosing spondylitis. BMJ 1974;1: 394.
369. Oh DH, Jun JB, Kim HT, et al. Transverse myelitis in a patient with longstanding ankylosing spondylitis. Clin Exp Rheumatol 2001;19:195–6.
370. Lan HH, Chen DY, Chen CC, et al. Combination of transverse myelitis and arachnoiditis in cauda equina syndrome of long-standing ankylosing spondylitis: MRI features and its role in clinical management. Clin Rheumatol 2007;26:1963–7.
371. Rath JJG, Ronday HK, Wirtz PW. Acute transverse myelitis in psoriatic arthritis. J Neurol 2010;257:457–8.
372. Weiss TD, Nelson JS, Woolsey RM, et al. Transverse myelitis in mixed connective tissue disease. Arthritis Rheum 1978;21(8):982–6.
373. Pedersen C, Bonen H, Boesen F. Transverse myelitis in mixed connective tissue disease. Case report. Clin Rheumatol 1987;6:290–2.
374. Flechtner KM, Baum K. Mixed connective tissue disease: recurrent episodes of optic neuropathy and transverse myelopathy. Successful treatment with plasmapheresis. J Neurol Sci 1994;126:146–8.
375. Mok CC, Lau CS. Transverse myelopathy complicating mixed connective tissue disease. Case report. Clin Neurol Neurosurg 1995;97:259–60.
376. Weatherby SJM, Davies MB, Hawkins CP. Transverse myelopathy, a rare complication of mixed connective tissue disease: comparison with SLE related transverse myelopathy. J Neurol Neurosurg Psychiatry 2000;68:532–41.
377. Bhinder S, Harbour K, Majithia V. Transverse myelitis, a rare neurological manifestation of mixed connective tissue disease—a case report and a review of literature. Clin Rheumatol 2007;26:445–7.
378. Torabi AM, Patel RK, Wolfe GI, et al. Transverse myelitis in systemic sclerosis. Arch Neurol 2004;61:126–8.
379. Franciotta D, Zardini E, Caporali R, et al. Systemic sclerosis in aquaporin-4 antibody-positive longitudinally extensive transverse myelitis. J Neurol Sci 2011; 303:139–41.
380. Brown JJ, Murphy MJ. Transverse myelopathy in progressive systemic sclerosis. Ann Neurol 1985;17:615–7.
381. Averbuch-Heller L, Steiner I, Abramski O. Neurologic manifestations of progressive systemic sclerosis. Arch Neurol 1992;49:1292–5.
382. Ray DW, Bridger J, Hawnaur J, et al. Transverse myelitis as the presentation of Jo-1 antibody syndrome (myositis and fibrosing alveolitis) in long-standing ulcerative colitis. Br J Rheumatol 1993;32:1105–8.
383. Bolla G, Disdier P, Verrot D, et al. Acute transverse myelitis and primary urticarial vasculitis. Clin Rheumatol 1998;17:250–2.
384. Nakashima I, Fujihara K, Endo M, et al. Clinical and laboratory features of myelitis patients with anti-neutrophil cytoplasmic antibodies. J Neurol Sci 1998;157(1):60–6.

385. Hamilton AJ, Whitehead DJ, Bull MD, et al. Systemic pANCA-associated vasculitis with central nervous involvement causing recurrent myelitis: case report. BMC Neurol 2010;10:118.
386. Bürk K, Farecki ML, Lamprecht G, et al. Neurological symptoms in patients with biopsy proven celiac disease. Mov Disord 2009;24:2358–62.
387. Hammond ER, Pardo CA, Kerr DA. Thymic hyperplasia in a patient with recurrent transverse myelitis with clinical resolution after thymectomy. J Neurol Neurosurg Psychiatry 2008;79:334–5.
388. Drobyski WR, Potluri J, Sauer D, et al. Autoimmune hemolytic anemia following T-cell-depleted allogeneic bone marrow transplantation. Bone Marrow Transplant 1996;17:1093–9.
389. Richard S, Fruchtman S, Scigliano E, et al. An immunological syndrome featuring transverse myelitis, Evans syndrome and pulmonary infiltrates after unrelated bone marrow transplant in a patient with severe aplastic anemia. Bone Marrow Transplant 2000;26:1225–8.
390. Perez-Montes R, Richard C, Baro J, et al. Acute transverse myelitis and autoimmune pancytopenia after unrelated hematopoietic cell transplantation. Haematologica 2001;86(5):556–7.
391. Kumar N, Hagan JB, Abraham RS, et al. Common variable immunodeficiency-associated myelitis: report of treatment with infliximab. J Neurol 2008;255(11): 1821–4.
392. Hermaszewski RA, Webster AD. Primary hypogammaglobulinemia: a survey of clinical manifestations and complications. Q J Med 1993;86:31–42.
393. Leypoldt F, Eichhorn P, Saager C, et al. Successful immunosuppressive treatment and long-term follow-up of anti-Ri-associated paraneoplastic myelitis. J Neurol Neurosurg Psychiatry 2006;77(10):1199–200.
394. Pittock SJ, Lucchinetti CF, Lennon VA. Anti-neuronal nuclear autoantibody type 2: paraneoplastic accompaniments. Ann Neurol 2003;53(5):580–7.
395. Pittock SJ, Lucchinetti CF, Parisi JE, et al. Amphiphysin autoimmunity: paraneoplastic accompaniments. Ann Neurol 2005;58:96–107.
396. Chamard L, Magnin E, Berger E, et al. Stiff leg syndrome and myelitis with anti-amphiphysin antibodies: a common physiopathology? Eur Neurol 2011;66:253–5.
397. Saiz A, Blanco Y, Sabater L, et al. Spectrum of neurological syndromes associated with glutamic acid decarboxylase antibodies: diagnostic clues for this association. Brain 2008;131:2553–63.
398. Vitaliani R, Mason W, Ances B, et al. Paraneoplastic encephalitis, psychiatric symptoms and hypoventilation in ovarian teratoma. Ann Neurol 2005;58: 594–604.
399. Kruer MC, Koch TK, Bourdette DN, et al. NMDA receptor encephalitis mimicking seronegative neuromyelitis optica. Neurology 2010;74:1473–5.
400. Pennington C, Livingstone S, Santosh C, et al. N-Methyl-D-aspartate receptor antibody encephalitis associated with myelitis. J Neurol Sci 2012;317:151–3.
401. Cay HF, Gungor HA, Sezer I, et al. Adverse effect of TNF-alpha blocker? Demyelination in an ankylosing spondylitis patient: a case report. J Clin Pharm Ther 2006;31(6):645–8.
402. Saieg NA, Luzar MJ. Etanercept induced multiple sclerosis and transverse myelitis. J Rheumatol 2006;33:1202–4.
403. Oleginski TP, Harrington TM, Carlson JP. Transverse myelitis secondary to sulfasalazine. J Rheumatol 1991;18(2):304.
404. Zhang M, Li B, Li J. Acute transverse myelopathy probably related to intravenous gemcitabine plus cisplatin. Ann Pharmacother 2011;45(4):544–5.

405. Wang MY, Arnold AC, Vinters HV, et al. Bilateral blindness and lumbosacral myelopathy associated with high-dose carmustine and cisplatin therapy. Am J Ophthalmol 2000;130:367–8.
406. Baker WJ, Royer GL Jr, Weiss RB. Cytarabine and neurologic toxicity. J Clin Oncol 1991;9:679–93.
407. Resar L, Phillips P, Kastan M, et al. Acute neurotoxicity after intrathecal cytosine arabinoside in two adolescents with acute lymphoblastic leukemia of B-cell type. Cancer 1993;71:117–23.
408. Crawford S, Rustin G, Bagshawe K. Acute neurological toxicity of intrathecal cytosine arabinoside: a case report. Cancer Chemother Pharmacol 1986;16: 306–7.
409. Dinsdale T. Spinal analgesia and cauda equina lesions. Anaesthesia 1947;2: 17–27.
410. Dawkins CJ. An analysis of the complications of extradural and caudal block. Anaesthesia 1969;24:554–63.
411. Newberry JM. Paraplegia following general anaesthesia. Anaesthesia 1977;32: 78–9.
412. Schreiner EJ, Lipson SF, Bromage PR, et al. Neurological complications following general anaesthesia. Three cases of major paralysis. Anaesthesia 1983;38:226–9.
413. Kitching A, Taylor S. A postoperative neurological problem. Anaesthesia 1989; 44:695–6.
414. Gutowsky NJ, Davies AO. Transverse myelitis following general anaesthesia. Anaesthesia 1993;48:44–5.
415. Martinez-Garcia E, Pelaez E, Roman JC, et al. Transverse myelitis following general and epidural anaesthesia in a paediatric patient. Anaesthesia 2005; 60:921–3.
416. Richter RW, Rosenberg RN. Transverse myelitis associated with heroin addiction. JAMA 1968;206(6):1255–7.
417. Ell JJ, Uttley D, Silver JR. Acute myelopathy in association with heroin addiction. J Neurol Neurosurg Psychiatry 1981;44:448–50.
418. McCreary M, Emerman C, Hanna J, et al. Acute myelopathy following intranasal insufflation of heroin: a case report. Neurology 2000;55:316–7.
419. Sahni V, Garg D, Garg S, et al. Unusual complications of heroin abuse: transverse myelitis, rhabdomyolysis, compartment syndrome, and ARF. Clin Toxicol (Phila) 2008;46(2):153–5.
420. Herregods P, Chappel R, Mortier G. Benzene poisoning as a possible cause of transverse myelitis. Paraplegia 1984;22:305–10.
421. Sauer GC. Transverse myelitis and paralysis from a brown recluse spider bite. Mo Med 1975;72(10):603–4.
422. Misra UK, Kalita K. Comparison of clinical and electrodiagnostic features in B12 deficiency neurological syndromes with and without antiparietal cell antibodies. Postgrad Med J 2007;83(976):124–7.
423. Lindenbaum J, Healton EB, Savage DG, et al. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. N Engl J Med 1988;318(26):1720–8.
424. Naidich MJ, Ho SU. Case 87: subacute combined degeneration. Radiology 2005;237:101–5.
425. Paliwal VK, Malhotra HS, Chaurasia RN, et al. “Anchor”-shaped bright posterior column in a patient with vitamin B12 deficiency myelopathy. Postgrad Med J 2009;85:186.

426. Vorgerd M, Tegenthoff M, Kuhne D, et al. Spinal MRI in progressive myeloneuropathy associated with vitamin E deficiency. Neuroradiology 1996;38:S111–3.
427. Gutmann L, Shockor W, Gutmann L, et al. Vitamin E-deficient spinocerebellar syndrome due to intestinal lymphangiectasia. Neurology 1986;36(4):554–6.
428. Nelson JS, Fitch CD, Fischer VW, et al. Progressive neuropathologic lesions in vitamin E deficient rhesus monkeys. J Neuropathol Exp Neurol 1981;40:166–86.
429. Pineles SL, Wilson CA, Balcer LJ, et al. Combined optic neuropathy and myelopathy secondary to copper deficiency. Surv Ophthalmol 2010;55(4):386–92.
430. Naismith RT, Shepherd JB, Weihl CC, et al. Acute and bilateral blindness due to optic neuropathy associated with copper deficiency. Arch Neurol 2009;66(8):1025–7.
431. Nations SP, Boyer PJ, love LA, et al. Denture cream: an unusual source of excess zinc leading to hypocupremia and neurologic disease. Neurology 2008;71(9):639–43.
432. Kumar N. Copper deficiency myelopathy (human swayback). Mayo Clin Proc 2006;81(10):1371–84.
433. Jaiser SR, Winston GP. Copper deficiency myelopathy. J Neurol 2010;257: 869–81.
434. Tatum WO, Bui DD, Grant EG, et al. Pseudo-Guillain-Barre syndrome due to "whippet"-induced myeloneuropathy. J Neuroimaging 2010;20(4):400–1.
435. Renard D, Dutray A, Remy A, et al. Subacute combined degeneration of the spinal cord caused by nitrous oxide anaesthesia. Neurol Sci 2009;30(1):75–6.
436. Ng J, O'Grady G, Pettit T, et al. Nitrous oxide use in first-year students at Auckland University. Lancet 2009;361:1349–50.
437. Spencer PS, Ludoph AC, Kisby GE. Neurologic diseases associated with use of plant components with toxic potential. Environ Res 1993;62:106–13.
438. Gerstner ER, Batchelor TT. Primary central nervous system lymphoma. Arch Neurol 2010;67(3):291–7.
439. Herrlinger U, Weller M, Kuker W. Primary CNS lymphoma in the spinal cord: clinical manifestations may precede MRI detectability. Neuroradiology 2002;44(3): 239–44.
440. Flanagan EP, O'Neill BP, Porter AB, et al. Primary intramedullary spinal cord lymphoma. Neurology 2011;77(8):784–91.
441. Beristain X, Azzarelli B. The neurological masquerade of intravascular lymphomatosis. Arch Neurol 2002;59:439–43.
442. Grove CS, Robbins PD, Kermode AG. Intravascular lymphoma presenting as progressive paraparesis. J Clin Neurosci 2008;15:1056–8.
443. Yang T, Tian L, Li Q, et al. A case of intravascular B-cell lymphoma presenting as myelopathy and diagnosed postmortem. J Neurol Sci 2008;272:196–8.
444. Kumar N, Keegan AM, Rodriguez FJ, et al. Intravascular lymphoma presenting as a longitudinally-extensive myelitis: diagnostic challenges and etiologic clues. J Neurol Sci 2011;303:146–9.
445. Podnar S. Epidemiology of cauda equina and conus medullaris lesions. Muscle Nerve 2007;35:529–31.
446. Schwarz S, Zoubaa S, Knauth M, et al. Intravascular lymphomatosis presenting with a conus medullaris syndrome mimicking disseminated encephalomyelitis. Neuro Oncol 2002;4(3):187–91.
447. Zeng M, Knisely J. Post-radiotherapy myelitis observed in an AIDS patient with a meningioma: case report and review of the literature. J Neurooncol 1999; 45(2):167–74.
448. Rampling R, Symonds P. Radiation myelopathy. Curr Opin Neurol 1998;11(6): 627–32.

449. Bleyer A, Choi M, Wang SJ, et al. Increased vulnerability of the spinal cord to radiation or intrathecal chemotherapy during adolescence: a report from the Children's Oncology Group. Pediatr Blood Cancer 2009;53:1205–10.
450. Alfonso ER, De Gregorio MA, Mateo P, et al. Radiation myelopathy in over-irradiated patients: MR imaging findings. Eur Radiol 1997;7(3):400–4.
451. Behrman AL, Harkema SJ. Physical rehabilitation as an agent for recovery after spinal cord injury. Phys Med Rehabil Clin N Am 2007;18(2):183–202.
452. Atrice MB. Lower extremity orthotic management for the spinal-cord-injured client. Spinal Cord Inj Rehabil 2000;5(4):1–10.
453. Bailey SN, Hardin EC, Kobetic R, et al. Neurotherapeutic and neuroprosthetic effects of implanted functional electrical stimulation for ambulation after incomplete spinal cord injury. J Rehabil Res Dev 2010;47(1):7–16.
454. Everaert DG, Thompson AK, Chong SL, et al. Does functional electrical stimulation for foot drop strengthen corticospinal connections? Neurorehabil Neural Repair 2010;24:168–77.
455. Swinnen E, Duerinck S, Baeyens JP, et al. Effectiveness of robot-assisted gait training in persons with spinal cord injury: a systematic review. J Rehabil Med 2010;42:520–6.
456. Jung R, Belanger A, Kanchiku T, et al. Neuromuscular stimulation therapy after incomplete spinal cord injury promotes recovery of interlimb coordination during locomotion. J Neural Eng 2009;6(5):055010. http://dx.doi.org/10.1088/1741-2560/6/5/055010.
457. Goodman AD, Brown TR, Edwards KR, et al. A phase 3 trial of extended release oral dalframpridine in multiple sclerosis. Ann Neurol 2010;68(4):494–502.
458. Kalsi V, Gonzales G, Popat R, et al. Botulinum injections for the treatment of bladder symptoms of multiple sclerosis. Ann Neurol 2007;62(5):452–7.
459. Morton SC, Shekelle PG, Adams JL, et al. Antimicrobial prophylaxis for urinary tract infection in persons with spinal cord dysfunction. Arch Phys Med Rehabil 2002;83:129–38.
460. Hess MJ, Hess PE, Sullivan MR, et al. Evaluation of cranberry tablets for the prevention of urinary tract infections in spinal cord injured patients with neurogenic bladder. Spinal Cord 2008;46:622–6.
461. Bosma R, Wynia K, Havlikova E, et al. Efficacy of desmopressin in patients with multiple sclerosis suffering from bladder dysfunction: a meta-analysis. Acta Neurol Scand 2005;112(1):1–5.
462. Khan F, Pallant JF, Pallant JI, et al. A randomised controlled trial: outcomes of bladder rehabilitation in persons with multiple sclerosis. J Neurol Neurosurg Psychiatry 2010;81:1033–8.
463. Dasgupta P, Haslam C, Goodwin R, et al. The 'Queen Square bladder stimulator': a device for assisting emptying of the neurogenic bladder. Br J Urol 1997;80(2):234–7.
464. Prasad RS, Smith SJ, Wright H. Lower abdominal pressure versus external bladder stimulation to aid bladder emptying in multiple sclerosis: a randomized controlled study. Clin Rehabil 2003;17(1):42–7.
465. Schwendimann RN. Treatment of symptoms in multiple sclerosis. Neurol Res 2006;28:306–15.
466. Bywater A, While A. Management of bowel dysfunction in people with multiple sclerosis. Br J Community Nurs 2006;11(8):333–41.
467. Wiesel PH, Norton C, Roy AJ, et al. Gut focused behavioural treatment (biofeedback) for constipation and faecal incontinence in multiple sclerosis. J Neurol Neurosurg Psychiatry 2000;69(2):240–3.

468. Lombardi G, Macchiarella A, Cecconi F, et al. Ten-year follow-up of sildenafil use in spinal cord-injured patients with erectile dysfunction. J Sex Med 2009;6(12): 3449–57.
469. Lombardi G, Nelli F, Celso M, et al. Treating erectile dysfunction and central neurological diseases with oral phosphodiesterase type 5 inhibitors. Review of the literature. J Sex Med 2012;9(4):970–85.
470. Dimitriadis T, Karakitsios K, Tsounapi P, et al. Erectile function and male reproduction in men with spinal cord injury: a review. Andrologia 2010;42(3):139–65.
471. Sipski ML, Alexander CJ, Gomez-Marin O, et al. Effects of vibratory stimulation on sexual response in women with spinal cord injury. J Rehabil Res Dev 2005; 42(5):609–16.
472. Billups KL, Berman L, Berman J, et al. A new non-pharmacological vacuum therapy for female sexual dysfunction. J Sex Marital Ther 2001;27:435–41.
473. Lahrmann H, Cortelli P, Hilz M, et al. EFNS guidelines on the diagnosis and management of orthostatic hypotension. Eur J Neurol 2006;13(9):930–6.
474. Faghri PD, Yount J. Electrically induced and voluntary activation of physiologic muscle pump: a comparison between spinal cord-injured and able-bodied individuals. Clin Rehabil 2002;16(8):878–85.
475. Raymond J, Davis GM, Bryant G, et al. Cardiovascular responses to an orthostatic challenge and electrical-stimulation-induced leg muscle contractions in individuals with paraplegia. Eur J Appl Physiol Occup Physiol 1999;80(3): 205–12.
476. Low PA, Gilden JL, Freeman R, et al. Efficacy of midodrine vs placebo in neurogenic orthostatic hypotension. A randomized, double-blind multicenter study. Midodrine study group. JAMA 1997;277(13):1046–51.
477. Singer W, Sandroni P, Opfer-Gehrking TL, et al. Pyridostigmine treatment trial in neurogenic orthostatic hypotension. Arch Neurol 2006;63(4):513–8.
478. Mathias CJ, Senard JM, Braune S, et al. L-threo-dihydroxyphenylserine (L-threo-DOPS; droxidopa) in the management of neurogenic orthostatic hypotension: a multi-national, multi-center, dose-ranging study in multiple system atrophy and pure autonomic failure. Clin Auton Res 2001;11:235–42.
479. Rabchevsky AG, Patel SP, Duale H, et al. Gabapentin for spasticity and autonomic dysreflexia after severe spinal cord injury. Spinal Cord 2011;49(1): 99–105.
480. Frankel HL, Mathias CJ. Severe hypertension in patients with high spinal cord lesions undergoing electro-ejaculation—management with prostaglandin E2. Paraplegia 1980;18(5):293–9.