

**Objectives:**

1. For multiple sclerosis, describe the pathogenesis, type and location of pathological changes; signs and symptoms; diagnostic criteria including CSF findings; and course of disease:
2. Know that Guillain-Barre Syndrome is a demyelinating disease of the peripheral nervous system, in contrast to multiple sclerosis, which is characterized by demyelination in the CNS.

## I. Multiple Sclerosis

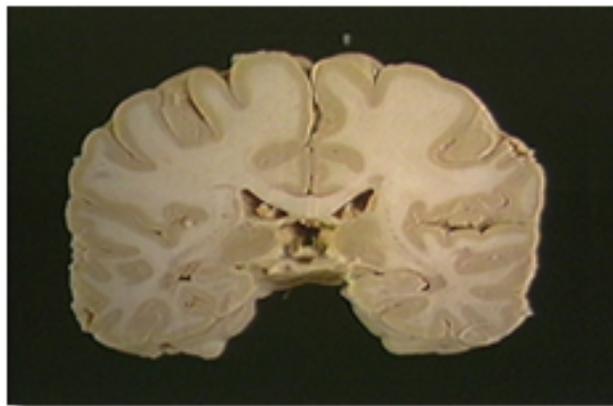
### **Multiple Sclerosis (MS) --**

MS is characterized by more than one episode of neurologic deficits separated in time, attributable to CNS white matter lesions that are separated in space. Lesions initially involve destruction of myelin; axonal damage may occur later in the process. Inflammatory brain lesions appear to arise from autoimmune responses involving activated lymphocytes and monocytes.

**Age of onset:** 20-50 years of age, usually; more common in women

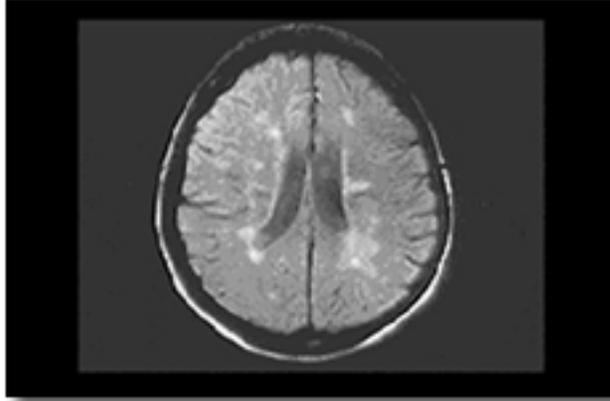
**Pathogenesis:** The lesions of MS are caused by a cellular immune response that is inappropriately directed against the components of the myelin sheath. One of the early events in the development of a new lesion is an increase in permeability of the blood-brain barrier associated with inflammation, generally in a perivenous distribution. Demyelination occurs early in the inflammatory phase, and apoptosis of oligodendrocytes has been documented at an early stage. Both CD4+ and CD8+ lymphocytes are present in active lesions. The regression of symptoms has been attributed to the resolution of inflammatory edema, to partial remyelination, and/or to redistribution of sodium channels to enhance conduction in demyelinated axons.

**Pathological changes:** Gross pathology: Multiple areas of demyelination (plaques) in white matter of the brain and spinal cord (not the peripheral nervous system). The plaques are frequently located adjacent to lateral ventricles (periventricular) in the cerebral hemispheres. In some patients the plaques are sharply demarcated centered on blood vessels; in other patients plaques show less demarcation and are not centered on vessels.



**DML 01**

**Gross coronal section showing plaques adjacent to lateral ventricles (note discolored areas at tips of ventricles)**

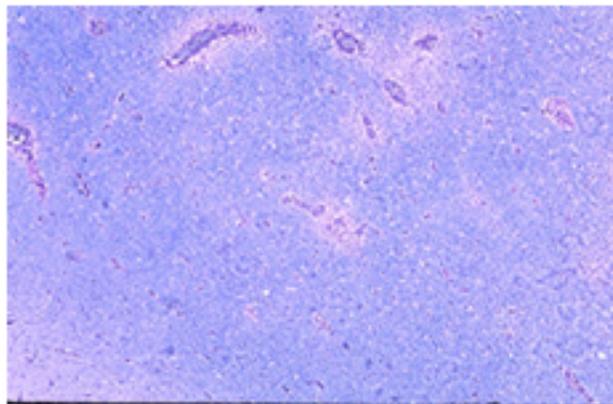


**DML 02**

**MRI showing multiple plaques (bright areas) around lateral ventricles.**

Microscopic pathology:

1. Loss of oligodendrocytes within plaques; gliosis within plaques
2. Axons usually remain intact initially in plaques, but axonal injury may occur late



**DML 03**

**Microscopic image (stained with luxol fast blue to show myelin) illustrating multiple small areas of myelin loss (lack of blue staining) around vessels.**



#### DML 04

Low power microscopic image. A lateral ventricle is located at top right. The absence of blue staining in tissue adjacent to the ventricle indicates a demyelinated plaque.

**Diagnosis** - The clinical diagnosis is based on clinical history, MRI, and/or CSF analysis. The relapsing forms are considered clinically definite when neurologic dysfunction becomes "disseminated in space and time." On MRI, findings of multifocal lesions of various ages, especially those involving the periventricular white matter, brainstem, cerebellum, and/or spinal cord white matter, support the clinical impression. The presence of gadolinium-enhancing lesions on MRI indicates current sites of presumed inflammatory demyelination (active lesions).

**CSF changes:** Moderate lymphocytic pleocytosis (less than 50 mononuclear cells). Gamma globulin elevated in most patients (due to proliferation of B cells within the nervous system); oligoclonal gamma globulin bands (more than one clone, usually about 5 distinct bands) are demonstrated on CSF electrophoresis.

**Clinical course** - variable (in all forms, presenting symptoms vary widely, but visual impairment due to optic neuritis is a common initial symptom). The most common course is remitting and relapsing over many years (about 80%). Some patients may have an acute progressively downhill course, a slowly progressive course, or a benign course. Many patients describe fatigue that is worse in the afternoon and is accompanied by physiologic increases in body temperature.

**Epidemiology:** In general, the frequency increases at higher latitudes (toward both poles). Individuals take on the relative risk of the environment in which they spent their first 15 years. There are significant genetic influences. Linkage studies have indicated associations with several MHC antigens.

**Treatment:** The goal of immunomodulating therapies is to slow the progression of MS by reducing or preventing inflammatory episodes that can lead, in later stages, to irreversible damage to oligodendrocytes and/or axons resulting in permanent neurological disability. Antigen-nonspecific immunomodulators include interferon (IFN)-beta 1b

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## II. Multiple Sclerosis Variants

Multiple Sclerosis Variants and Other Types of Encephalomyelitis Demyelinating Diseases:

Multiple Sclerosis variants: Examples include:

- Neuromyelitis optica (also called Devic disease) - more prevalent in Asians: the course is variable
- Acute MS ( Marburg form) - tends to occur in young individuals; rapid course over several months

Acute Disseminated encephalomyelitis (ADEM, perivenous encephalomyelitis)

- Demyelinating disease that usually follows a viral infection; diffuse brain involvement; prognosis ranges from death to complete recovery

Acute Necrotizing Hemorrhagic Encephalomyelitis (ANHE)

- Rapidly progressing syndrome of CNS demyelination; usually preceded by upper respiratory infection; more common in young adults and children; prognosis ranges from death to complete recovery; lesions are more devastating than ADEM and include disseminated necrosis with acute hemorrhage.

## III. Guillain-Barre Syndrome

**Guillain-Barre Syndrome** (Acute Inflammatory Demyelinating Polyradiculopathy) is a demyelinating disease that occurs in the **peripheral nervous system**. It is probably immune-mediated. A typical clinical presentation includes rapidly ascending weakness, often after a patient has the flu.