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Pediatric Acute Transverse Myelitis Overview and Differential Diagnosis

Varina L. Wolf, MD¹, Pamela J. Lupo, MD¹, and Timothy E. Lotze, MD¹

Abstract
Acute transverse myelitis is a clinical syndrome affecting the spinal cord, which is characterized by acute onset of motor, sensory, and autonomic dysfunction. Approximately 20% of cases of acute transverse myelitis occur in children. This review summarizes the current published literature on acute transverse myelitis, including epidemiology, diagnostic criteria, pathogenesis, clinical presentation, clinical evaluation, and differential diagnosis. The article also summarizes the neuroimaging features, acute and chronic complications, treatments, and prognosis of acute transverse myelitis in the pediatric population. The initial evaluation centers on differentiation from other causes of myelopathy, and cases are further divided into idiopathic or disease-associated acute transverse myelitis. Correct diagnosis is important for treatment and prognosis. Treatment begins with intensive surveillance for acute life-threatening respiratory or autonomic complications. Immunomodulating therapy is recommended for noninfectious causes, using high-dose intravenous corticosteroids or plasma exchange. Other therapeutic options are also discussed. Prognosis depends on a number of factors, and evidence suggests that the majority of children have a good outcome. A small percentage of children diagnosed with acute transverse myelitis later are diagnosed with other demyelinating diseases, especially neuromyelitis optica, or multiple sclerosis. The most common long-term complications of acute transverse myelitis are urinary, motor, or sensory dysfunction.

Keywords
acute transverse myelitis, myelopathy, demyelinating, acute weakness, pediatric

Epidemiology
Across all age populations, the incidence of acute transverse myelitis is reported to be 1 to 8 cases per million people in the United States, resulting in approximately 1400 new cases per year being diagnosed in the United States.¹ Thirty-four thousand adults and children have residual disabilities secondary to acute transverse myelitis. Approximately 20% of acute transverse myelitis cases occur in children.¹ The Canadian Pediatric Surveillance Program provided an incidence of 2 cases per million children.² There are 2 peaks of pediatric incidence, between 0 and 2 years of age and 5 to 17 years of age, with the age of highest incidence between birth and 2 years, although this may reflect referral center bias.³ One study has demonstrated a slight male predominance (female/male = 0.81/1).² However, a more recent report of Canadian children with acute

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transverse myelitis found a slight female predominance of 1.2:1 in children under the age of 10 years, which became more pronounced at 2.6:1 for children over 10 years. This is similar to adult populations in which transverse myelitis secondary to multiple sclerosis and other inflammatory causes is more often seen in women.

**Diagnostic Criteria**

Diagnostic criteria, defined by the 2002 American Academy of Neurology (AAN) Transverse Myelitis Consortium Working Group, outline proposed exclusion and inclusion guidelines. As transverse myelitis is a diagnosis of exclusion, the initial approach is to exclude such conditions as extrinsic spinal compression, ischemia, tumor, arteriovenous malformation, and toxicities such as those produced by vitamin B12 deficiency or previous spinal radiation. In the absence of such exclusionary diagnoses, cases are then further divided into 2 groups: idiopathic acute transverse myelitis and disease-associated acute transverse myelitis, the latter encompassing cases secondary to identified causes such as connective tissue disease, multiple sclerosis, and neuromyelitis optica. Additional inclusion criteria include both of the following:

1. Evidence of spinal cord inflammation as demonstrated by the following:
   a. an enhancing spinal cord lesion, or
   b. cerebrospinal fluid finding of either pleocytosis (greater than 10 cells/mm$^3$) or increased immunoglobulin type G (IgG) index.
2. Time to nadir of dysfunction (ie, maximal disability) greater than 4 hours and less than 21 days.

Specific testing to differentiate disease-associated acute transverse myelitis from idiopathic acute transverse myelitis is discussed below. Two recent studies discuss these specific inclusion criteria in a pediatric population. In the first study ($n = 47$), 74% met the gadolinium enhancement magnetic resonance imaging (MRI) criteria, and 50% met the cerebrospinal fluid pleocytosis criteria. It is not known by this study as to how many patients met both of the cord enhancement and cerebrospinal fluid finding criteria. The IgG index was not sufficiently reported to be included. Time to nadir was reported at a mean of 48 hours. The number of patients progressing to their nadir of dysfunction at greater than 21 days is not reported. In the second pediatric study ($n = 47$), 23% (9 of 38) had gadolinium enhancement, 67% (21 of 31) had a cerebrospinal fluid white blood cell count greater than 10 cells/μL, and mean time to nadir was 3.7 days, with 6% (3 of 47) progressing to nadir at greater than 21 days. The IgG index was not reported. Given these results, it is possible that not all lesions concerning acute transverse myelitis will demonstrate enhancement or meet cerebrospinal fluid inclusion criteria as outlined above. This suggests that the 2002 consortium guidelines may underdiagnose pediatric acute transverse myelitis, but this needs further study.

**Immunopathogenesis**

There are several theories explaining the inciting events of immune-mediated infiltration of the spinal cord. These theories include molecular mimicry, superantigen effect, humorally based dysregulation, interleukin 6–mediated toxicity (IL-6), and a secondary effect of allergy with elevated immunoglobulin E (IgE) levels, as discussed further below. There are unifying elements to all of these theories found in pathology-based studies, demonstrating intraparenchymal and perivascular cellular infiltrates associated with demyelination and neuronal injury. The cellular makeup of the infiltrates are monocytes and sometimes CD4$^+$ and CD8$^+$ T lymphocytes. The glia and microglia demonstrate activation. In some cases, necrosis with cavitation is found. The intact subpial parenchyma yields evidence that ischemia may be the common end effect of the cellular infiltration, producing the cord lesions in longitudinally extensive transverse myelitis.

**Presentation of Idiopathic and Disease-Associated Acute Transverse Myelitis**

**Prodrome**

Pediatric acute transverse myelitis is typically preceded by a mild illness in the 3 weeks prior to symptom onset, as reported in 50% to 100% of cases. Other less common provoking factors reported include vaccine, allergy shot, and mild trauma. No single infectious pathogen, vaccine type, or specific allergy shot prevails as a leading risk factor for idiopathic acute transverse myelitis. Mild spinal trauma has been reported.
as a prodromal risk factor. However, some of these cases are described to have imaging evidence for displacement of the posterior spinal ligament, narrowing and protrusion of intervertebral discs, and nucleus pulposus T2 hypointensity perhaps more suggestive of ischemic myelopathy secondary to fibrocartilagenous embolism. Alternatively, mild trauma may be coincidently incurred secondary to gait instability in the early stages of acute transverse myelitis. In addition, lesions due to trauma can have secondary demyelination but is not thought to be due to a primary immune-related derangement as in idiopathic acute transverse myelitis.

Signs and Symptoms

The spinal cord is a relatively narrow structure in which motor, sensory, and autonomic tracts are in close proximity. Therefore, lesions in the spinal cord can have effects in all of these modalities. However, such effects are not necessarily uniform in severity or symmetric across different modalities. Clinical examination, with a focus on investigation for a spinal sensory and motor level, will aid in lesion localization.

One of the most common initial symptoms in children is pain (60%). Other common symptoms in children include motor deficits, numbness, ataxic gait, and loss of bowel or bladder control. Priapism and visual loss are also reported. Weakness is most commonly found in the lower extremities but is also frequent in the torso and upper extremities. Involvement of the posterior columns can cause fine motor dyscoordination and an ataxic gait, which may be mislocalized to the cerebellum. Occasionally, weakness can be unilateral. Ninety percent of patients will have sensory loss, most often at a thoracic level. Sensory loss in any primary modality is often found in a band-like or transverse level, with a noticeable decrease in severity or symmetric across different modalities. Clinical examination, with a focus on investigation for a spinal sensory and motor level, will aid in lesion localization.

In the initial phase, spinal shock may be present, which causes a transient physiological suspension of spinal cord function and loss of reflexes below the level of the injury, lasting days to 12 weeks. Deafferentation from the sympathetic control center in the medulla oblongata to the spinal sympathetic neurons in the intermediolateral nuclei of thoracic level 1 through lumbar level 2 cord segments results in reduced sympathetic activity below the level of injury and unopposed parasympathetic outflow through the intact vagal nerve, manifesting as arterial hypotension and bradycardia. Resolution of spinal shock is heralded by a return of increased deep tendon reflexes and increased tone. The initial absence of reflexes can sometimes raise consideration for Guillain-Barré syndrome rather than acute transverse myelitis as the etiology for the presenting complaints. However, additional aspects of the neurological examination and occasional ancillary studies can help to distinguish the conditions as discussed below.

Autonomic dysreflexia appears after the beginning of spinal shock resolution and is a potentially life-threatening syndrome of imbalanced reflex sympathetic discharge occurring in patients with lesions above the splanchnic sympathetic outflow from thoracic level 5 to 6. Autonomic symptoms are virtually always part of the clinical course of acute transverse myelitis. Urinary retention causing postvoid residuals is found in 95% of patients during the acute phase, secondary to disruption of the signal between the pontine micturition center and the sacral level. Chronically, there may be detrusor muscle spasticity causing incontinence, an areflexic bladder leading to urinary retention, or dyscoordination of the internal and external sphincters for micturition (ie, detrusor sphincter dys-synergia). The urinary symptoms do not correlate with either MRI signal changes or with the degree of motor and sensory deficit but instead with reflex and tone changes. Constipation can be severe and may present in children as increased irritability with fullness in the left lower quadrant. Horner syndrome, resulting from lesions above thoracic level 2 that decrease sympathetic signal to the superior cervical ganglion, may not initially be recognized or attributed to a spinal cord lesion.

Encephalopathy is not classically part of the presentation of acute transverse myelitis itself. However, acute transverse myelitis may present in association with acute disseminated encephalomyelitis in which encephalopathy is (by definition) present. Headache, fatigue, ataxia, seizure, and tremor have all been reported in pediatric acute transverse myelitis and most likely represent part of the acute disseminated encephalomyelitis spectrum.

Infantile Acute Transverse Myelitis

Signs and symptoms of acute transverse myelitis in the infant can be difficult to recognize given limited cooperation and communication. Irritability related to pain from allodynia or Lhermitte sign may suggest a primary encephalopathy. Alternatively, signs of myelopathy in the setting of acute disseminated encephalomyelitis may not be obvious on examination in an infant with severe encephalopathy. As such, imaging of the spine should be performed in such cases. Detection of sensory deficits can also be confounded by an irritable infant, and less dramatic signs of weakness may be overlooked. Clues to the diagnosis are reduced movements, especially of the lower extremities, and decreased urinary output. Priapism was a principal symptom in an infant presenting at our institution.

Evaluation Strategy

Emergent spinal imaging is warranted in all patients with acute myelopathic symptoms. Presentation of compressive lesions such as extramedullary tumor or hemorrhage can be identical to transverse myelitis. Examination and imaging direct critical neurosurgical intervention for the relief of compressive lesions with the aim of preventing permanent deficits. Communication between the examining physician and neuroradiologist optimizes diagnostic MRI resources. Ultimately, comprehensive spine and brain MRI is indicated, including gadolinium-enhanced studies. Once compressive etiologies are ruled
out, lumbar puncture and serological tests are the next necessary steps in diagnosis. Tables 1 and 2 provide lists of common cerebrospinal fluid and serological tests. Specific studies are guided by the differential diagnosis.

**Ophthalmological Evaluation**

Ophthalmological examination, ideally to include patterned visual evoked potentials and ocular coherence tomography, is recommended for all patients presenting with acute transverse myelitis. While patient complaints of vision impairment provide a clear indication of comorbid optic neuritis, younger patients and patients with an encephalopathy may not report this symptom. In addition, experience at our institution has discovered neurophysiological evidence for subclinical optic neuritis in children with no such reported history. This has implications as to the diagnosis of disease-associated transverse myelitis and recurrence risk.

**Differential Diagnosis**

**Compressive Myelopathy**

Neurological symptoms caused by extramedullary mass effect on the spinal cord can be the first signs of the underlying pathology. Depending on the underlying etiology, additional constitutional symptoms can include back pain and fever. Traumatic injury can result in vertebral body compression, intervertebral disk herniation, and epidural hematoma. Compressive extramedullary tumors presenting in childhood include Ewing sarcoma, neuroblastoma, granulocytic sarcoma, T cell and malignant lymphoma, and Hodgkin disease. In addition, spinal cord abscesses may result in symptoms of compressive myelopathy.

**Ischemic Myelopathy**

Ischemia of the spinal cord is uncommon in children. Anterior spinal artery infarction presents with motor, autonomic, and spinothalamic-related sensory deficits localized to the anterior two thirds of the spinal cord, with sparing of vibration and proprioception. Anterior spinal artery infarction is reported after both mild and major trauma, aortic dissection, anterior spinal artery dissection, embolism, and primary thrombus. The most sensitive imaging results are diffusion-weighted sequences demonstrating restricted diffusion in the distribution of a T2 hyperintense lesion. Short T1-weighted inversion recovery images may have improved contrast over T2 images by reducing fat saturation. Hyperintensity is reported first in the anterior cortical spinal tract, progressing to include the entire anterior two thirds of the cord over 2 to 3 days. However, patterns of ischemia on spinal MRI are more difficult to detect and interpret, especially in children, secondary to the smaller diameter of the cord. Specific MRI modalities can improve visualization at 7 to 10 days. Repeat imaging on day 2 may demonstrate lesions in a previously normal cord. Absence of cerebrospinal fluid pleocytosis and normal protein are more typical with infarct and may distinguish this from an inflammatory myelopathy.

**Fibrocartilagenous Embolism**

Fibrocartilagenous embolism causes the same symptoms as anterior spinal artery infarction and can occur after mild trauma or straining in children. The intervertebral disc’s nucleus pulposus material embolizes and obstructs arterial flow to the associated spinal cord. Imaging may demonstrate ischemic changes in the anterior spinal cord with unusual T2 isointensity and narrowing of the associated disc(s), which are normally hyperintense on T2-weighted images.

**Previous Spinal Radiation**

With corresponding clinical history, postradiation myelopathy may be considered and range from acute transient myelitis, presenting with Lhermitte sign, to chronic progressive necrotic myelitis with severe paralysis. Latent period can be 3 months to 6 years. Treatments include steroids and hyperbaric oxygen.

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### Table 1. Cerebrospinal Fluid Evaluation

<table>
<thead>
<tr>
<th>Cerebrospinal fluid component</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell count</td>
<td>&gt;50 white blood cell/μL infectious</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>Elevated in multiple sclerosis</td>
</tr>
<tr>
<td>IgG index</td>
<td>Elevated in one third of longitudinally extensive transverse myelitis</td>
</tr>
<tr>
<td>Oligoclonal bands</td>
<td></td>
</tr>
<tr>
<td>Viral and bacterial culture</td>
<td></td>
</tr>
<tr>
<td>Viral DNA PCR</td>
<td>Herpes simplex, varicella, EBV, CMV</td>
</tr>
<tr>
<td>Aquaporin 4 IgG</td>
<td>Obtain if serum negative and suspect NMO disease</td>
</tr>
<tr>
<td>Measles, rubella, zoster IgG level</td>
<td>Normal levels in NMO and paraneoplastic</td>
</tr>
</tbody>
</table>

IgG, immunoglobulin type G; PCR, polymerase chain reaction; EBV, Epstein-Barr virus; CMV, cytomegalovirus; NMO, neuromyelitis optica.

### Table 2. Serum Evaluation

<table>
<thead>
<tr>
<th>Serology</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td></td>
</tr>
<tr>
<td>Mycoplasma IgM and IgG with throat swab PCR</td>
<td></td>
</tr>
<tr>
<td>Cat scratch, Bartonella henselae titers</td>
<td></td>
</tr>
<tr>
<td>Lyme disease in endemic areas RPR</td>
<td></td>
</tr>
<tr>
<td>Autoimmune</td>
<td></td>
</tr>
<tr>
<td>ANA, RF, anti–dsDNA antibody, antiphospholipid antibodies Aquaporin 4 IgG</td>
<td></td>
</tr>
</tbody>
</table>

IgM, immunoglobulin type M; IgG, immunoglobulin type G; PCR, polymerase chain reaction; RPR, rapid plasma reagin test for syphilis; anti-nuclear antibody; RF, rheumatoid factor; dsDNA, double-stranded DNA.
Intramedullary Tumor

Intramedullary tumors, such as gliomas, can present similarly to acute transverse myelitis. Astrocytomas, the most common childhood primary cord neoplasm, typically demonstrate an enhancing infiltrating mass with fusiform expansion of the cord, usually extending less than 4 vertebral segments. A syrinx above and below the lesion is often present secondary to obstruction of the central canal by the tumor. Sometimes, hyperintense proteinaceous cerebrospinal fluid (Froin syndrome) may be present below the mass, occasionally associated with hemorrhage. Pilocytic astrocytomas may have a cyst adjacent to the tumor. Ependymomas are well circumscribed with cord expansion. These tumors may be cystic or be associated with a syrinx and frequently hemorrhage. Occasionally, it can be difficult to distinguish acute transverse myelitis from an intramedullary mass in the setting of diffuse cord swelling with increased T2 signal, gadolinium enhancement, and elevated protein. Inflammatory markers such as cerebrospinal fluid pleocytosis can help to distinguish the two. However, patients with large expansile lesions associated with cysts or those who do not improve with standard therapy for acute transverse myelitis or continue to worsen past 30 days should be reimaged. Biopsy should be considered if there is progressive disease.

Spinal Arteriovenous Malformation

Arteriovenous malformation or fistula of the spine classically presents with fluctuating motor, sensory, and/or autonomic symptoms related to a vascular steal phenomenon. A vascular bruit can sometimes be auscultated over the back. The flow voids, which may or may not be visualized on MRI, represent engorged veins. Increased T2 signal and cord swelling can mimic acute transverse myelitis. Spinal angiography is the modality of choice but, in small children and infants, is often not possible secondary to the very small vessel caliber. Time of flight and phase contrast magnetic resonance angiography can prove useful.

Infectious Myelitis

Presentation and MRI findings of direct infection of the spinal cord can be similar to acute transverse myelitis, with cord swelling, focal T2 hyperintensity, and enhancement. Cerebrospinal fluid protein and cell count are classically markedly elevated, typically with protein elevation above 100 to 500 mg/dL, cell count greater than 50 cells/μL, and decreased glucose. Exceptions to these findings are numerous, and acute transverse myelitis can have similar white cell count and protein findings. Fever can occur as part of autonomic dysfunction in acute transverse myelitis, further confusing the picture. A variety of pathogens have been reported to include human herpes virus-1 and -6; varicella zoster virus; Epstein-Barr virus; cytomegalovirus; influenza viruses; enteroviruses; hepatitis A, B, and C; and bacteria such as Mycoplasma pneumoniae, Bartonella henselae, and Borrelia burgdorferi.

Testing for a specific infectious agent should be based upon associated exposures and additional clinical features suggestive of a particular pathogen. Detection of a pathogen by cerebrospinal fluid polymerase chain reaction is most sensitive. Alternatively, 4-fold increases in IgG titers or evolution from elevated IgM to IgG at 2 and 6 weeks can provide evidence for an associated direct infection.

Guillain-Barré Syndrome

Guillain-Barré syndrome can present similarly to acute transverse myelitis, with depressed reflexes, weakness, bowel and bladder dysfunction, and autonomic dysregulation. Differentiating factors of Guillain-Barré syndrome include lack of a prominent sensory component and the presence of cranial neuropathies (excluding the optic nerve). Magnetic resonance imaging can also help to distinguish the 2 conditions by demonstrating enhancement of spinal nerve roots in Guillain-Barré syndrome and the absence of intramedullary disease. While both acute transverse myelitis and Guillain-Barré syndrome may have elevation of cerebrospinal fluid protein, Guillain-Barré syndrome will not demonstrate pleocytosis as is often seen in acute transverse myelitis. In cases that remain unclear, nerve conduction studies can be of use to demonstrate an acquired neuropathy. Rarely, acute transverse myelitis and Guillain-Barré syndrome have occurred together in a patient.

Disease-Associated Acute Transverse Myelitis

While idiopathic acute transverse myelitis is a diagnosis of exclusion, it accounts for 89% of cases in pediatric studies, compared to 36% of adult cases. The purpose of investigating the presence of disease-associated acute transverse myelitis is primarily to identify those at risk for recurrence and to initiate appropriate treatment and surveillance to improve outcomes. Diseases associated with pediatric acute transverse myelitis include multiple sclerosis, acute disseminated encephalomyelitis, neuromyelitis optica, and rheumatological conditions such as systemic lupus erythematosus and antiphospholipid antibody syndrome. The results of brain and spinal cord MRI as well as serum and cerebrospinal fluid studies are useful in such diagnoses. Table 3 summarizes key differentiating features from the AAN evidence-based guideline with regard to MRI, cerebrospinal fluid, and serum interpretation in disease-associated acute transverse myelitis.

MRI Features

The cord involvement of idiopathic acute transverse myelitis has a pattern that is central and more uniform and symmetric when compared to the pattern found in multiple sclerosis, in which the cord has a patchier and peripheral lesion distribution. Longitudinally extensive transverse myelitis is defined as acute transverse myelitis involving 3 or more consecutive vertebral levels and is clinically most often associated with acute complete transverse myelitis. Similar to adults, longitudinally...
extensive transverse myelitis is common in pediatric idiopathic acute transverse myelitis, with 2 studies reporting a mean lesion length of 6 spinal cord segments.2,48 In addition, longitudinally extensive transverse myelitis is more typically seen in children with acute disseminated encephalomyelitis–associated transverse myelitis and in neuromyelitis optica. Multiple sclerosis is more typically associated with segmental transverse myelitis occupying fewer than 3 vertebral segments, as in Figure 1.

**Life-Threatening Acute Complications**

Certain spinal lesion locations warrant increased attention and consideration for a higher level of care with close cardiac and respiratory monitoring, especially early in the course. Upper cervical lesions can affect cranial nerve 11, the spinal accessory nerve, which innervates the pharyngeal muscles, and can result in loss of upper airway patency. Lesions above cervical level 5 (C5) can weaken the diaphragm and can result in loss of inspiratory excursion and respiratory compromise.

Importantly, thoracic lesions above T6 can result in autonomic dysreflexia. Noxious sensory stimuli, such as urinary retention or muscle spasms, below the lesion travel through peripheral sensory nerves to neurons located in the intermediolateral thoracolumbar nuclei, releasing sympathetic outflow discharge, resulting in peripheral hypertension, sweating, and headache secondary to cerebral vasodilation.18 Parasympathetic response to hypertension mediated through the vagus nerve generates inhibitory impulses that cannot be transmitted below the lesion but triggers bradycardia.18 The constellation of symptoms includes elevated systolic blood pressure, headache, visual impairment due to cerebral vasodilation, and reflex bradycardia.18 Treatment includes the avoidance of triggers with prophylactic intermittent urinary catheterization, bowel decompression, spasticity management, elevated position of the head and trunk, and, if needed, prophylactic α-adrenergic blocker such as terazosin. Ablative agents can include sublingual nifedipine or, in extreme circumstances, general anesthesia blocking sympathetic response.18

**Pediatric Acute Transverse Myelitis Treatment**

The initial treatment of patients suspected to have spinal cord lesions includes evaluation of airway, breathing, and circulation. A history of trauma requires initial immobilization of the spinal cord until imaging studies and neurological evaluations rule out trauma-related myelopathy. Attendance to acute urinary retention should be managed with catheterization.

Class I evidence for treatment in children does not exist. However, recently published guidelines following typical practice suggest first-line treatment of noninfectious immune-mediated acute transverse myelitis to be intravenous methylprednisolone 30 mg/kg/d for 5 to 7 days, with a maximum dose of 1 g/d. Use of high-dose corticosteroids can reduce the length of disability and improve outcomes.22,49,50 One small study compared a group of 12 children with complete acute transverse myelitis treated with high-dose corticosteroids to a historical control of 17 children not receiving such treatment.50 The proportion of children walking at 1 month in the treated group was 66% versus 17% in the control group. In addition, 55% of patients in the treated group were reported to have had complete recovery at 12 months compared to only 12% in the control group. The time to independent walking was also significantly shorter in the treated group at a mean of 25 days versus 120 days in the control group. Normal sphincter function was also more common in the treated patients (9 of 12) compared to only 3 of 17 in the control group. Intravenous steroid treatment should be followed by an oral corticosteroid taper starting at 1 mg/kg patient weight per day over 3 to 4 weeks. If clinical improvement does not begin or symptoms are

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**Table 3. Differentiating Factors in Disease-Associated Acute Transverse Myelitis: American Academy of Neurology Evidence-Based Guideline**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Evidence level</th>
<th>Investigation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromyelitis optica</td>
<td>I</td>
<td>Serum and CSF aquaporin 4 IgG</td>
<td>Diagnostic of disease when present</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>MRI in longitudinally extensive transverse myelitis</td>
<td>More common in NMO than multiple sclerosis</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>II</td>
<td>CSF OCB</td>
<td>Rarely, OCB can be found in NMO, ADEM, and infectious myelopathies (Lyme, measles, syphilis)</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Acute partial transverse myelitis</td>
<td>More common in multiple sclerosis</td>
</tr>
<tr>
<td>Connective tissue disease related</td>
<td>II</td>
<td>Brain MRI with multiple sclerosis–like lesions</td>
<td>More common in multiple sclerosis</td>
</tr>
</tbody>
</table>

CSF, cerebrospinal fluid; IgG, immunoglobulin type G; MRI, magnetic resonance imaging; AAN, anti-nuclear antibody; SLE, systemic lupus erythematosus; SS, Sjögren syndrome; NMO, neuromyelitis optica; OCB, oligoclonal bands; ADEM, acute disseminated encephalomyelitis.
worsening within 24 to 48 hours of beginning corticosteroid treatment, consideration should be given for initiation of plasma exchange therapy, especially for longitudinally extensive transverse myelitis. A recent evidence-based guideline on the utilization of plasma exchange in the treatment of neurological diseases noted a single study with class II evidence for effectiveness of plasmapheresis in fulminant demyelinating conditions. At the authors’ institution, they will typically perform 6 exchanges of 1.1 plasma volumes over 14 days. Limited evidence exists for additional therapies but can include intravenous immunoglobulin and cyclophosphamide. Intravenous immunoglobulin is typically dosed at 2 g/kg divided over 2 to 5 days. Cyclophosphamide 500 to 750 mg/m² once may be another alternative.

Patients with acute transverse myelitis of any lesion length and having brain MRI consistent with multiple sclerosis and meeting the 2010 McDonald multiple sclerosis criteria can be considered for initiation of typical immunomodulatory agents after the acute period. Those patients meeting diagnostic criteria for neuromyelitis optica should likewise be started on prophylactic disease treatment.

Clinical Course

Deficits can start abruptly but can initially be subtle and progress over a 2- to 30-day period. The most recent American Academy of Neurology diagnostic guidelines of 2002 propose a nadir of symptoms between 4 hours and 21 days. The primary purpose of this timeline is to differentiate acute transverse myelitis from ischemic myelopathy, which progresses and nadirs rapidly, and chronic hereditary myelopathies, which progress over months to years. Applicability of this timeline in pediatric populations is further reviewed later in this article.

Symptoms of pain along with motor, sensory, and autonomic dysfunction begin over hours and progress within 5 days (range, 2-30 days) to a nadir of function. This plateau of symptoms is typically 1 week in duration (range, 1-40 days). Autonomic instability is common during the worsening and plateau phases and manifests with fluctuating temperature, respiratory rate, heart rate and rhythm, and bowel and bladder function.

Time from symptom onset to initial recovery averages 9 days (range, 2-50 days). In those patients with spinal shock associated with flaccid weakness and loss of deep tendon reflexes, upper motor neuron signs of increased tone spasticity typically evolve over a 2-week period. Time to the return to ambulation is the least predictable, averaging approximately 1 month (range, 2-365 days).

Rehabilitation

Rehabilitation should begin as soon as possible through consultation with physical medicine and rehabilitation specialists as well as physical and occupational therapy. Typical goals include maintaining range of motion, strengthening,
prescribing adaptive equipment to include orthotics, and bowel and bladder continence programs. The latter can additionally require consultation with urology specialists. Patients continuing to demonstrate recovery from severe deficits after completion of their acute treatment with intravenous steroids and plasmapheresis can benefit from a more intensive inpatient rehabilitation program as directed by physical medicine consultants. Depending on the amount of recovery, ongoing life-long follow-up with physical medicine and rehabilitation specialists may be needed. Specific symptomatic treatment is addressed in Table 4.

### Cognitive and Psychosocial Issues

While cognitive impairment is reported in multiple sclerosis and neuromyelitis optica, there are currently no published data on school performance or neuropsychological outcomes following acute transverse myelitis. A 2009 study that surveyed parents of 20 children after acute transverse myelitis attending a special needs camp reported subjective cognitive impairment in 10% of patients, suggesting this population should be monitored for such sequelae.52

Children with chronic neurological disability secondary to spinal cord lesions are at higher risk of depression and anxiety.52-54 Particular concern arises in later childhood and adolescence when children’s concept of self-worth becomes increasingly influenced by perceived body image as interpreted by peers.54 Clinicians should provide routine assessment of self-perception and family relationships. Preventative cognitive-behavioral interventions for depression and anxiety include counseling focused on the child’s discovery of personally important developmental opportunities in which he or she feels competent. Such interventions can assist in the management of negative body self-perceptions as found in a study of children with normal cognition and spina bifida.54 Interventions aimed at promoting parent-child communication and in balancing the child’s autonomy in the context of disability are recommended.

### Prognosis and Outcomes

The prognosis of acute transverse myelitis in children is dependent on a number of factors. Outcomes range from complete recovery with no residual deficit to complete paralysis, to even death.

In general, the prognosis in adult cases of acute transverse myelitis (based mainly on older studies of myelopathies) indicates that approximately one third of patients have a good outcome, one third have a fair outcome, and one third have a poor outcome. Good outcome implies complete recovery or minimal residual symptoms. Fair outcome implies that the patient is functional and ambulatory but may have some degree of urinary and bowel symptoms and/or sensory changes. Poor outcome implies that the patient is mainly nonambulatory, has poor or no sphincter control, and has severe sensory deficits.55

The prognosis in children has been reported in several case series as complete recovery in 33% to 50% of patients, with poor outcome in 10% to 20% of cases.55,56 A 2007 prospective study from India of 15 patients with acute transverse myelitis showed 53% with complete recovery, 46% with bladder disturbance, 20% with mild motor sequelae, and 20% wheelchair bound.57 A 2009 retrospective Australian study showed that 73% had good motor outcome, 77% had normal urinary function, and 9% had residual sensory symptoms.50 A 2007 study of 47 cases of idiopathic acute transverse myelitis in patients who initially presented before age 18 years at a tertiary care center reported 2 deaths and showed that of the survivors, 40% remained wheelchair dependent, 80% had deficits in sphincter control, and 27% required assistance for tasks of daily living.3 The majority of patients did report independence with activities of daily living and locomotion. Most recently, a 2012 prospective study of 38 Canadian children with acute transverse myelitis reported 16% needing a wheelchair for mobility and 22% having sphincter dysfunction.4 In general, patients with better motor recovery appear to also have been those with better urinary control recovery.58 Infants tend to have worse outcomes.52 The reason for this is unclear but can relate to acute complete and longitudinally extensive transverse myelitis being more common in this younger age group. In addition, the immature nervous system may not be able to recover from damage sustained in a fulminant inflammatory attack.

Many previous studies have reported little improvement after 6 months,19 but Pidcock et al3 reported that a longer time to follow-up was associated with better functional outcome, suggesting that recovery can continue even over several years.

Factors that have been associated with poorer prognosis are rapid onset of symptoms, severe motor weakness at nadir, need for ventilator support, and longer time at symptom nadir. More recent data add elevated cerebrospinal fluid white blood cell count, younger age at onset, longer time to diagnosis, lack of increased deep tendon reflexes at onset, higher anatomic rostral border of the sensory level, and longitudinal extent of the cord lesion.3,30,56 Transverse myelitis associated with acute disseminated encephalomyelitis or multiple sclerosis has a better prognosis for recovery compared to idiopathic transverse myelitis and neuromyelitis optica–related transverse myelitis.

The length of the lesion in the context of idiopathic transverse myelitis is a major determinant of prognosis for
recurrence, as reflected by classifying terminology. Those with longitudinally extensive transverse myelitis have a higher risk for neuromyelitis optica. However, in the absence of neuromyelitis optica diagnostic criteria to include pathological aquaporin 4 IgG, such individuals have a lower risk of recurrence and lower risk of developing multiple sclerosis compared to patients with shorter lesions and those with acute partial transverse myelitis.51,59 In general, transverse myelitis is a rare presenting symptom in pediatric multiple sclerosis.10 However, acute transverse myelitis can be the initial manifestation of multiple sclerosis, with higher risk in those with patchy lesions between 1 to 3 spinal segments.13 The presence of cerebrospinal fluid oligoclonal bands increases the risk for multiple sclerosis, as they are found in over 90% of this population. Positive oligoclonal bands can also be found in up to 30% of patients with neuromyelitis optica.13 Pidcock et al3 reported 2 cases of recurrent longitudinally extensive transverse myelitis (4%), 1 case later diagnosed as neuromyelitis optica (2%), and 1 as multiple sclerosis (2%). Kalra57 reported no cases of progression to neuromyelitis optica or multiple sclerosis. The 2012 Canadian study reported progression to multiple sclerosis in 13% of children with acute transverse myelitis.2

Summary
Pediatric acute transverse myelitis is a clinical syndrome reflecting spinal cord pathology due to inflammation, with clinical examination often revealing a band-like sensory level. Deficits can include sensory, motor, and autonomic symptoms. Pain and bowel/bladder symptomatology are frequently seen, and reflexes can initially be increased or decreased. By and large, symptoms begin over a period of 2 days; nadir of function typically occurs between 4 hours and 30 days. It is vital to work up a patient expeditiously, not only to ensure that appropriate treatment can be started but also so that other causes of myelopathy can be excluded (especially compressive myelopathies requiring rapid surgical intervention). Diagnostic workup includes MRI of the spine and brain, lumbar puncture, and serology directed to investigate for specific disease-associated myelopathies. Treatment of noninfectious acute transverse myelitis typically consists of pulse-dose intravenous methylprednisolone for 5 days, followed by oral corticosteroid taper; plasma exchange should be considered if prompt improvement is not seen. Prognosis in children is not clear cut; although most data suggest perhaps as many as 30% to 50% make a full recovery, a significant portion will have residual debilitating motor sequelae.

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