

MIAMS 2008

Clinical MRI for the non clinicians

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Objective:

The goal of this educational session is to provide background on the clinical impact of MS on individuals. This lecture reviewed the epidemiology, pathogenesis, common symptoms, natural history, diagnosis and treatment of MS. A video with patient vignettes is also available through the EndMS network (www.endmsnetwork.ca).

Epidemiology

MS is an autoimmune disorder of the central nervous system. The cause is unknown but is felt to be a combination of genetic and environmental factors. The genetic risk of the disease is only 4% for offspring of affected individuals. It typically affects young adults between the ages of 20 and 40, but can occur at any age, even as young as 3. Like most autoimmune disorders, women are more often affected than men (2:1 to 3:1 ratio). More than 1 million people worldwide have MS with 450,000 in the US and 50,000 in Canada. Prevalence increases with increasing distance from the equator, leading to some theories that vitamin D deficiency could be a significant contributor to overall risk.

Figure 1: Prevalence of MS per 100,000 population. North America rates are 100-200/100,000 in contrast to Japan where rates are 10/100,000.

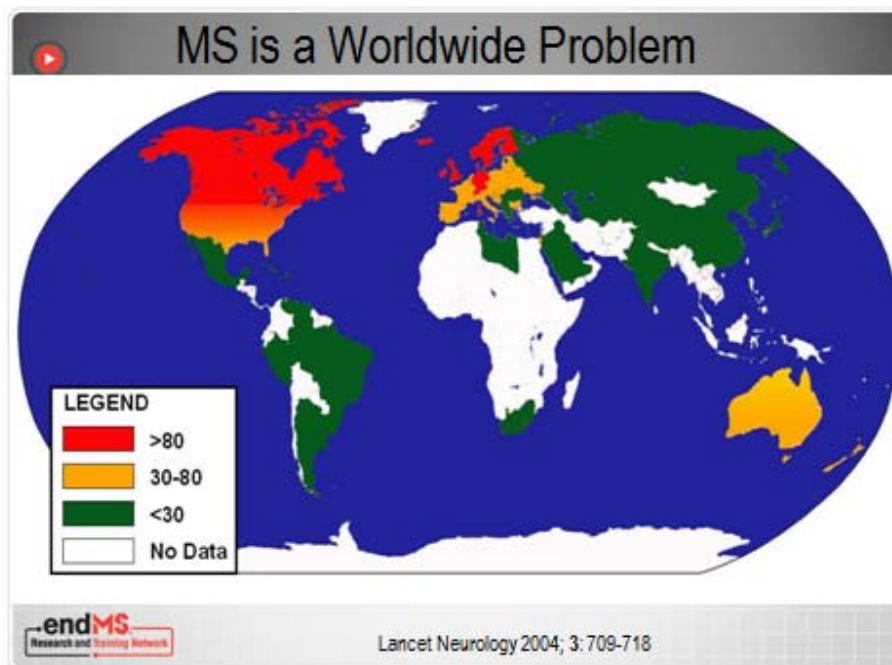


Figure 2: Cause of MS is unknown





Why do people get Multiple Sclerosis?

- Mostly environmental issues.
- Possibly a virus in childhood.
- Possibly vitamin D deficiency.
- Small genetic risk of 4% only.
- We don't know the cause.

The diagram consists of a white rectangular box on a grey grid background. At the top left, the word 'ENVIRONMENT' is written in blue capital letters. At the top right, the word 'GENETICS' is written in green capital letters. Below each word is a blue circular arrow pointing clockwise. A plus sign '+' is centered between the two arrows. Below the plus sign, the words 'MULTIPLE SCLEROSIS' are written in red capital letters.

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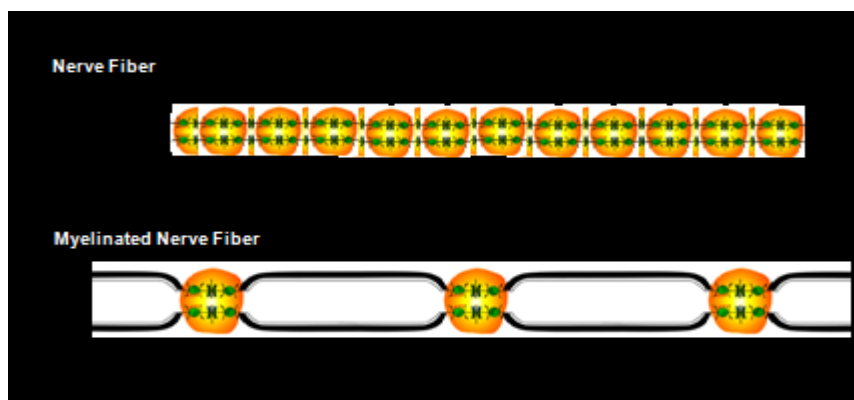
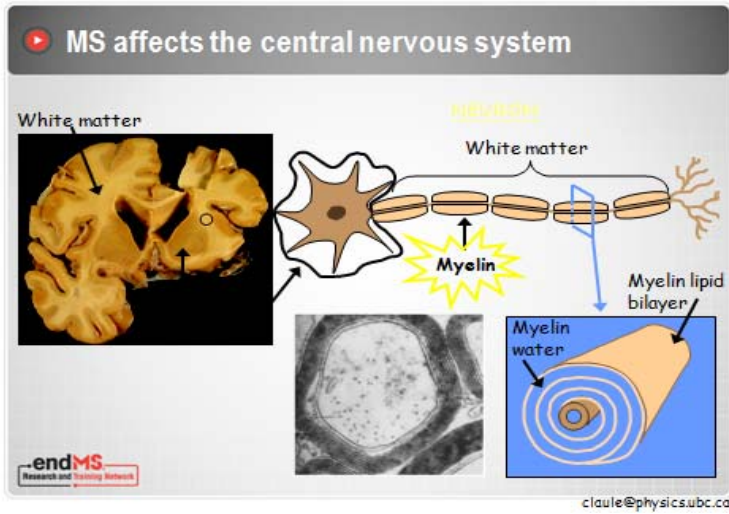
Multiple Sclerosis: Significance

-  Affects an estimated 50,000 Canadians, 350,000 Americans, and more than 1 million persons worldwide
-  Most common, non-traumatic cause of disability in young adults
 - 15 years after onset, 50% of affected persons require assistance to walk
 - High rate of unemployment
-  Negative impact on family & social roles
-  Annual cost of MS in the U.S. in 1994 >\$34,000 per person → \$6.8 billion annually (national level)

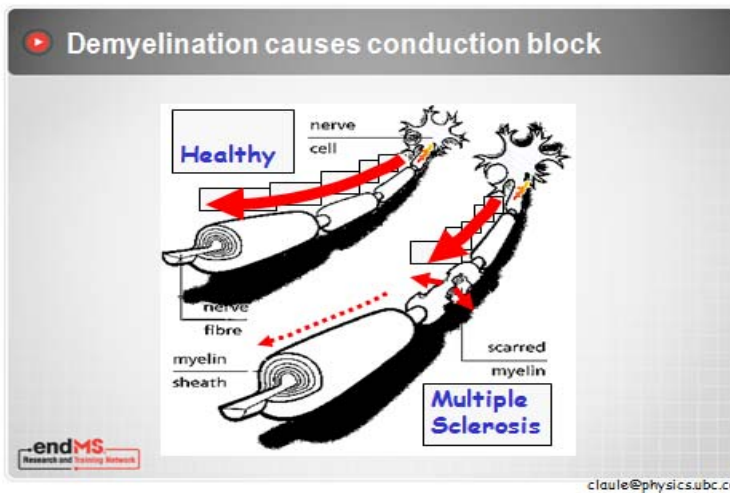
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Immunology and Pathogenesis

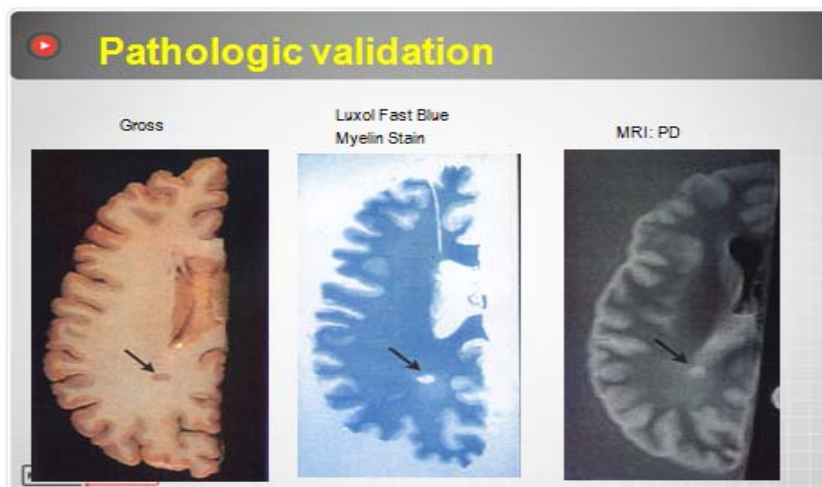
The nervous system contains two main components: neurons with their long processes (axons) for communication between cells, and oligodendrocytes that coat these axons with myelin to speed conduction of electrical discharges and decrease the amount of energy required for transmission.



The immune system normally surveys the body, and has the ability to distinguish normal tissue from foreign (ie. bacteria or virus) or damaged tissue. Detection of abnormal tissue can lead to an inflammatory cascade (cytokine release, recruitment of other immune cells) to remove the unwanted cells. Normally, the blood brain barrier minimizes the number of immune cells trafficking into the central nervous system. In MS, there is an aberrant signal that leads to breakdown of the blood brain barrier and immune mediated attack of the myelin sheath around axons. The trigger (antigen) for this cascade is not known, and this occurs sporadically and frequently throughout the life of a patient with MS. The damage to myelin coating (demyelination) can block or slow signal transmission in the affected pathways.




This process is self limiting, and some repair (remyelination) occurs. However there is often a permanent residual scar (figure below) that remains with variable degrees of permanent demyelination and to a lesser degree, axonal loss. These permanent scars are easily seen on MRI and correlates well with histopathology. While the acute demyelination is associated with the onset of symptoms, and remyelination (along with resolution of toxic substances such as nitrous oxide) is associated with improvement, it is the permanent loss of axons that contributes to irreversible clinical disability in MS.



The classic symptoms of MS (attacks) occur when new episodes of inflammation occur in strategic pathways such as the optic nerves (optic neuritis), brainstem (double vision, ataxia) and spinal cord (ascending numbness, bladder dysfunction, l'Hermittes (electric shocks down spine with neck flexion)).

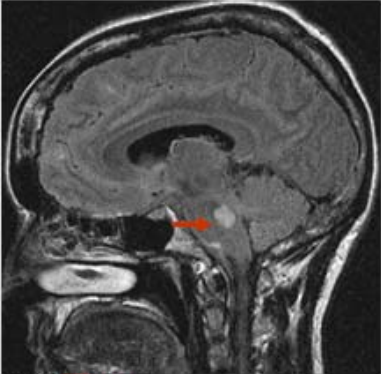

Symptomatic MRI Relapses: Optic Neuritis



The left image is an axial MRI scan of the head showing the optic nerves. A red oval highlights a hyperintense area in the right optic nerve, indicating inflammation. The right image is a photograph of a person in a blue dress walking, whose face is heavily blurred, illustrating the visual symptoms of optic neuritis.

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Left image from Kidd Brain 2003.

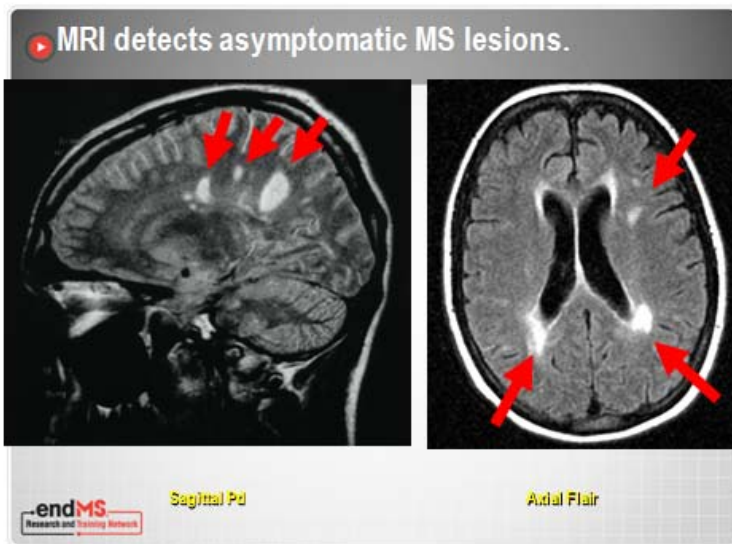
Symptomatic lesions

Brainstem	Spinal Cord
	

The left image is a sagittal MRI scan of the brain, showing a red arrow pointing to a lesion in the brainstem. The right image is a sagittal MRI scan of the spinal cord, showing a red arrow pointing to a lesion in the spinal cord.

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However, most new episodes affect regions of the central nervous system without any direct clinical symptoms. MRI is highly sensitive for detecting these silent lesions.



Serial MRI studies have demonstrated that new lesions are occurring frequently, often in the absence of clinical symptoms and the concept of clinical “remission” does not reflect ongoing pathologic changes.

▶ **Most new episodes of inflammation occur in “silent” regions of the brain that are easily seen with MRI.**

- New lesions may decrease in size, but almost always leave a residual scar (plaque) behind that is visible on MRI.
- On average, patients develop 4 new lesions on MRI per year.
- For every 10 new lesions, only one is associated with new clinical symptoms.

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Dr. T. Traboulsee, UBC Neurology, slides may be used for educational purposes

▶ **MRI detects clinically silent disease**

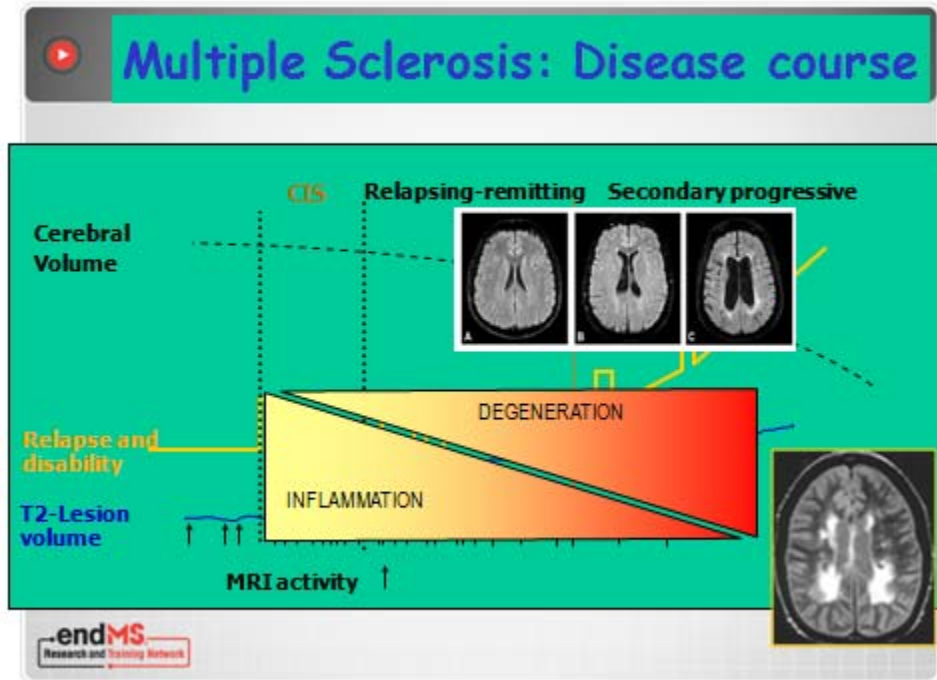
Symptoms

MRI lesions

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Disability in MS is due to incomplete recovery from attacks, and due to the accumulation of ongoing clinically silent disease (both MRI visible and processes that are invisible on standard MRI scans). The obvious disability for patients is when mobility is affected. However, there is significant impact due to “invisible disability” including bladder dysfunction, poor vision, cognitive impairment, psychiatric illness and medication side effects. The natural history of MS is summarized below. The early years of the disease is dominated by new inflammation. It is this stage that seems most responsive to the current treatments available for MS (disease modifying therapies or DMT). Overtime, most patients show some progression of disability that is occurring without any relapses, and it is possible that other mechanisms are driving the degenerative aspect of the disease. This is an important area of research. This stage of

the disease is not (or only minimally) clinically responsive to current DMTs. Therefore, we often promote treatment when patients have minimal disability to prevent future disability. Unfortunately, we have no treatments that can reverse established disability.



Three Components to Treatment

- Relapse management
 - Corticosteroids, rehabilitation
- Disease-modifying therapies
 - Prevent disability
- Chronic symptom management
 - Multidisciplinary

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DIAGNOSIS OF MS

There is no single test that is diagnostic of MS. The diagnosis is made after careful assessment of the symptoms. MRI has been extremely helpful in establishing an earlier diagnosis and for ruling out common alternative diagnosis. However, many conditions can look similar on MRI and in the absence of a clear clinical story, caution is required not to over interpret “white spots”

▶ Diagnosing MS

The symptoms and examination are important for the neurologist to determine if someone might have MS.

After that, additional tests are performed including an MRI, Visual evoked potentials, blood tests and sometime a lumbar puncture (spinal tap).



CONCLUSION

MS is a common disease, and an important cause of disability. It is highly variable amongst individuals and has significant physical and psychological impact on their well being. While the cause remains unknown, the dynamic nature of the inflammatory processes, making it a disease with a reasonable chance of developing effective treatments that will prevent further damage. MRI will remain in the forefront of these efforts.