Myelin Diseases of the CNS

Disease	Features and causes	Pathogenesis	Clinical appearance and manifestations	Epidemiology	Dx
Multiple Sclerosis *Demyelinating*	**Most common demyelinating disease** -**Autoimmune disease**: loss of tolerance of self-proteins in the myelin sheath. -**At any age (20-40)** -Rare in children & >50. -**Immune response against an auto antigen (Myelin antigen)** -Genetic + environmental triggers are needed to develop this disease.	-**T-cell mediated immune response.** Most common: T HELPER CELLS: 1.Myelin antigen is recognized by T helper cells as non-self. 2.Upon recognition, T helper cells differentiate into **Th1 and Th17** 3.Th1 produces IFN Gamma, which recruits macrophages 4.Th17 produces cytokines (17) which recruits WBC's. 5.WBC's secrete cytokines that cause tissue destruction (myelin destruction). -T KILLER CELLS may be involved	-**Episodic** -Episodes are **separated in time** -**White matter lesions/plaques** separated in space, and are: -Multiple -Well circumscribed -Slightly depressed -Grey/tan -Irregularly shaped -Grossly firmer than normal white matter (**SCLEROTIC**) **Location of plaques:** 1.Paraventricular 2.Cerebellum 3.Spinal cord 4.Optic nerve & optic chiasm 5.Brainstem Plaques are either **Active or Quiescent.** -**Symptoms depend on the location of the plaque.**	-More common in **females (Female: Male ratio= 2:1)**	-Oligoclonal bands in the CSF (Lumbar puncture) and electrophoresis → Immunoglobulins that aren't found in the serum.

	-**Genetic susceptibility:** **1.HLA DR2** **2. IL2, IL7 receptors** -**Environmental trigger:** Viral infection 1st degree relative: 15 times more likely to have MS. Homozygotic Twins: 25% chance of getting MS.	-B CELLS may be involved. Proof: When we examine the CSF, there are oligoclonal bands. Patients may also respond well to B cell depletion therapies.	**Symptoms** are: 1. **Visual**: Optic neuritis, diplopia, nystagmus. 2. **Throat**: Dysphagia 3. **Musculoskeletal** weakness 4. **Central**: Fatigue, depression, cognitive impairment. 5. **Sensation**: Pain, paresthesia, hypoesthesia - Disease may **recur, with different symptoms than the first time.** **Outcome**: Repeated attacks of autoimmune destruction, associated inflammation and toxic effects from lymphocytes and macrophages leads to **axonal damage (Secondary).**		

Clinical course of MS is variable and unpredictable:

1. **Relapsing remitting:** Symptoms (relapses) separated by periods of remission (no symptoms).
2. **Primary progressive**: Symptoms start, and the patient has them continuously (No remission), and symptoms get worse with time.
3. **Secondary progressive**: Starts the same way as 1 (relapse then remission), but changes into 2 (Primary progressive) at some point.
4. **Progressive relapsing:** Same as primary progressive, except symptoms get even worse.

Neuromyelitis Optica *Demyelinating*	**Demyelination that is caused by antibodies.**	**Optic nerve and spinal cord are affected** **B cells** are involved (Unlike MS which involves T cells)		-Females are more affected than males. -Rarer than MS.	-Antibodies to aquaporin-4 (**AQP4**) are diagnostic.
Post-infectious demyelination *Demyelinating*	Occurs in CNS **after viral infection** (1-2 weeks). **NOTE: The demyelination is NOT due to direct effect of the virus.** **Two types:** 1. **Acute disseminating encephalitis** 2. **Acute necrotizing hemorrhagic encephalomyelitis**	Has immunologic mechanism due to cross reaction between **viral antigens and myelin antigens.**	-Acute onset -Monophasic (Not episodic like MS). -More severe than MS 1. **Acute Disseminating Encephalitis** has **non localizing (non-specific) symptoms:** - Headache - Weakness - Coma **-Fatal in 20% of cases** **-Rapid progression** **-Complete recovery** (Those who survive it recover completely) 2. **Acute Necrotizing Hemorrhagic Encephalomyelitis:** More severe (Higher fatality rate).		

Central Pontine Myelinolysis *Demyelinating*	-**No viral or immunologic reaction.** -**NON-IMMUNE.** -**Most common cause: Iatrogenic rapid correction of hyponatremia.** (That's why it's important to correct hyponatremia slowly at a **rate no higher than 8-12 mmol/L of Na per day**). -Other causes: Any sudden change in osmotic pressure.	Abnormality in fluid balance around the myelin (electrolyte imbalance) → Osmotic pressure changes → **edema of oligodendrocytes →Lysis of myelin → it separates from the axons.**	**Location** (Central Pontine) Central part of the pons. **Motor signals aren't transmitted** → Affects motor functions → Can result in complete paralysis 1. Rapid quadriplegia 2. **Locked in syndrome** (Patient cannot move but is aware/conscious of his surroundings – pons is nonfunctional, but the cortex is functioning) caused by **damage in the ventral part of the pons.** 3. **Intact vertical eye movements and blinking.** The patient is able to communicate by movement of the eyelids. Note: Anything or any conditions that involves damage or destruction to the pons usually cause Locked in Syndrome.		

Dysmyelinating diseases (Leukodystrophies)	**Inherited** diseases: -Most: a**utosomal recessive** -Some: X linked Causes: 1.**Inherited disorder in the enzymes that regulate myelin** → Imbalance between destruction and regeneration of myelin. 2. **Dysfunctional structure of myelin**		**Affected children are:** **At birth:** Normal **During infancy and Childhood:** Start losing developmental milestones**.** **Affected children have:** Deterioration in motor skills, Ataxia, spasticity. **Diseases are progressive and fatal.**	More common in **children**	

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