Neuroscience II Pathology

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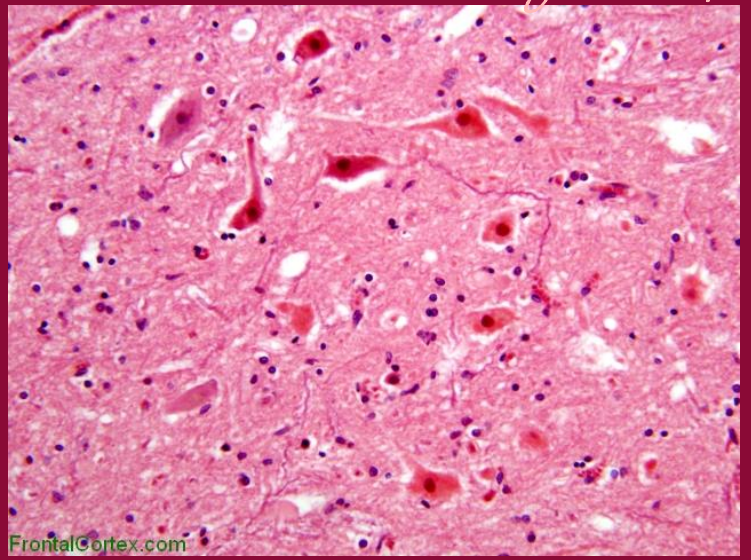
Central nervous system

Characteristic Features of Cellular Pathology in CNS

Neurons – Acute neuronal injury

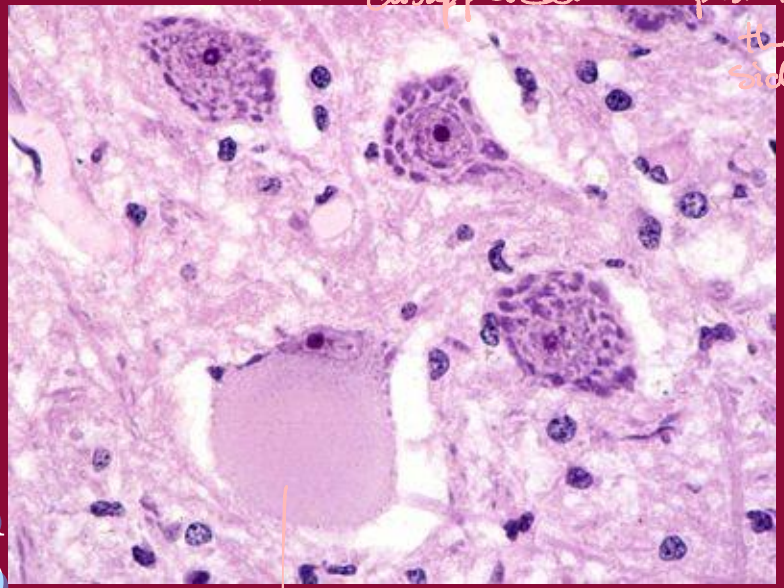
- Within **12-24 hours** of an irreversible hypoxic-ischemic insult, **neuronal injury** becomes evident microscopically
- (1) Shrinkage of the cell body, (2) pyknosis of the nucleus, (3) disappearance of the nucleolus, (4) loss of Nissl substance, and (5) intense eosinophilia of the cytoplasm **"red neurons"**

Dead cell, bright esinophilic.



Neurons – Axonal injury/reaction

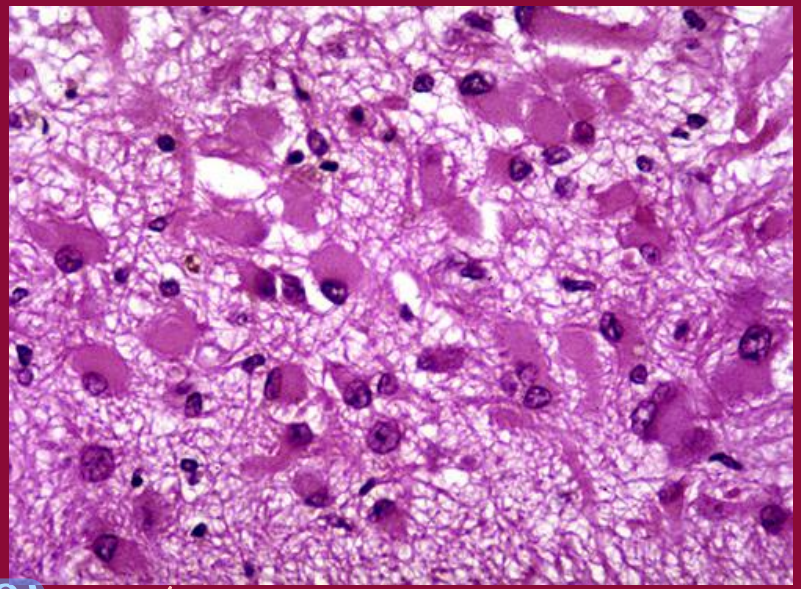
- A change observed in the cell body of the neurons during regeneration of the axon (sprouting).
- Cell body enlargement and rounding, peripheral displacement of the nucleus, enlargement of the nucleolus, and peripheral dispersion of Nissl substance (central chromatolysis)



Astrocyte Injury and Repair

Very small with many processes.

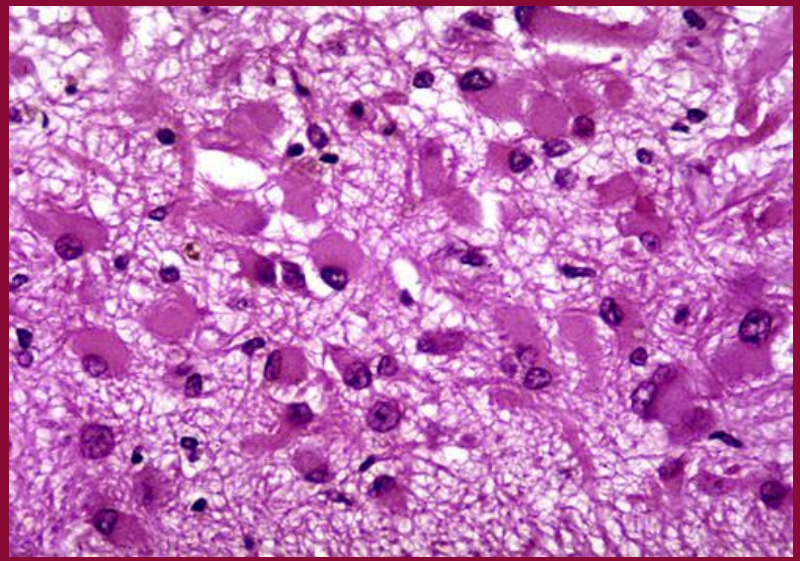
- Astrocytes → repair & scar formation in CNS, (gliosis)
- After injury they undergo hypertrophy and hyperplasia.
- The nucleus enlarges (more vesicular) & the nucleolus becomes prominent. The cytoplasm expands with bright pink hue & extends multiple processes (gemistocytic astrocyte).



Vesicular → بكون كبير مع أماكن بيضا "حبيبات"

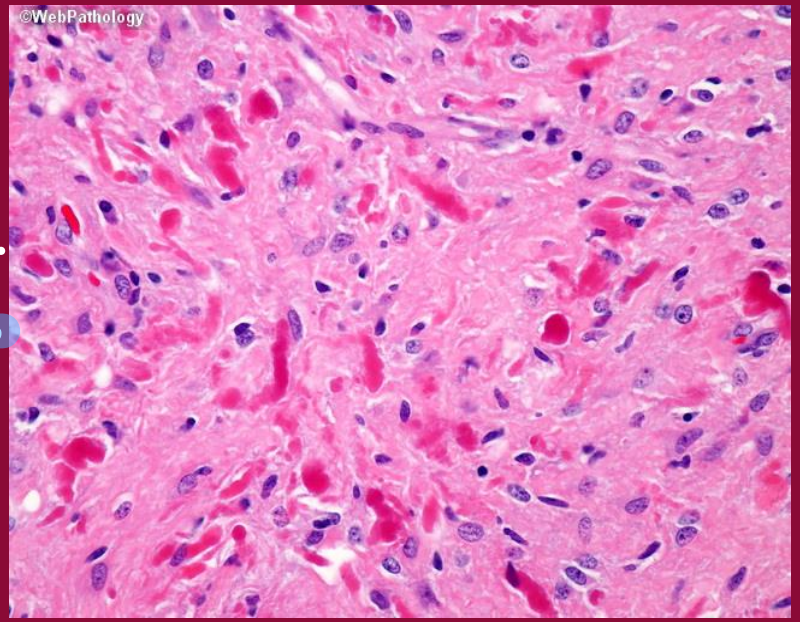
Astrocyte Injury and Repair

- Unlike elsewhere in the body, fibroblasts participate in healing after brain injury to a limited extent except in specific settings (penetrating brain trauma or around abscesses).



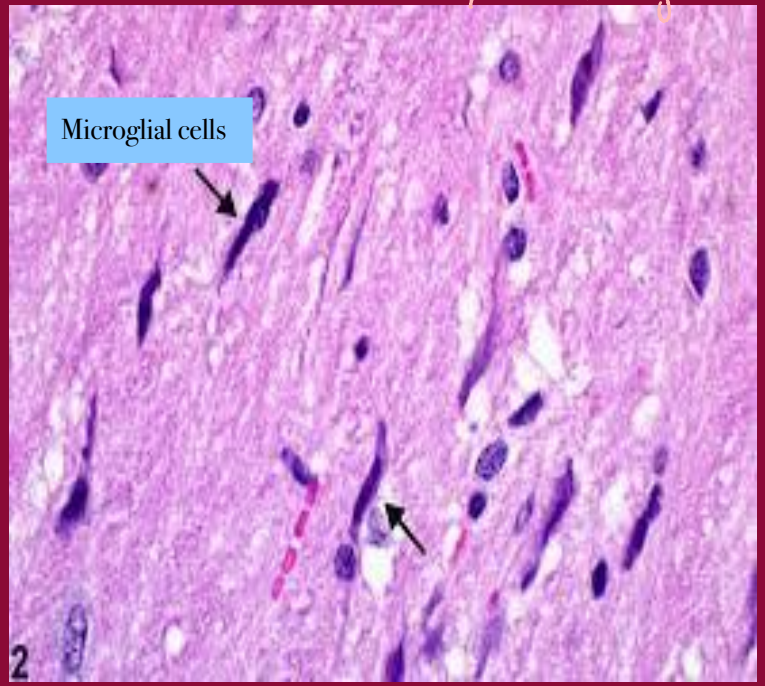
Astrocyte Injury and Repair

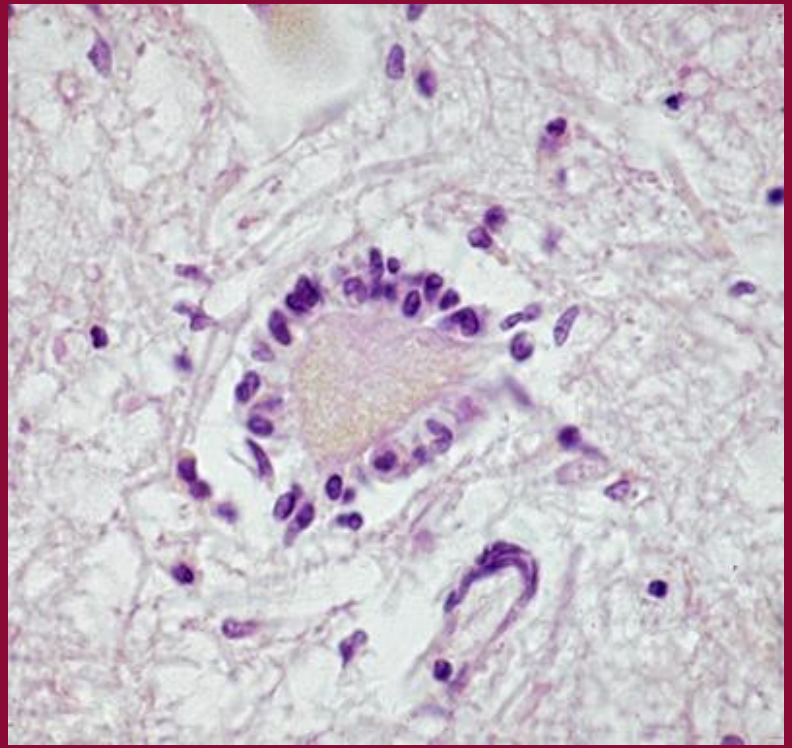
- In long-standing gliosis, the cytoplasm of reactive astrocytes shrinks in size, & cellular processes become tightly interwoven (fibrillary astrocytes).
- **Rosenthal fibers:** thick,elongated, brightly eosinophilic protein aggregates found in astrocytic processes in chronic gliosis & in some low-grade gliomas. (pilocytic astrocytoma)

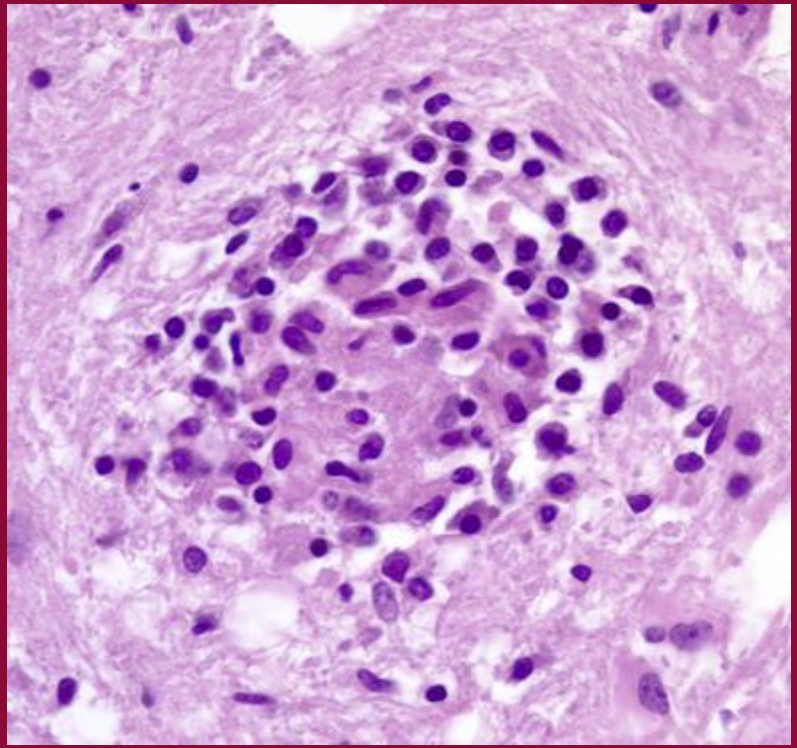


Microglial cells

- Long-lived resident phagocytes in CNS, derived from embryonic yolk sac.
- Activated by tissue injury, infection, or trauma.
- May develop elongated nuclei - rod cells (infections).
- Aggregates around necrosis → microglial nodules .
- Or around a dying neuron → Neuronophagia.







Demyelinating & degenerative diseases of CNS (1)

Myelin..

- Axons in CNS are tightly ensheathed by myelin.
- It is an electrical insulator → allows rapid propagation of neural impulses.
- Consists of multiple layers of highly specialized, closely apposed plasma membranes.
- Assembled by oligodendrocytes. → CNS
- Dominant component in the white matter, so most diseases of myelin are primarily white matter disorders.

Schwann cell's → PNS.

Differences b/w CNS & PNS Myelin

1) PNS myelin is made by Schwann cells, CNS made by oligodendrocytes. → Parenchyma 'Background'.
2) In PNS each Schwann cells provides myelin for only one internode, while in the CNS, many internodes are created by processes coming from a single oligodendrocyte.
3) The specialized proteins and lipids are also different.
4) Most diseases of CNS myelin do not involve the PNS to any significant extent, and vice versa.

Diseases of myelin are separated to two groups:

I. Demyelinating diseases

+acquired conditions.

+damage to previously normal myelin.

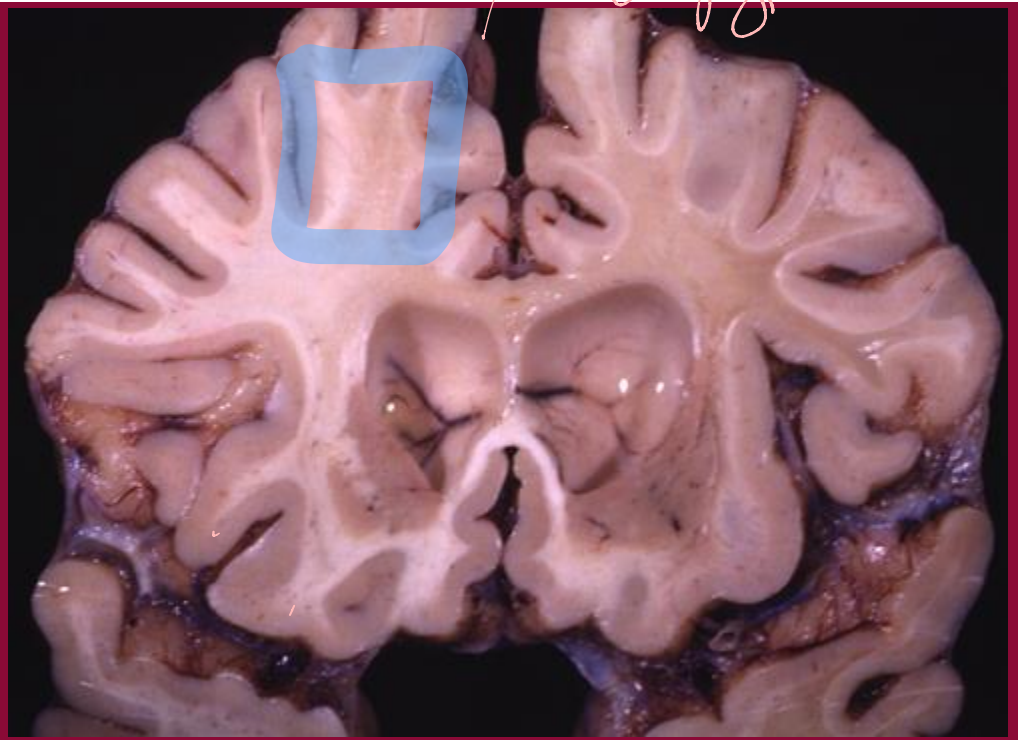
+causes: (1)immune mediated, (2)oligodendrocytes viral infection (progressive multifocal leukoencephalopathy → JC virus, a polyomavirus), or (3) injury caused by drugs and other toxic agents.

diseases of myelin are separated to two groups:

II. Leukodystrophy or dysmyelinating diseases:

+Myelin is not formed properly or has abnormal kinetics

+Caused by mutations that disrupt the function of proteins required for the formation of normal myelin sheaths.



Leukodystrophies

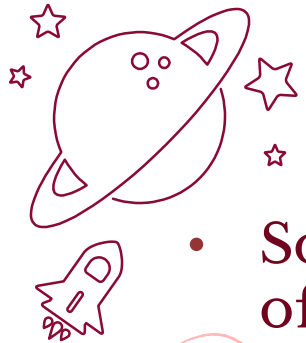
- Inherited dysmyelinating diseases. (Most autosomal recessive).
- Mutations of the genes involved in the generation, turnover, or maintenance of myelin.
- Clinically, Each disorder of the various types has a characteristic presentation→ diagnosed by genetic or biochemical methods.
- Affected children are normal at birth but begin to miss developmental milestones during infancy & childhood

Leukodystrophies - morphology

- Pathologic change mainly in the white matter → diffusely abnormal in color (gray and translucent) and volume (decreased). Leading to deterioration in motor skills, spasticity, hypotonia, or ataxia.
- Later the brain becomes atrophic, the ventricles enlarge, & changes can be found in the gray matter.
- Compared to demyelinating diseases they have insidious presentation & progressive loss of function at younger age, & associated with symmetric changes on MRI.

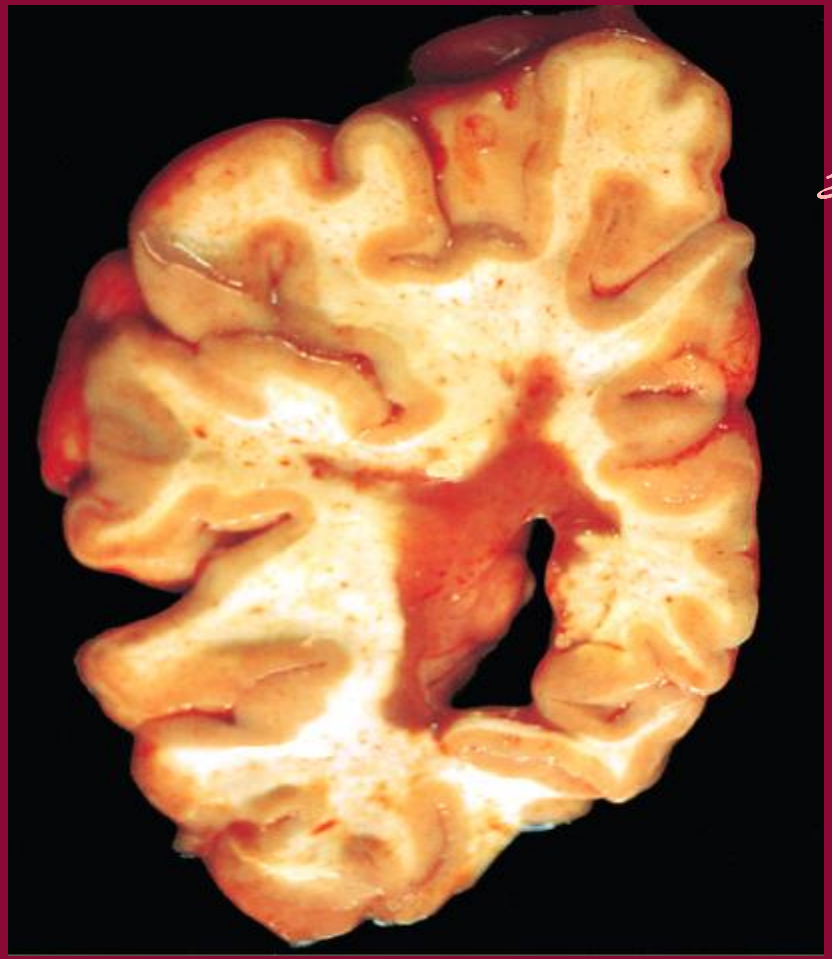
Multiple Sclerosis (MS)

- The most common demyelinating disease.
- Episodes of disease activity, separated in time which produce white matter lesions, separated in space.
- M:F 1:2, rare in childhood & after the age of 50.
- The lesions of are caused by an autoimmune response directed against components of the myelin sheath.
- Course is variable, commonly multiple relapses followed by episodes of remission; typically, recovery during remissions is not complete.

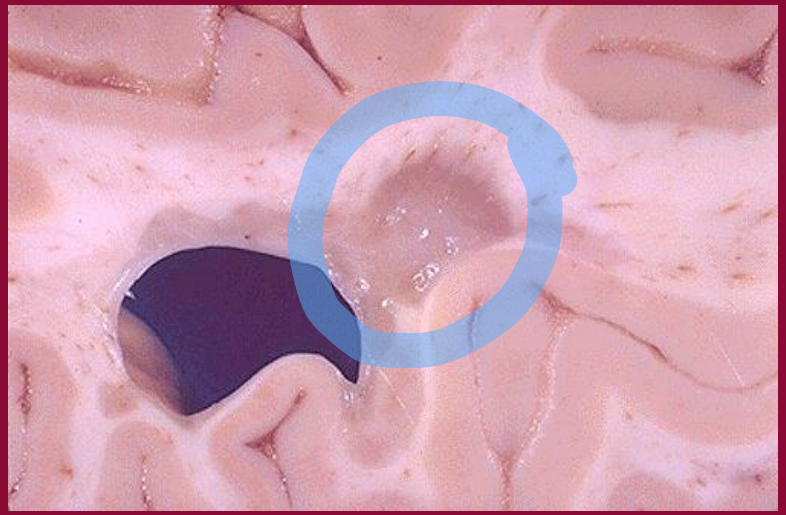


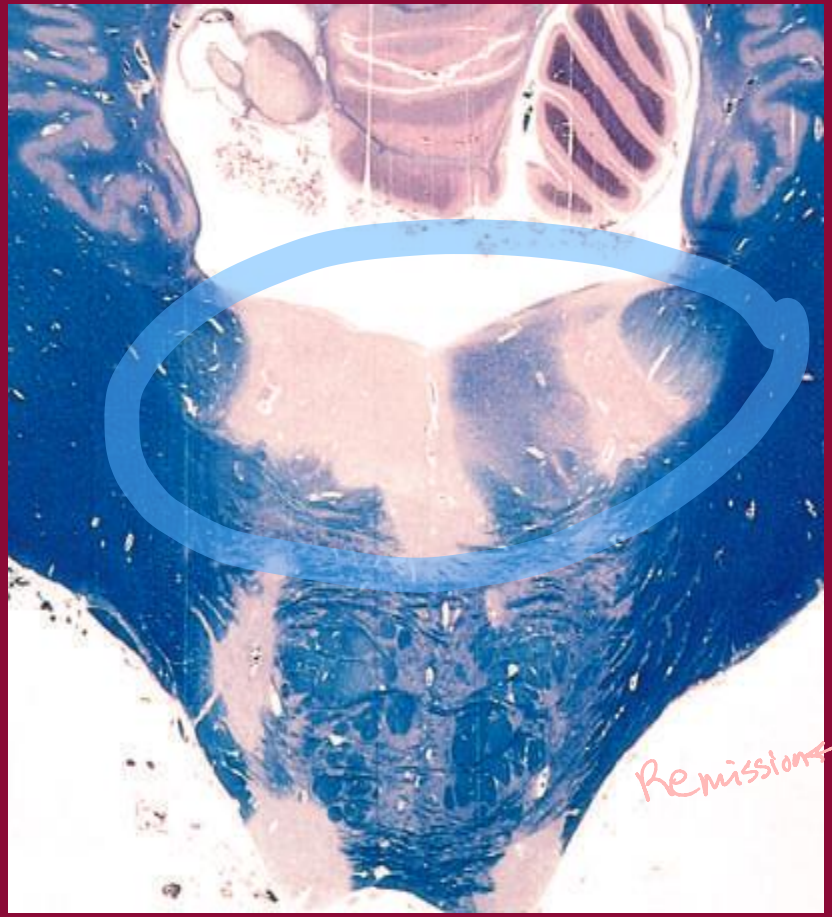
Multiple Sclerosis (MS)

- So over time there is usually a gradual accumulation of neurologic deficits.
- Unilateral visual impairment due to optic nerve involvement is a frequent initial manifestation.
- Brainstem involvement produces cranial nerve signs; ataxia & nystagmus, while spinal cord lesion give rise to motor & sensory impairment.
- The CSF in patients shows a mildly elevated protein level, moderate pleocytosis, & increased immunoglobulin(Ig) with oligoclonal bands.



A white matter disease.
Lesions → **plaques**:
واضحة **discrete**, slightly depressed, glassy-appearing, and gray in color, and commonly near the ventricles.





lesions are sharply defined microscopically:

+ **Active plaques** (ongoing myelin breakdown): contain abundant macrophages stuffed with myelin debris (lipid), also perivascular cuffs of Lymphocytes.

+**Inactive plaques** (quiescent): inflammation mostly disappears, leaving little to no myelin, & gliosis.

#Pt.1