



# Recognizing and treating acquired demyelination of the central nervous system in children

**Brenda Banwell, MD, Jennifer Hamilton, Julia Kennedy**

The Hospital for Sick Children, Toronto

Multiple sclerosis (MS) is a neurological disease defined by recurrent attacks of immune cells on the white matter of the brain and spinal cord, leading to temporary or permanent disability. The cause of MS is believed to involve stimulation of immune cells by one or more environmental agents (i.e., viruses) and misdirection of these cells to attack white-matter proteins (a process called demyelination).

Individuals experiencing an initial attack, also known as “clinically isolated syndrome (CIS)” face an uncertain future as not all go on to experience recurrent attacks that characterize MS. Carefully documented outcomes of paediatric CIS patients attending a tertiary paediatric care center have shown that approximately 25% of children with CIS will have an MS-defining event. The mean time from CIS to second attack was 0.71 years, and all children experienced their second attack by 2.7 years. Why some patients experience a single attack (CIS), while others have recurrent attacks (MS) is unknown. It is likely that progression from CIS to MS relates to differences in the environmental exposures, activation of the immune cells, or particular genetic or target organ susceptibilities. Understanding these differences is the focus of the CPSP acquired demyelinating syndromes of the central nervous system study.

## **Signs and symptoms of demyelination of the central nervous system (CNS)**

Symptoms vary depending on which part of the brain and/or spinal cord is affected by the attacks on the myelin. Therefore, what the patient feels depends entirely on where the attack is situated. Symptoms can include:

- Impaired vision
- Double vision
- Tremor

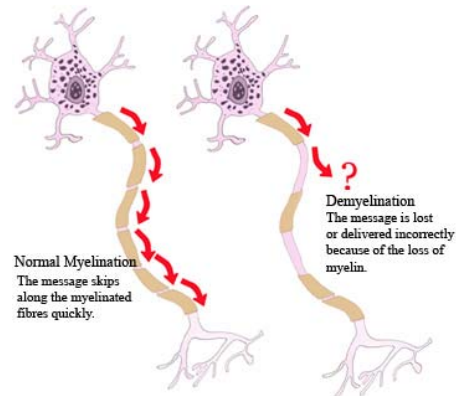
RESOURCES



- Numbness, tingling or weakness in arms and/or legs
- Inability to walk due to weakness in both legs
- Difficulty maintaining balance
- Bladder retention

The above symptoms may also be associated with:

- Confusion, restlessness, irritability
- Fatigue
- Vomiting
- Fever
- Headache
- Seizures
- Stiff neck
- Coma



### Diagnosis

The diagnosis of CNS demyelination requires exclusion of other possibilities. The following examples are not an exhaustive list:

- Previous radiation to the spine within the last 10 years
- Arterial distribution clinical deficit consistent with vascular ischemia
- Arteriovenous malformation
- Serologic or clinical evidence of connective tissue disease, such as sarcoidosis, Behcet's disease, Sjögren's syndrome, systemic lupus erythematosus, mixed connective tissue disorder, etc.
- Acute CNS manifestations of syphilis, Lyme disease, HIV, HTLV-1, West Nile virus, or other acute CNS infection with documented CSF pleocytosis and microbiological confirmation of a causal organism.
- Biochemical or biopsy evidence of metabolic disease.

### Investigations

The investigations must be tailored to the clinical presentation of the child and might include amongst others:

- Ophthalmology exam
- Viral serologies
- CSF analysis, biochemistry and cultures
- CT/MRI of brain and/or spinal cord

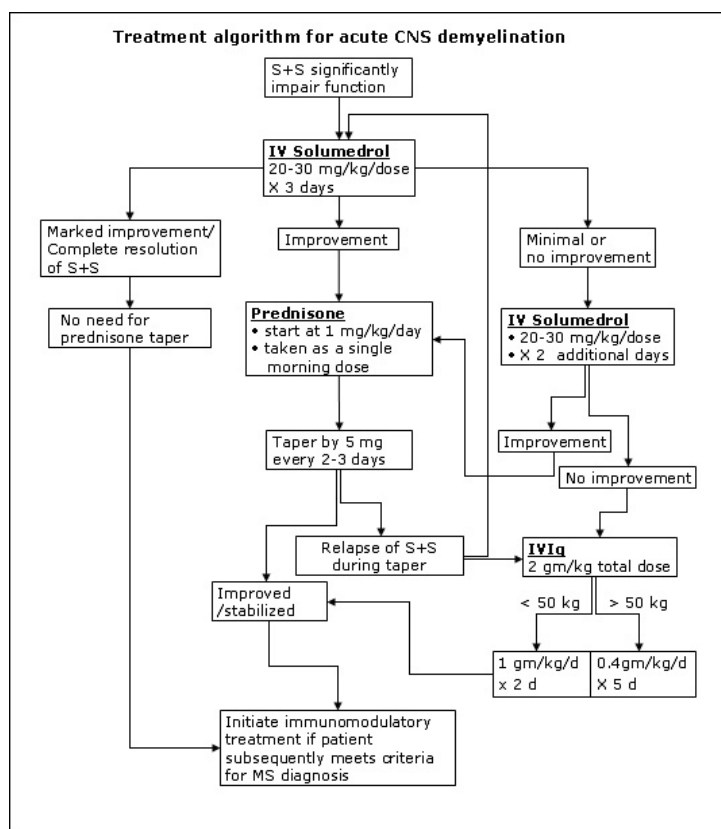
### Treatment and management

Treatment of acute demyelination of the CNS should be considered when symptoms are of a severity as to interfere with daily function. Mild sensory symptoms may not require medication, but would prompt detailed investigation.



## Recognizing and treating acquired demyelination of the central nervous system in children (continued)

There are no randomized, controlled trials of corticosteroids or immune globulins in paediatric demyelination of the CNS. The following algorithm represents a current protocol; however, all treatments must be individualized based on clinical severity and concurrent medical issues.



# RESOURCES

### Goals of research

Important questions that can be answered through research on pediatric demyelination include:

- Who is at risk for future attacks that are characteristic of multiple sclerosis?
- What are the clinical features of CIS and demyelination?
- What are the possible triggers of disease? Viral infection, abnormal immune function, diet, environment?
- What goes “wrong” with the immune systems in children with demyelination?
- What does MS look like in a child on MRI images, and can these images teach us about recovery and MS risk?



## Quiz

- 1. MS is a neurological disease characterized by recurrent attacks of what type of cells on the white matter?**
  - a) Red blood cells
  - b) Stem cells
  - c) Mitochondrial cells
  - d) Immune cells
  - e) All of the above
- 2. What are the symptoms of demyelination?**
  - a) Double vision
  - b) Impaired vision
  - c) Tremor
  - d) Inability to walk due to weakness in both legs
  - e) Bladder retention
  - f) Numbness in the face, arms or legs
  - g) All of the above
- 3. What is the first-line medication currently used to treat the symptoms of demyelination?**
  - a) IVIG
  - b) Cyclophosphamide
  - c) Oral prednisone
  - d) IV solumedrol
  - e) None of the above
- 4. What possible other diagnosis needs to be considered when a child presents with symptoms of demyelination?**
  - a) CNS infections, such as Herpes simplex, Lyme disease, West Nile virus and syphilis
  - b) Rheumatological disease, such as systemic lupus erythematosus
  - c) Metabolic disorders
  - d) Inherited disorders of cerebral white matter (leukodystrophies)
  - e) All of the above
- 5. What is the approximate likelihood that a child with an initial attack of demyelination will experience further attacks, leading to a diagnosis of MS?**
  - a) 5%
  - b) 10%
  - c) 25%
  - d) 50%
  - e) 75%

Answers:  
1-d, 2-g, 3-d, 4-e, 5-c