



Neuropathology

Primary diseases of myelin

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I. Primary diseases of myelin

Demyelinating diseases

- **Normally structured myelin**
- **Acquired**
- **Causes:**
 - **Immune-mediated injury**
 - **Viral infections**
 - **Toxic agents**
- **Multiple Sclerosis**
- **Others**

Dysmyelinating diseases

- **Abnormal formation or turnover of myelin**
- **Inherited**
- **Causes:**
 - **Mutations**
- **Leukodystrophies**

Multiple Sclerosis (MS)

- **„multifocal demyelination”**
- **Common (1/1000 person)**
- **~30-40 years of age; Femal : Male = 2 : 1**
- **Autoimmune disease**
- **Clinical sy: distinctive episodes of neurologic deficits (visual disturbances, numbness/ weakness of limbs, unsteady gait, dysphagia, dizziness (vertigo), etc.)**
- **Clinical course: Relapses-remissions or chronic progressive**

Pathogenesis of MS – immune-mediated myelin damage

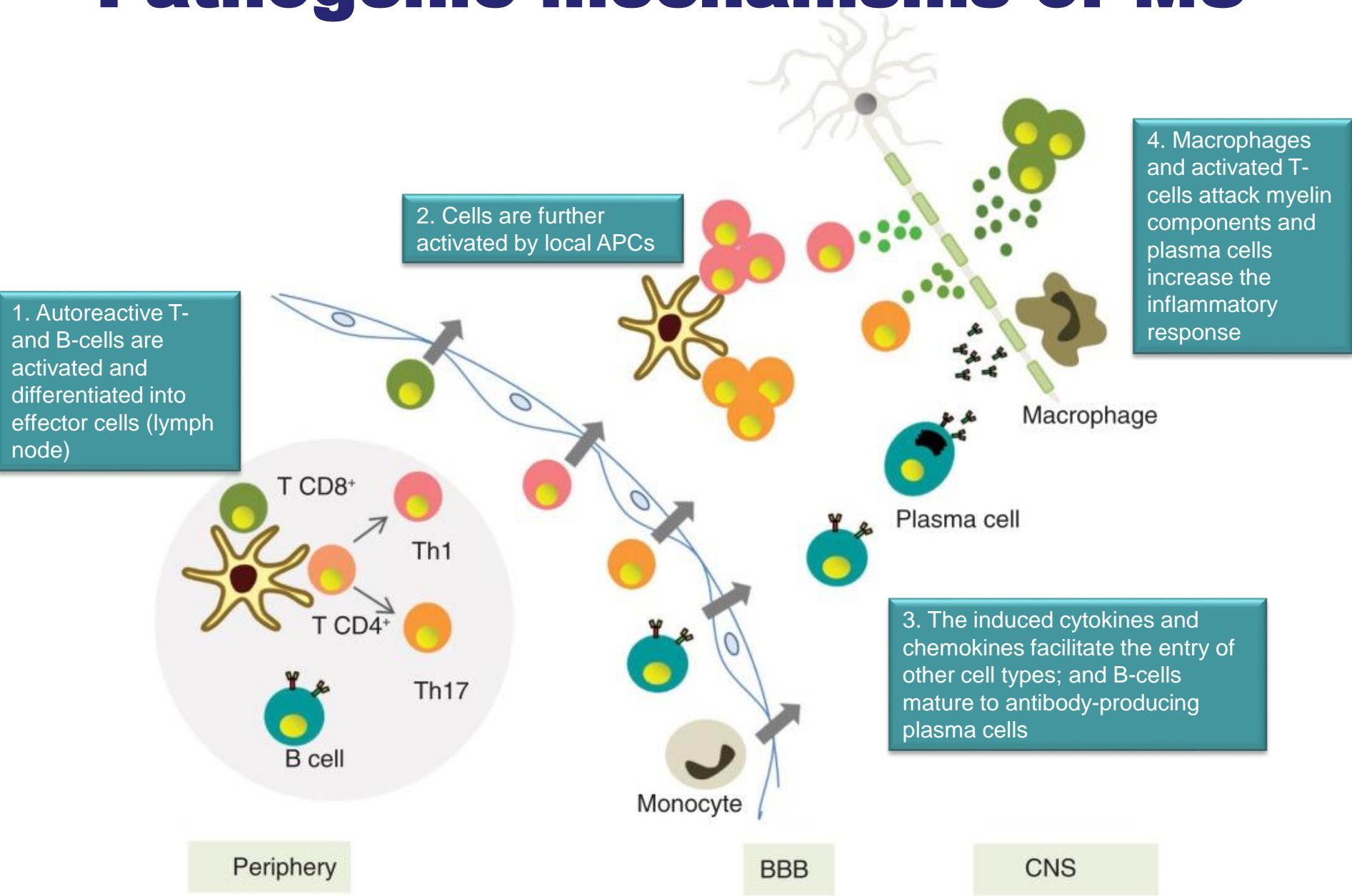
- **Multiple genetic (HLA-DRB1*1501 allele; polymorphism of IL-2 and IL-7 receptor genes) and environmental factors**
- **Loss of tolerance to myelin antigens**
- **Central role of CD4+ T-cells (T_H17 & T_H1 cells)**
- **In addition to myelin loss axonal and neuronal damage also occurs**

Pathogenic mechanisms of MS

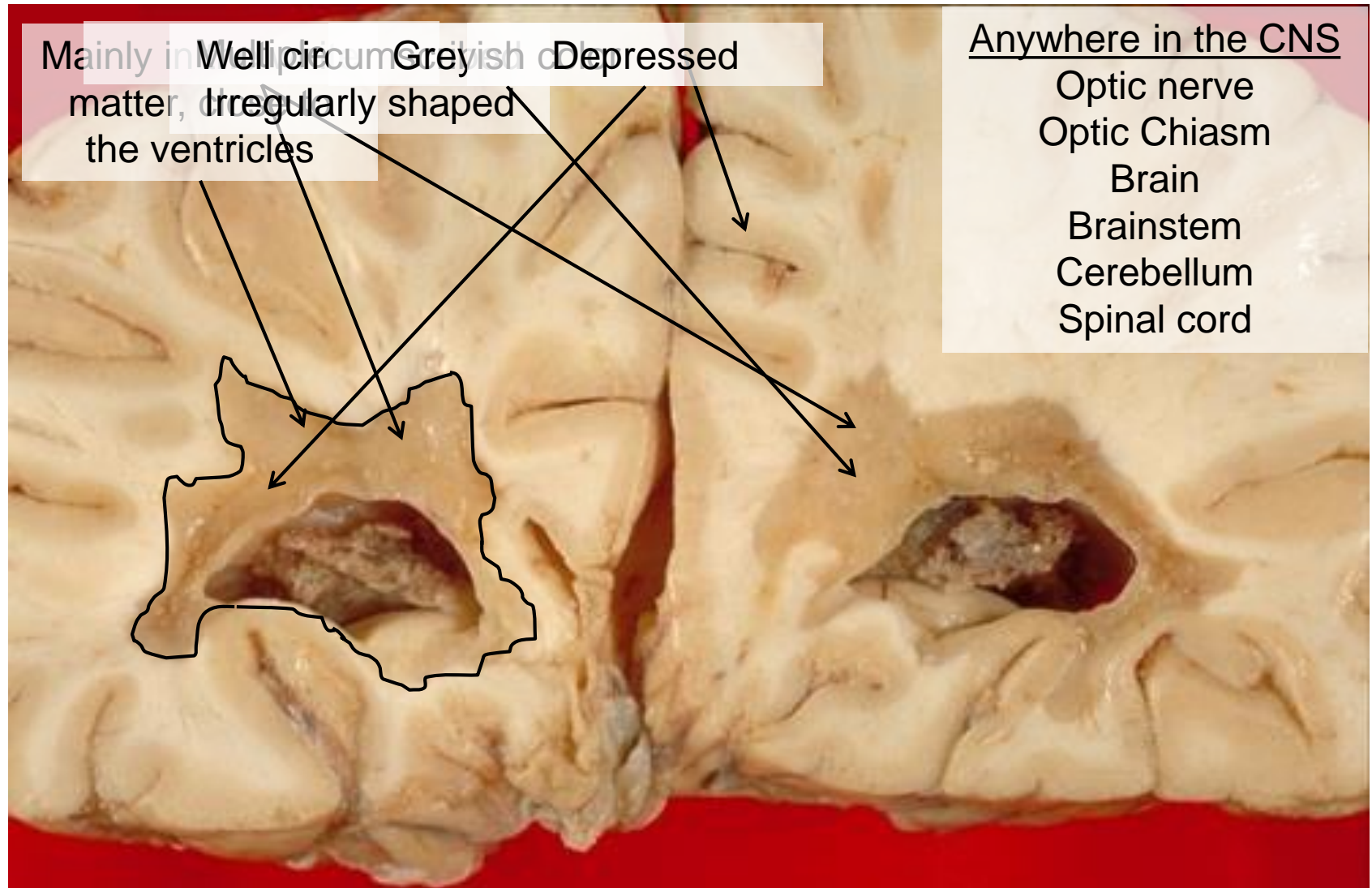
1. Autoreactive T- and B-cells are activated and differentiated into effector cells (lymph node)

2. Cells are further activated by local APCs

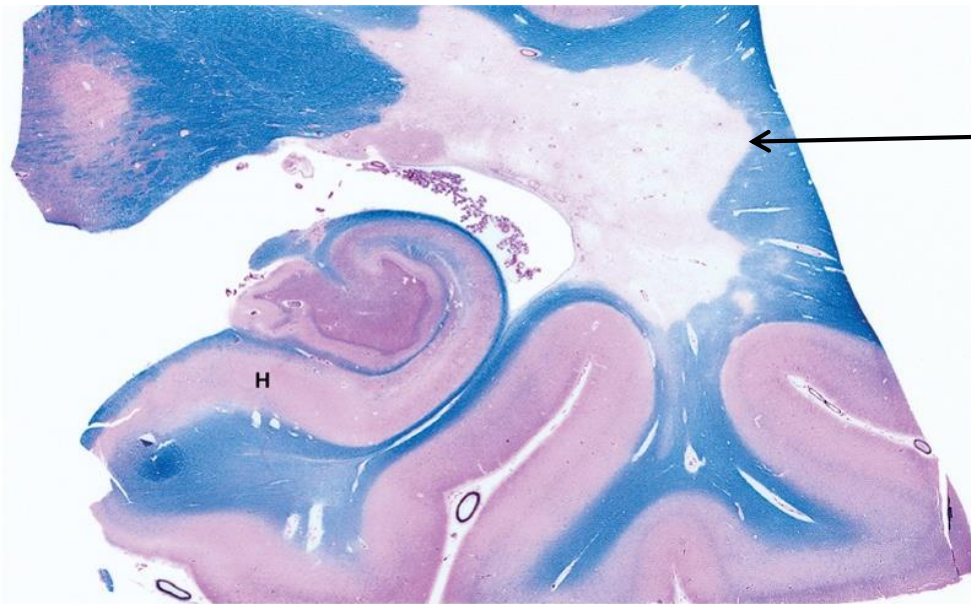
4. Macrophages and activated T-cells attack myelin components and plasma cells increase the inflammatory response



MS macro-morphology: Plaques

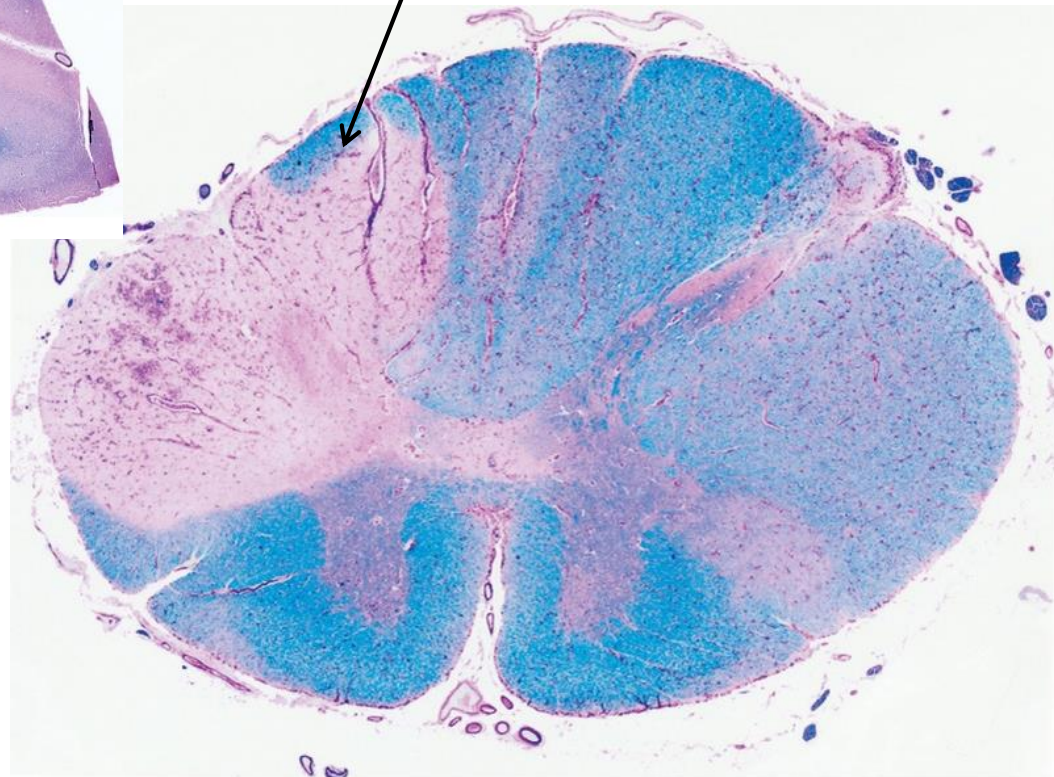


MS micro-morphology: Plaques



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Well circumscribed
Sharp margin

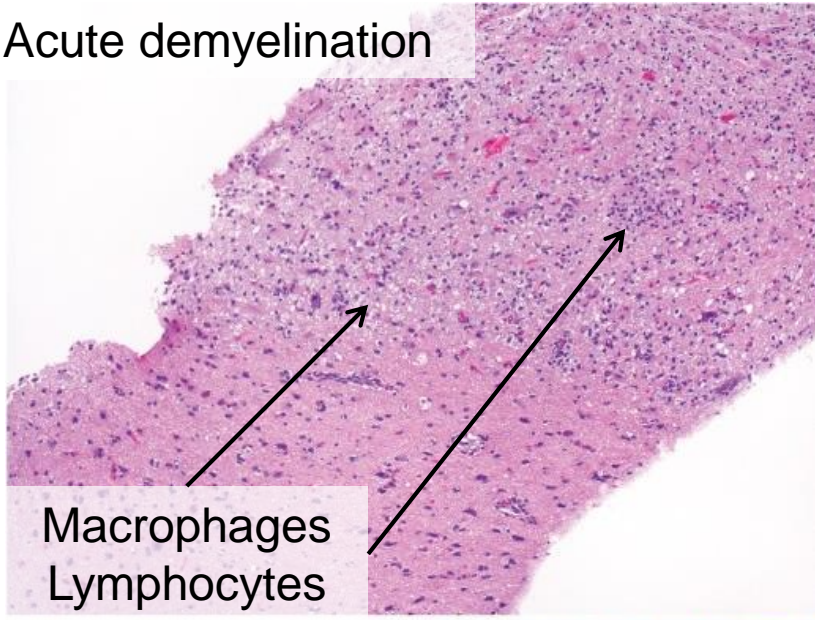


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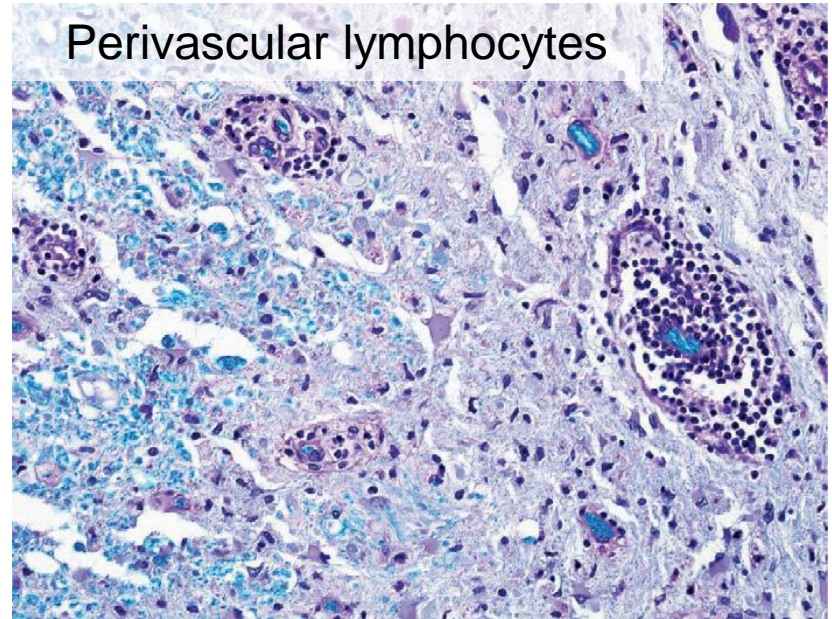
- Active plaques
- Inactive plaques

MS – Active plaques

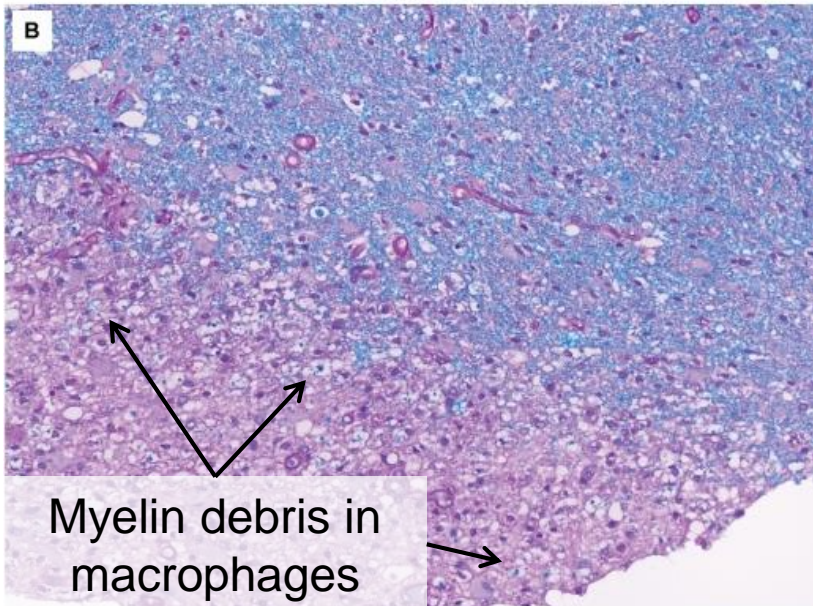
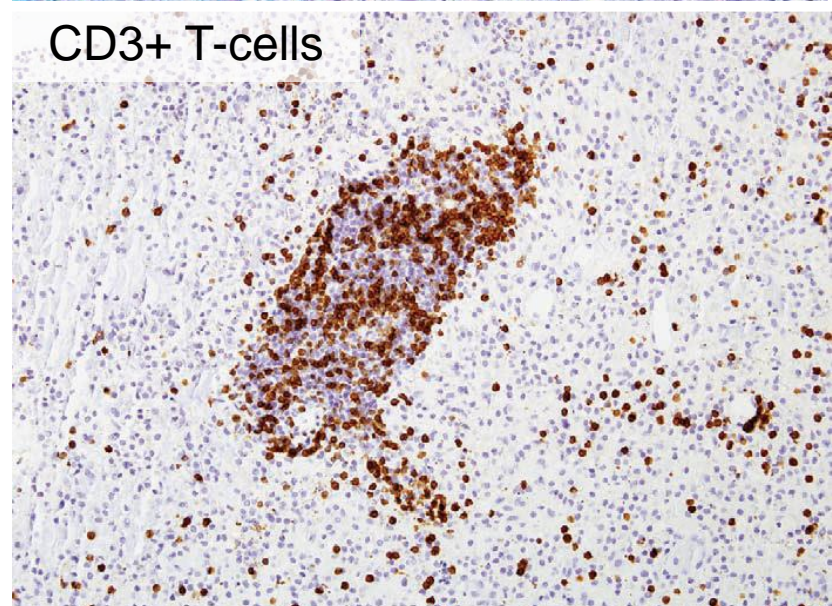
Acute demyelination



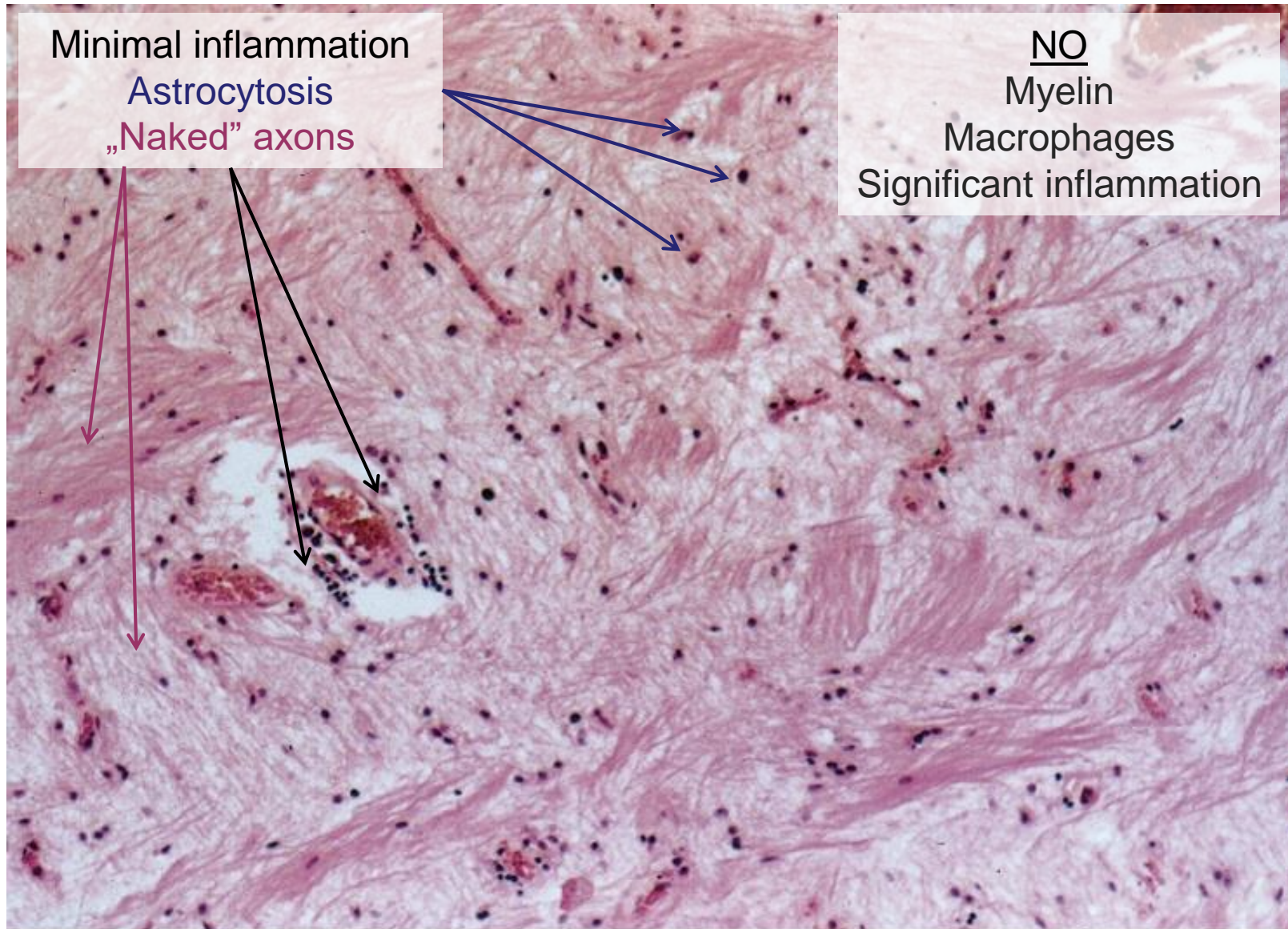
Perivascular lymphocytes



CD3+ T-cells



MS – Inactive plaques



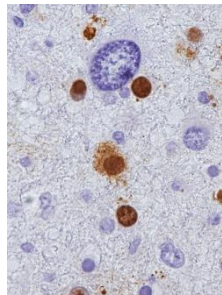
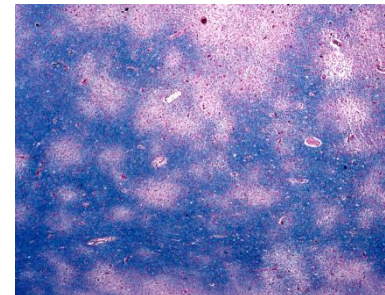
Other acquired demyelinating disorders

Immune-mediated

- **Postinfectious**
(cross-reaction with myelin antigens)
 - Acute disseminated encephalomyelitis (ADEM)
 - Acute necrotizing haemorrhagic encephalomyelitis (necrotizing vasculitis)
- **Neuromyelitis optica**
(Devic disease)
 - Aquaporin-4 autoantibodies (astrocytes)

Nonimmune-mediated

- **Central pontine myelinolysis**
 - After rapid correction of hyponatraemia
 - In alcoholism or severe electrolyte and osmolar imbalance
- **Progressive multifocal leukoencephalopathy**
 - JC virus



Leukodystrophies

- **autosomal recessive inheritance (some X-linked)**
- **begin at younger ages**
- **diffuse involvement of white matter (symmetric)**
- **deterioration in motor skills, spasticity, hypotonia, ataxia**
- **progressive loss of function**

