Electron microscopy in diagnosis of peripheral neuropathy

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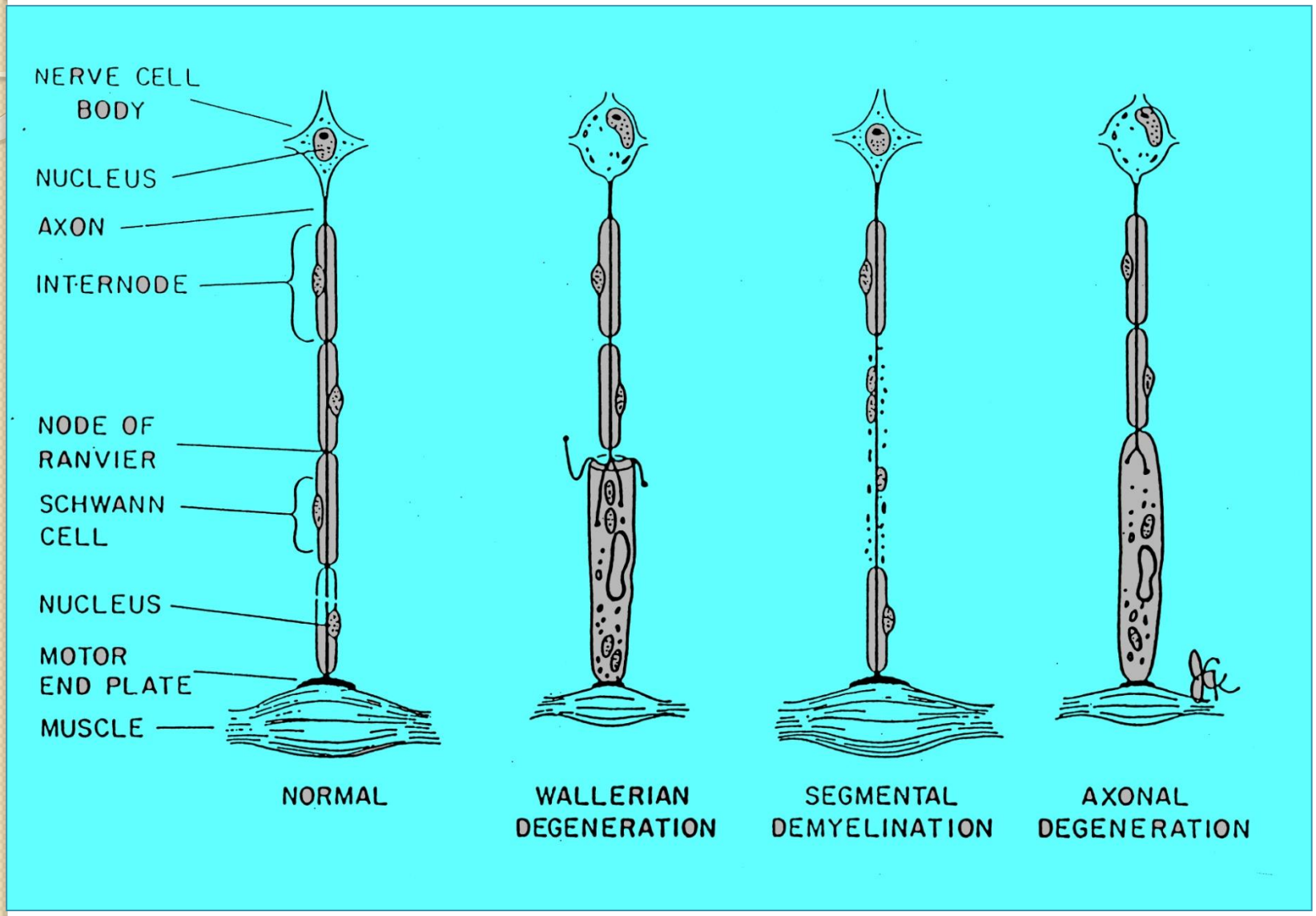
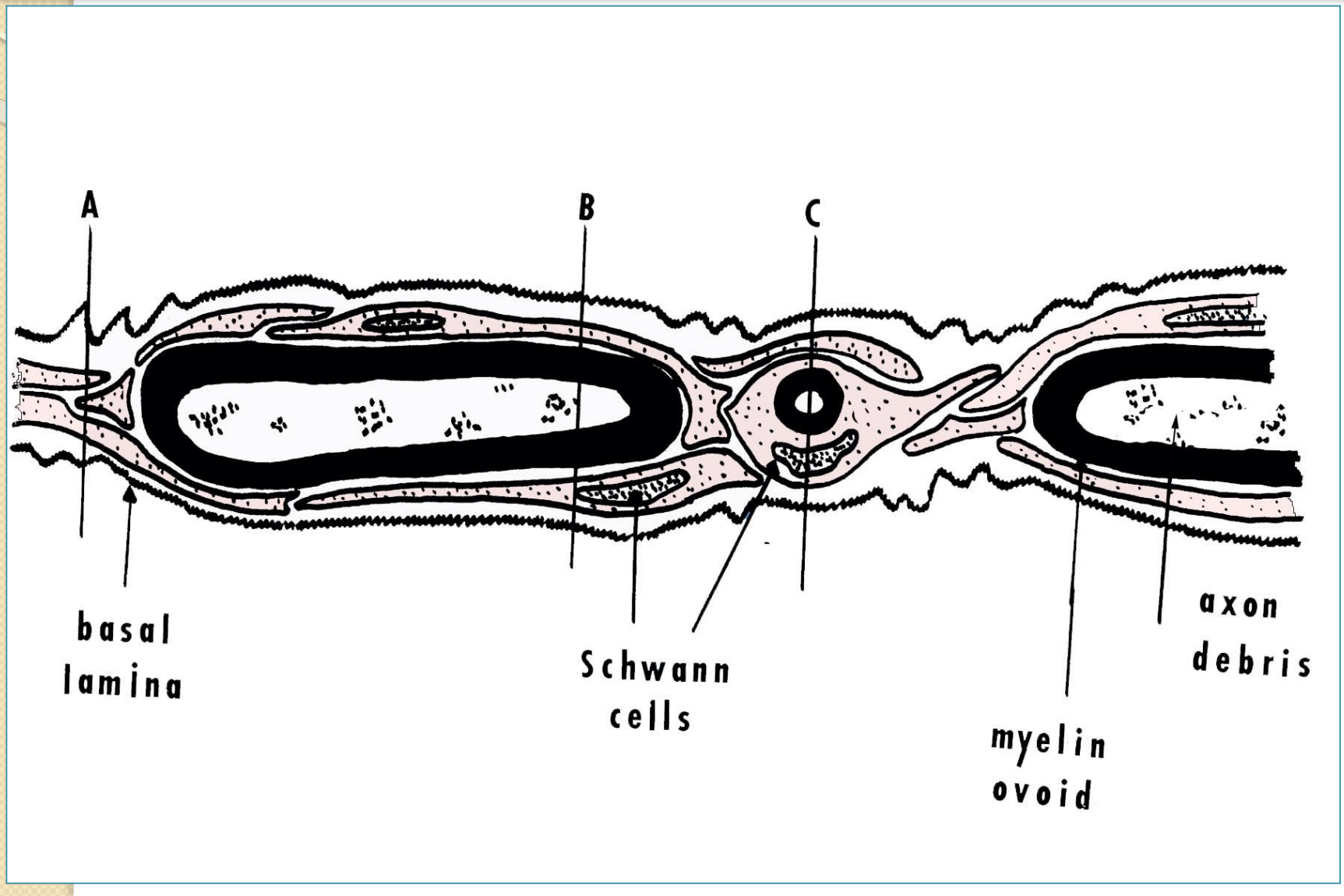
Usefulness of EM in diagnosis

- Essential, e.g. leprosy, amyloid, unmyelinated axons, widely spaced myelin, SC & axonal inclusions,
- Useful, e.g. CIDP, congenital neuropathies
- Confirmatory, e.g. diabetes, HMSN
- Caveats
  - Misinterpretation
  - Surprises
  - Artefacts

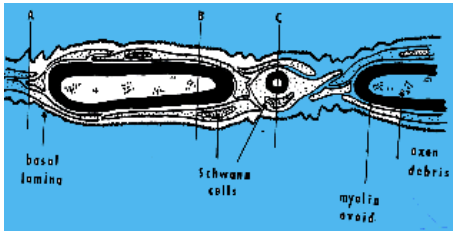
Types of injury



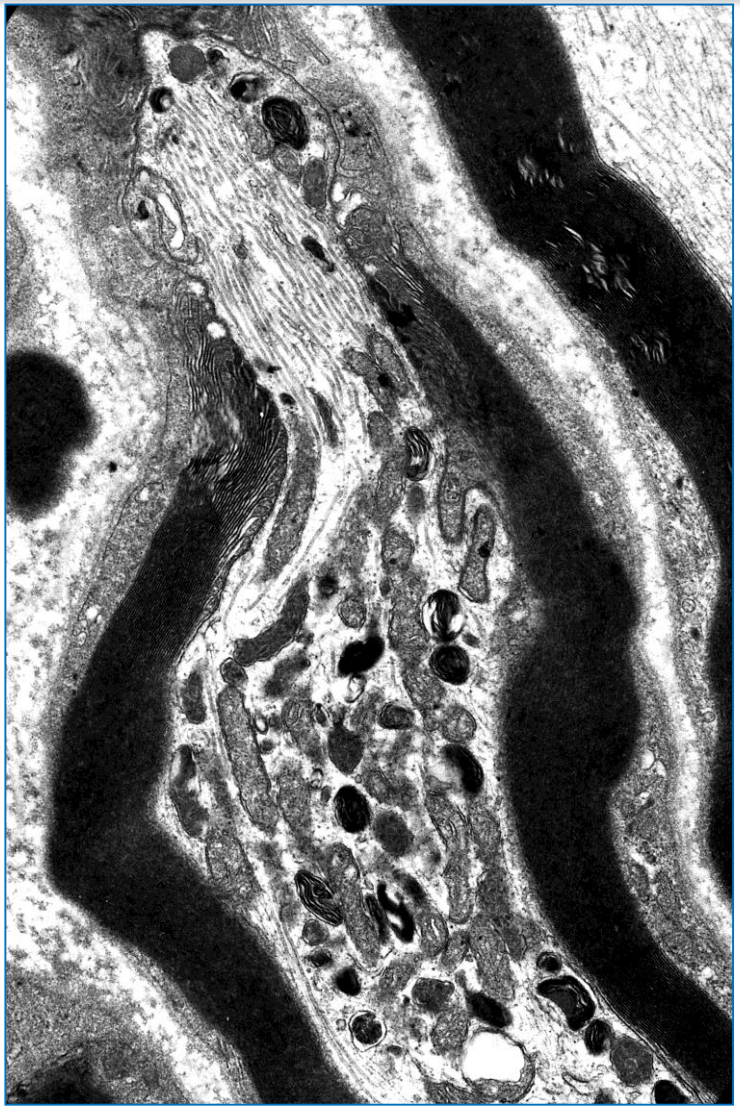
Wallerian-type degeneration



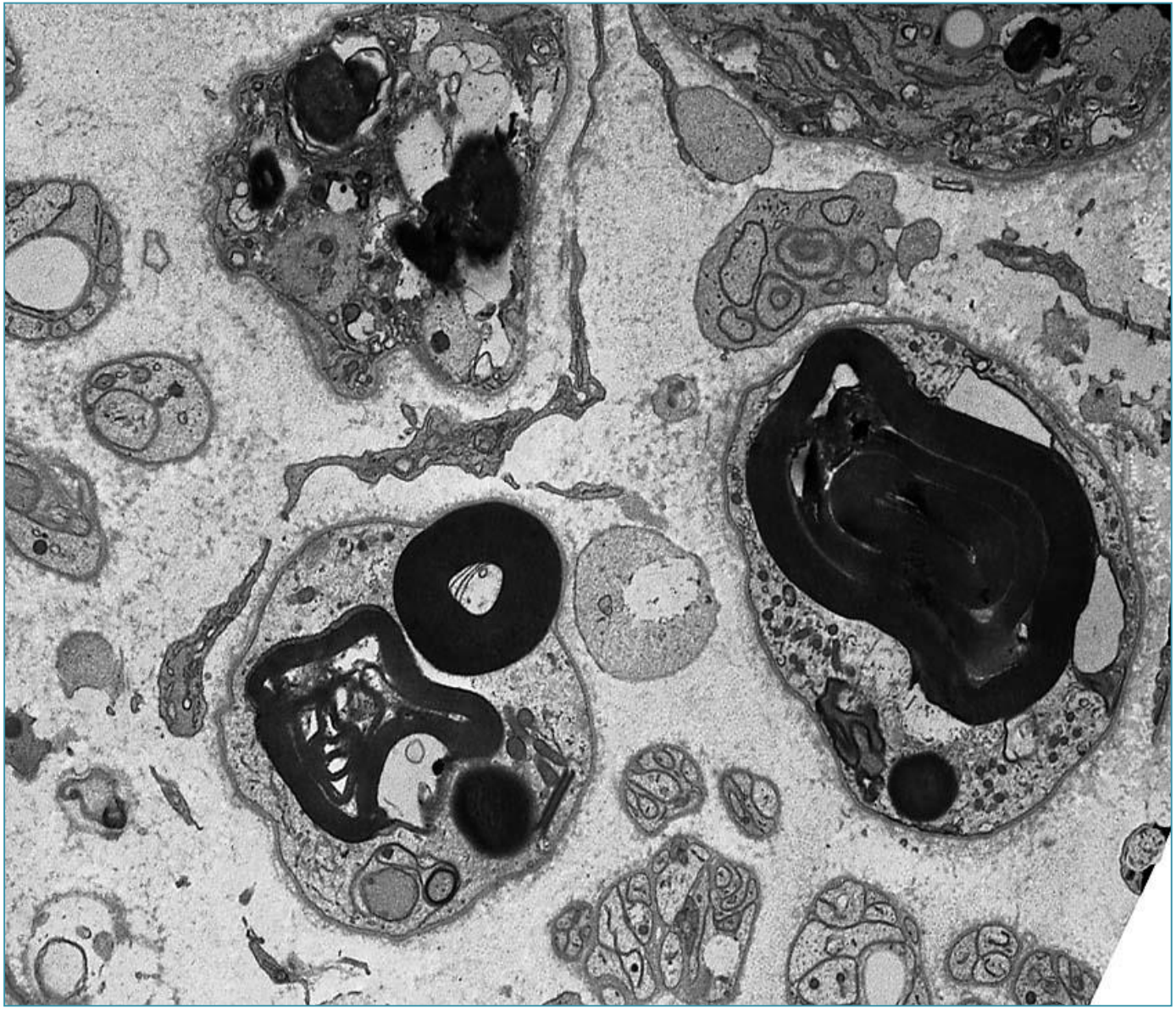
Axonal degeneration



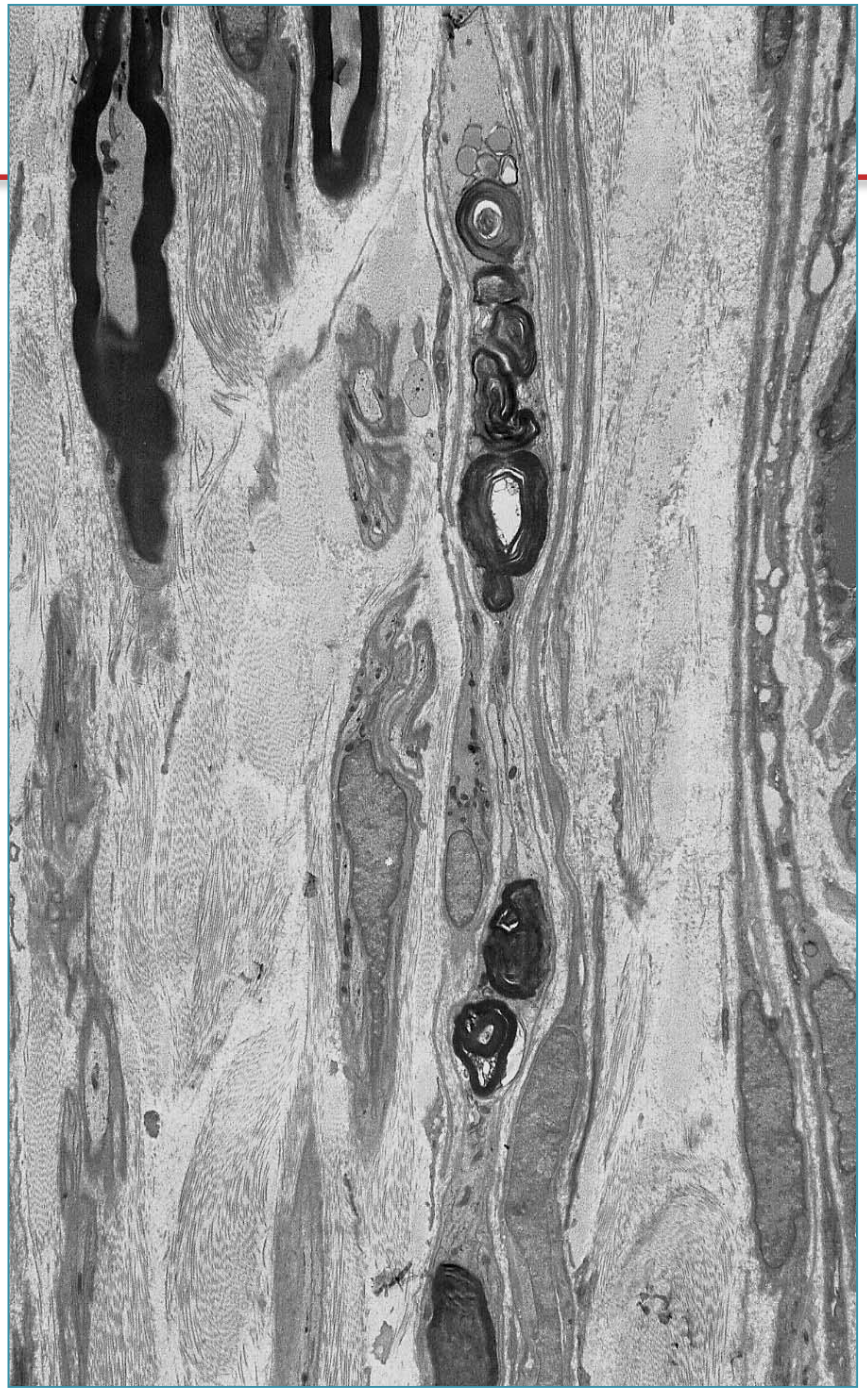
Organelles collect as flow ceases, often above nodes



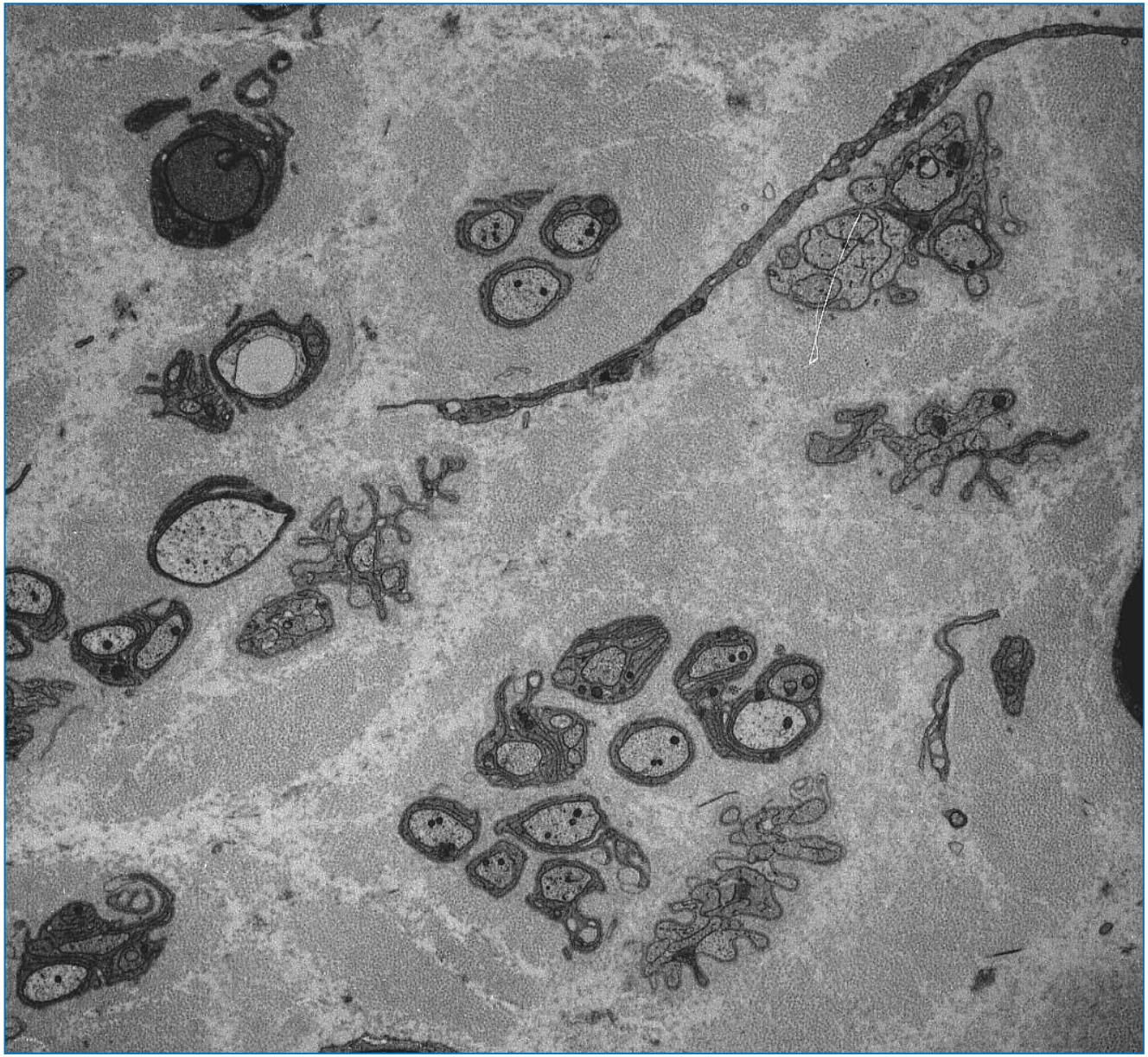
Axonal degeneration



Degeneration



Myelinated fibre loss

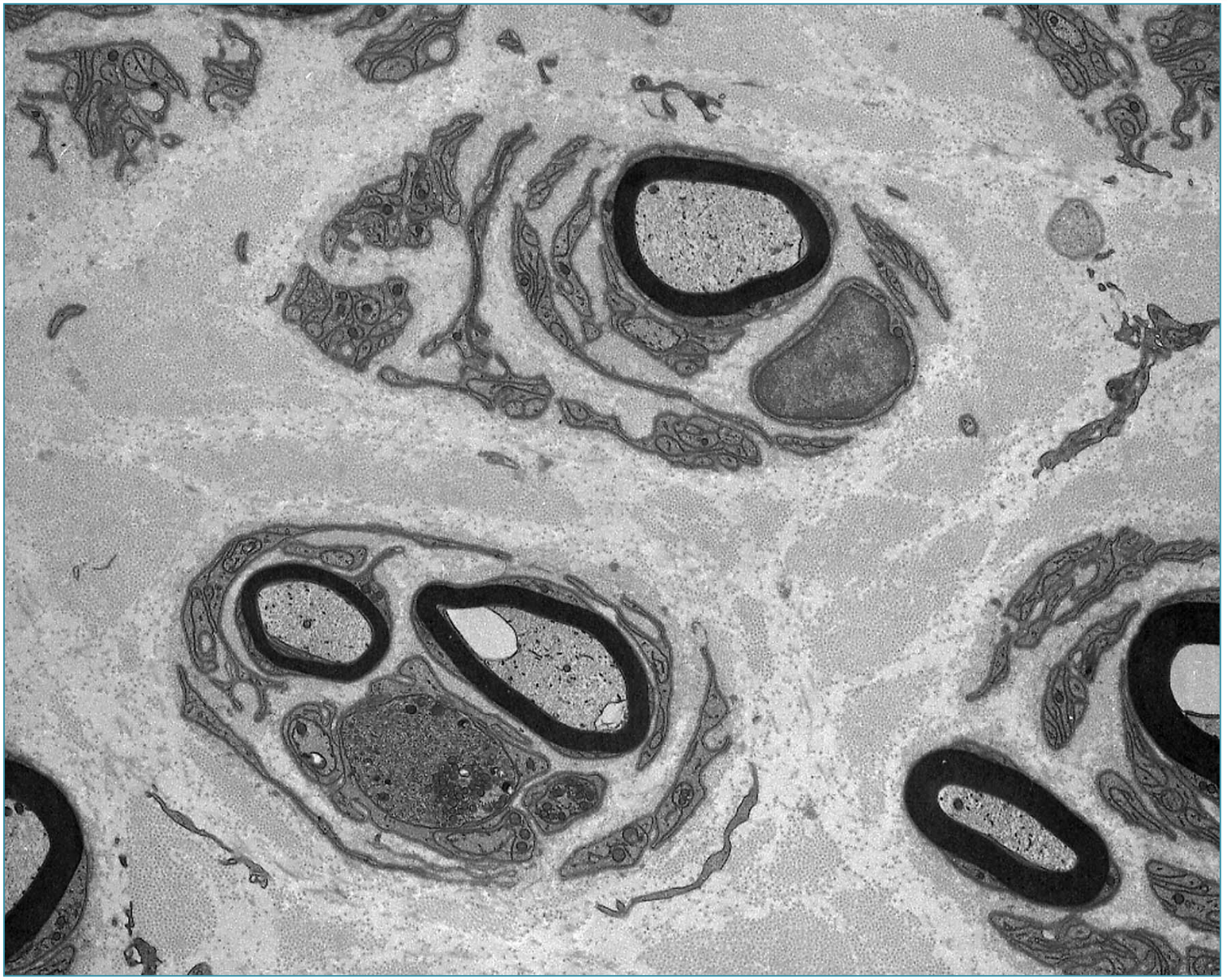


Regeneration

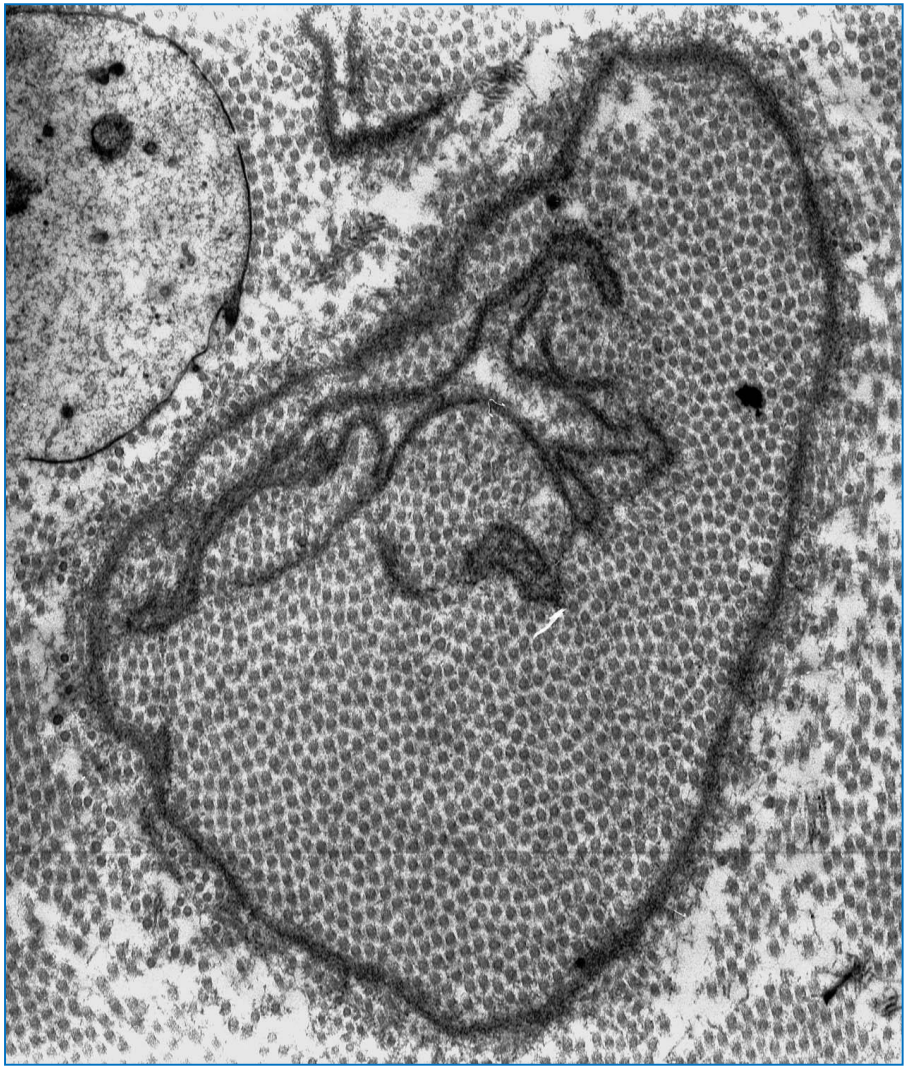
Band of Büngner

Regenerating axon sprouts

Axonal regeneration

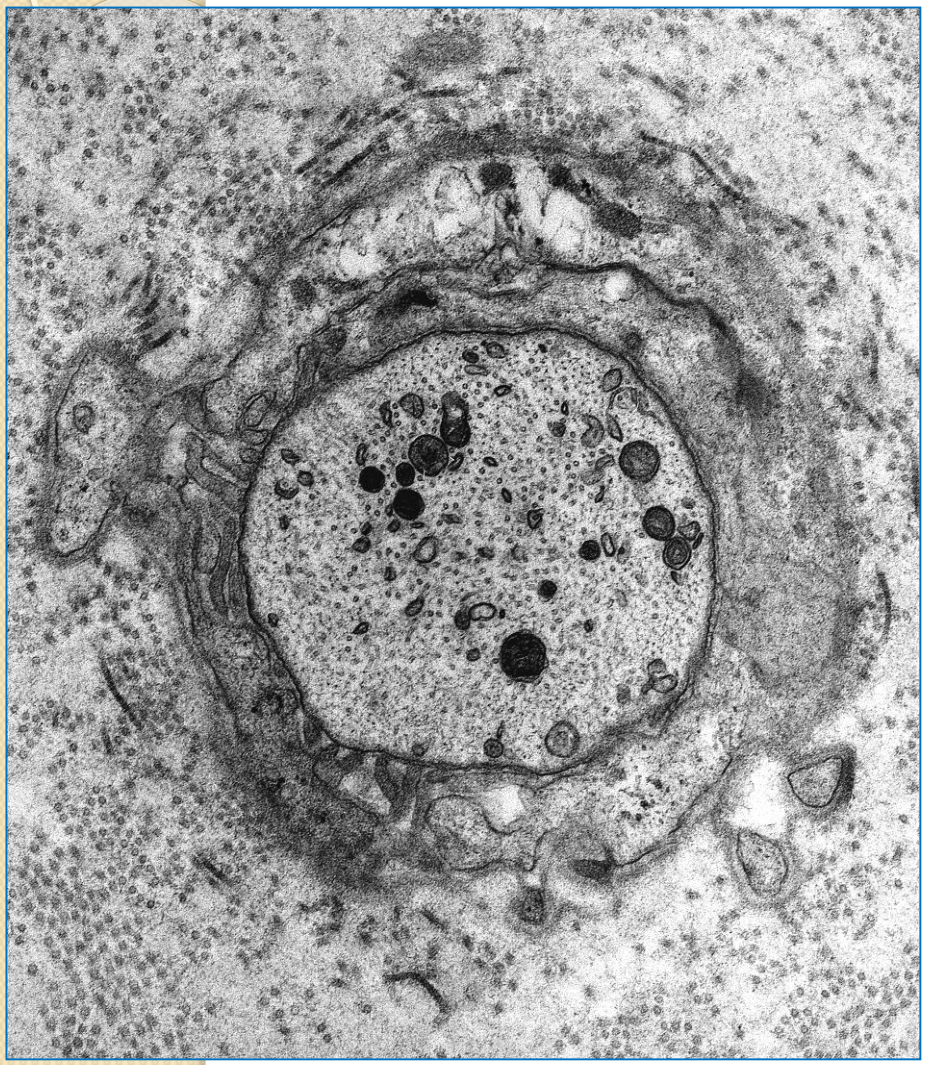


Diabetic neuropathy

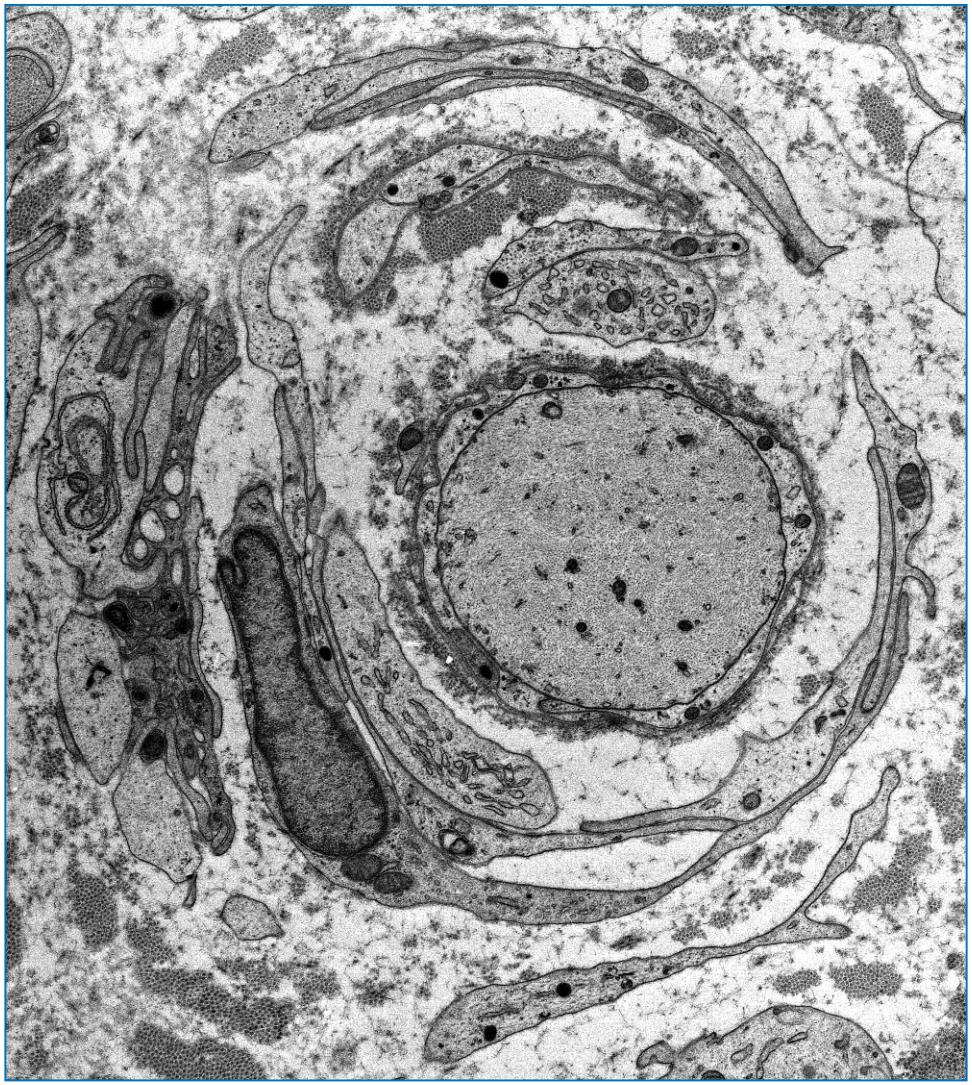


Persistent Schwann cell basal laminal sheath

Demyelination?

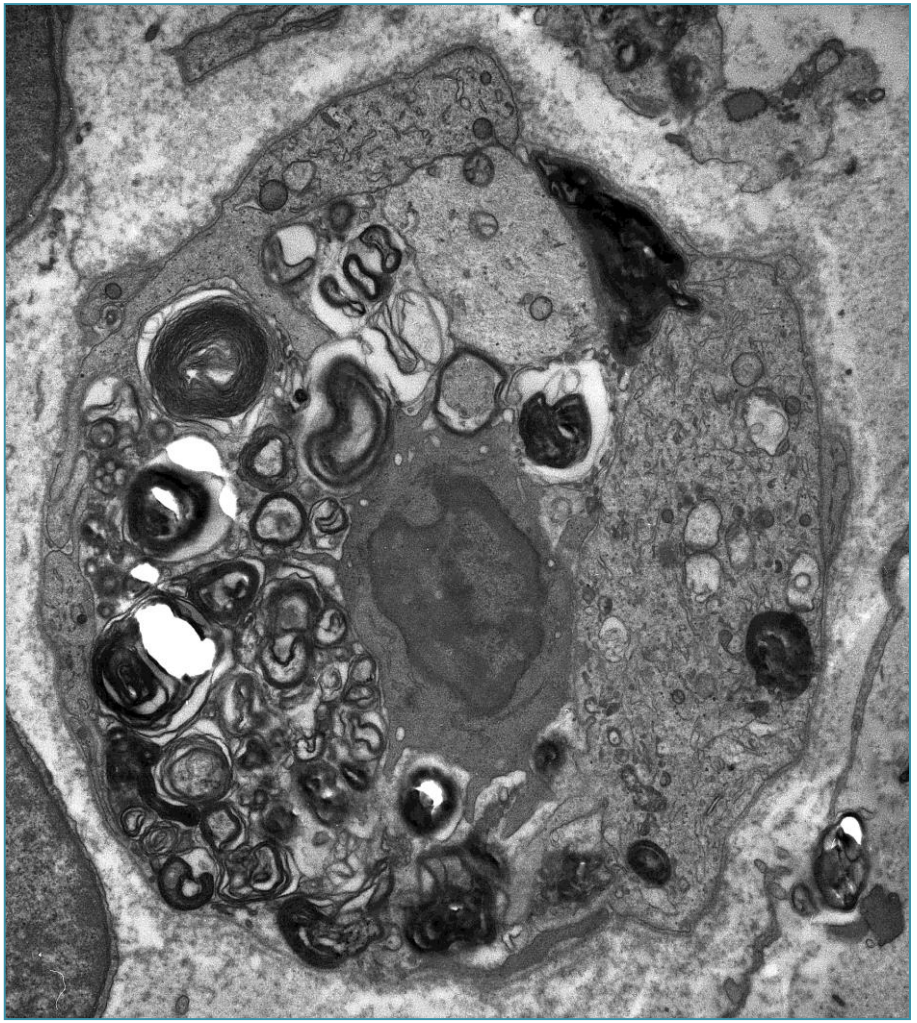


No

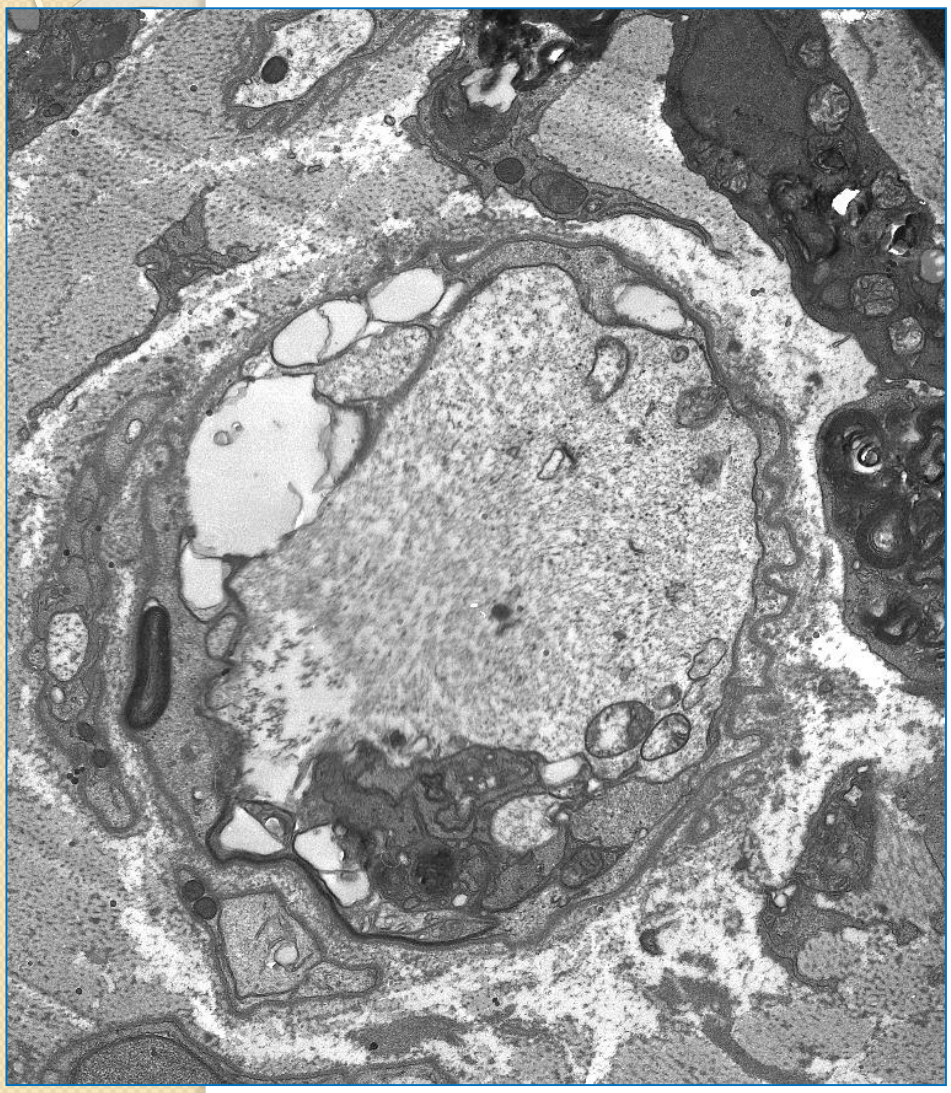


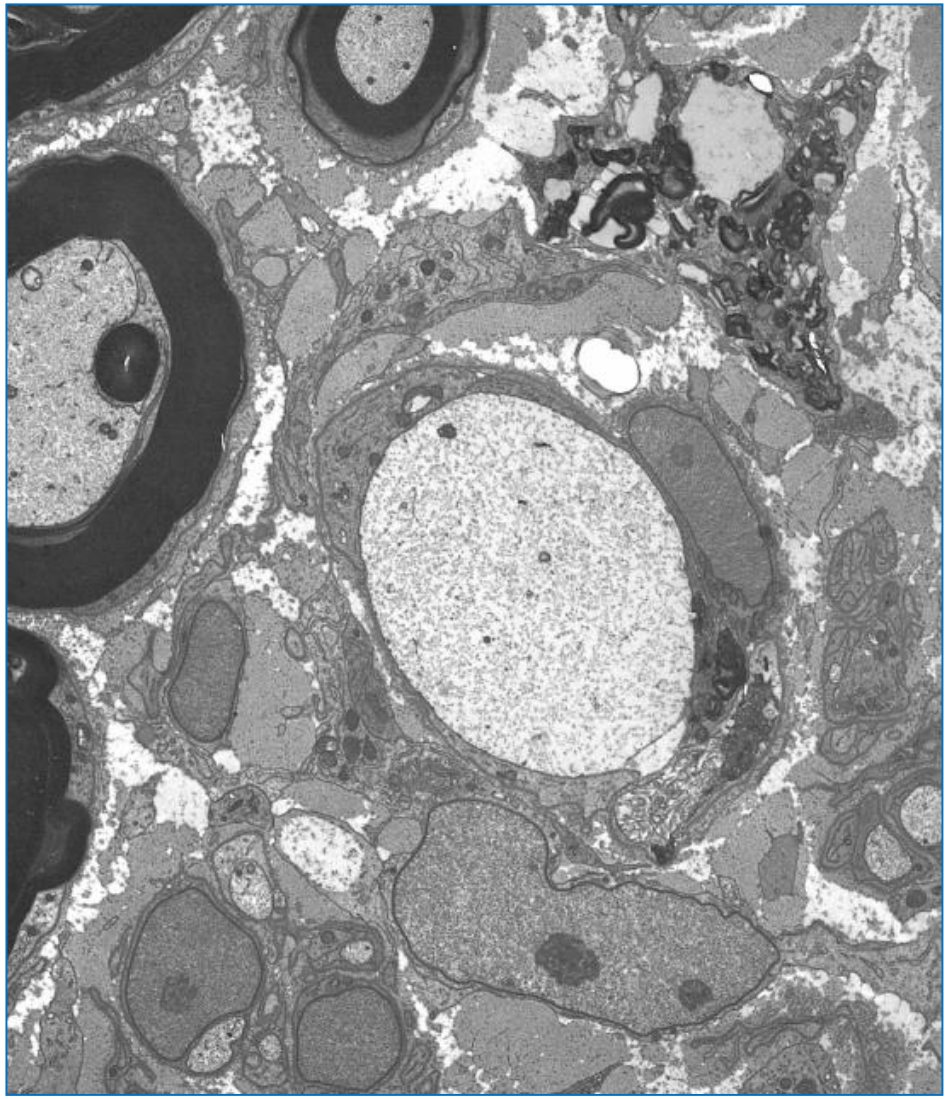
Yes

Demyelination



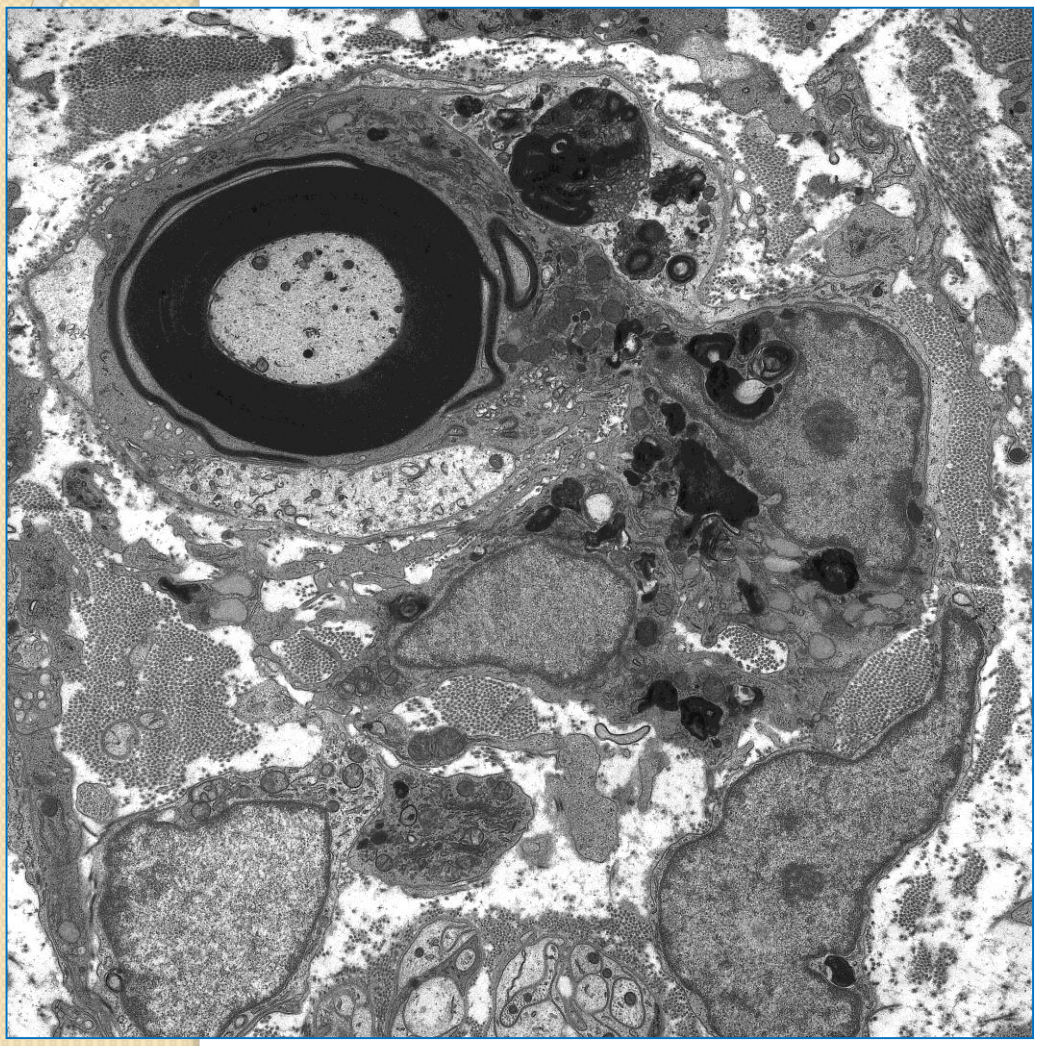
Demyelination

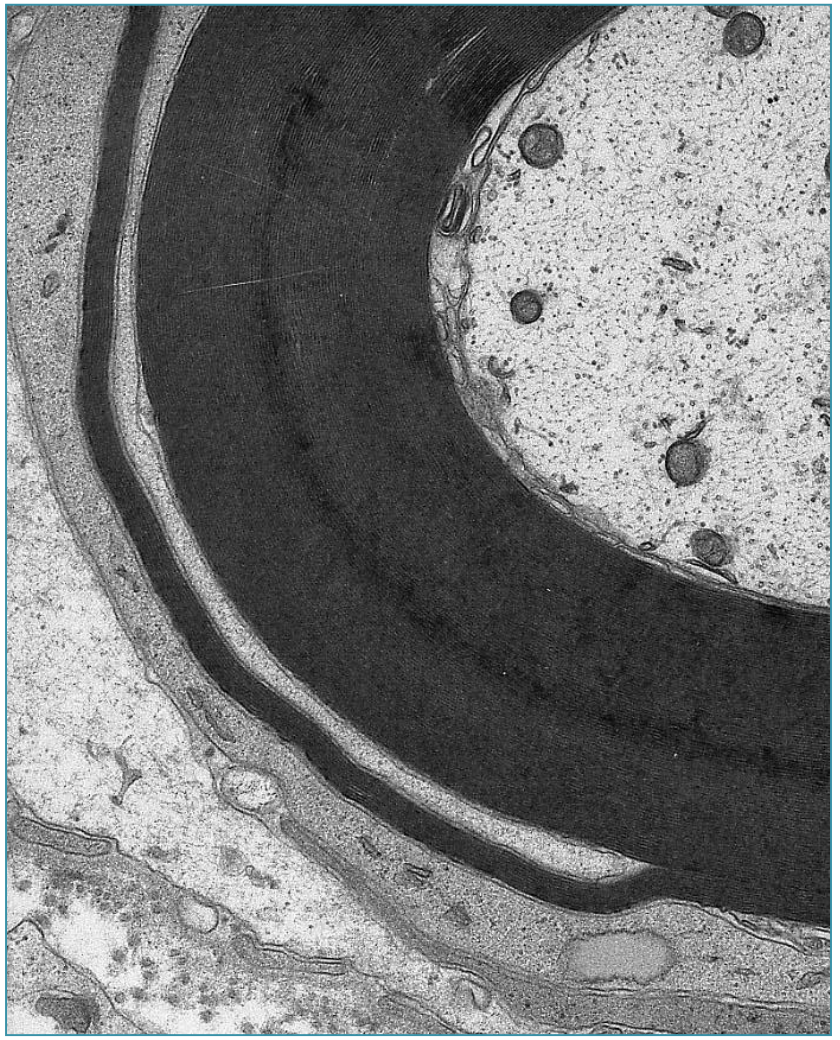




CIDP, 59F

Immune mediated demyelination





Macrophage attack

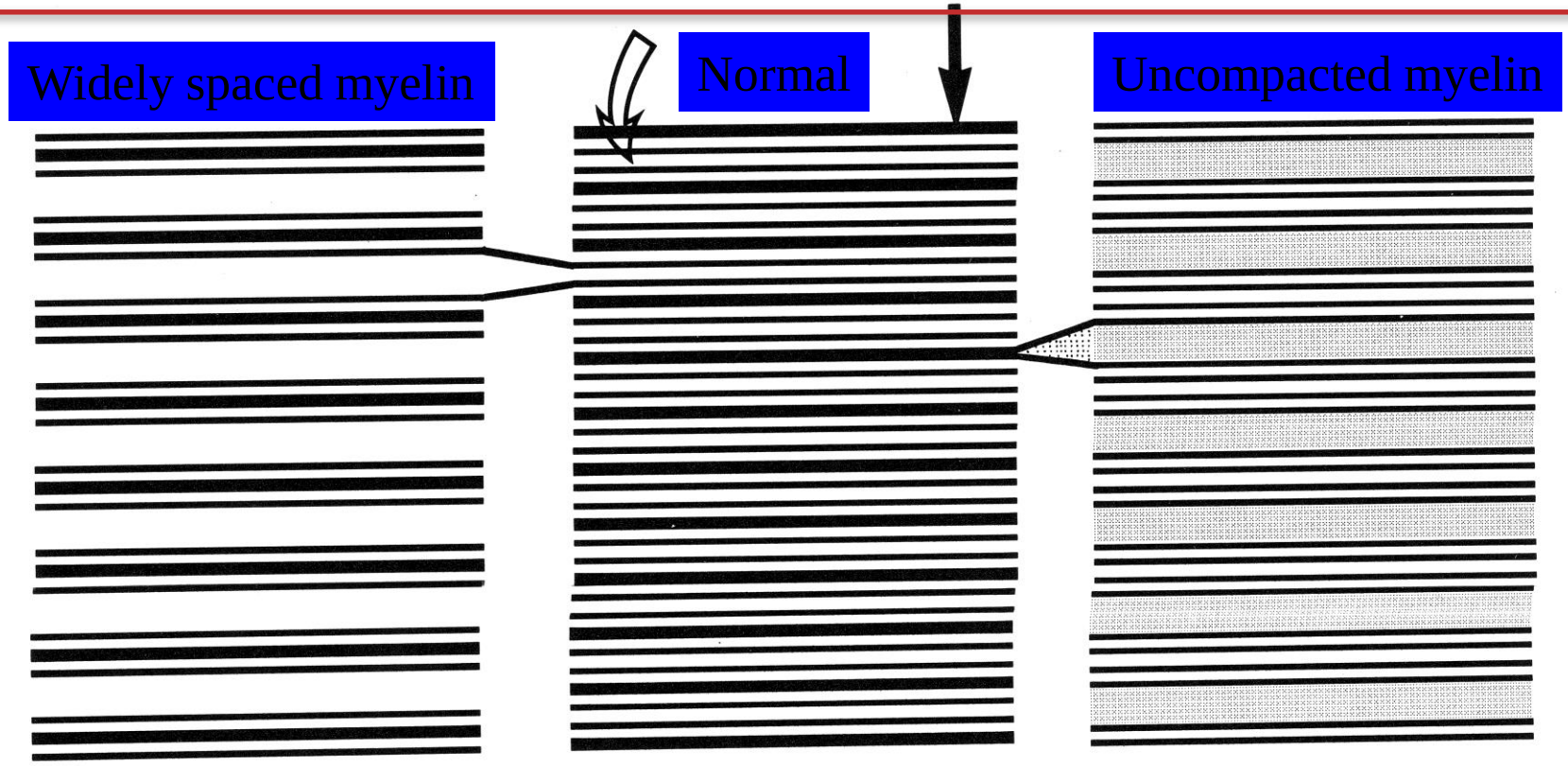
No axon

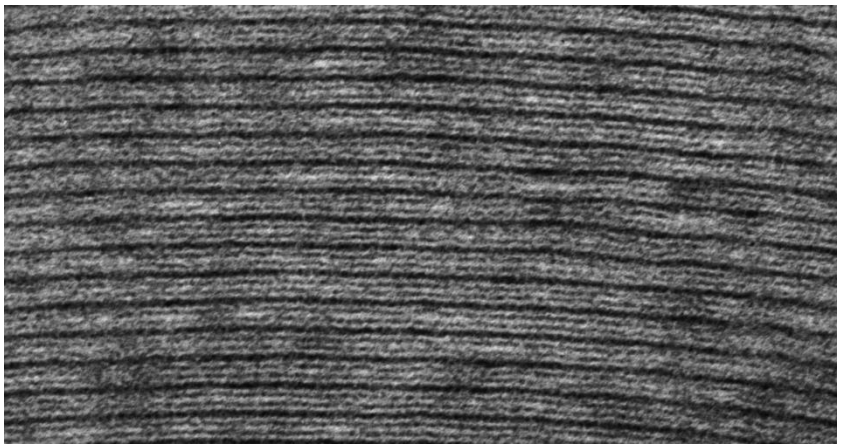
Stripping

Abnormal myelin

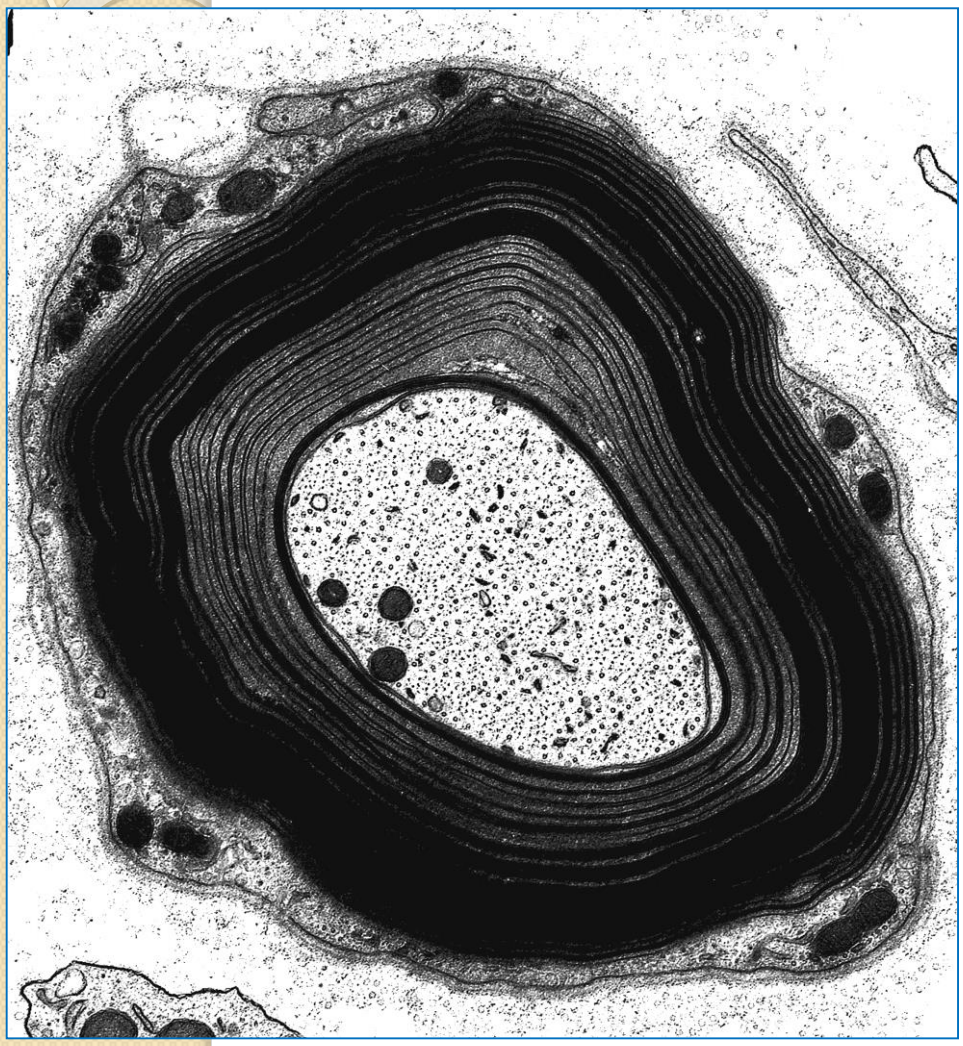
- Identification of myelin stripping
- Identification of demyelination
- Identification of remyelination
- Abnormal myelin periodicity

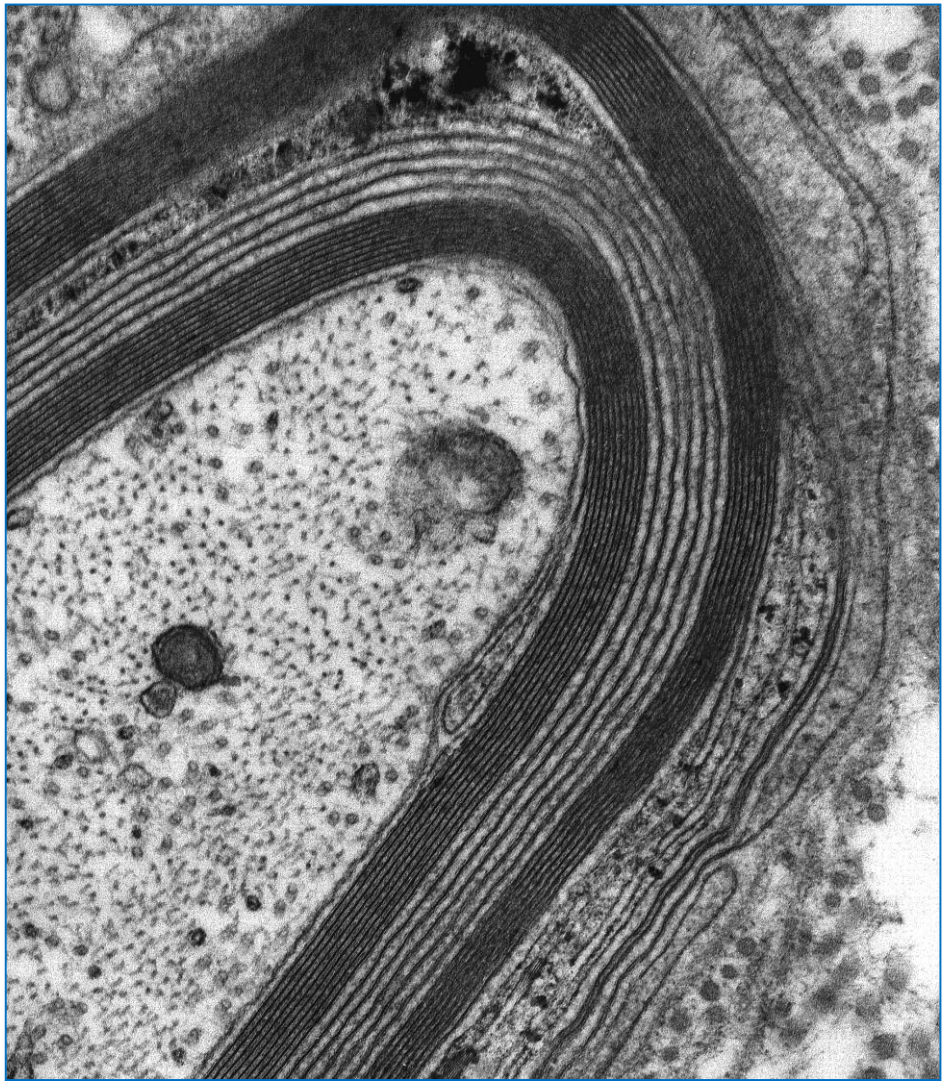
Myelin abnormalities





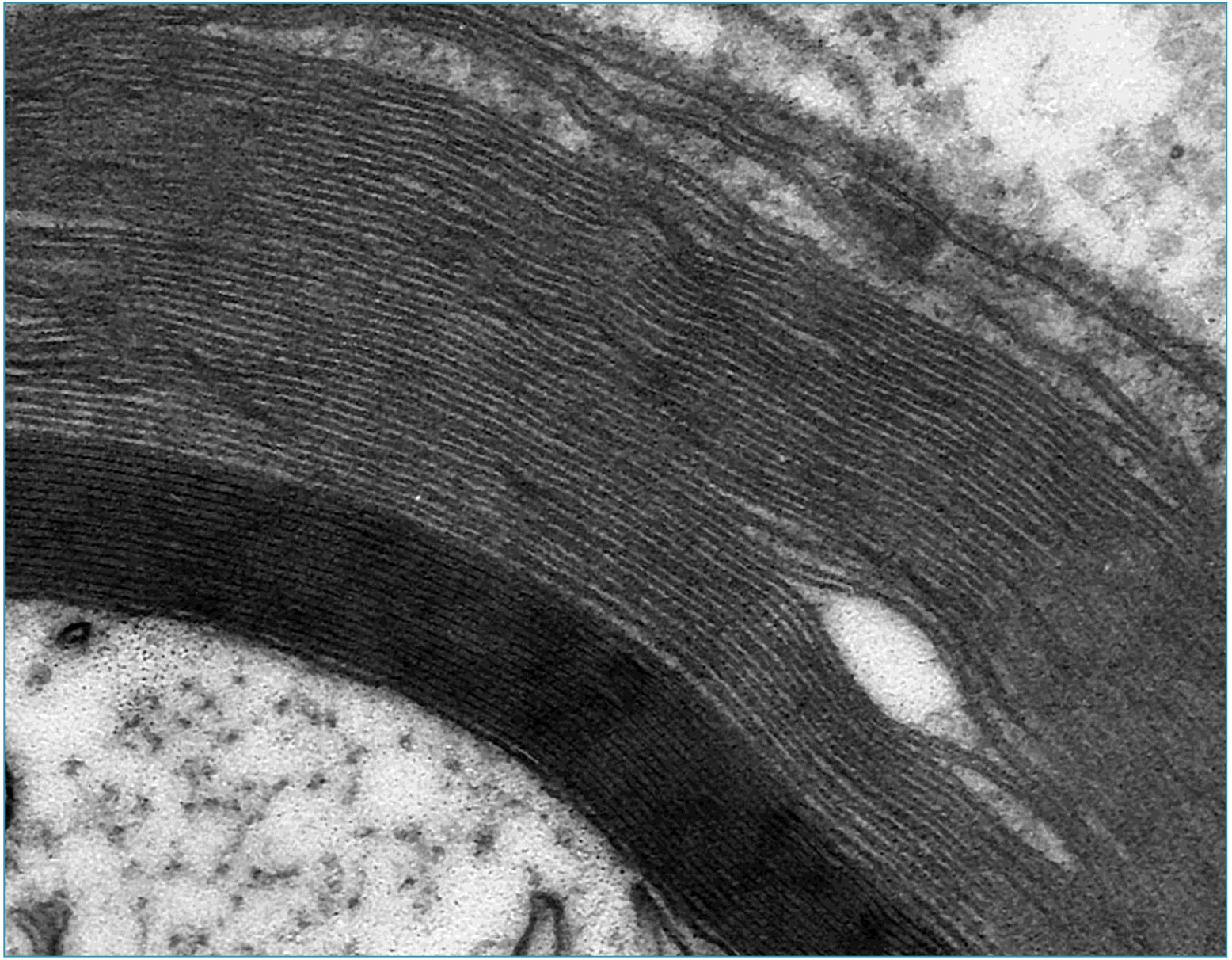
Widely spaced myelin





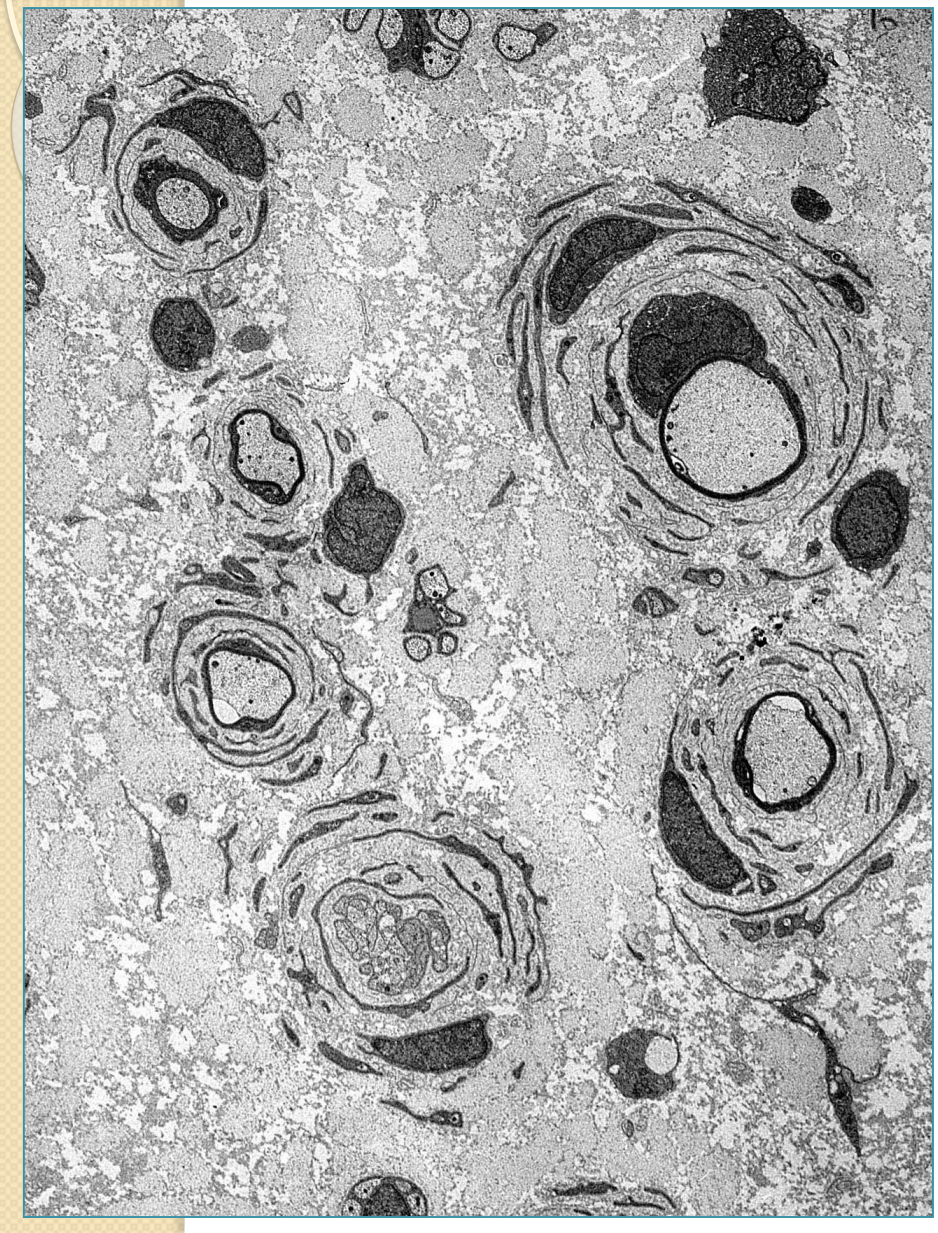
Normal periodicity ≈ 14nm, ws myelin 2.5X

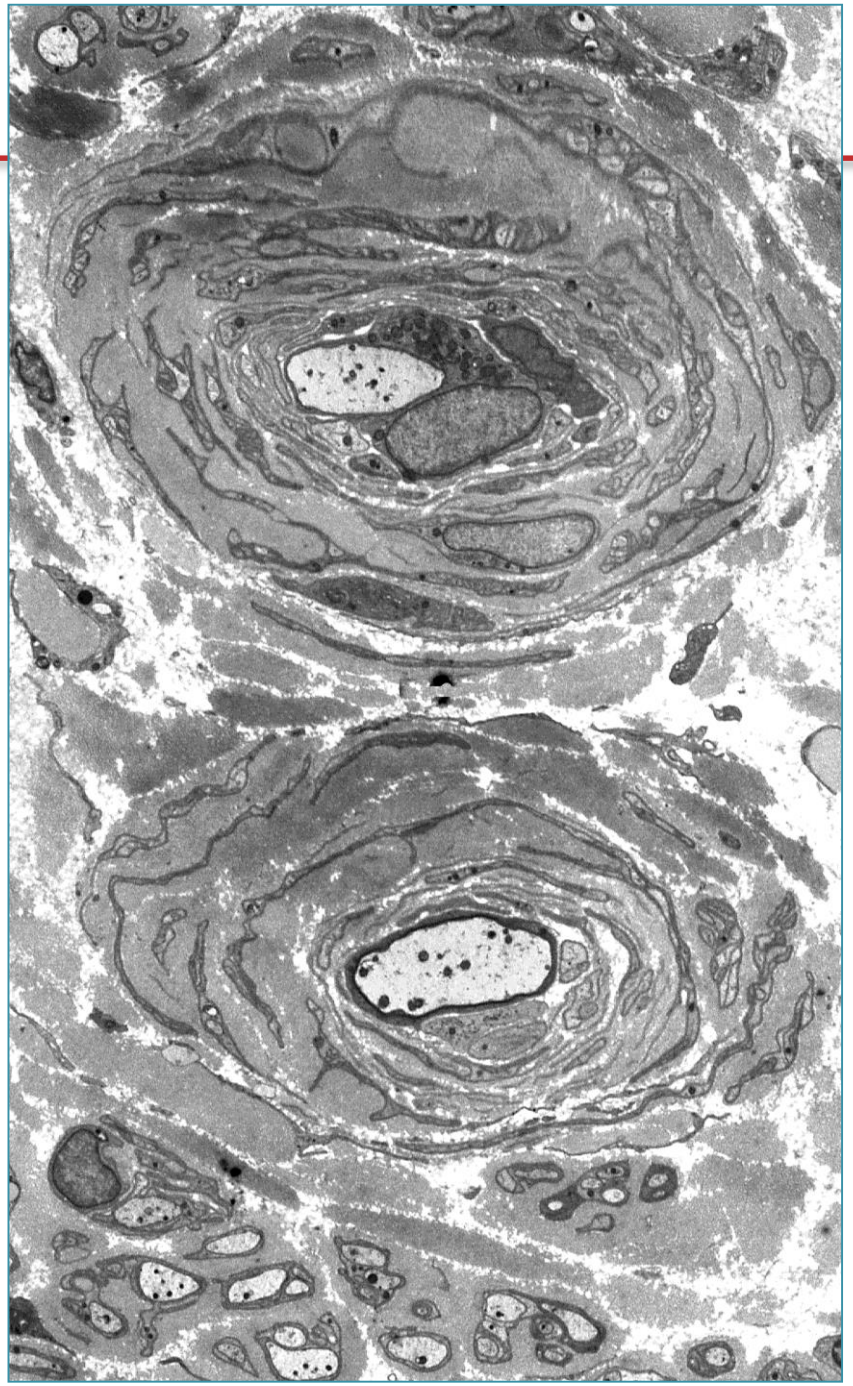
Uncompacted myelin



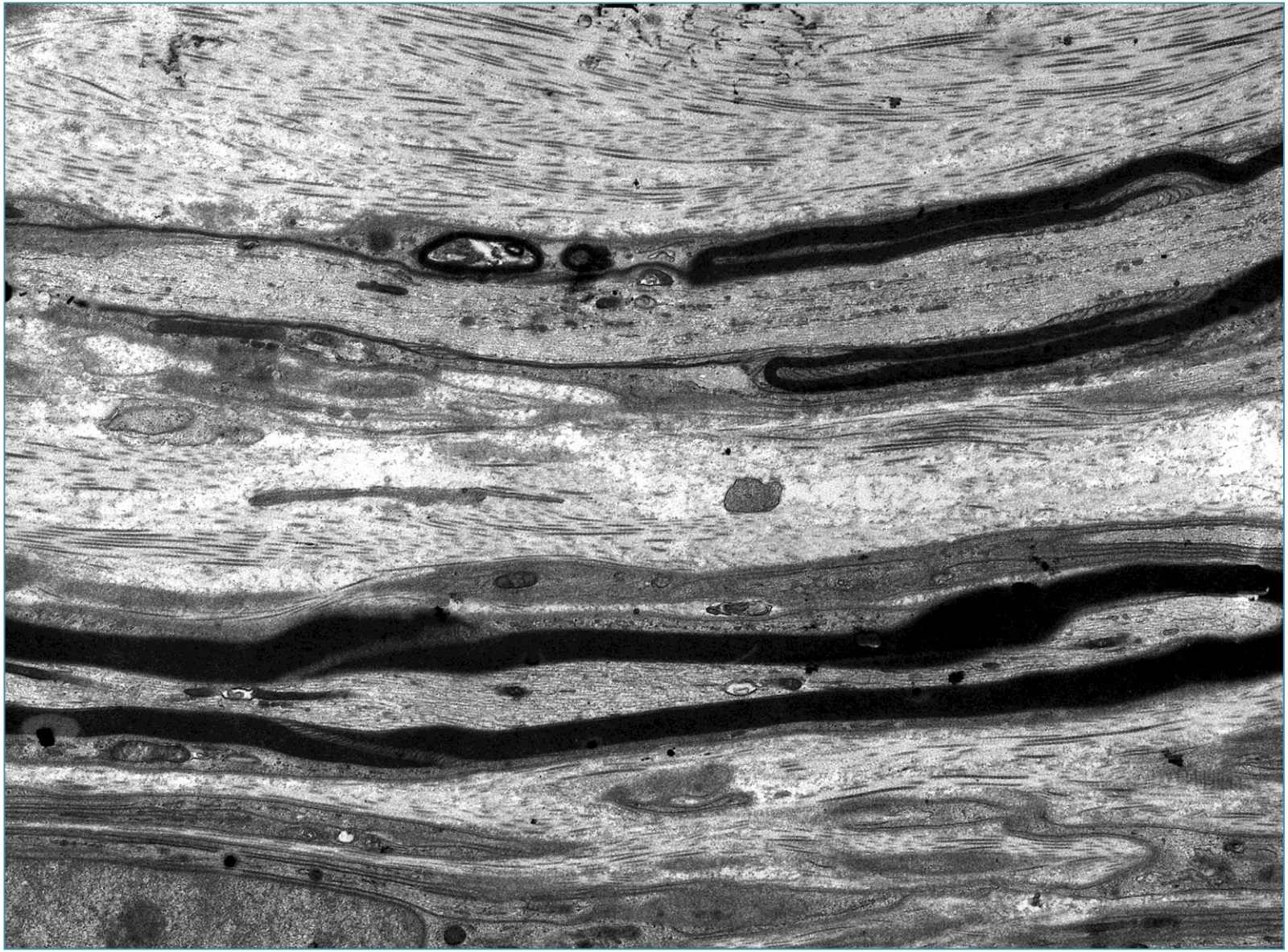
Intramyelinic oedema

Remyelination

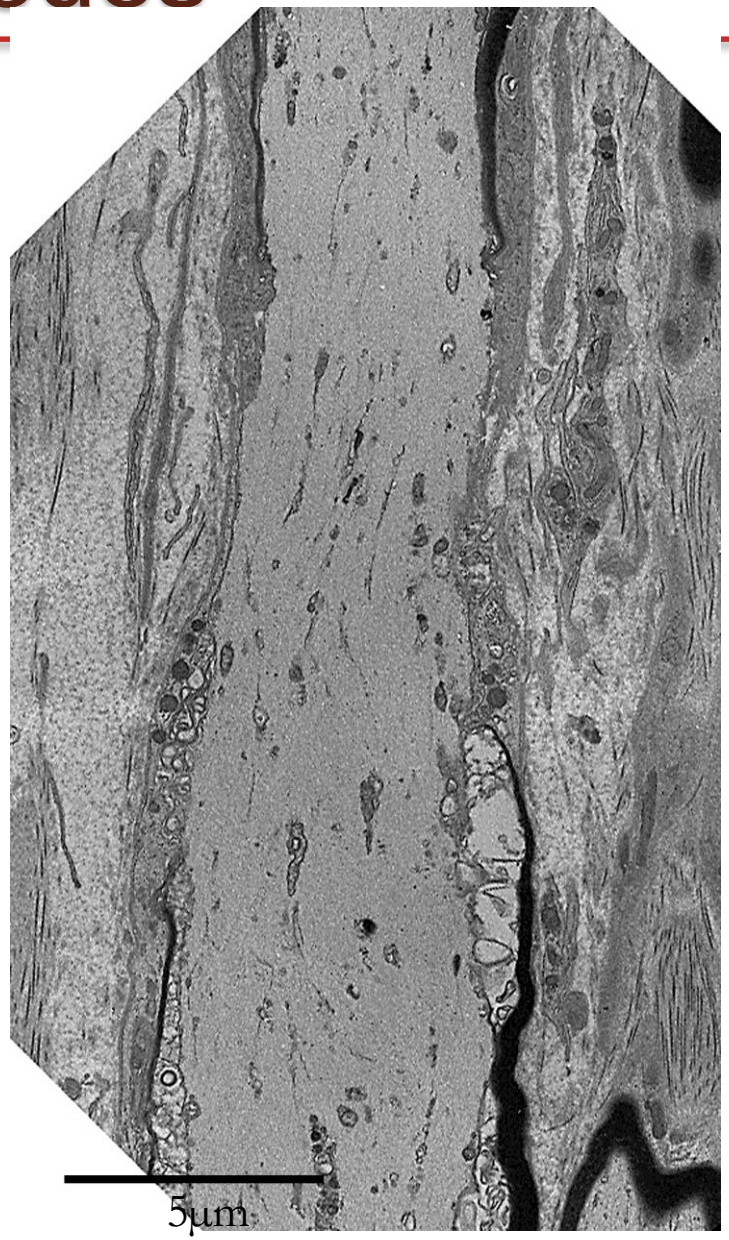




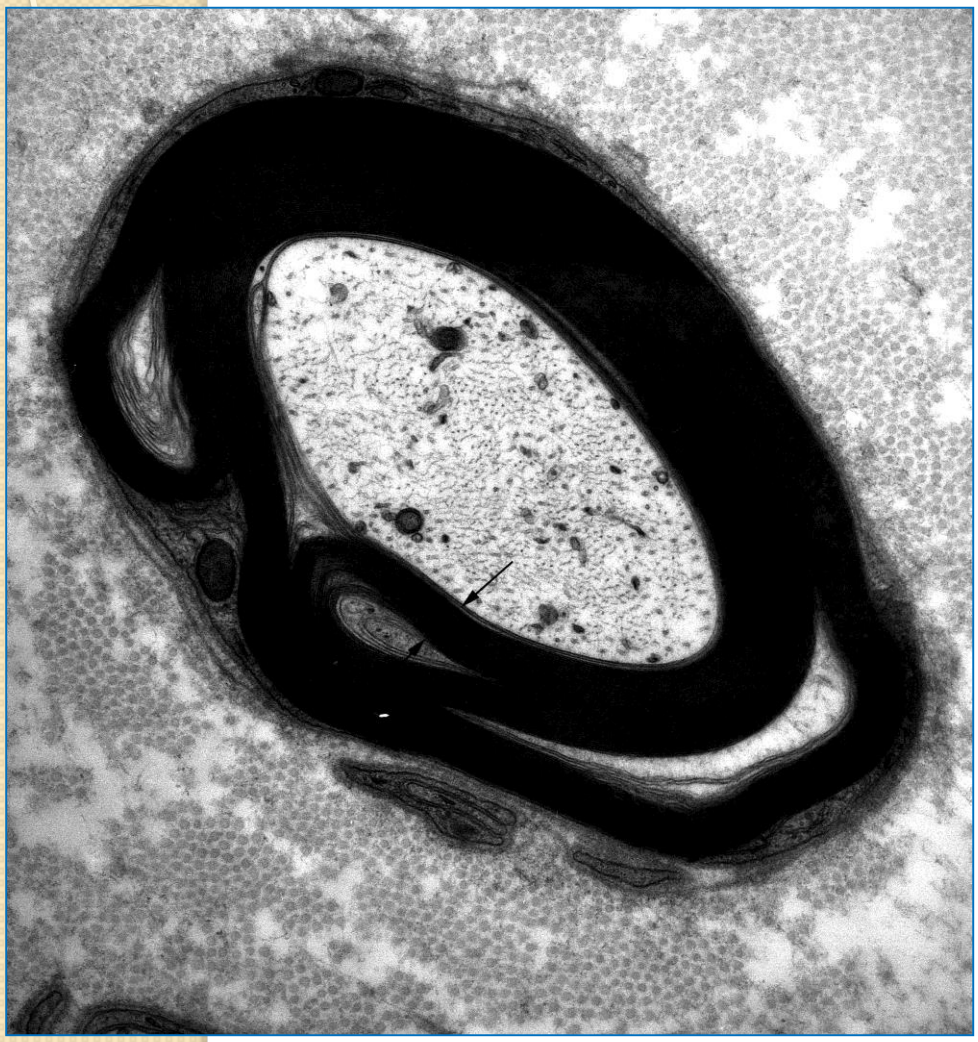
Remyelination



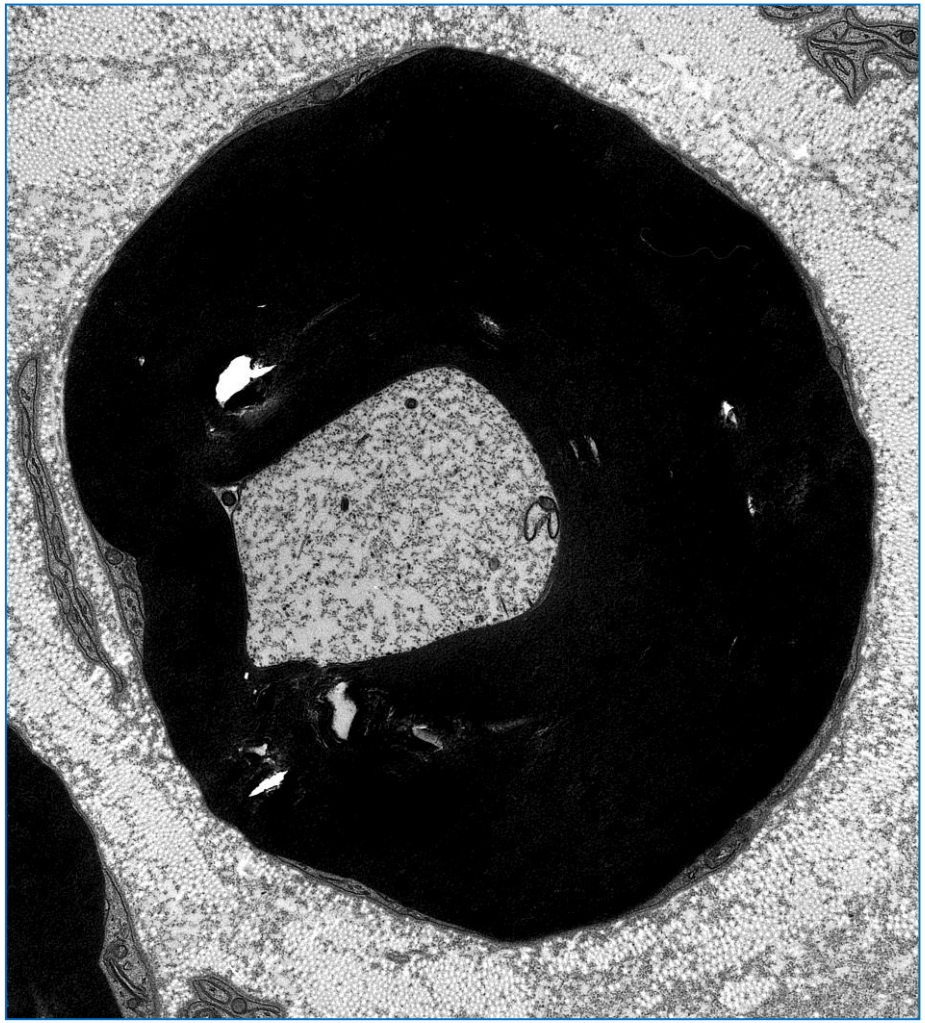
Remyelinating nodes



Abnormal myelin sheath

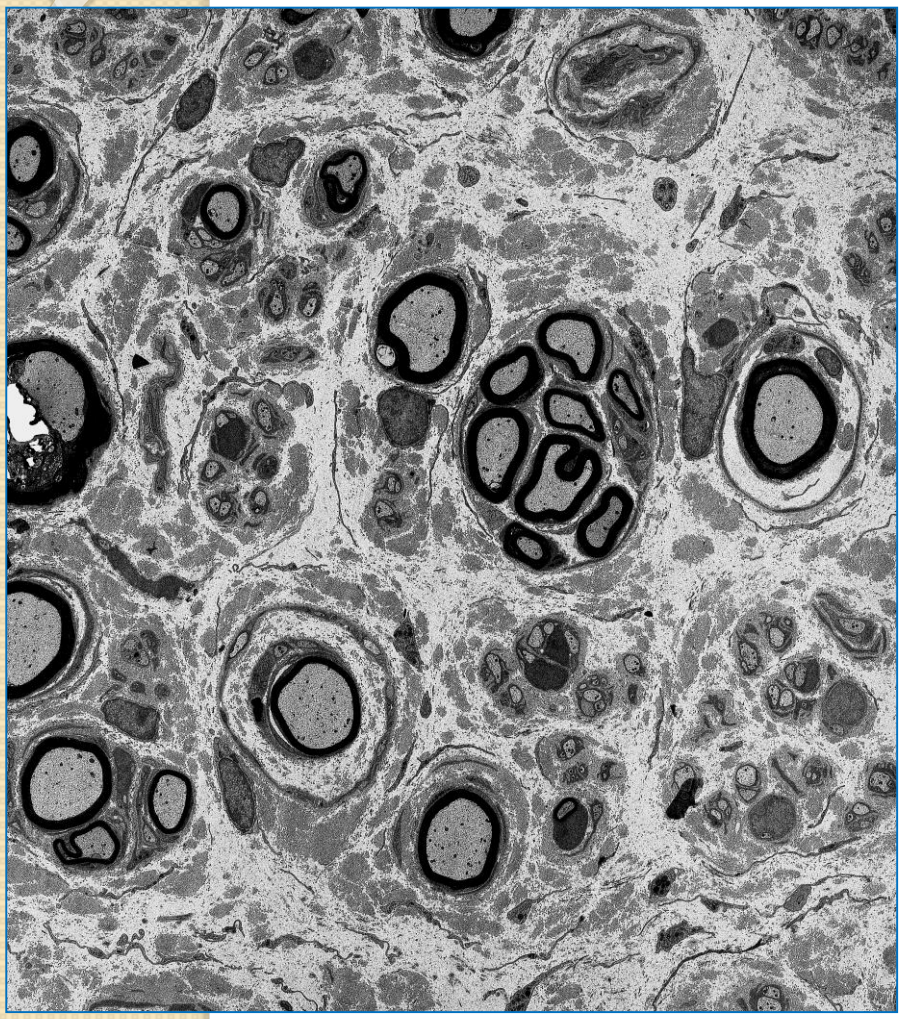


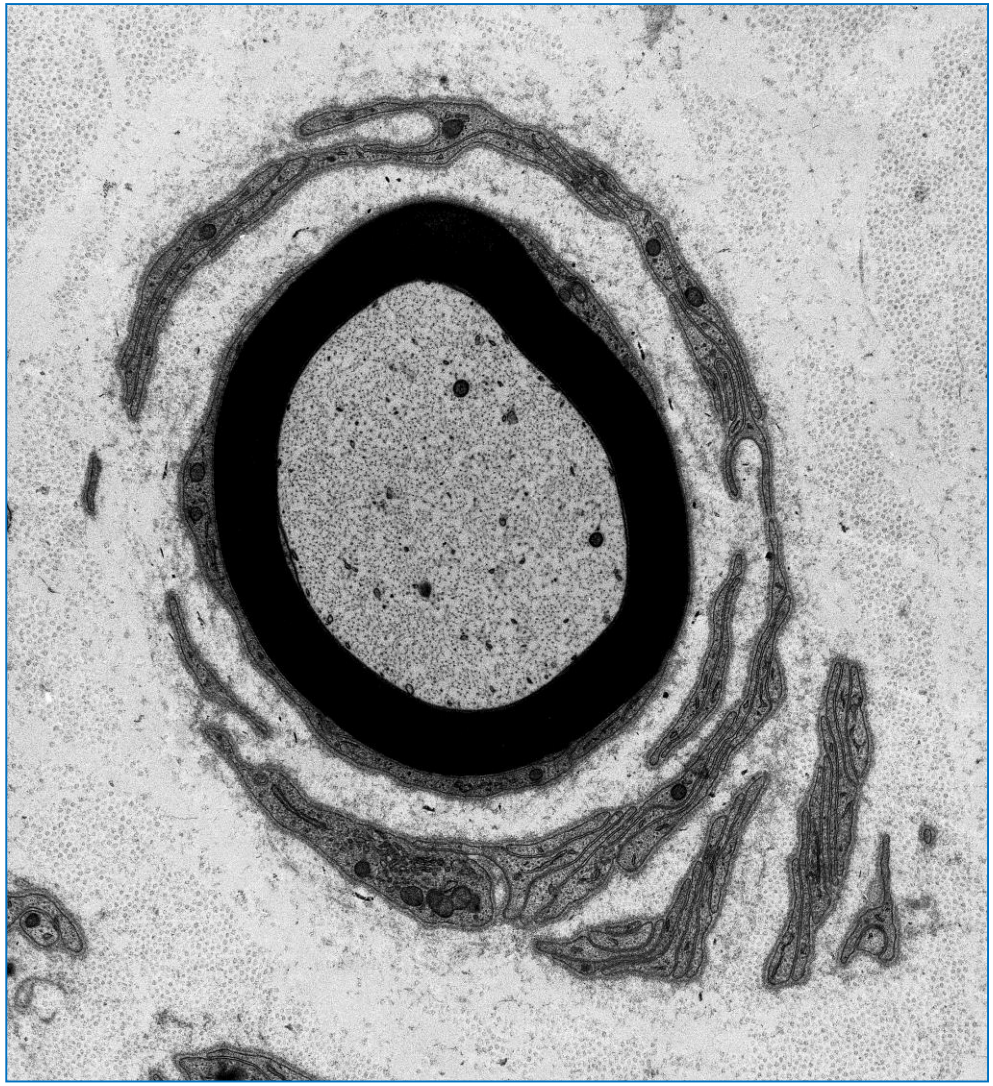
Double wrapped myelin; CIDP



Tomacula (HNPP)(PMP22 deletion)

Remyelination or regeneration?





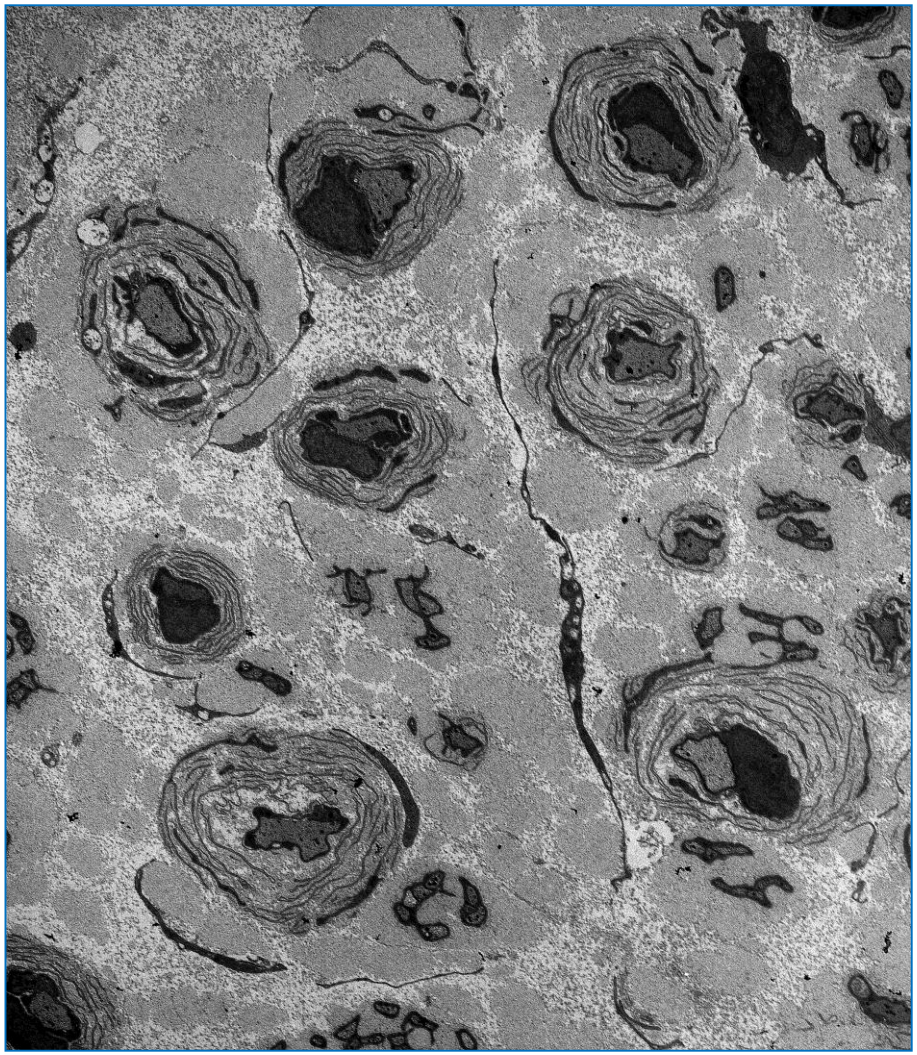
Hypertrophic neuropathies

- Onion bulbs
  - Schwann cells
    - Chronic demyelinating neuropathies
      - E.g. HMSN1

        CIDP
  - Perineurial cells
    - Localized hypertrophic neuropathy
    - Neuroma
    - Neurofibromatosis

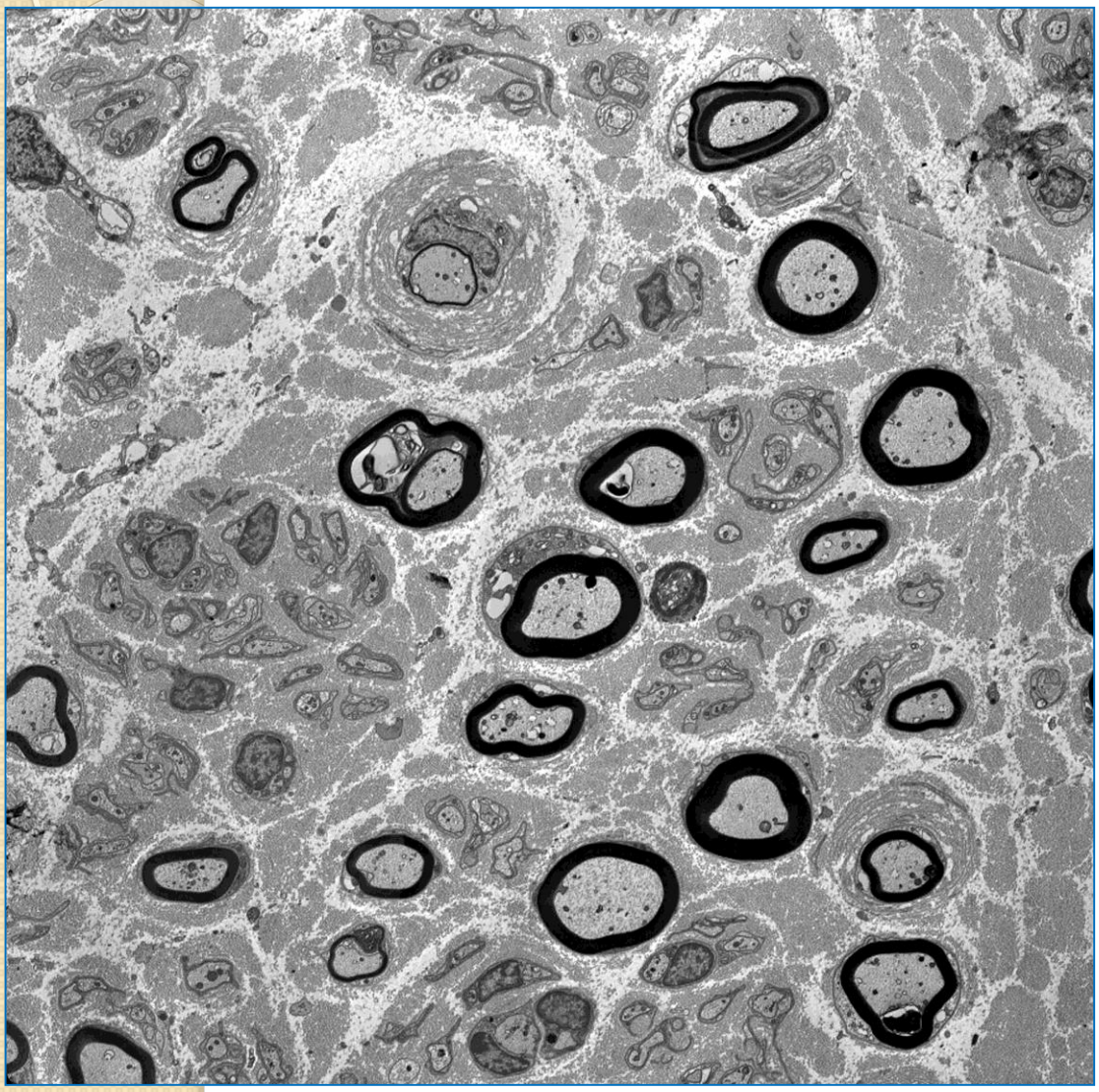
Onion bulbs

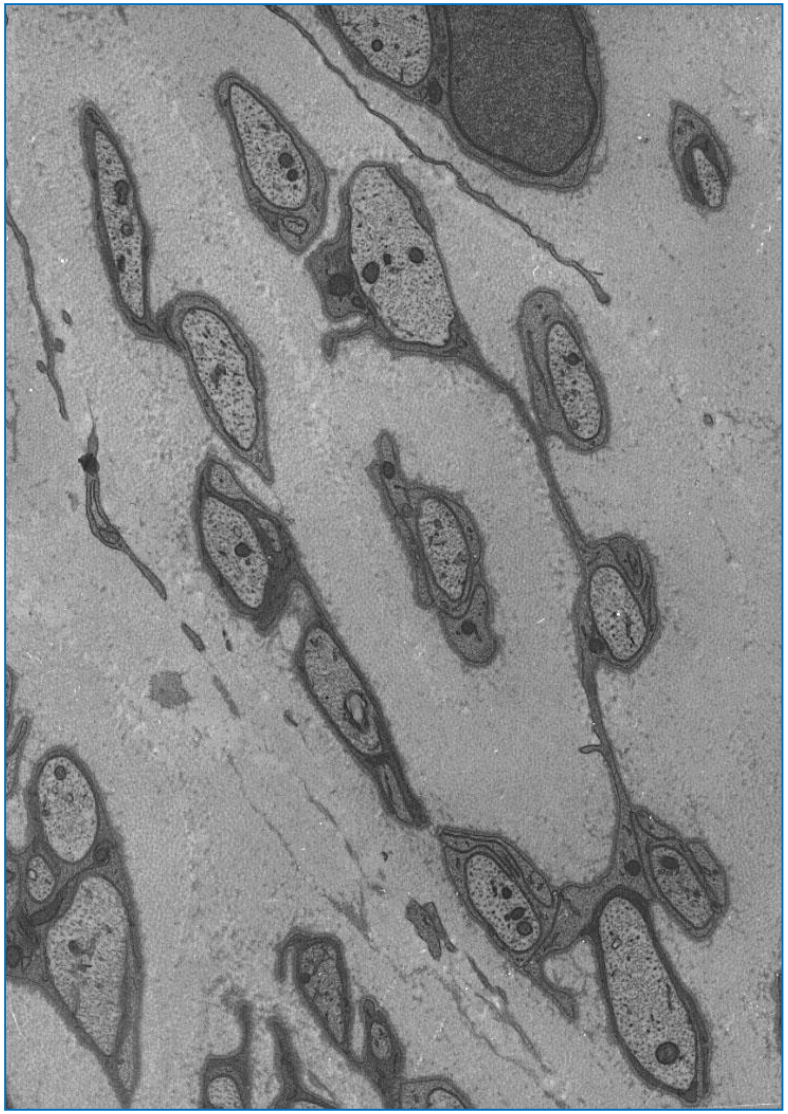
Classical



Basal laminal onion bulbs

CMT 4C (KIAA1985, SH3TC2)

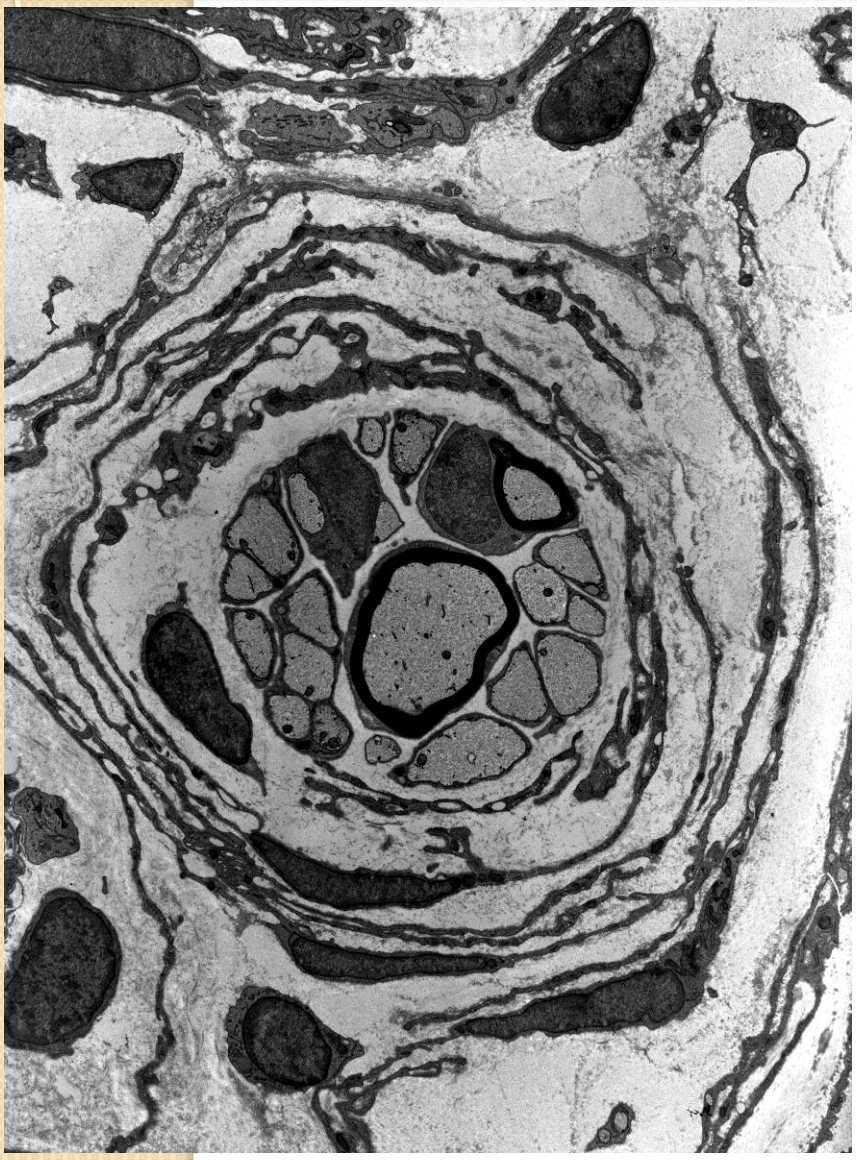


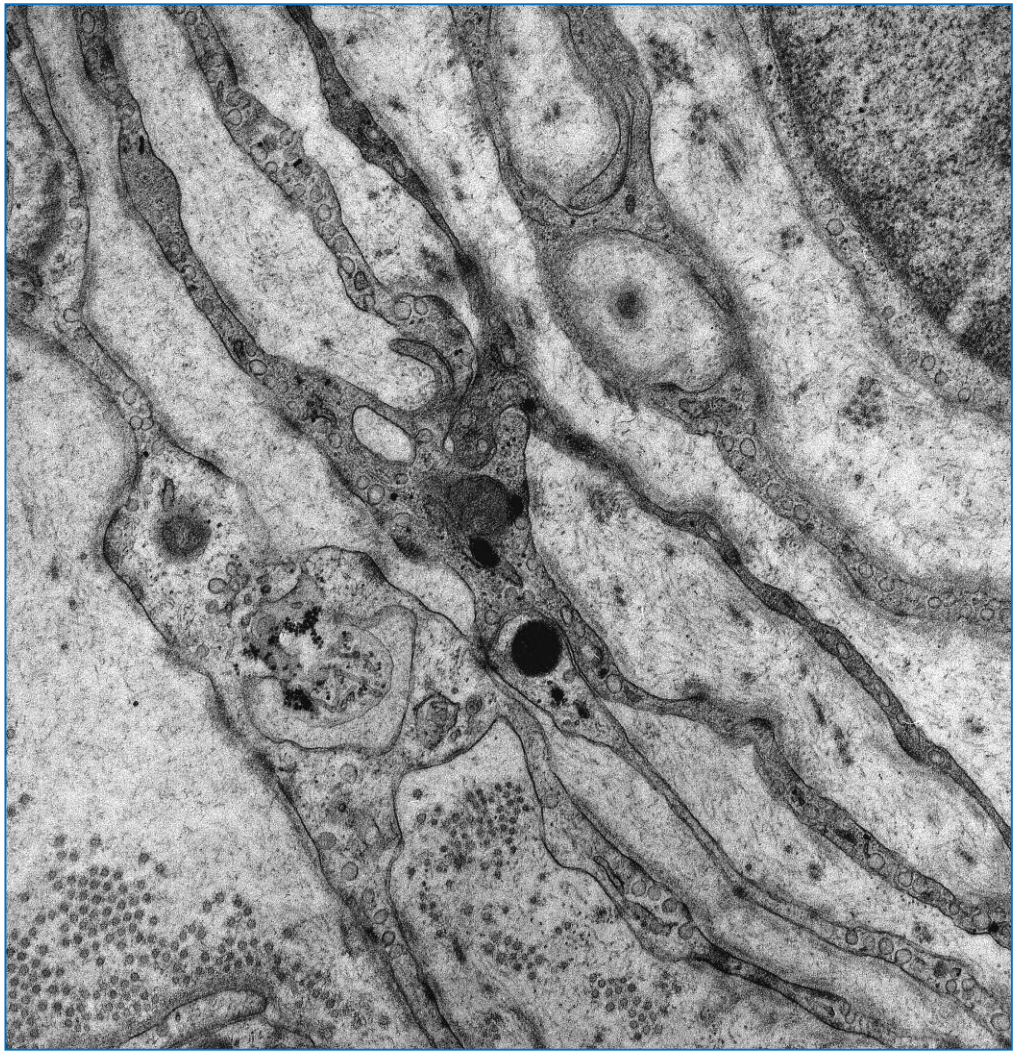


CC F 16

SP F 24

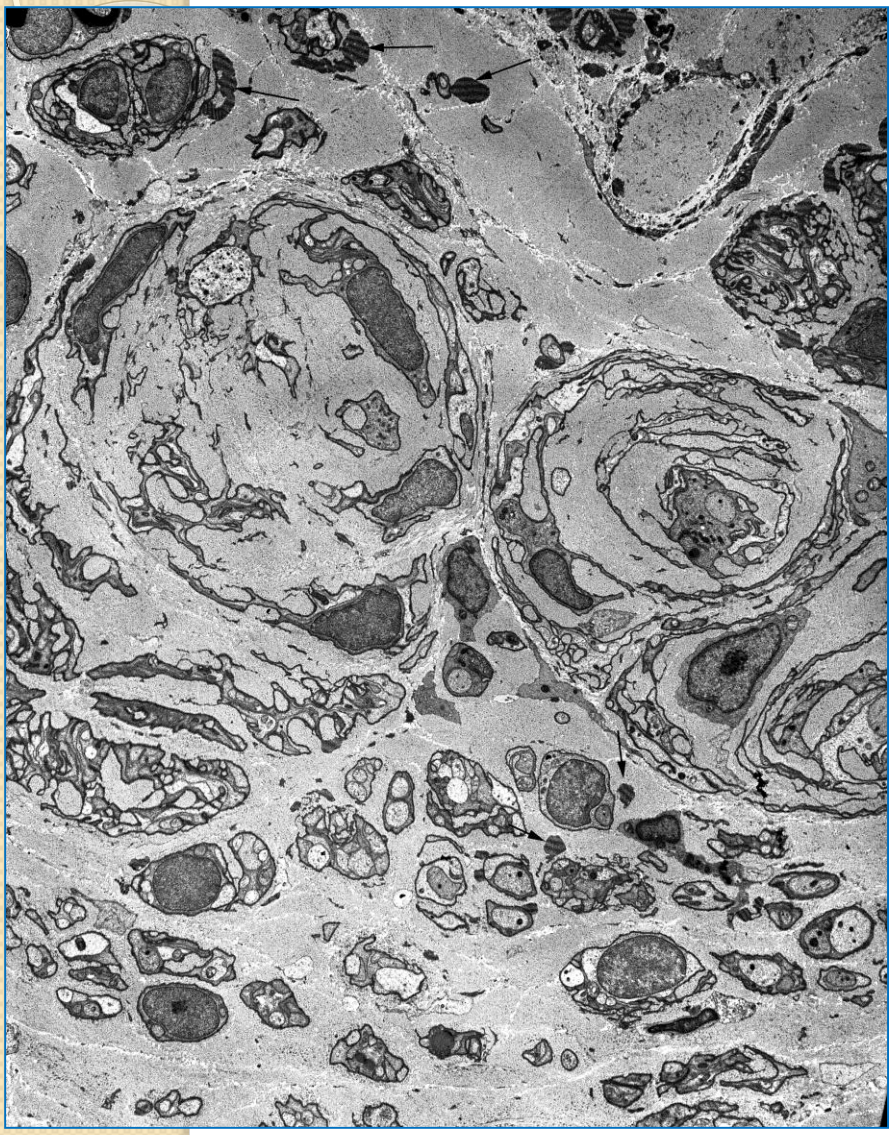
Pseudo-onion bulbs



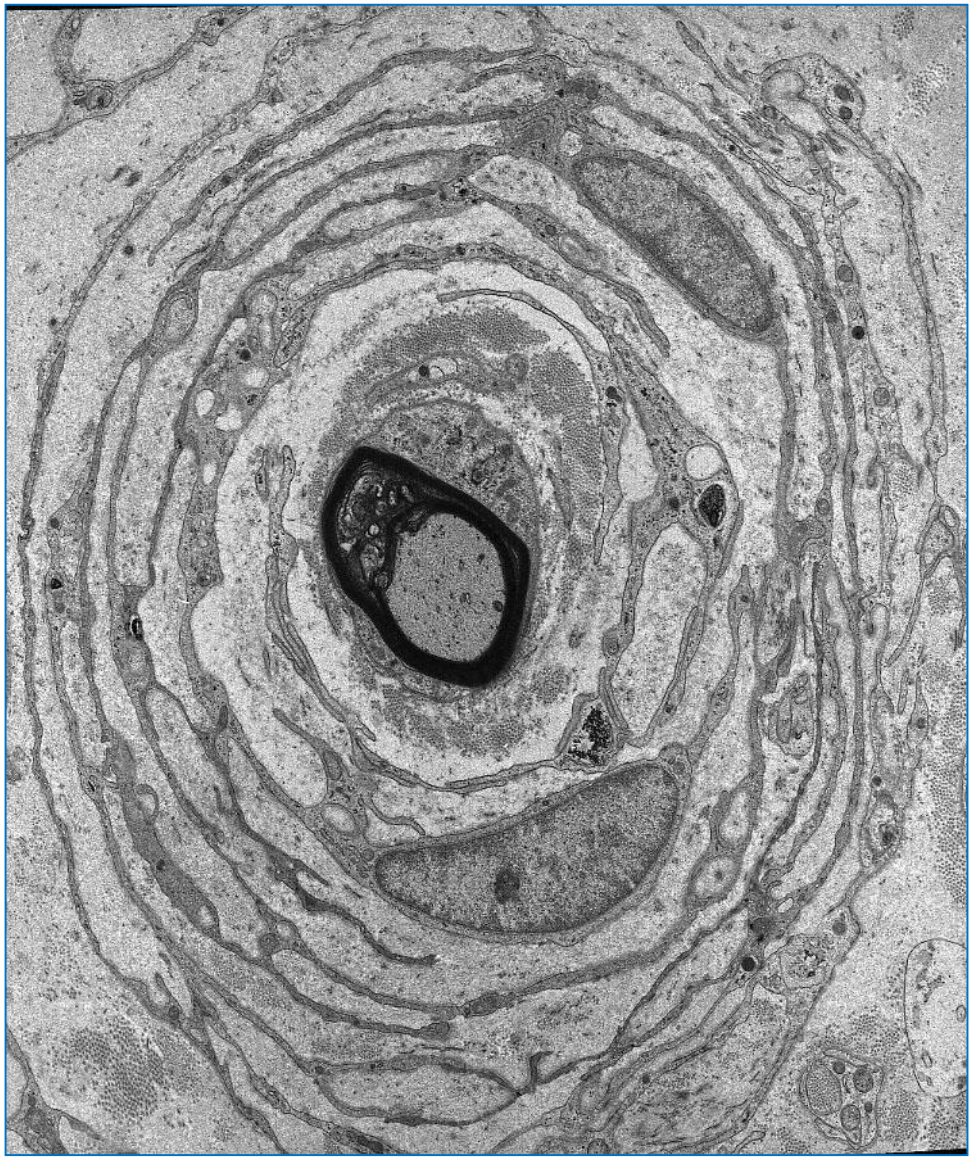


Localised hypertropic neuropathy

Pseudo-onion bulbs

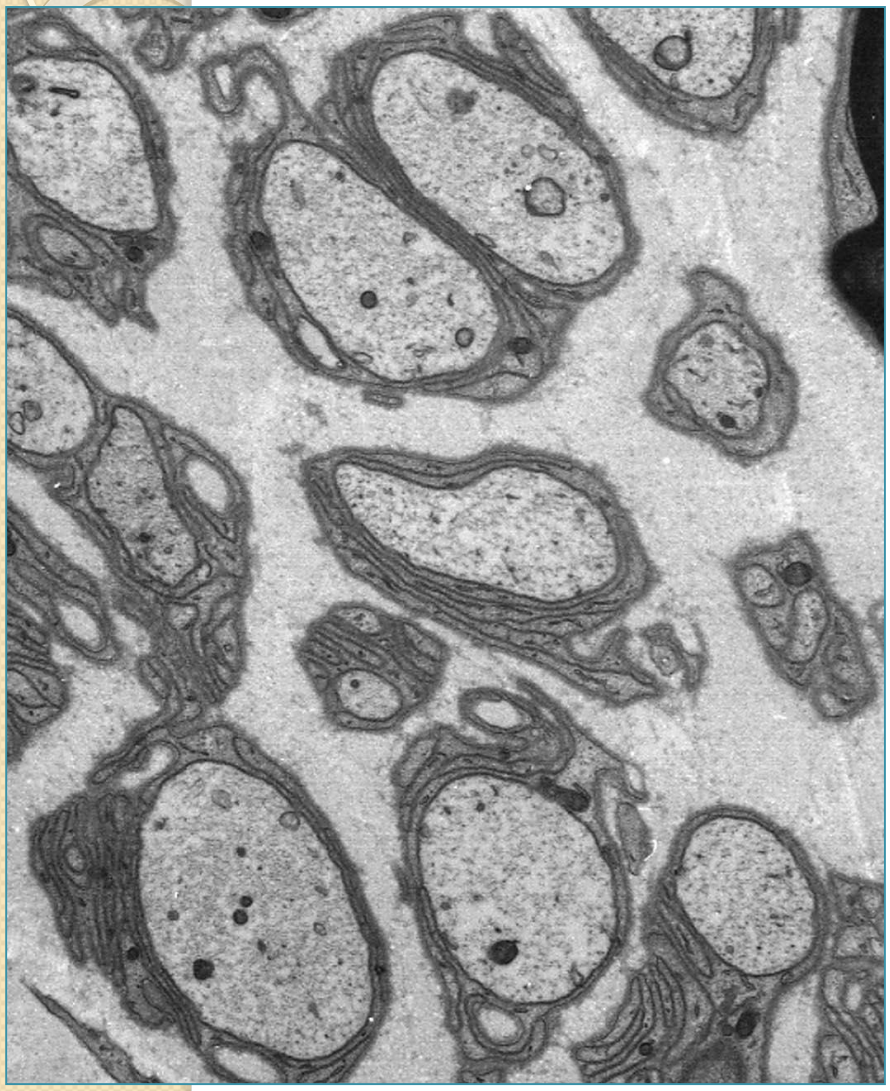


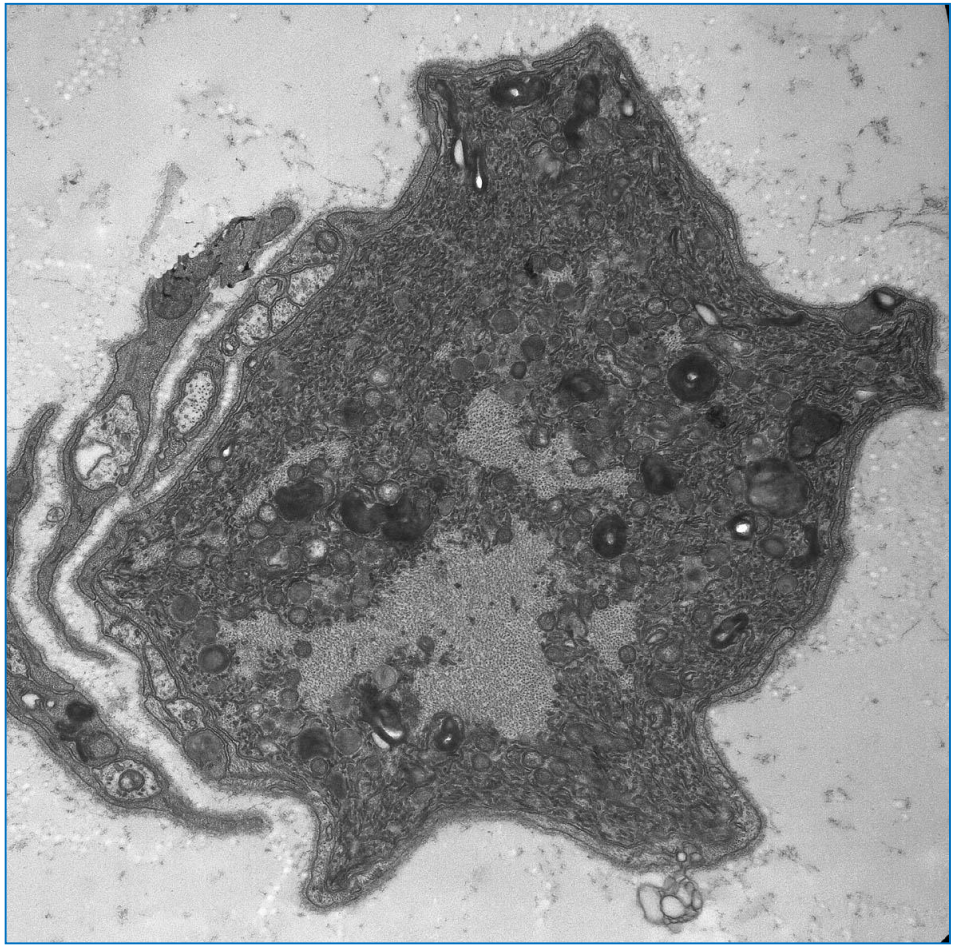
Neurofibroma



Neuroma

Unmyelinated axons (Remak fibres)



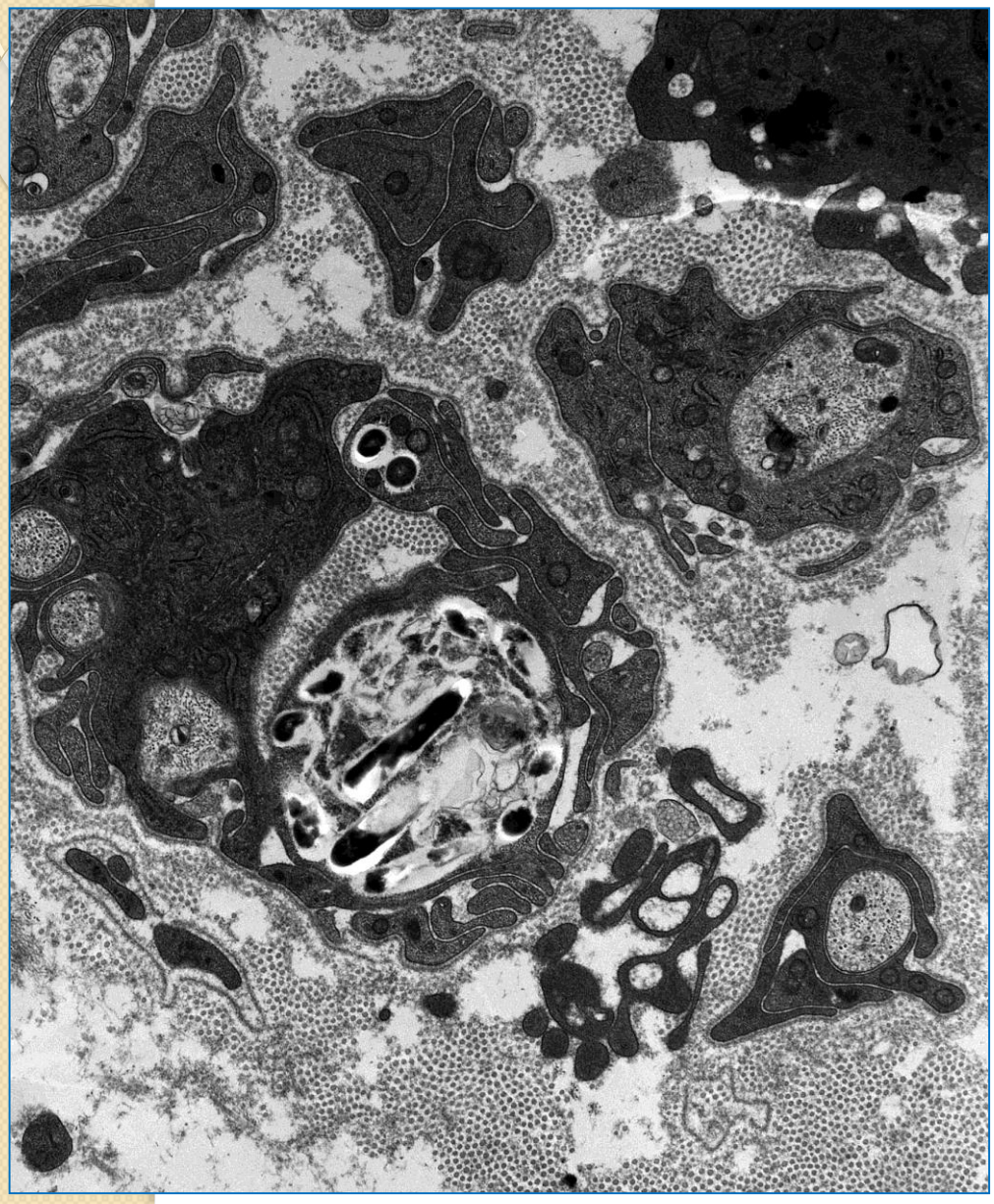


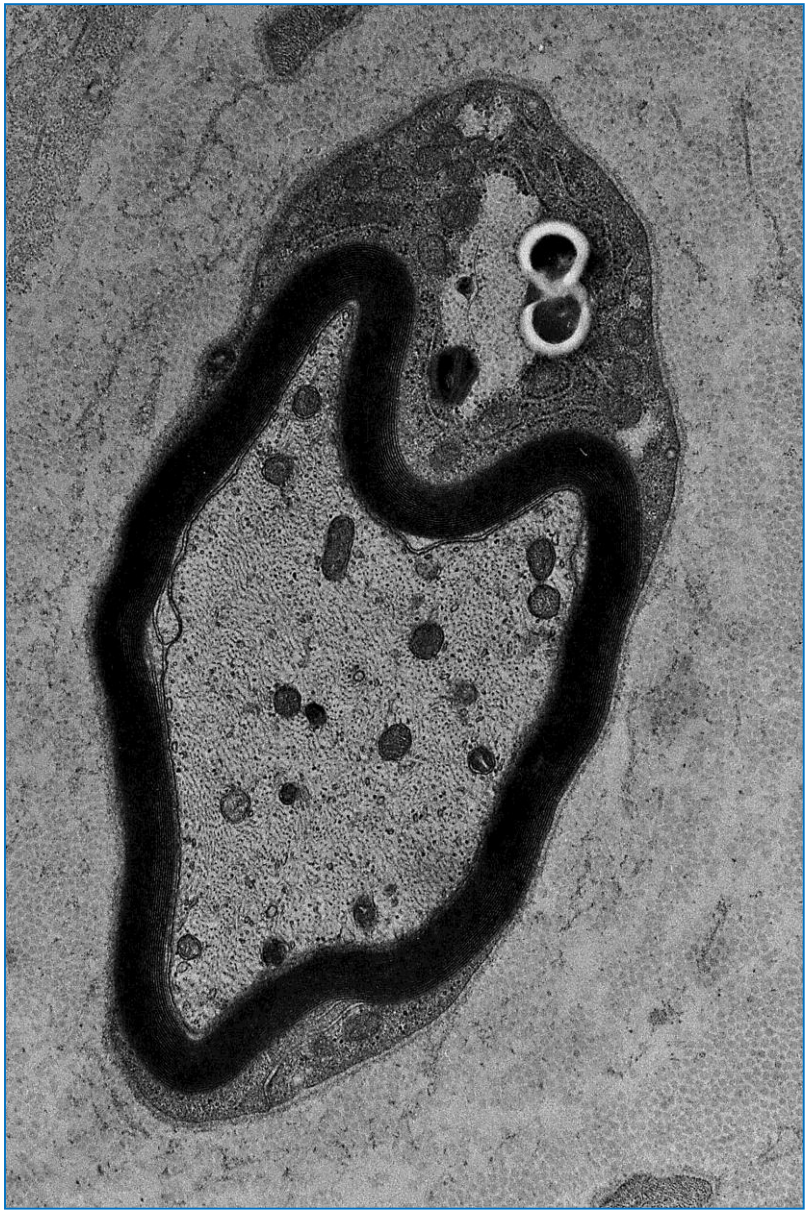
Unmyelinated axon degeneration

Identification of abnormal inclusions

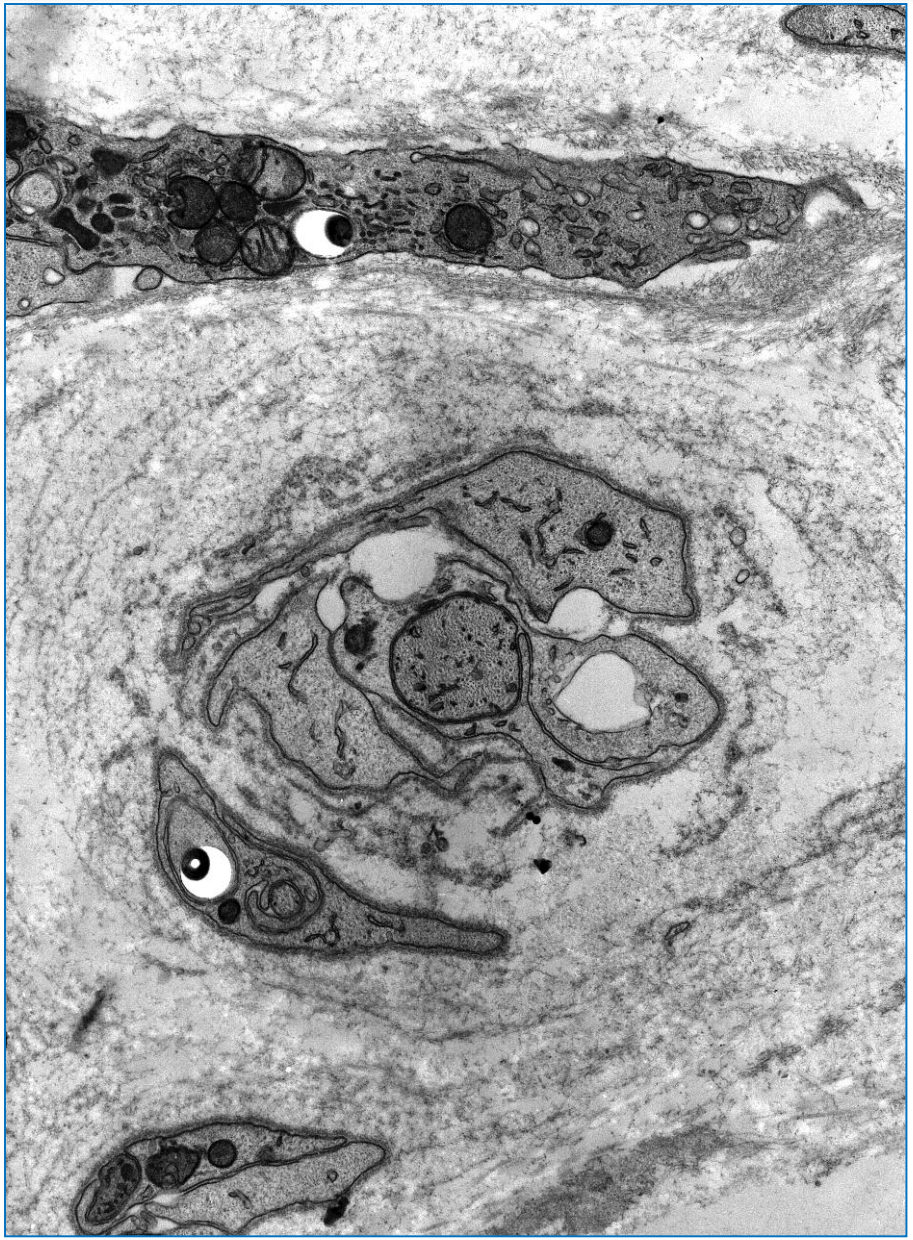
- Axonal inclusions
  - Early degeneration
  - Abnormal cytoskeleton
- Schwann cell inclusions
  - Leucodystrophies
- Perineurial inclusions
  - Fabry's disease
- Extracellular deposits
  - Amyloid
  - Fibrin

Leprosy

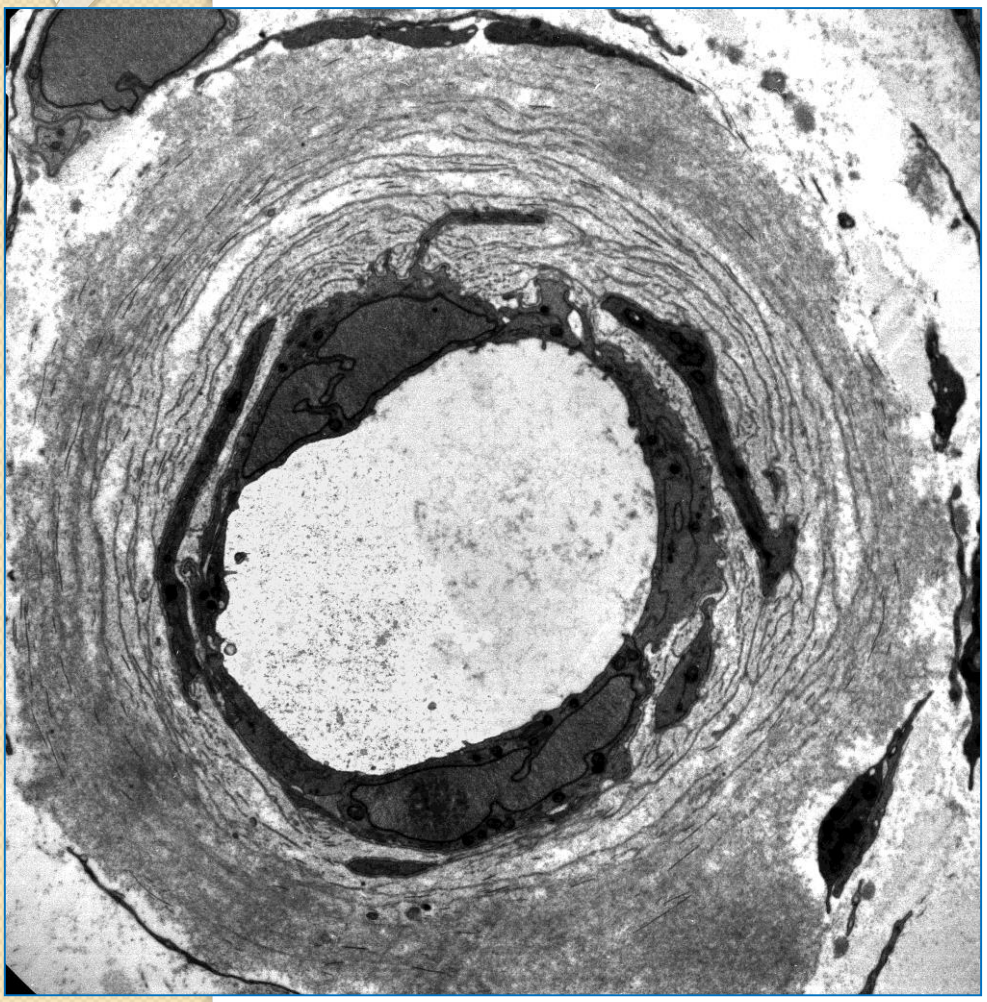




Leprosy



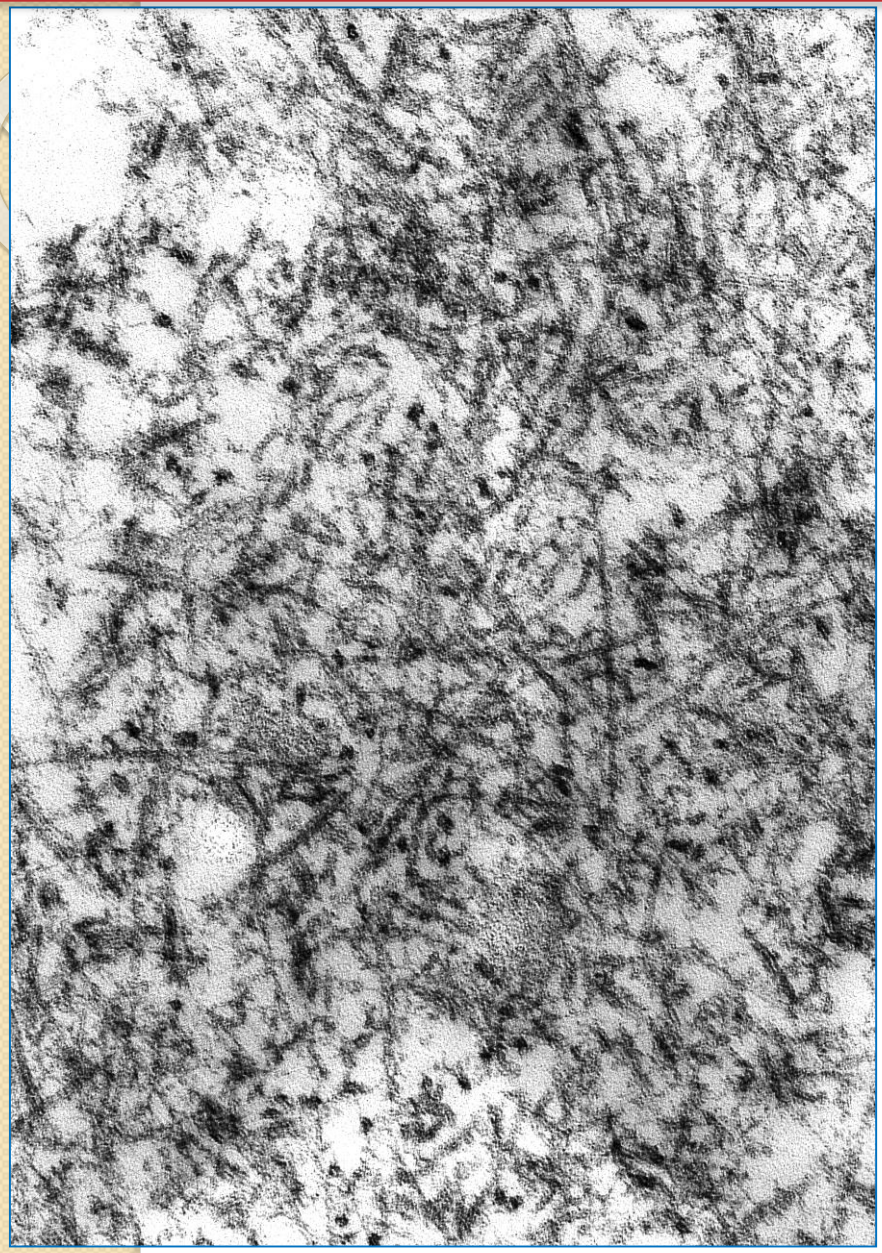
Blood vessel basal laminal thickening

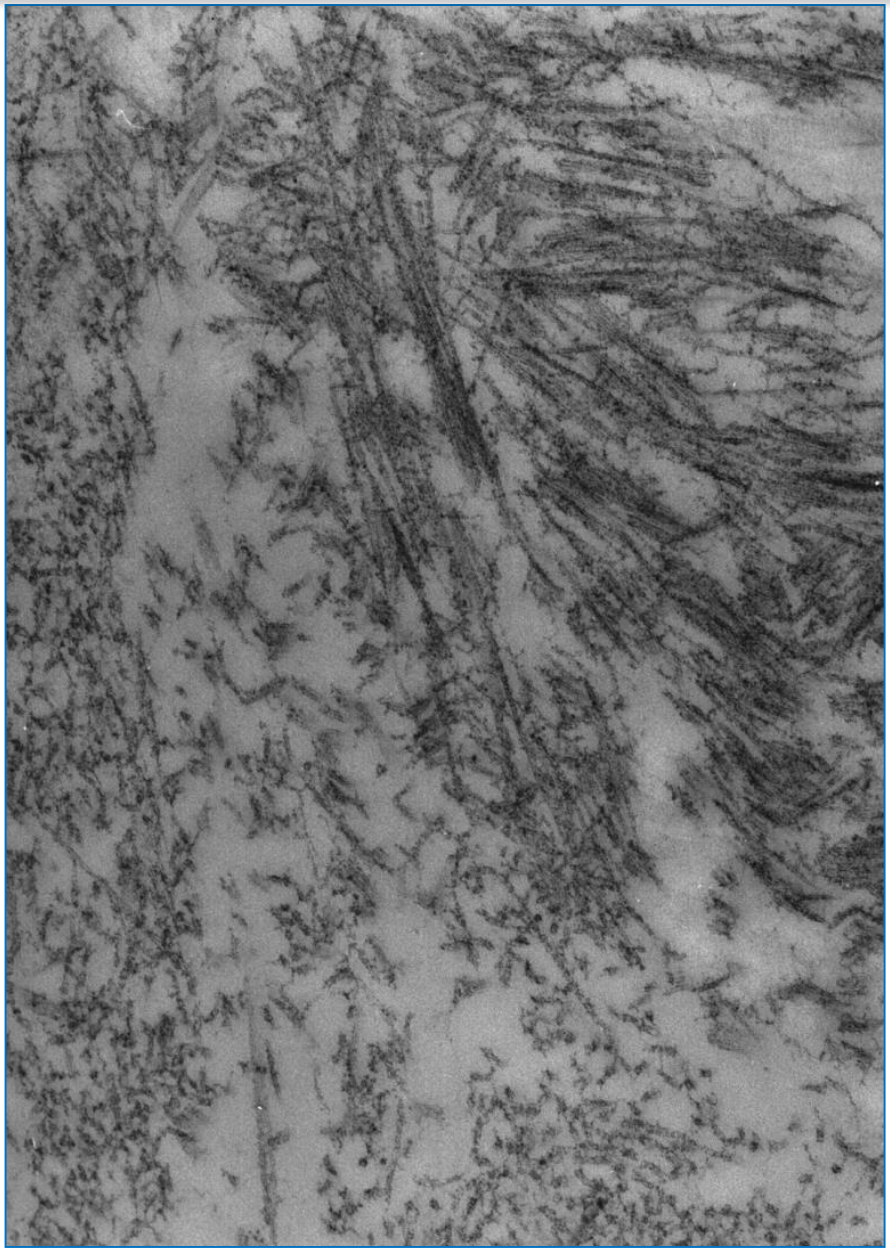


Amyloid

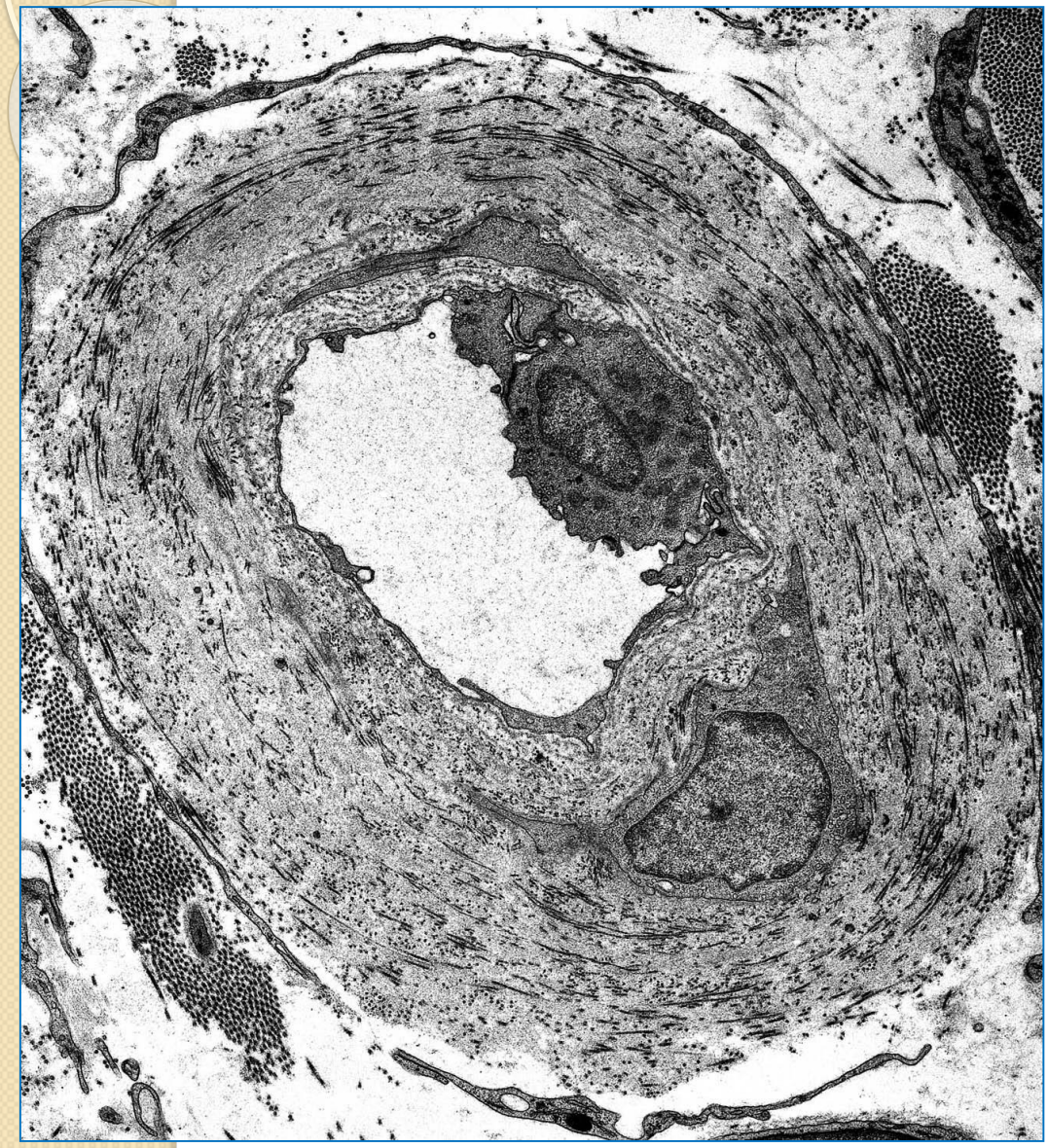
Diabetic, basal laminal reduplication

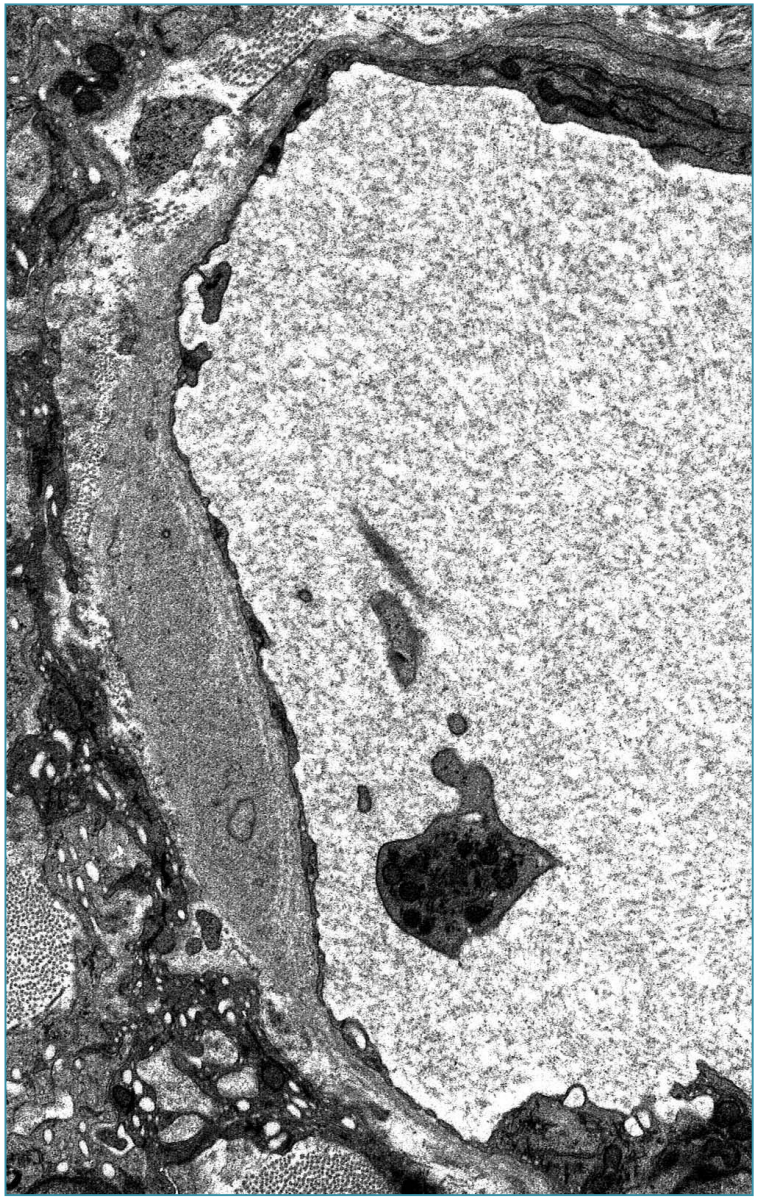
Amyloid fibrils



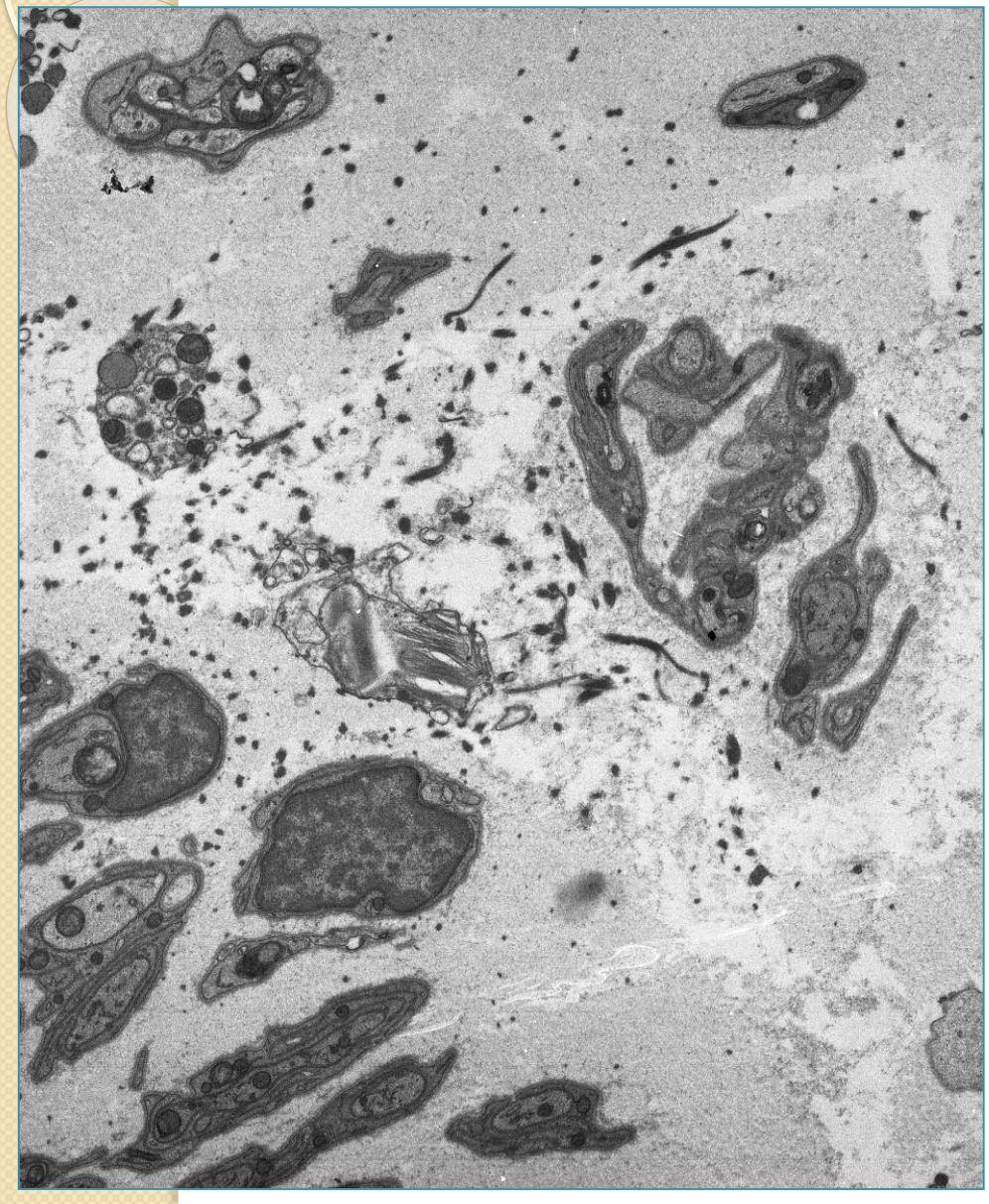


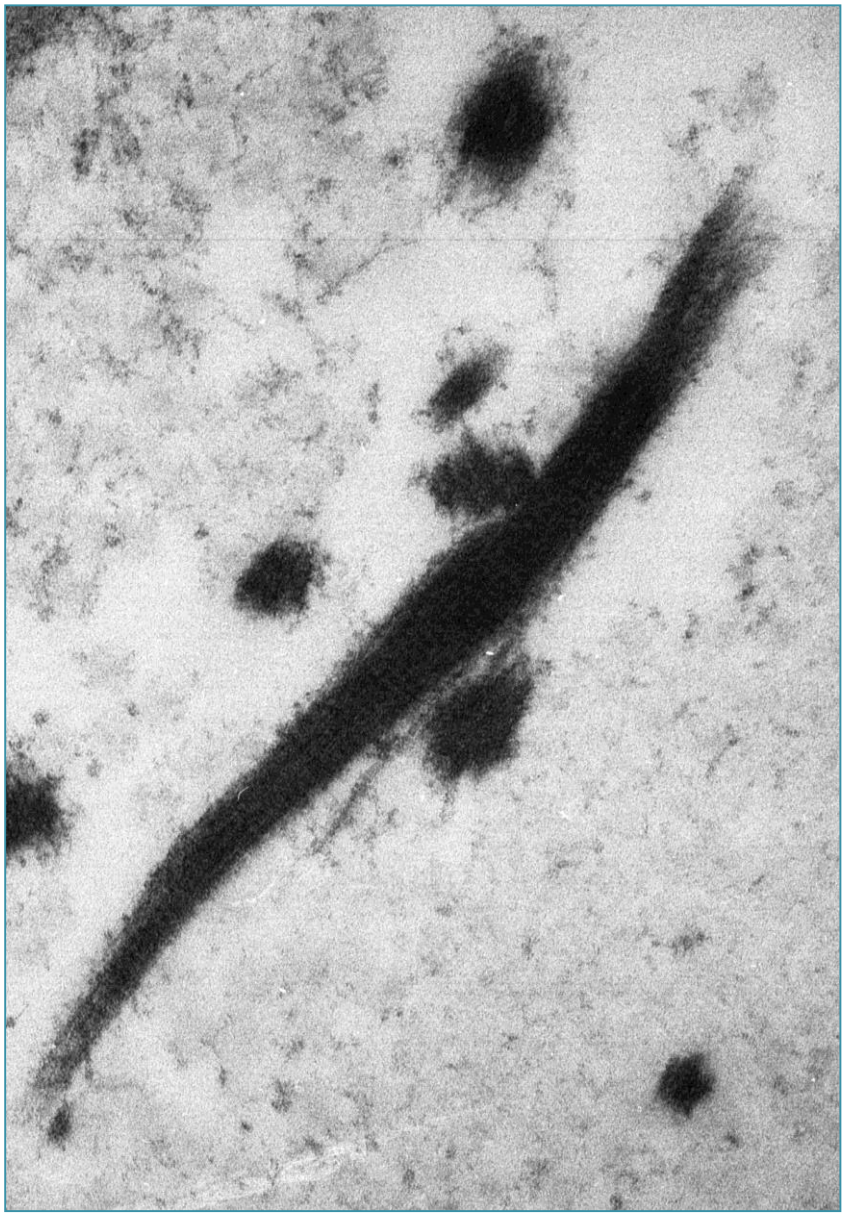
Fenestrated blood vessels



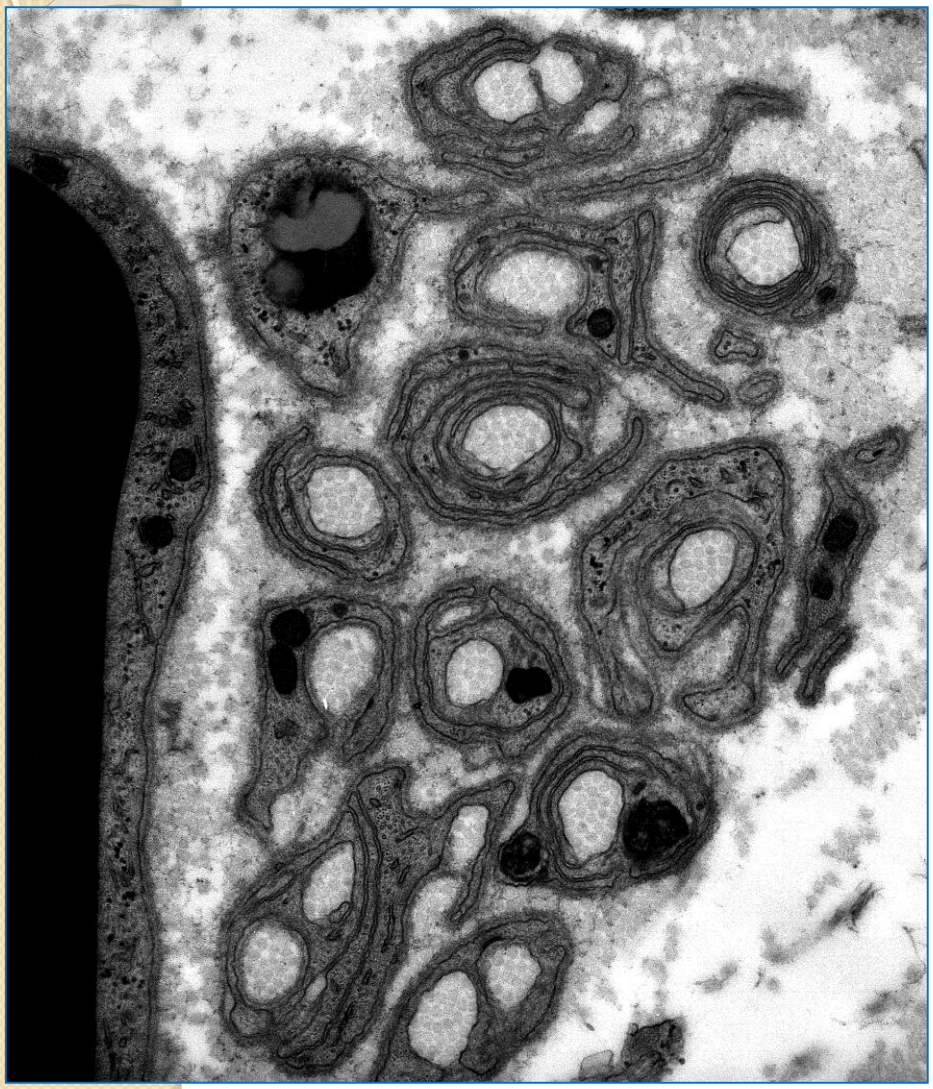


Fibrin leakage

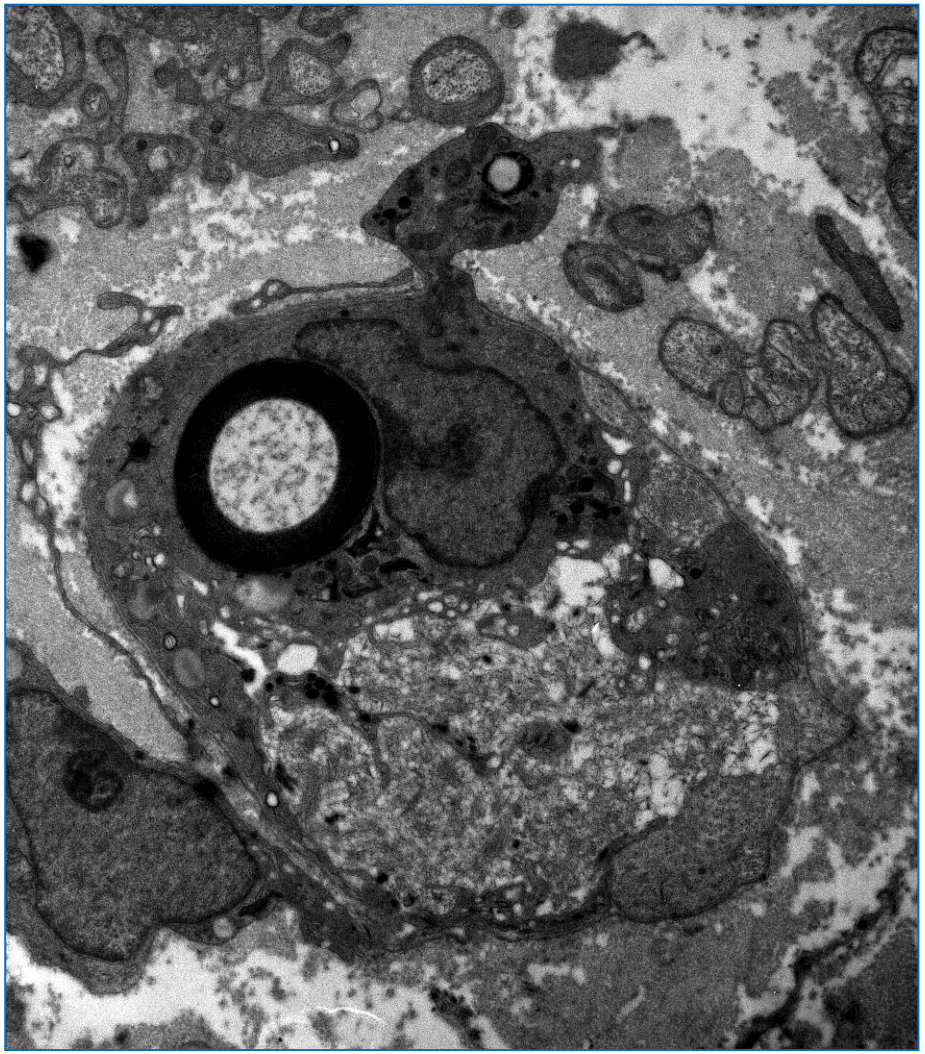




Axons?



Collagen pockets

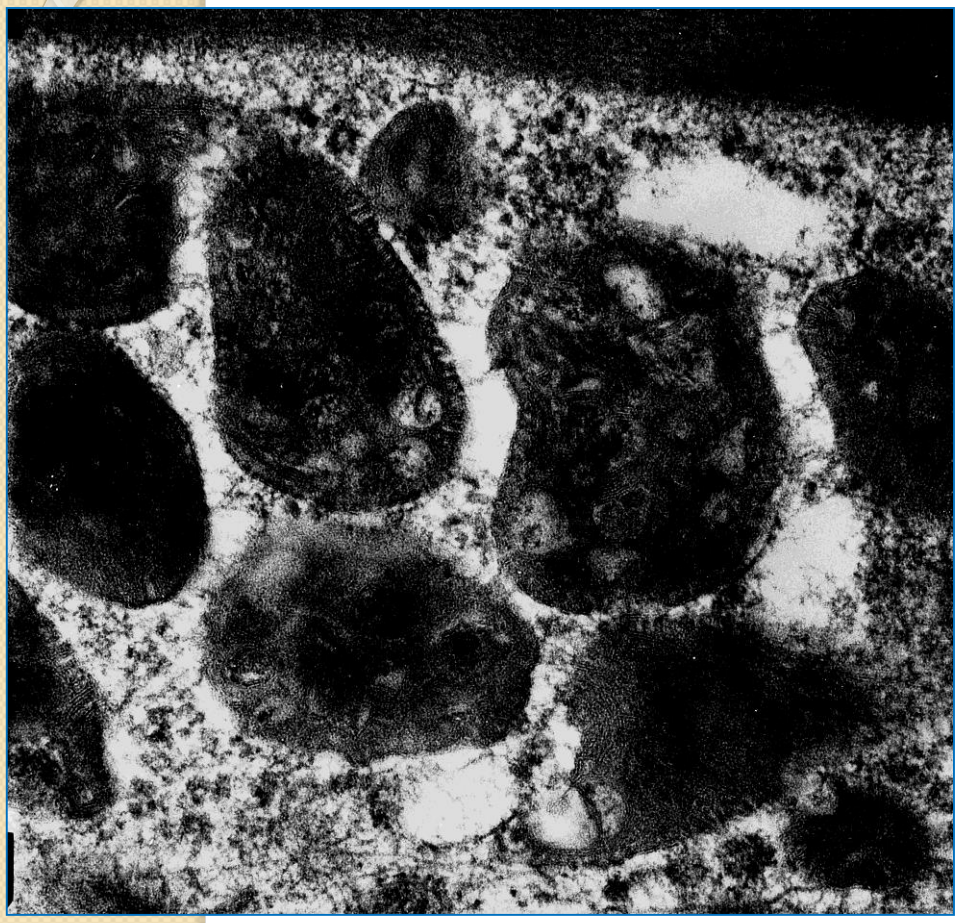


Macrophage debris

Metachromatic leucodystrophy

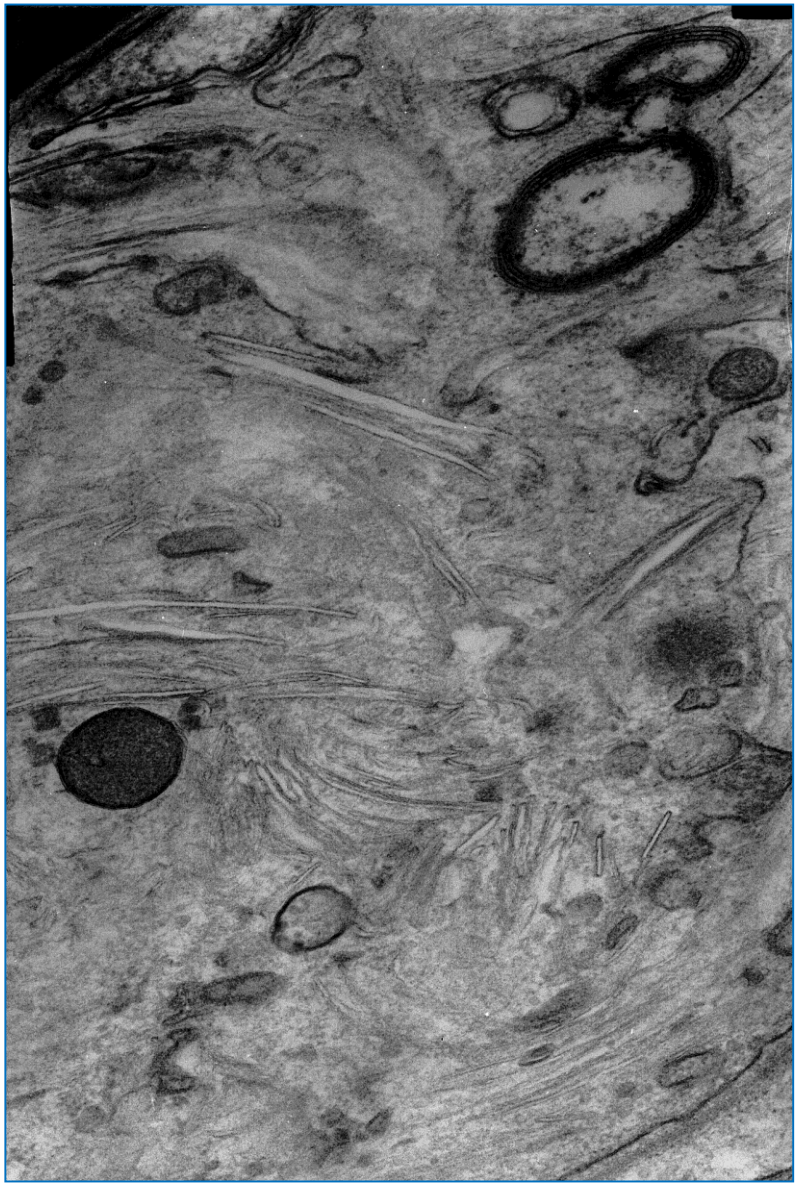
Aryl sulphatase A deficiency, sulphatide deposits

Metachromatic leucodystrophy

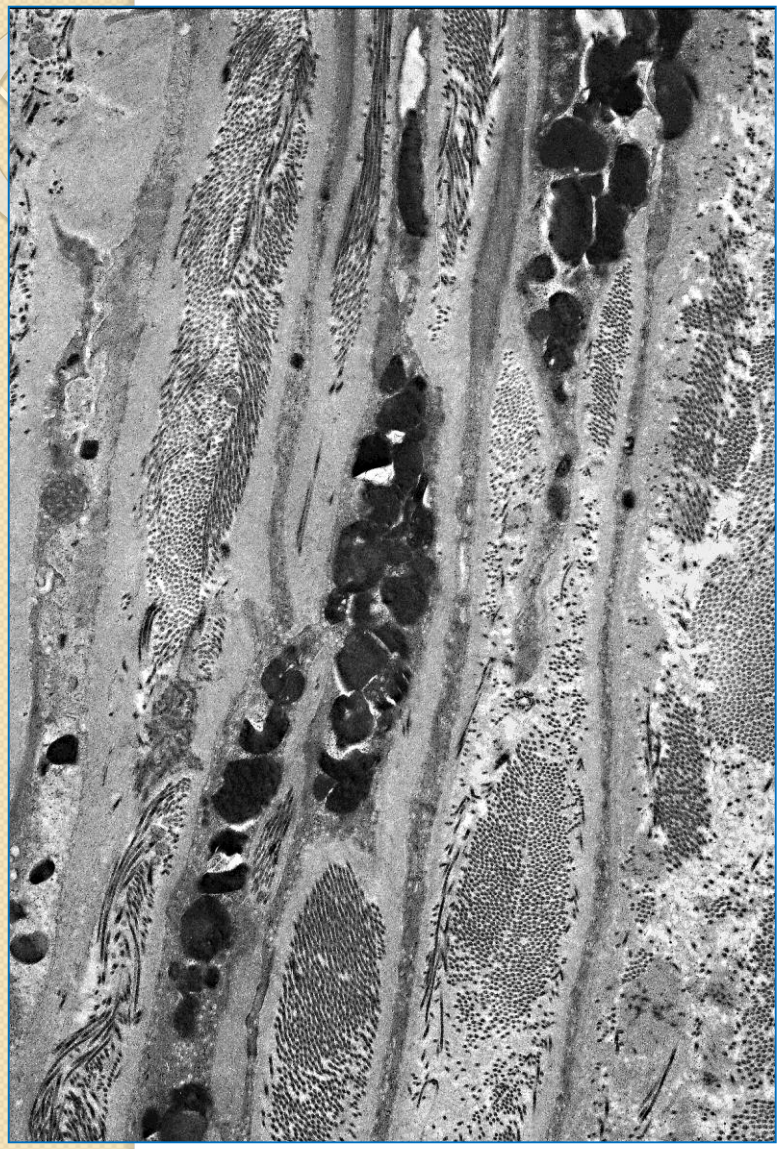


Periodicity of sulphatide 5.6 -5.8nm

Krabbe's disease (Galactosyl ceremide lipidosis)

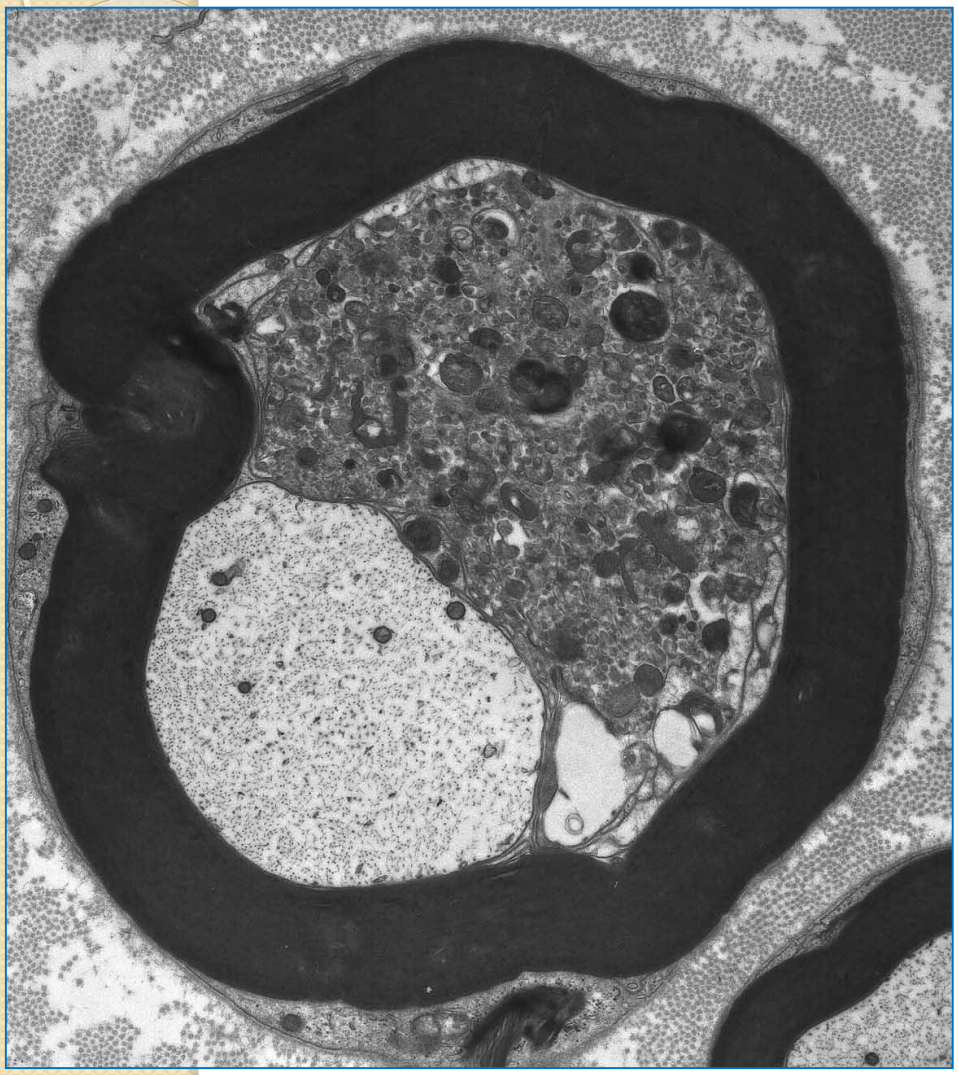


Fabry's disease (angiokeratoma corporis diffusum)

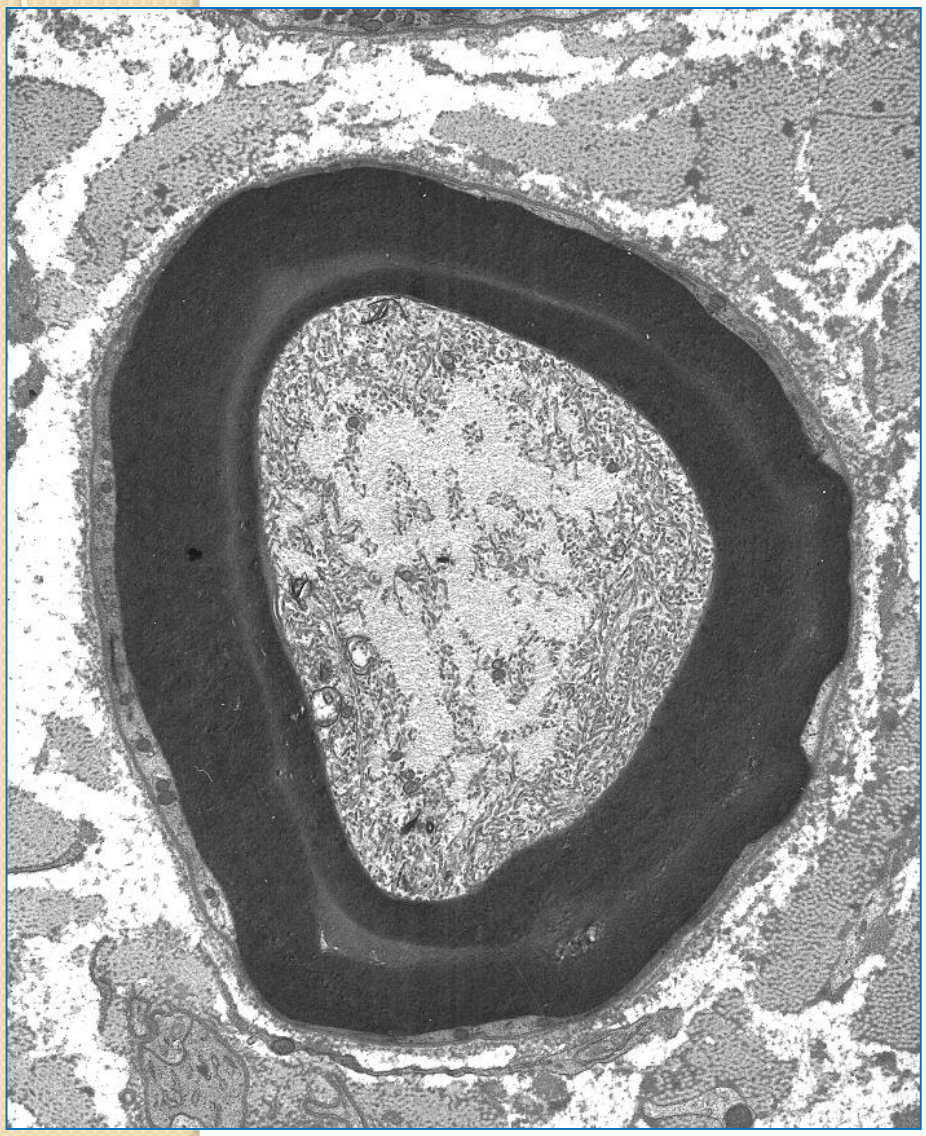


Glycosphingolipid, 5nm periodicity

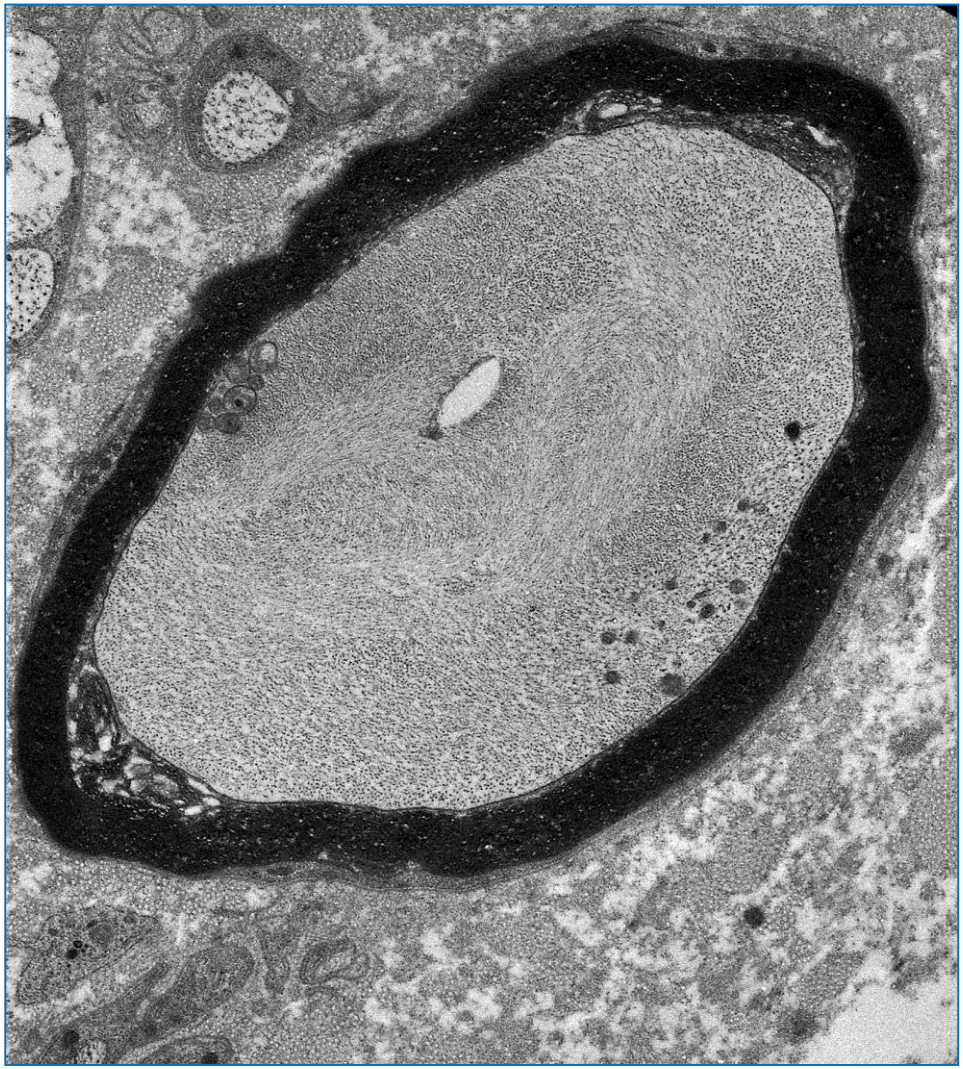
Schwann cell inclusions



Axonal inclusions

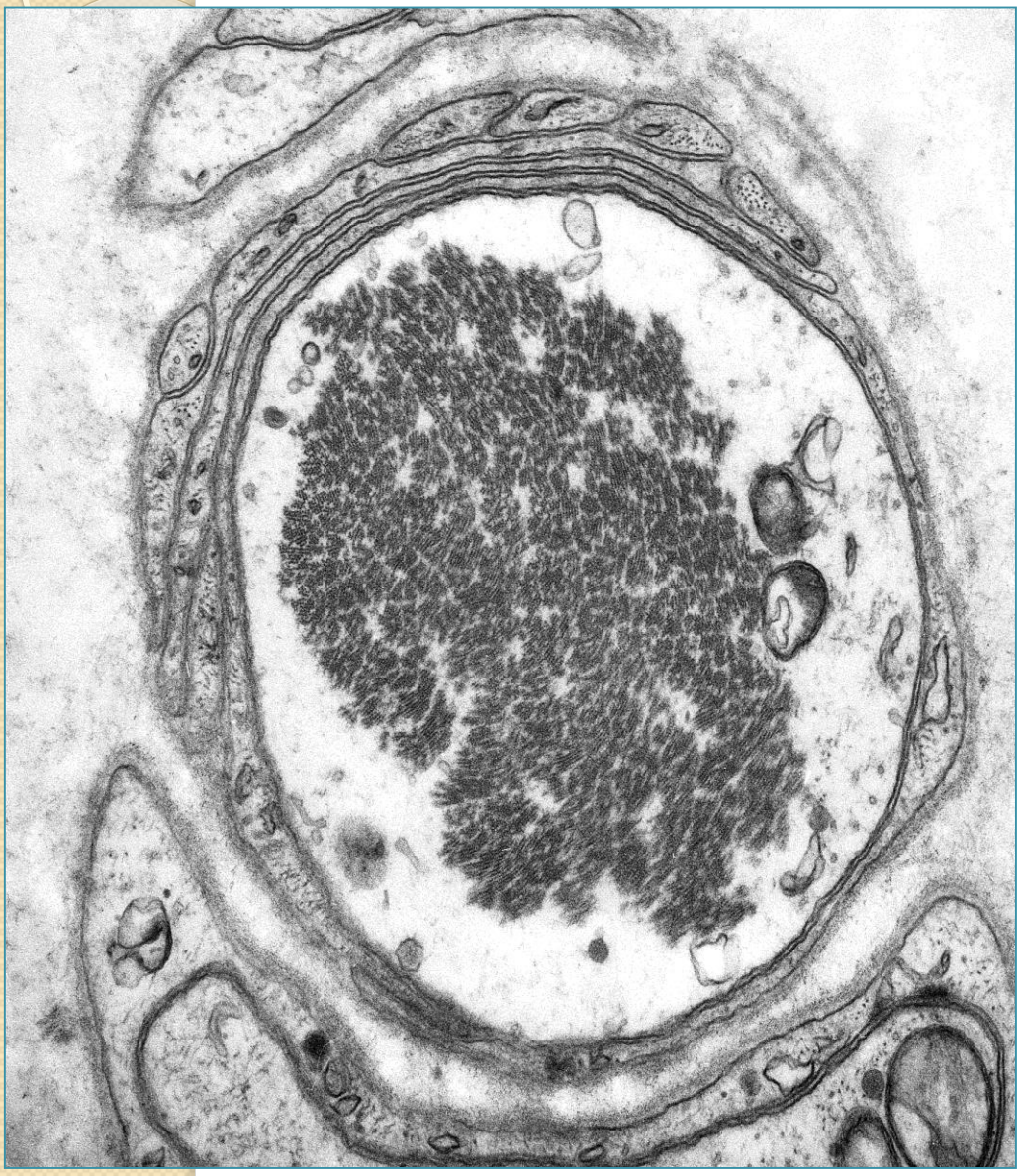


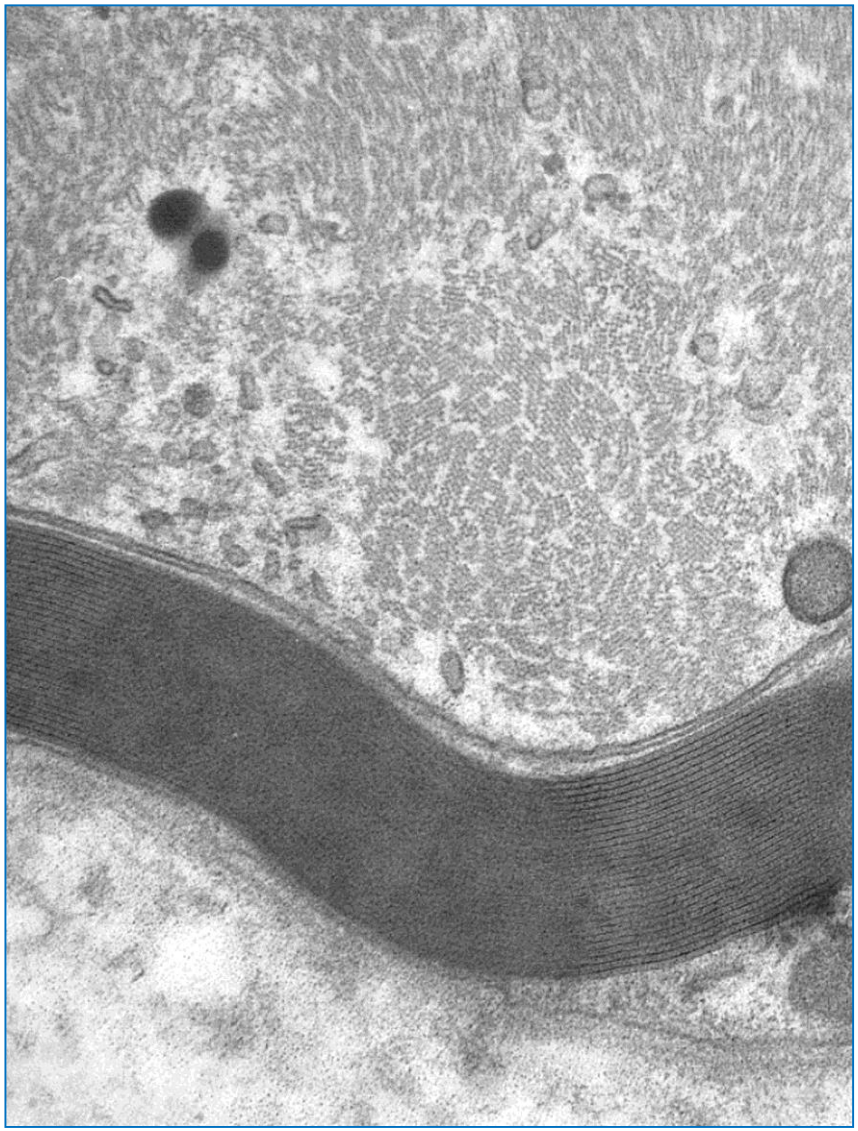
Early axonal degeneration



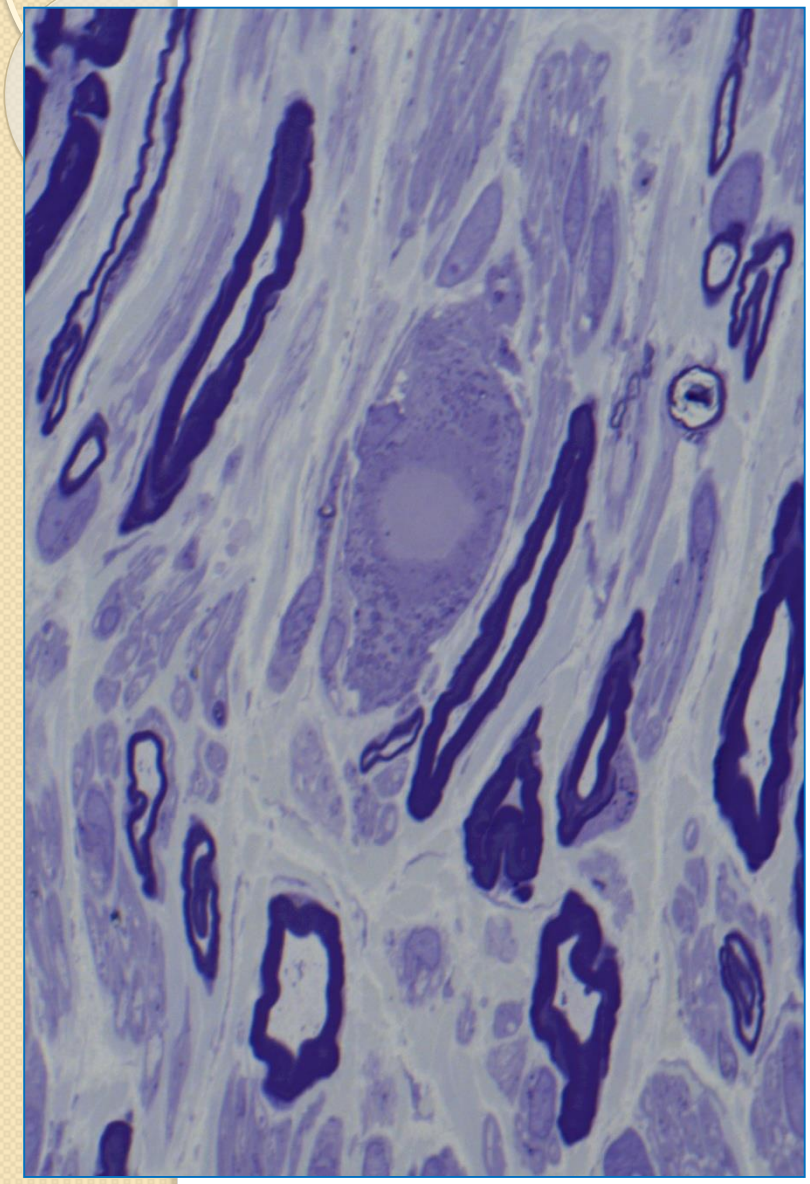
Toxic neuropathy

Crystalline inclusions

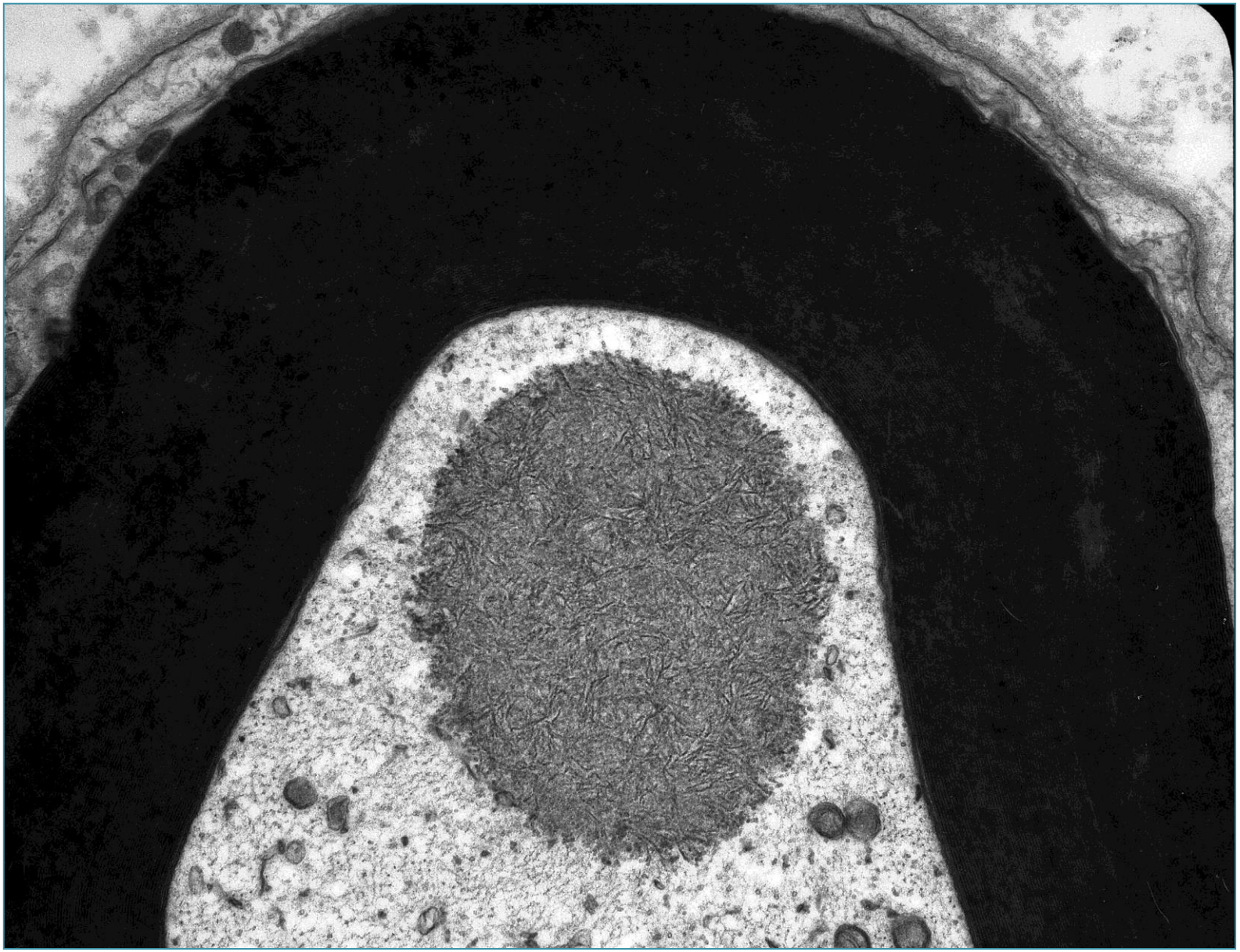




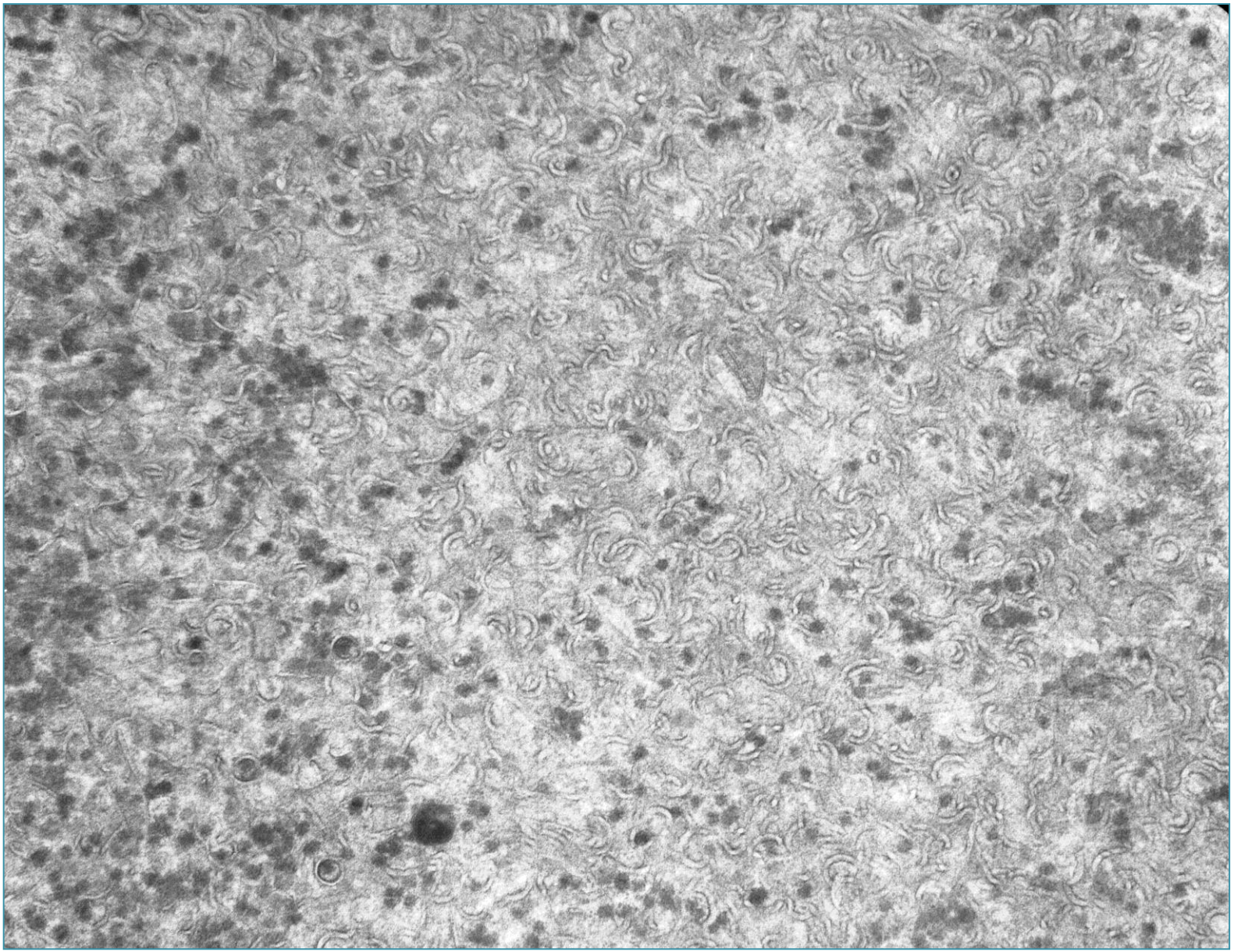
Polyglucosan bodies



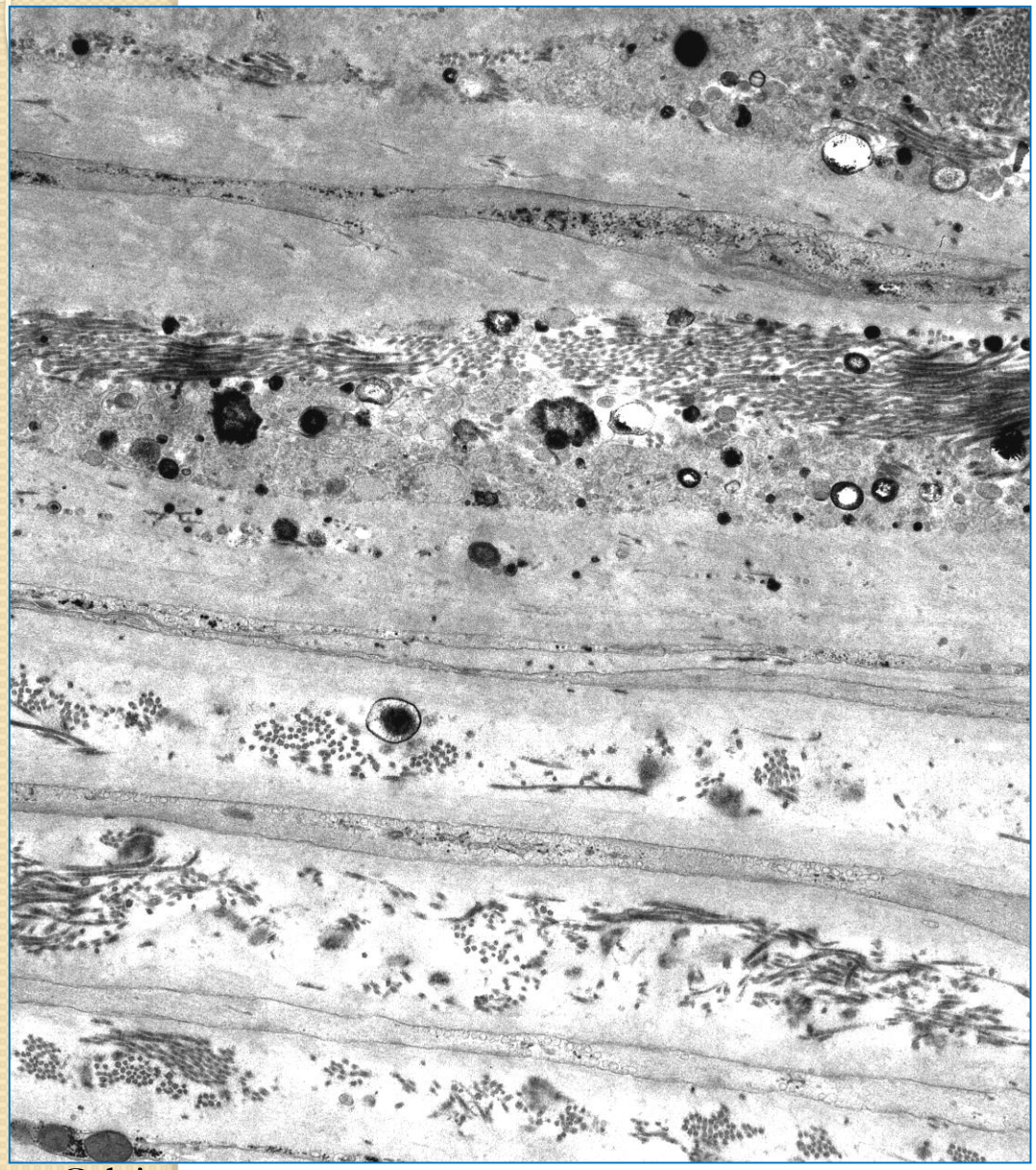
Polyglucosan bodies



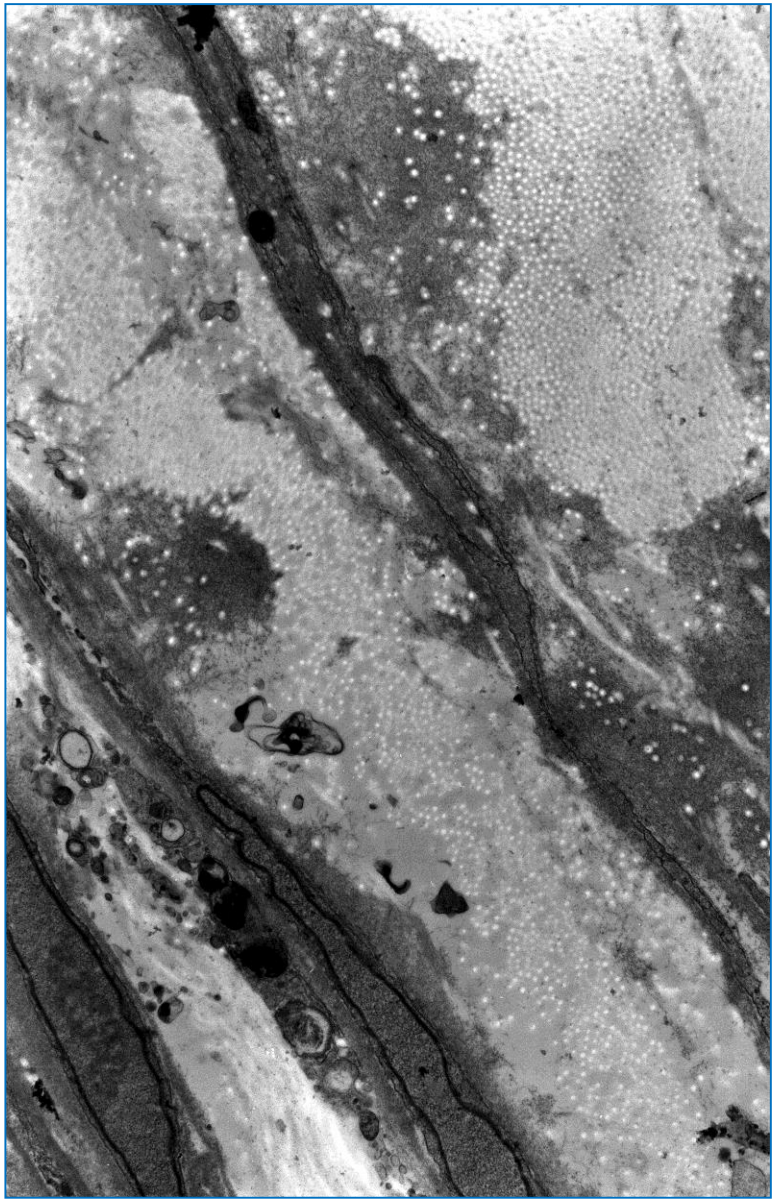
Curved axonal inclusions



Perineurium

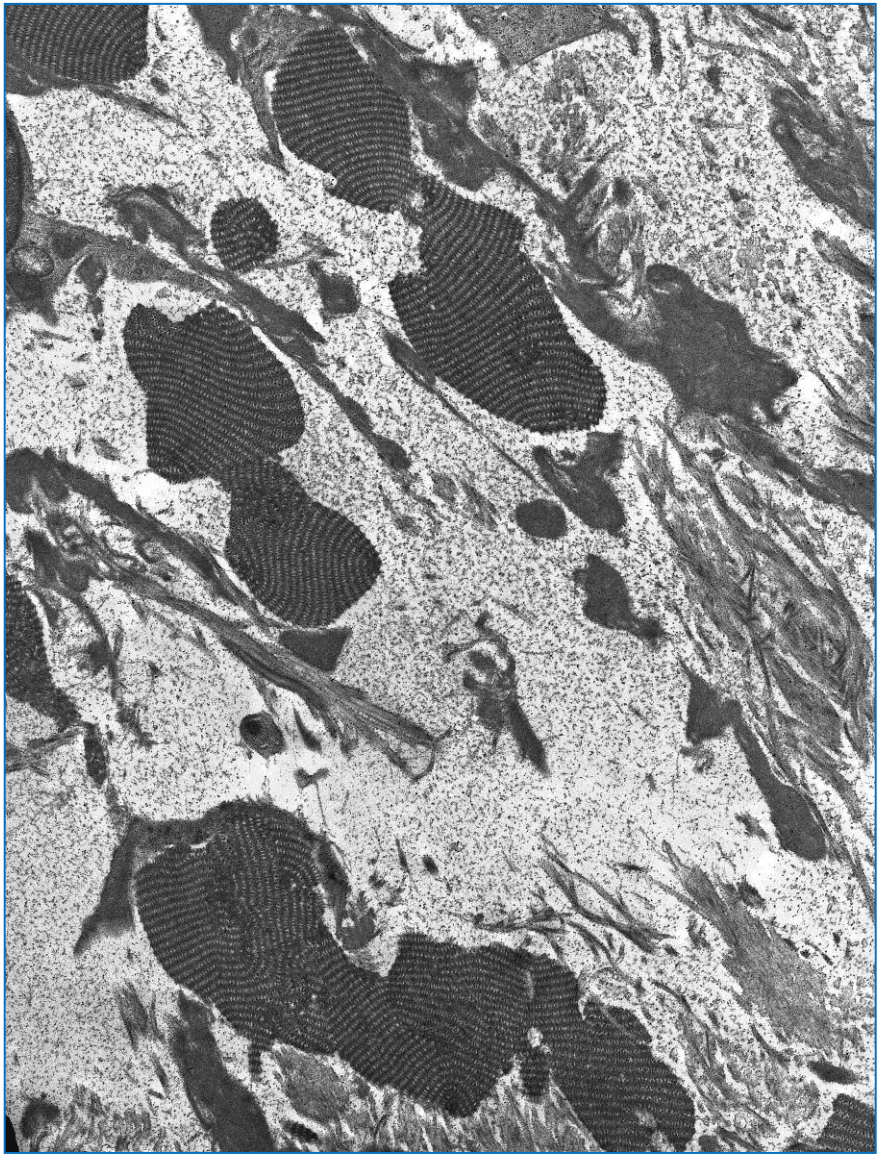


Calcium

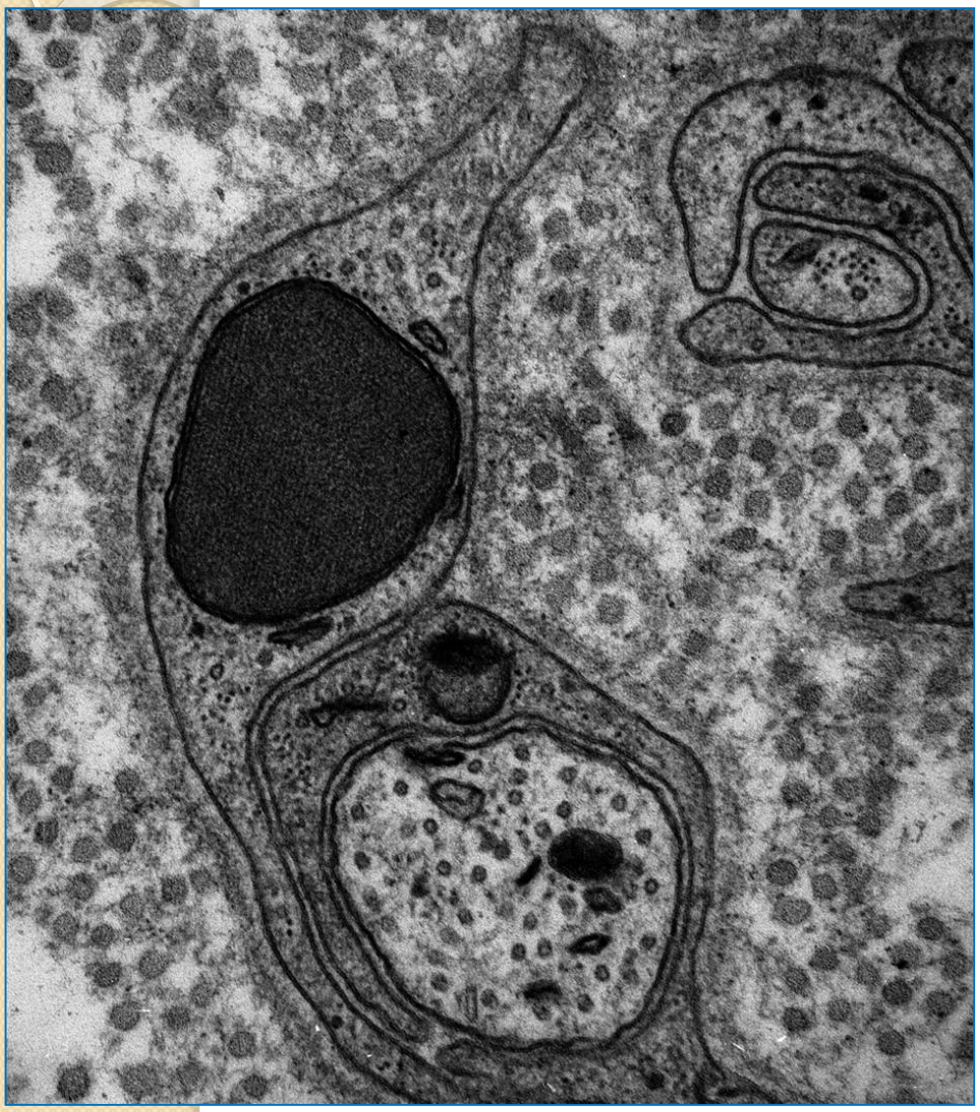


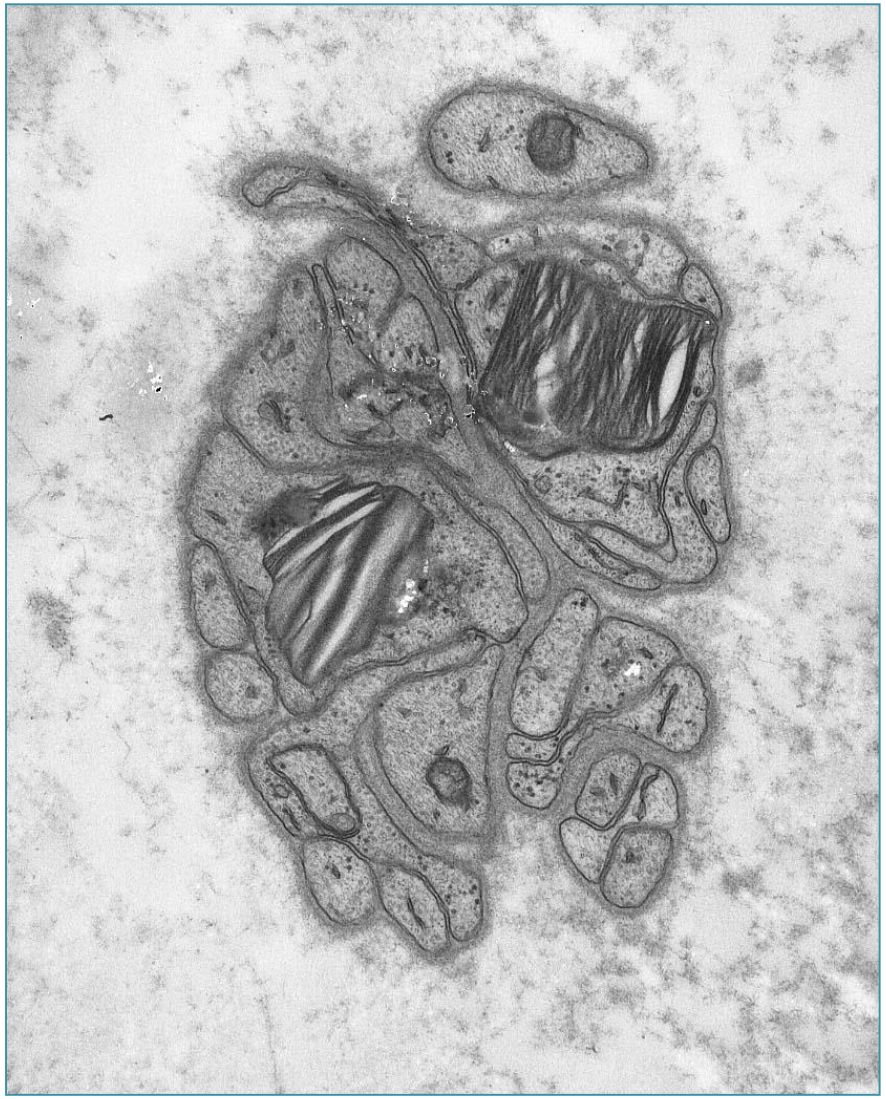
Amyloid

Fibrous long spacing collagen



Remak fibre inclusions





Surprises

M.Leprae in axon, lepromatous leprosy