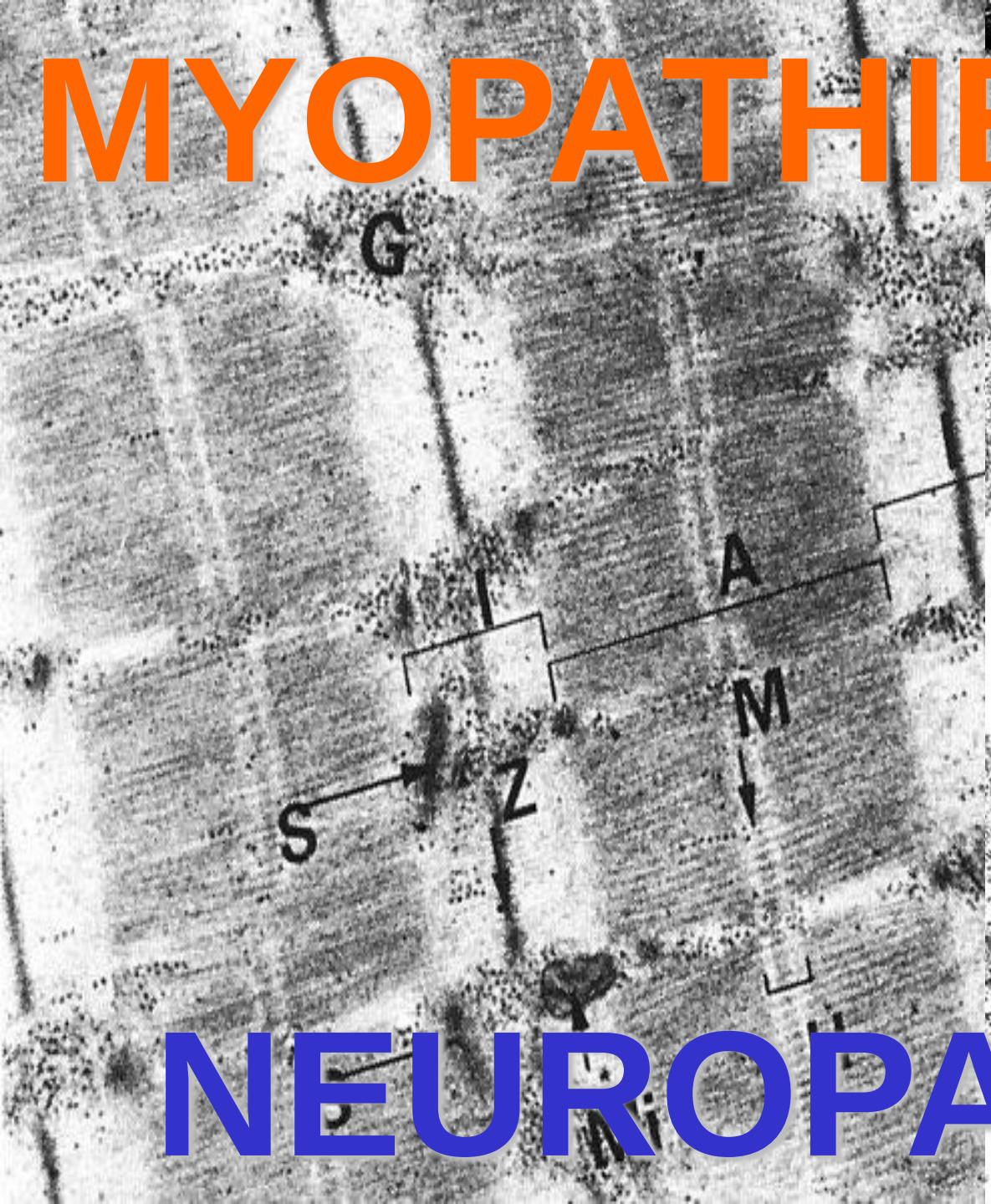
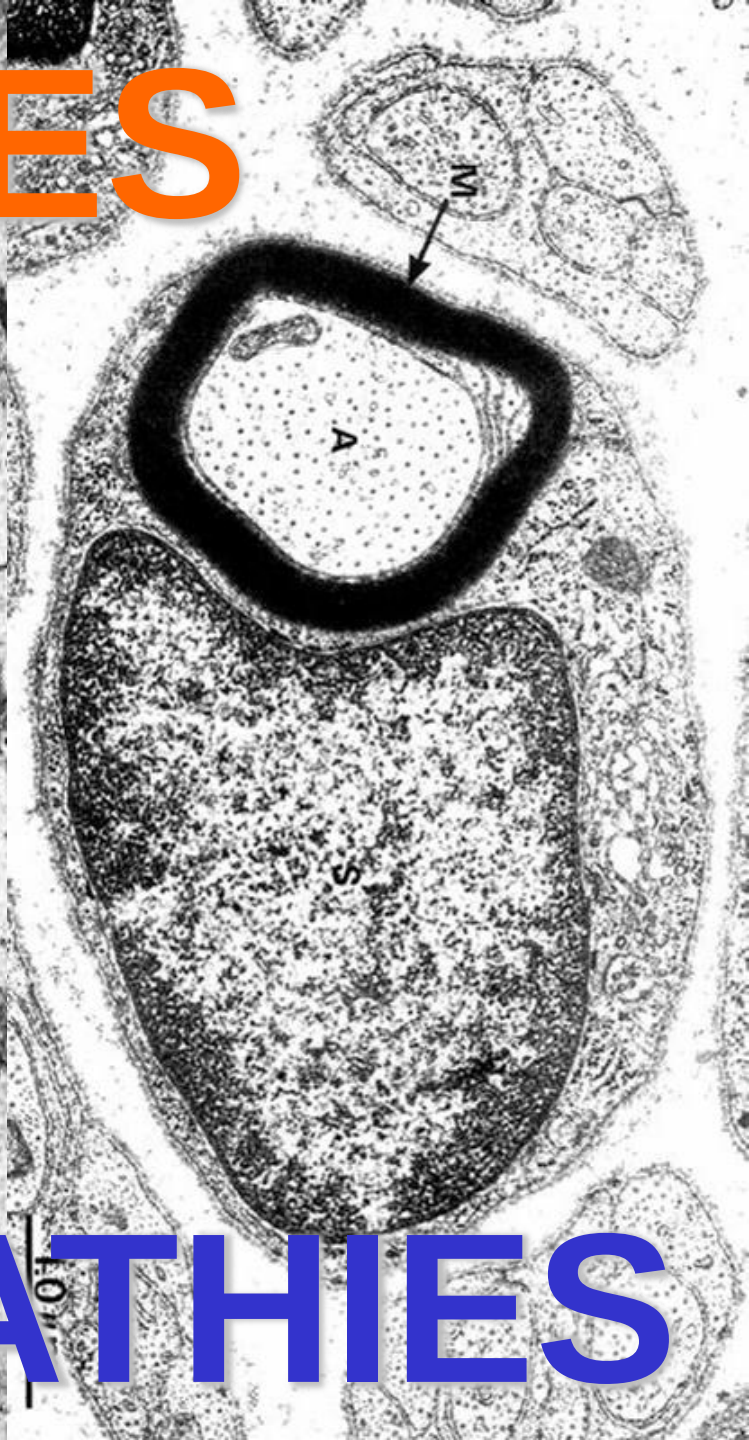
MYOPATHIES

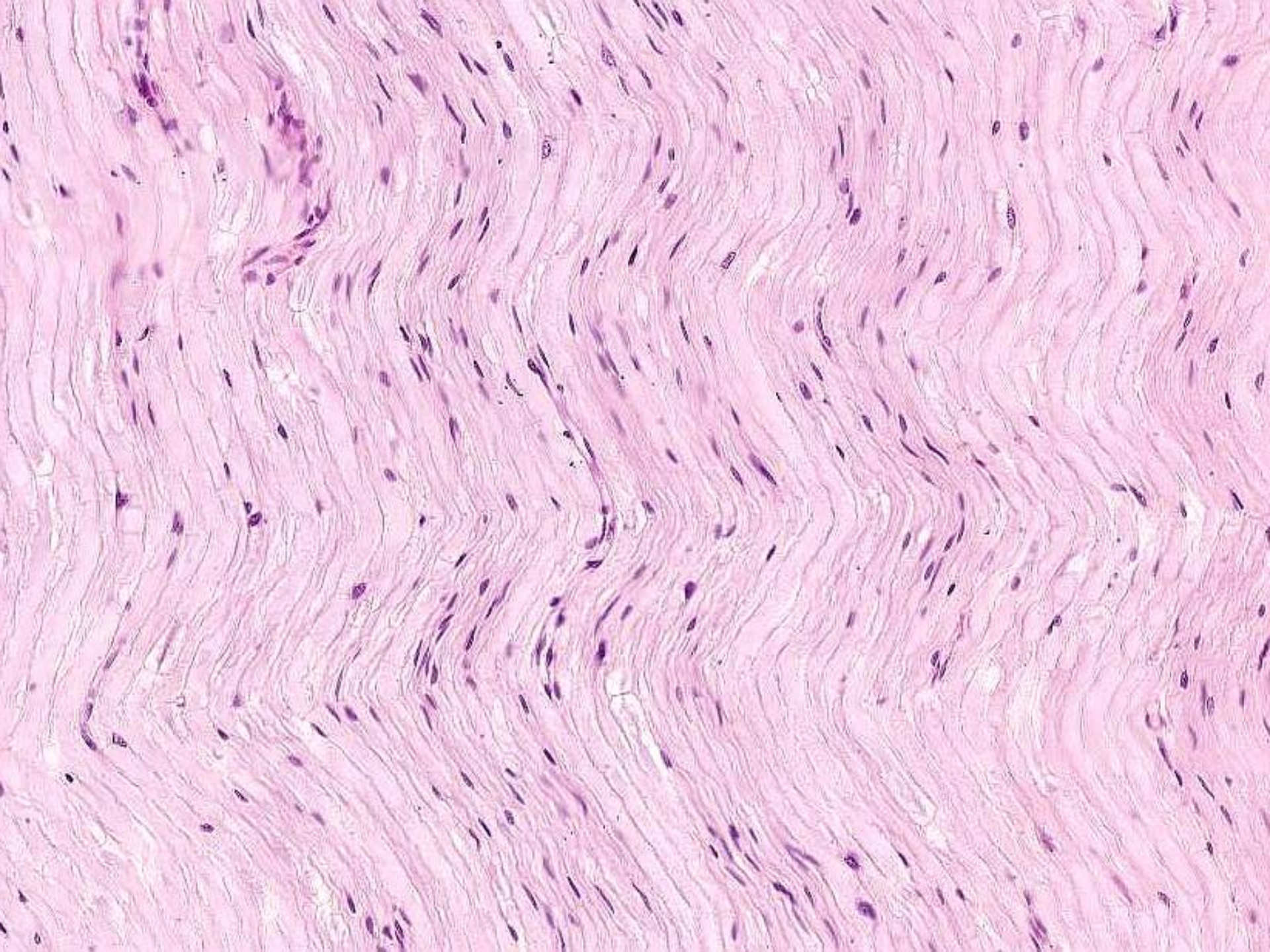


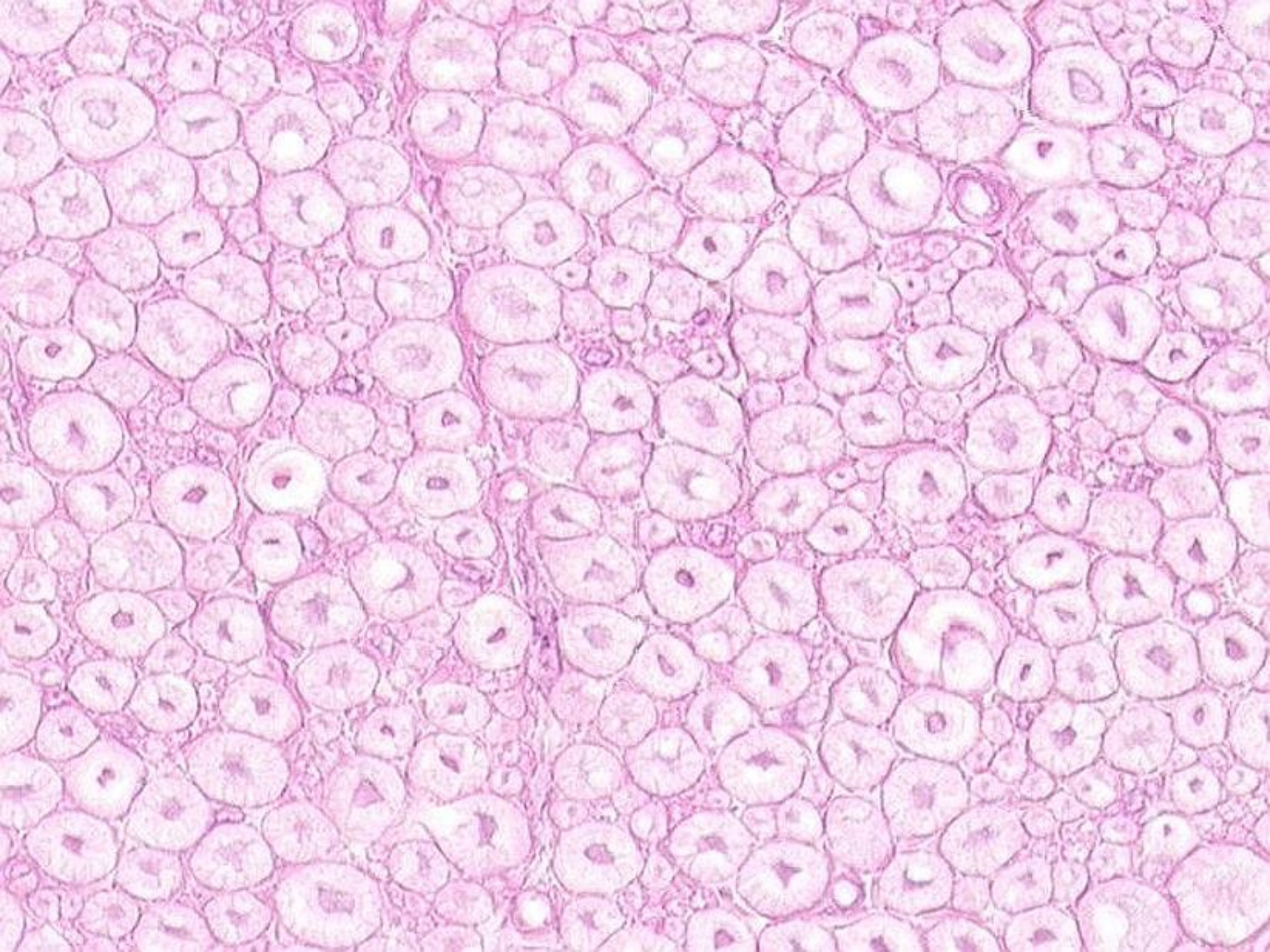


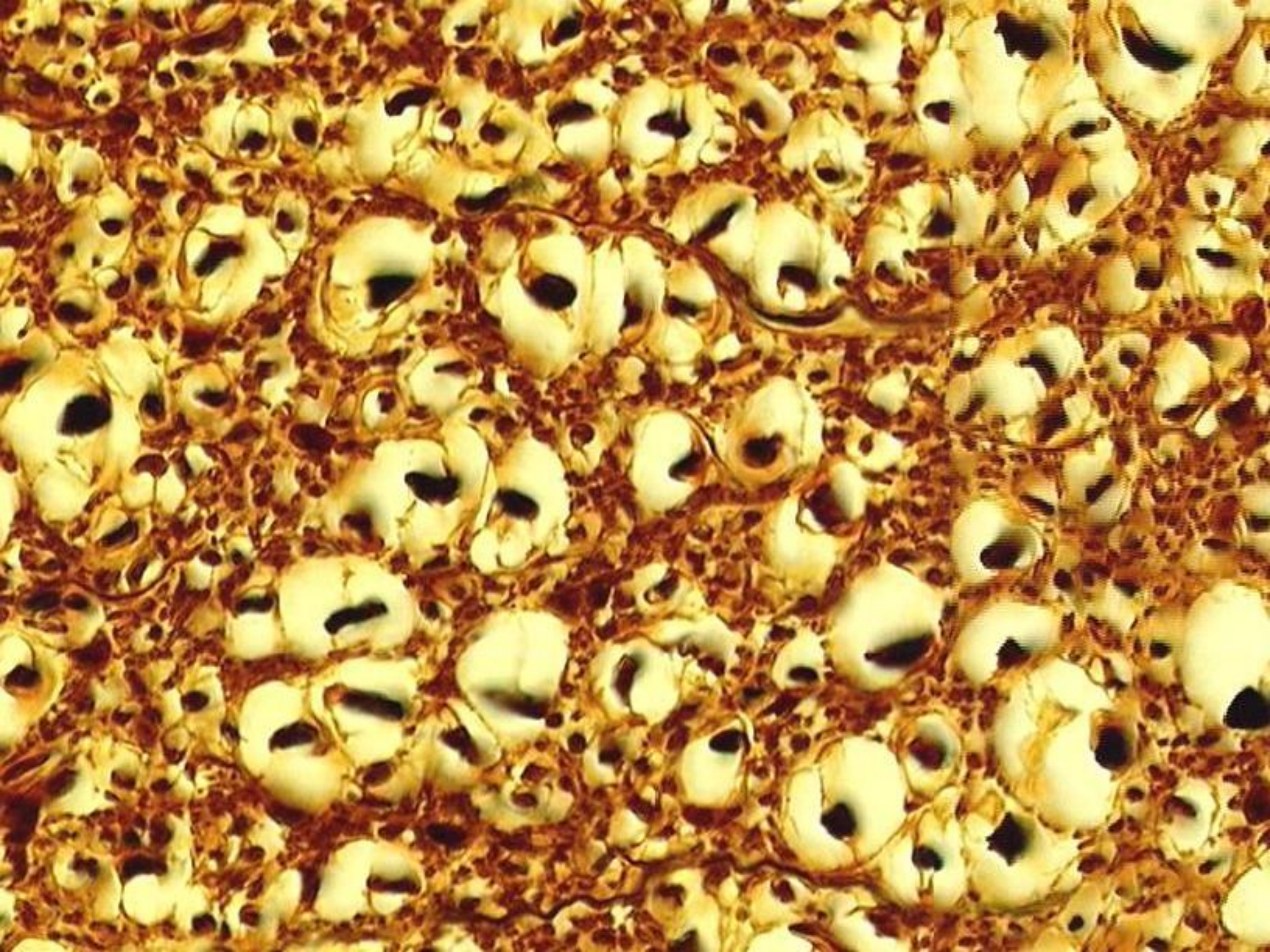
NEUROPATHIES

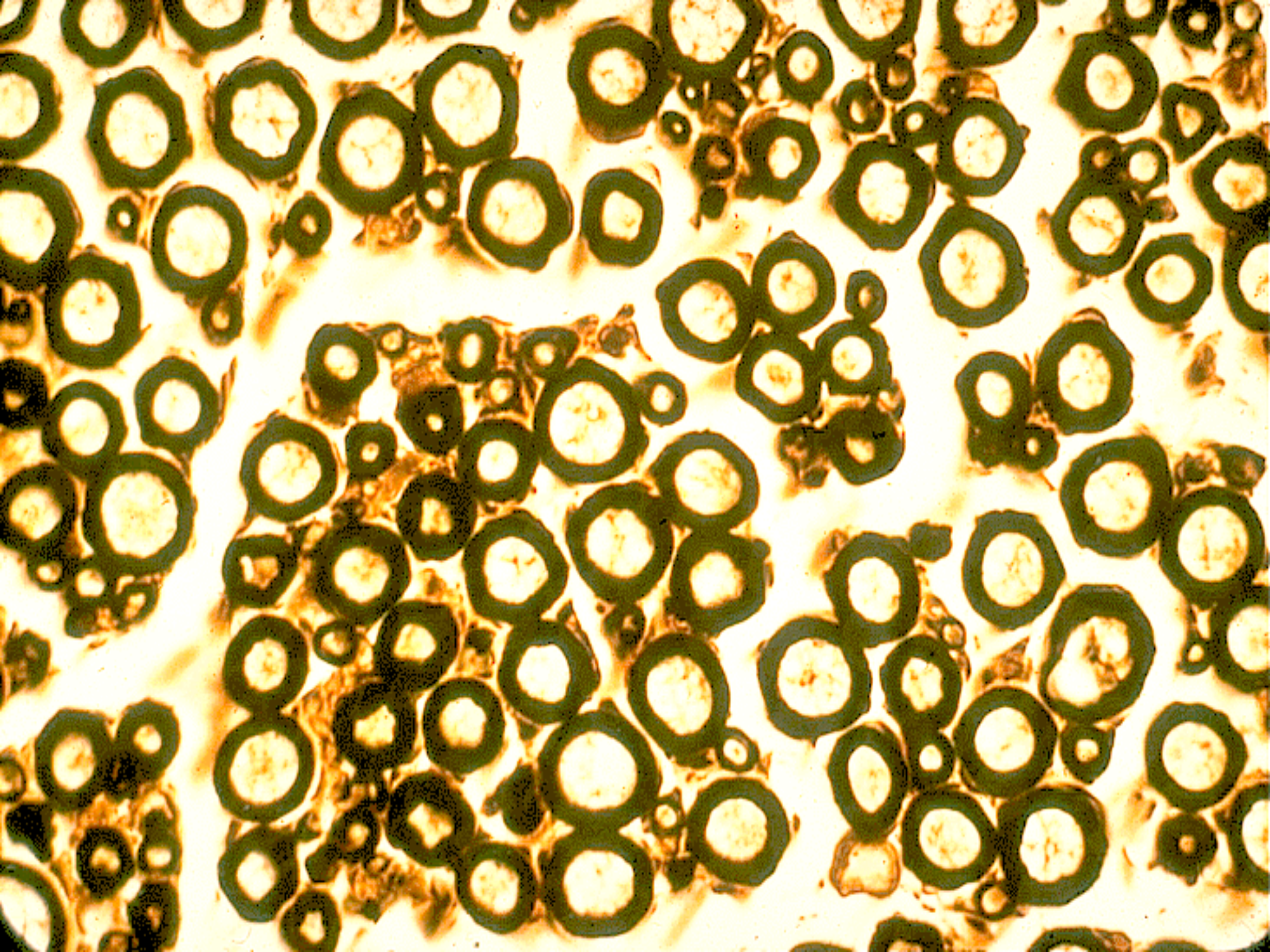
NEUROPATHIES, MYOPATHIES

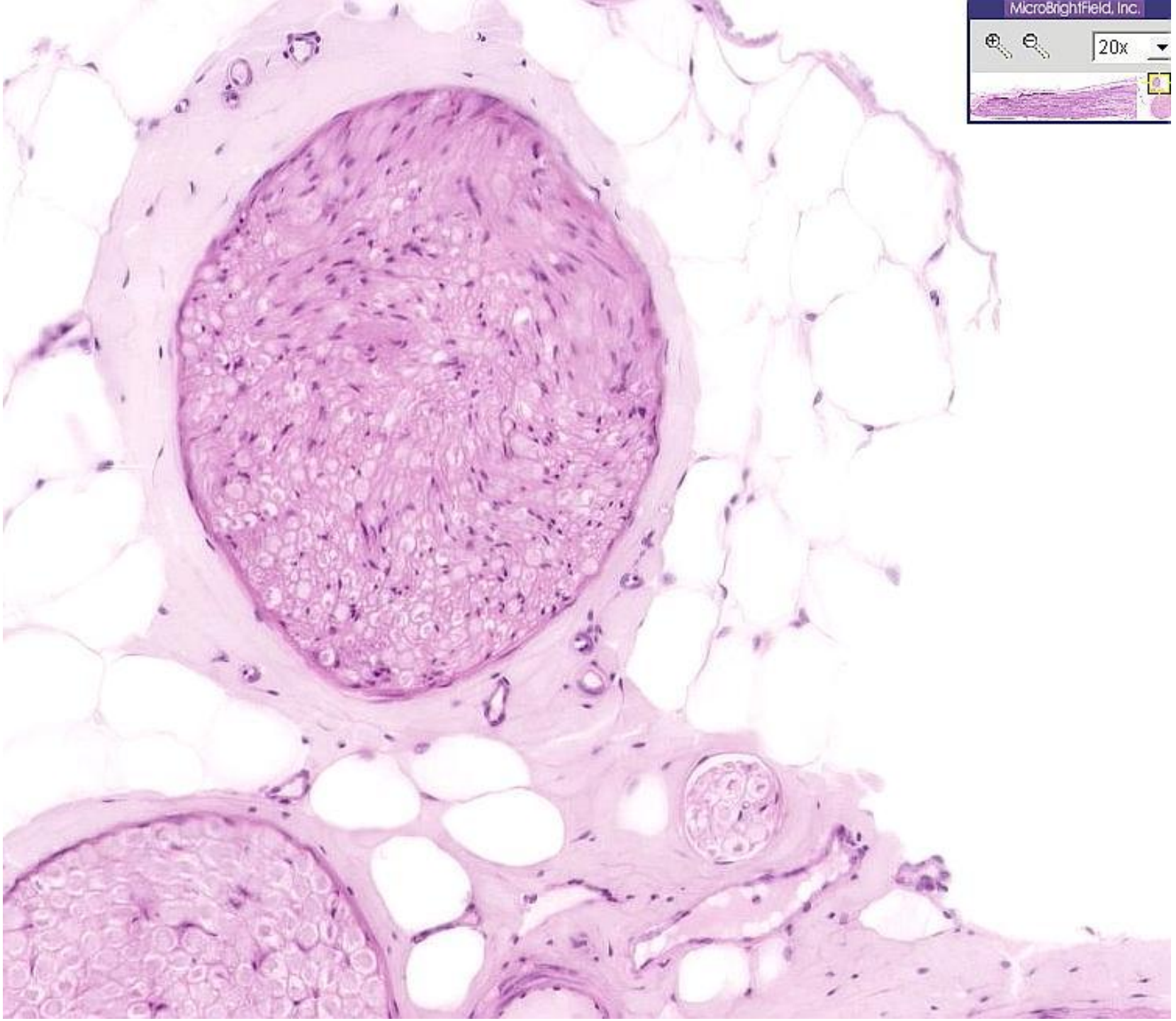
- **NEUROPATHIES (7)**
  - Inflammatory
  - Infectious
  - Hereditary (HMSN-I)
  - HMSN-II, HMSN-III
  - **Acquired (Toxic/Metabolic)**
  - Traumatic
  - Neoplasms
- **MYOPATHIES (9)**
  - **Denervation**
  - Dystrophies
  - Ion Channel
  - Congenital
  - Genetic Metabolic
  - Inflammatory
  - Toxic
  - NeuroMuscular Junction
  - Neoplasms

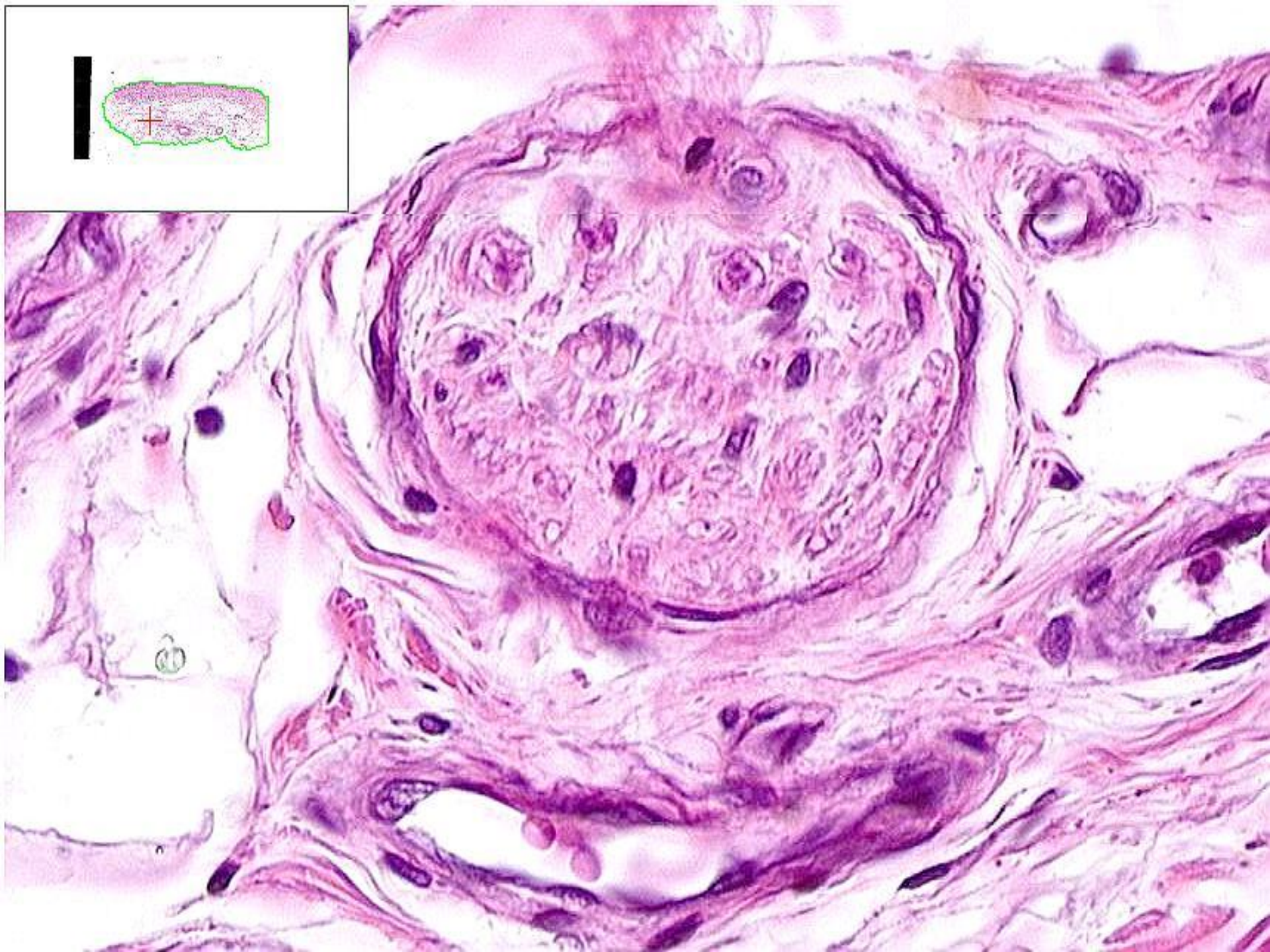


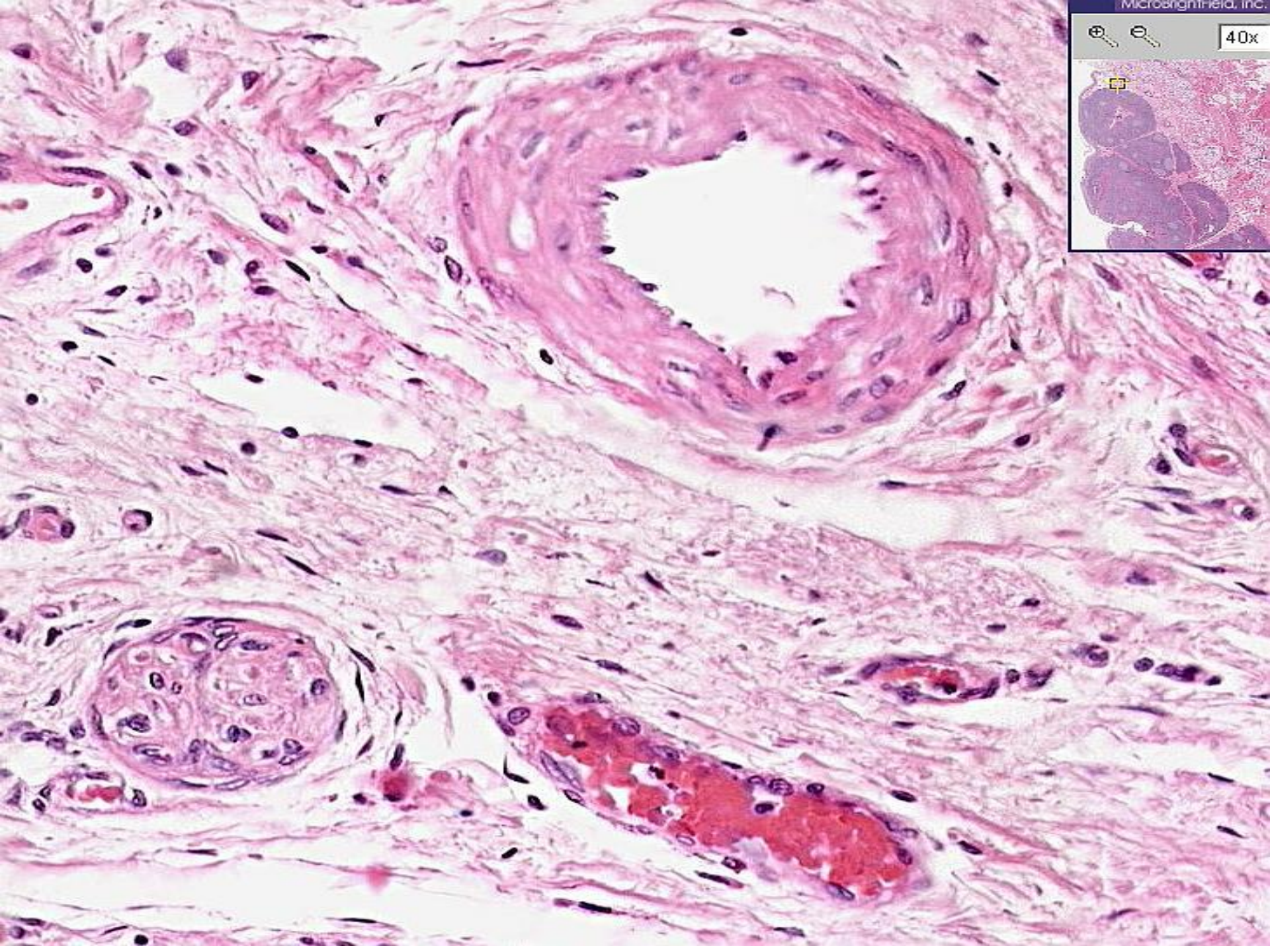







MicroBrightField, Inc.
20x

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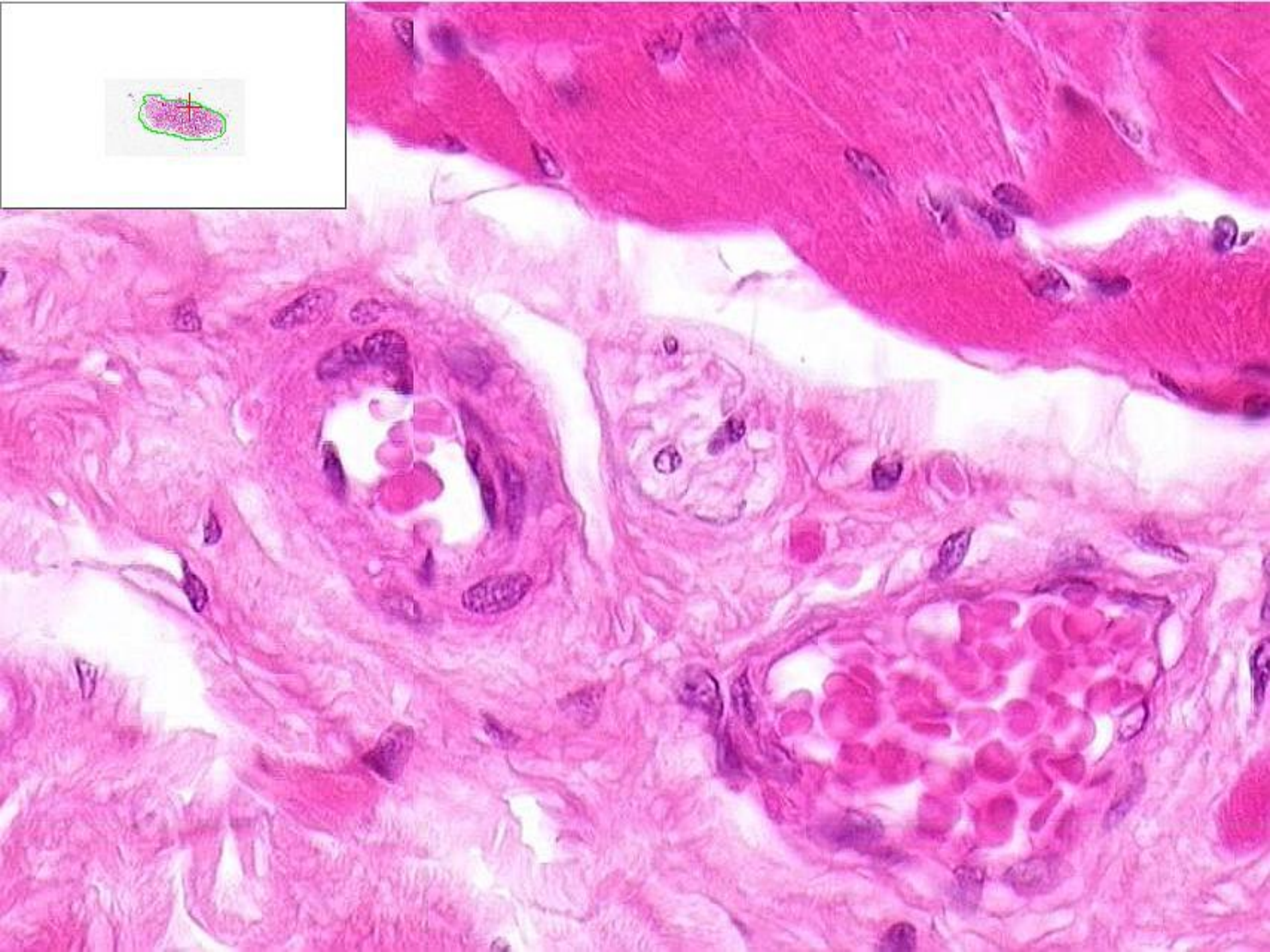
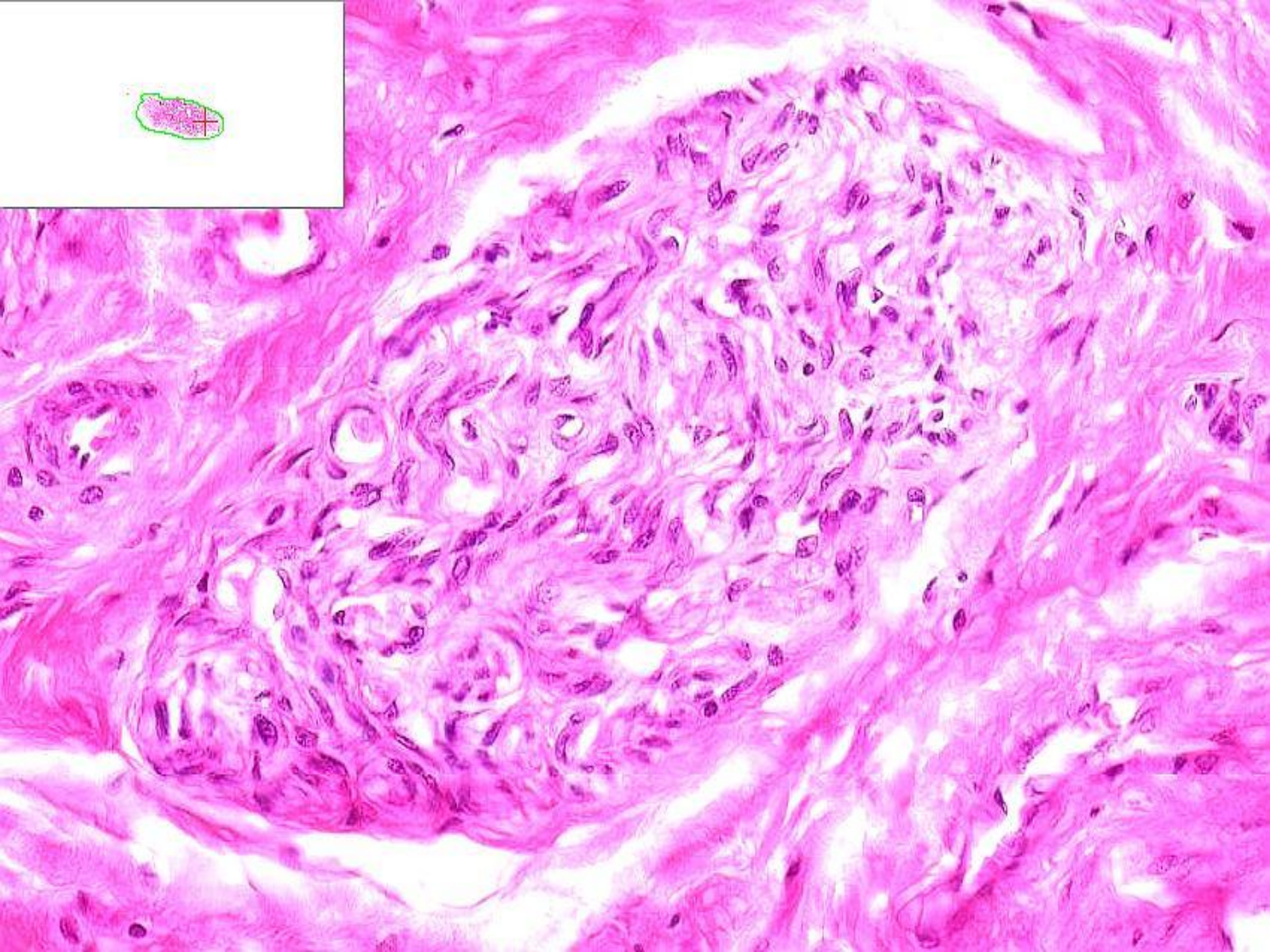
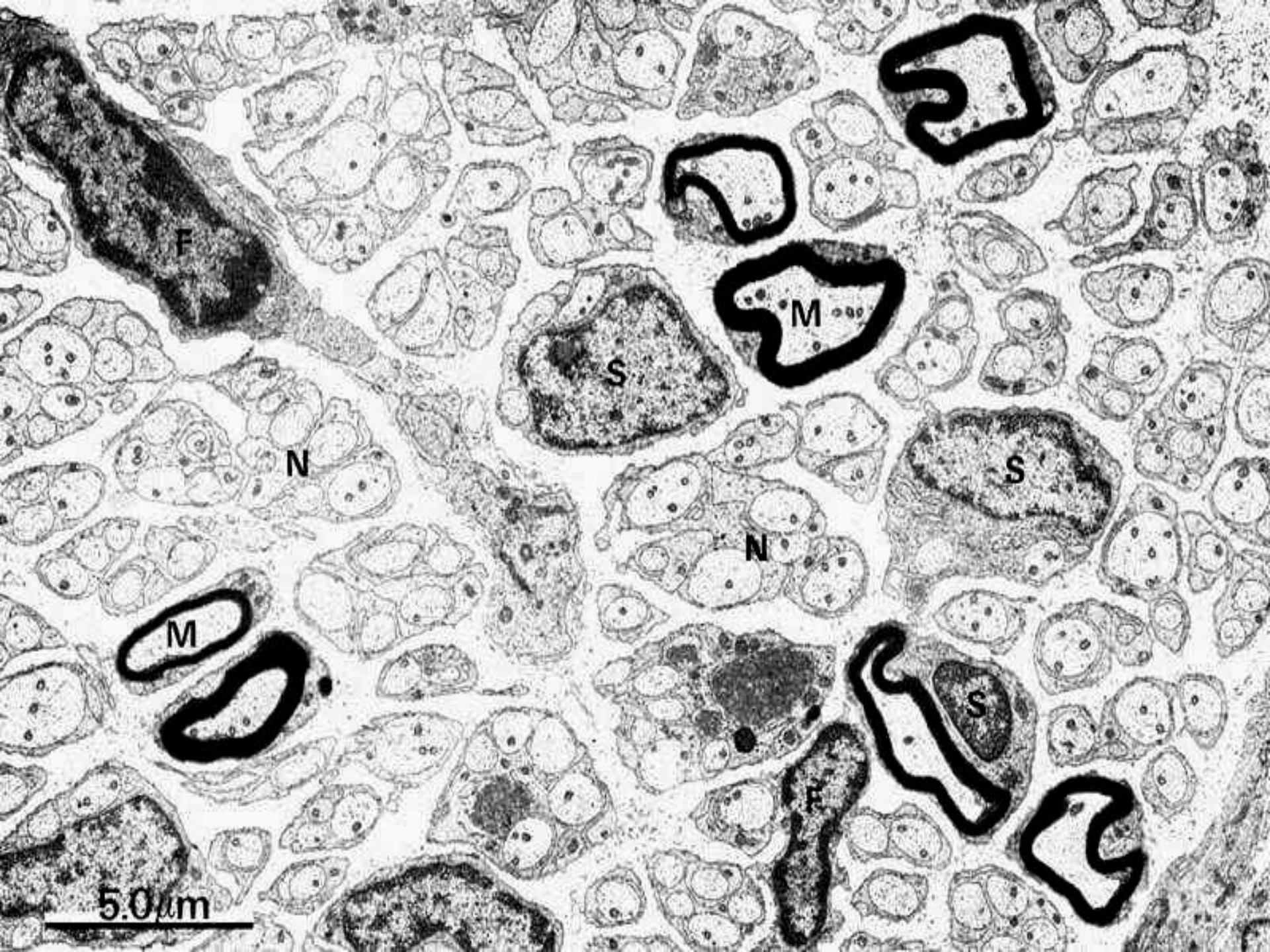
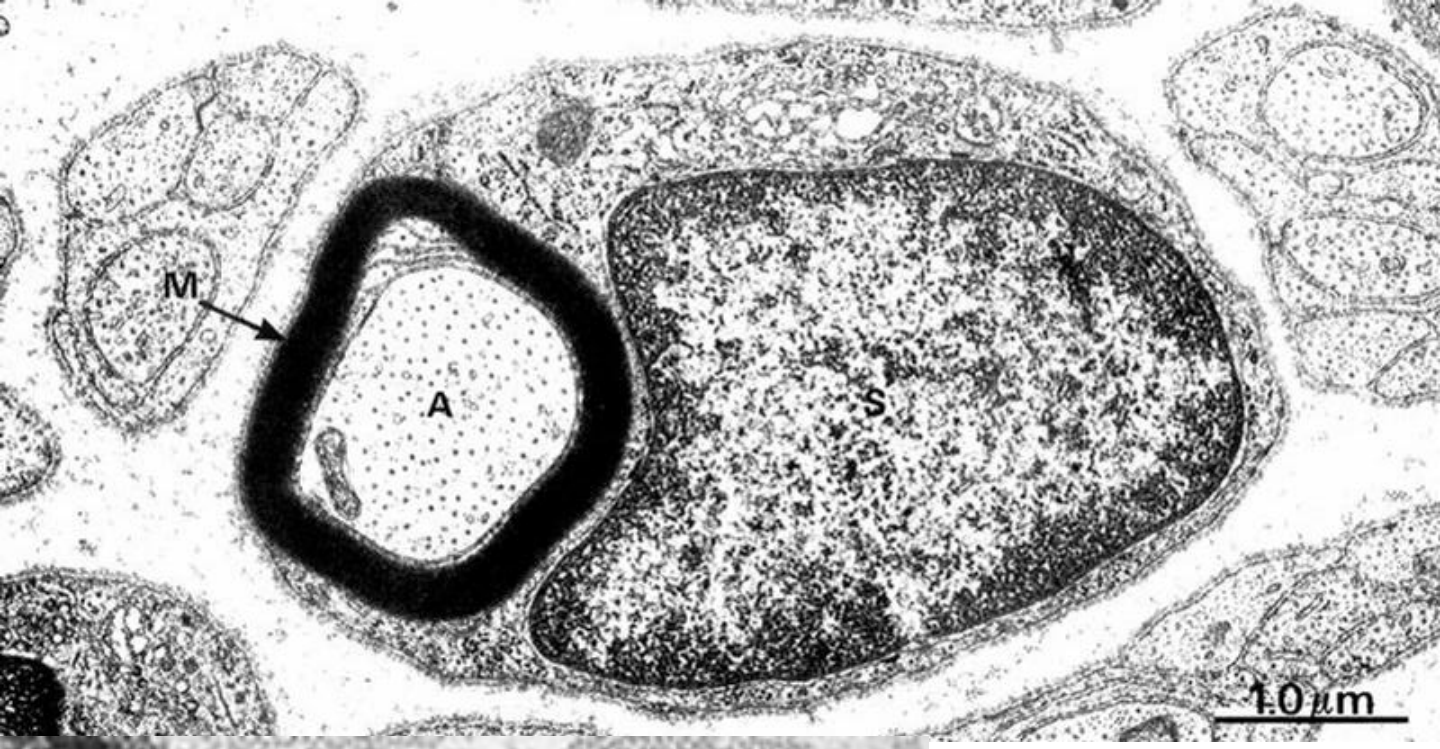
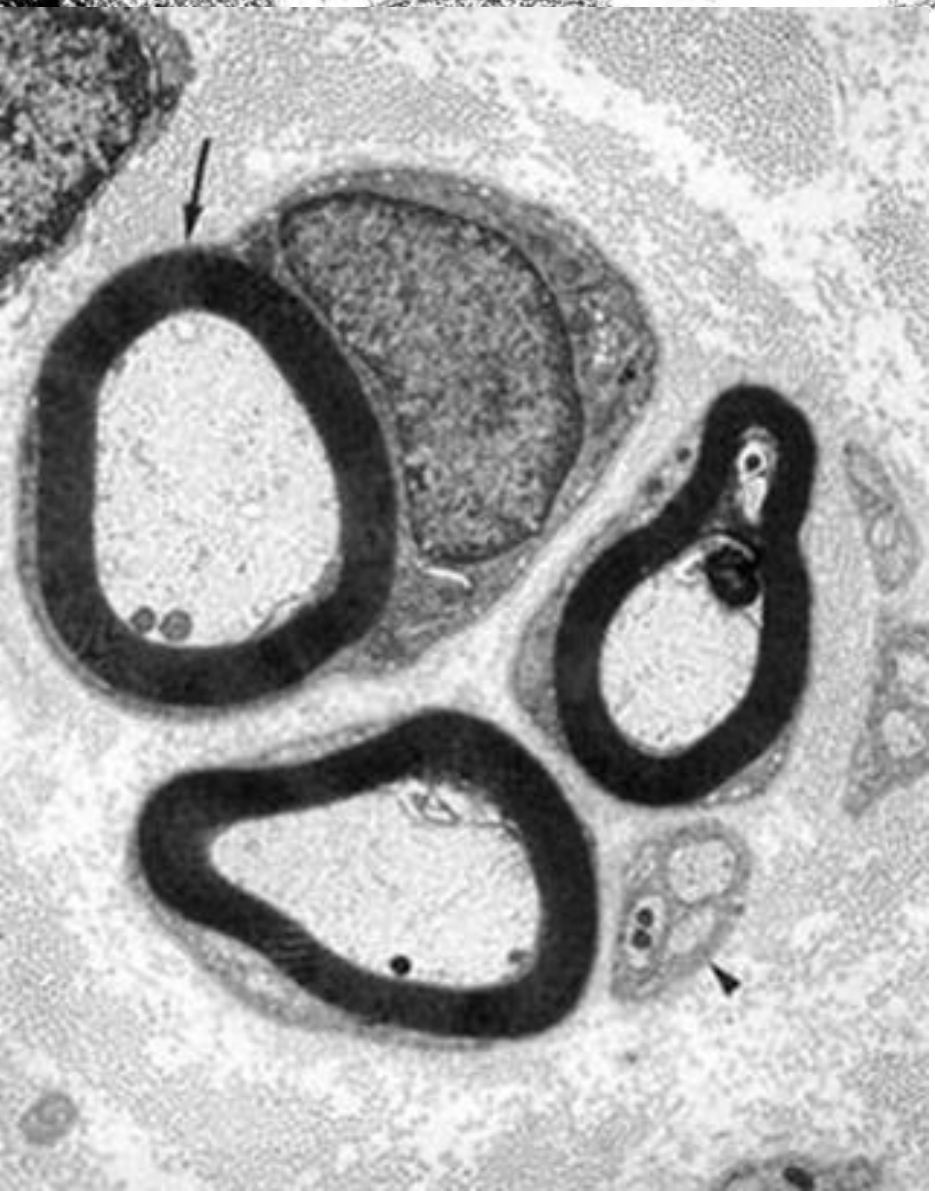
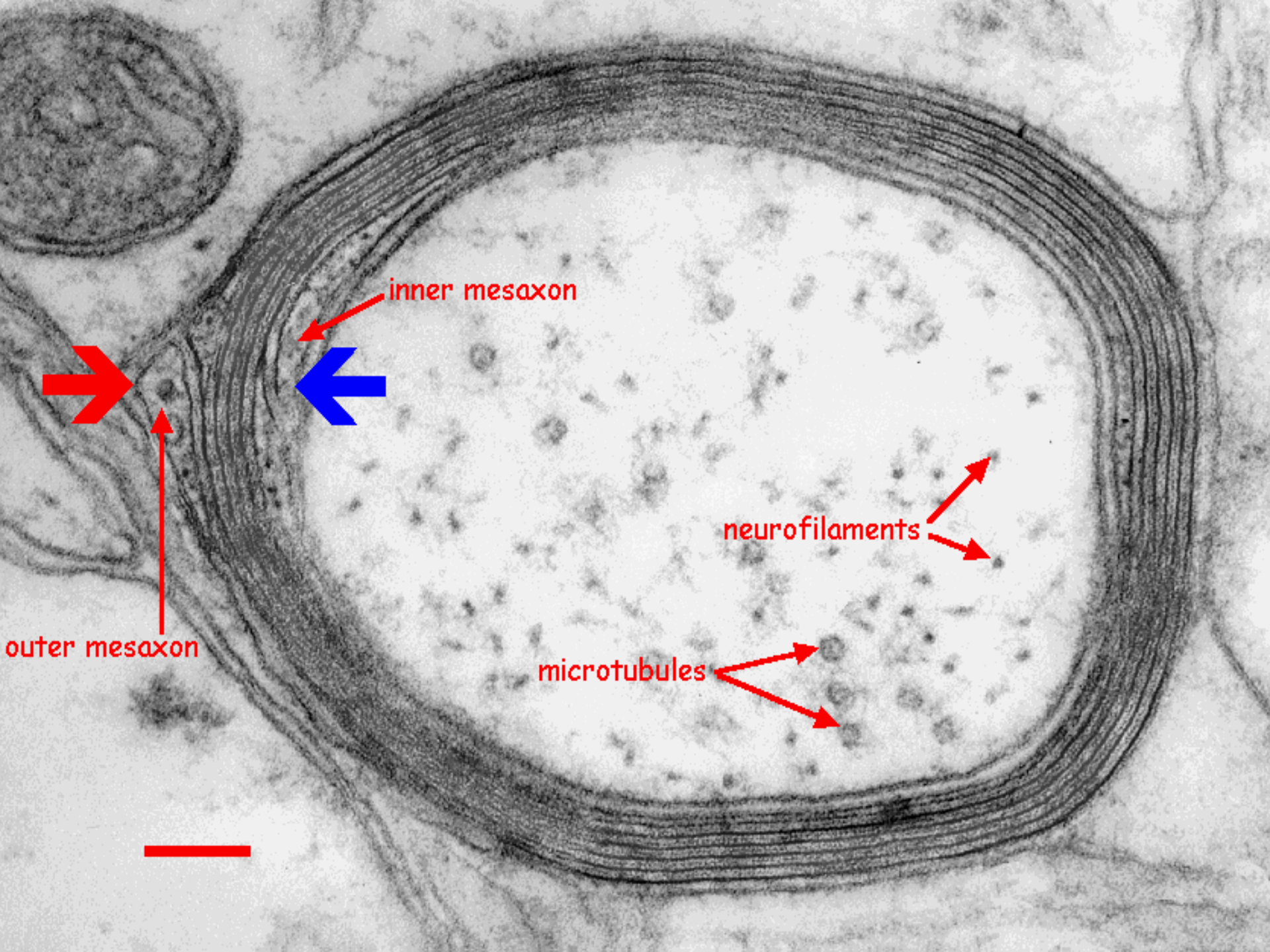


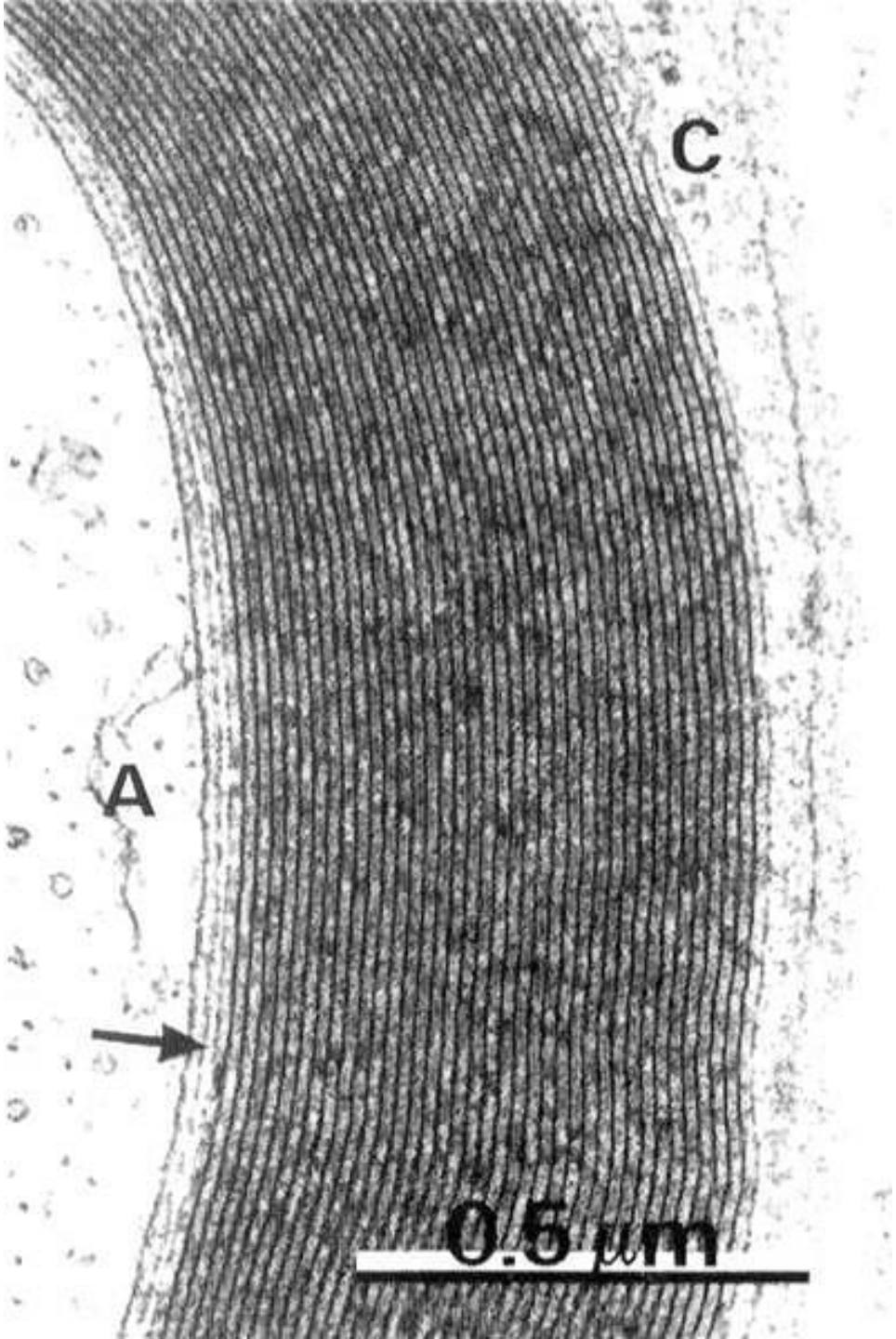


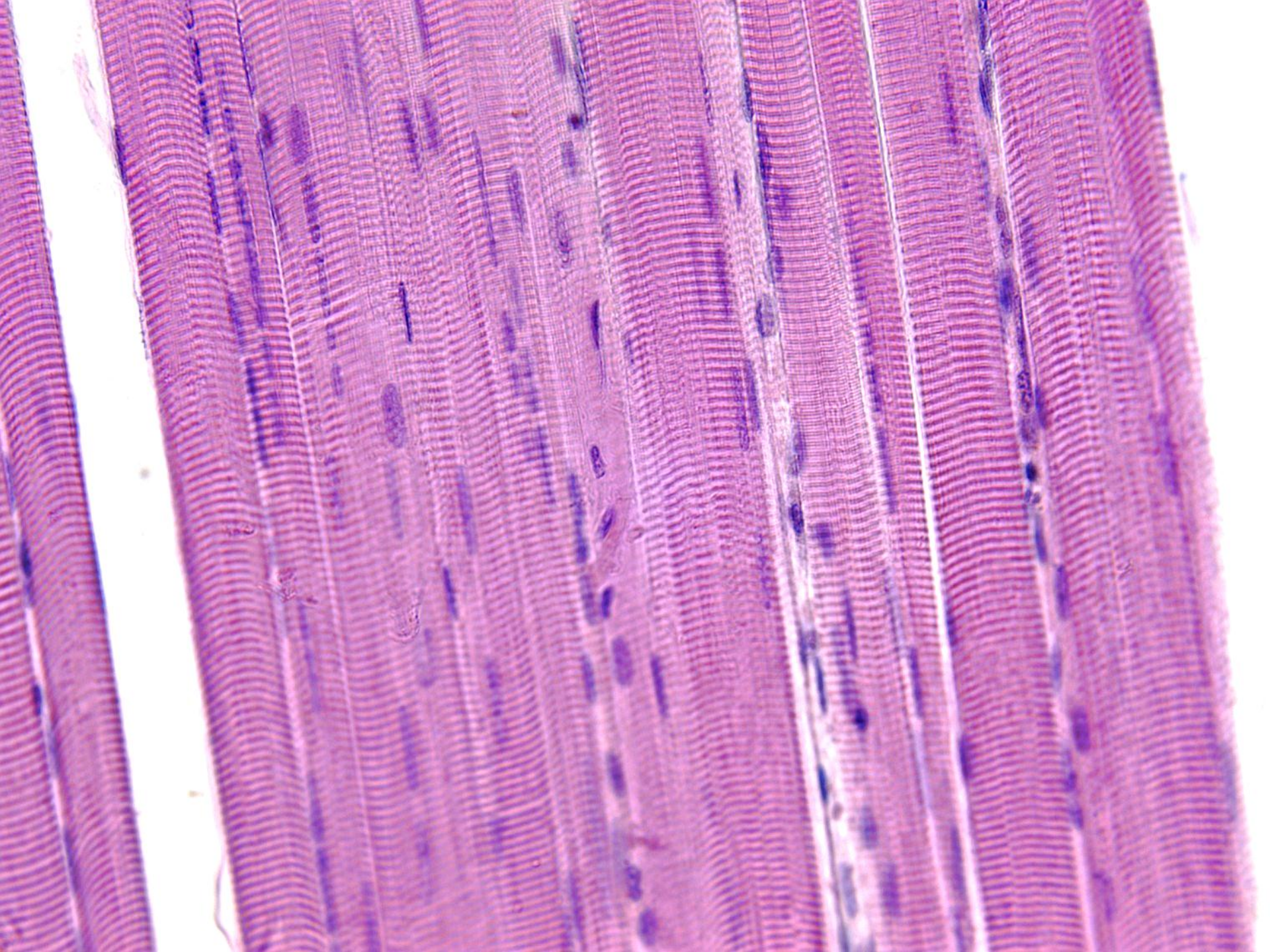

F
M
S
N
S
N
M
S
F
5.0μm

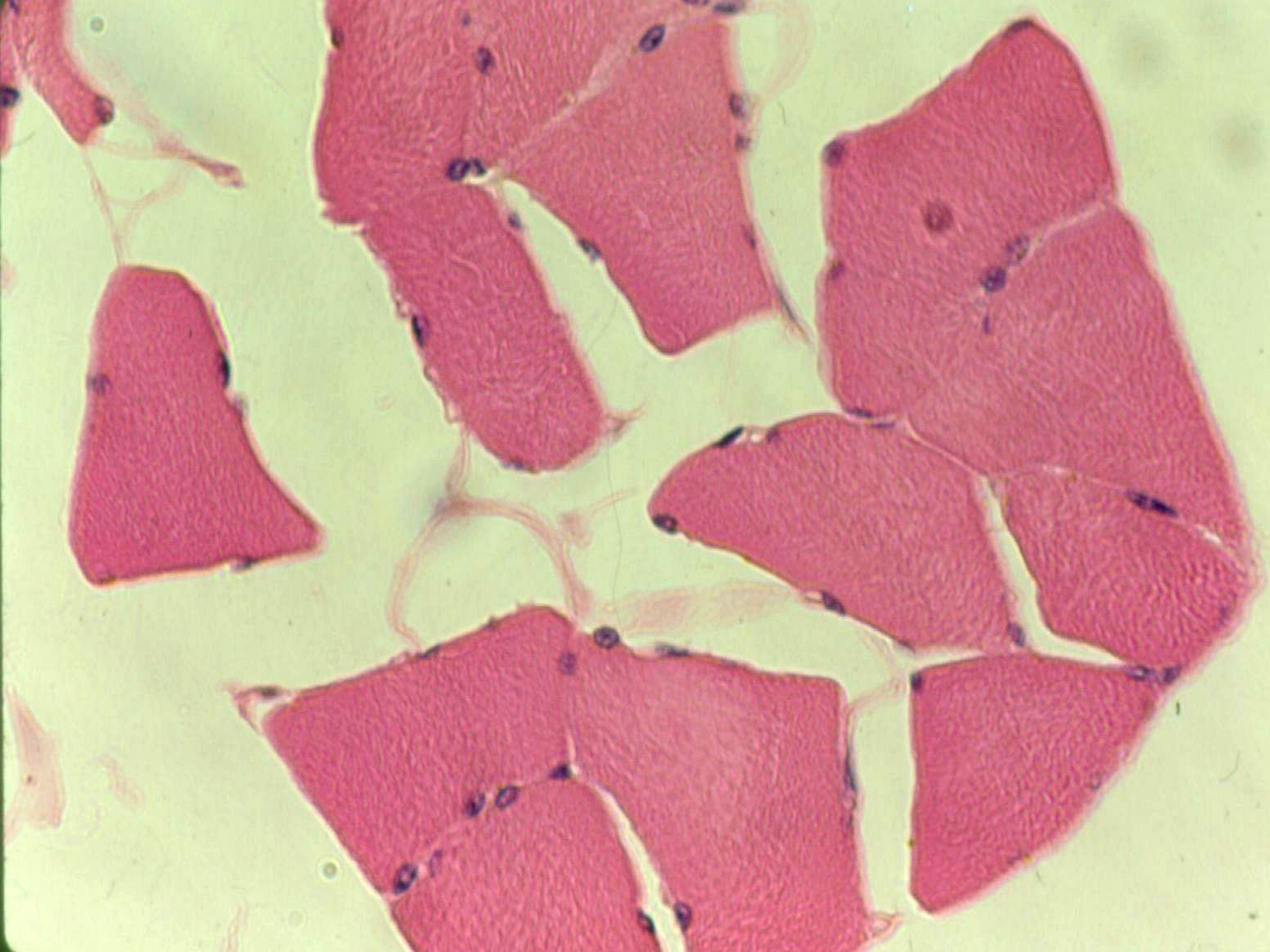

M
A
S
1.0 μm

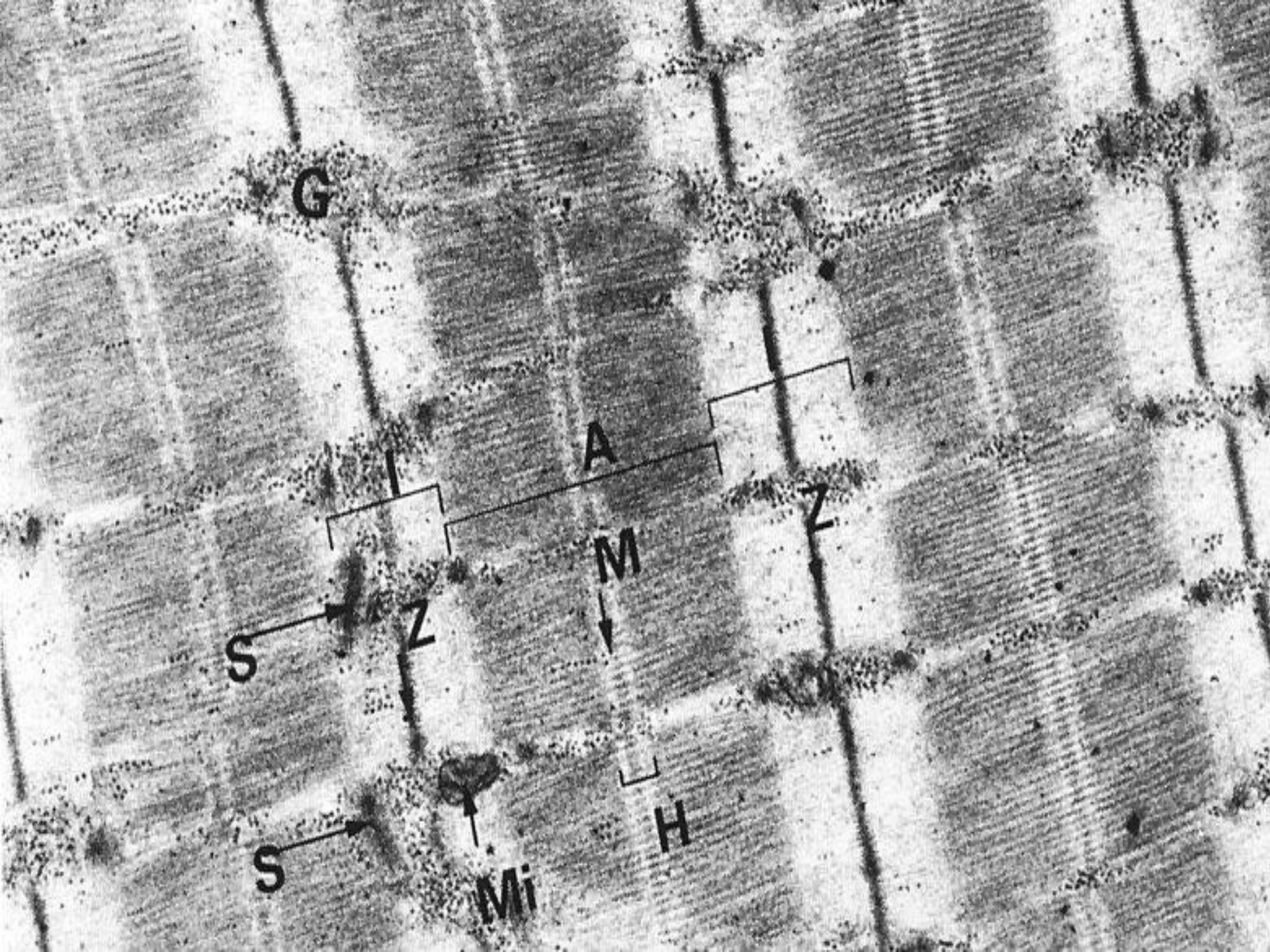


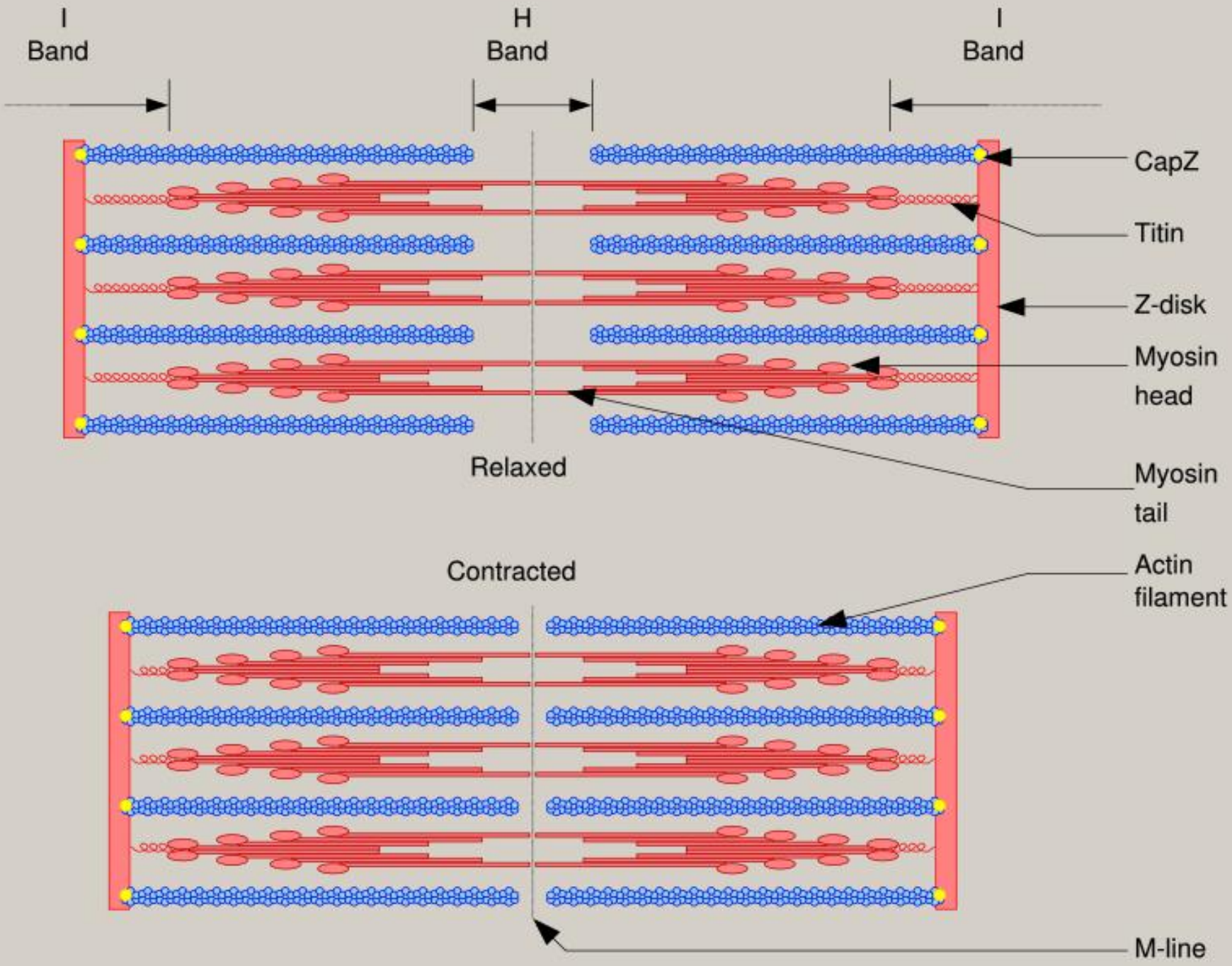

inner mesaxon
outer mesaxon
neurofilaments
microtubules

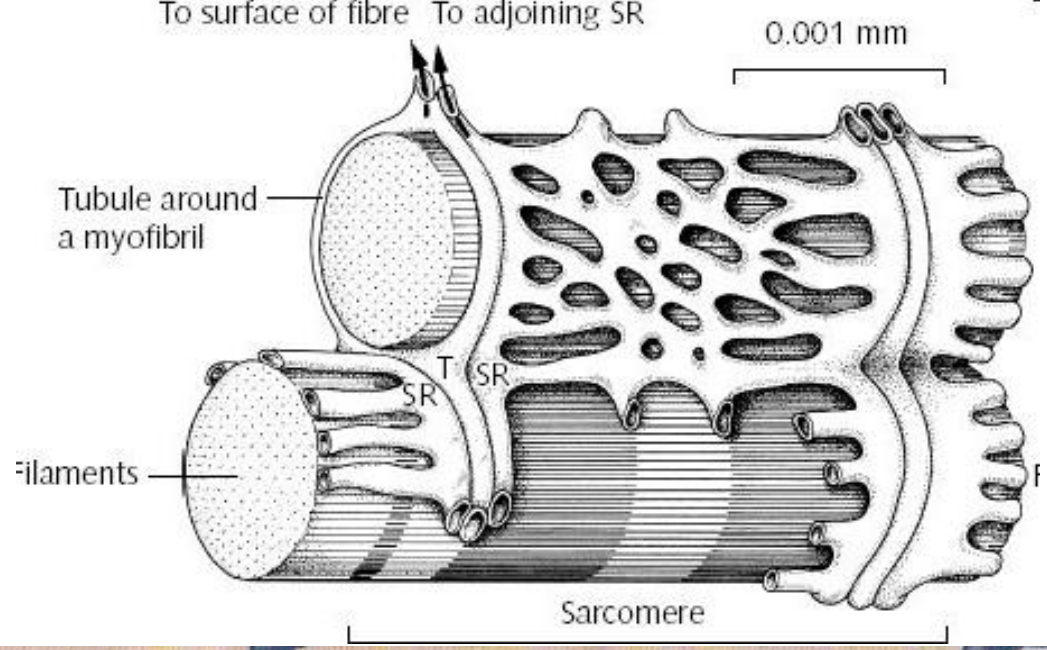

C
A
0.5 μm

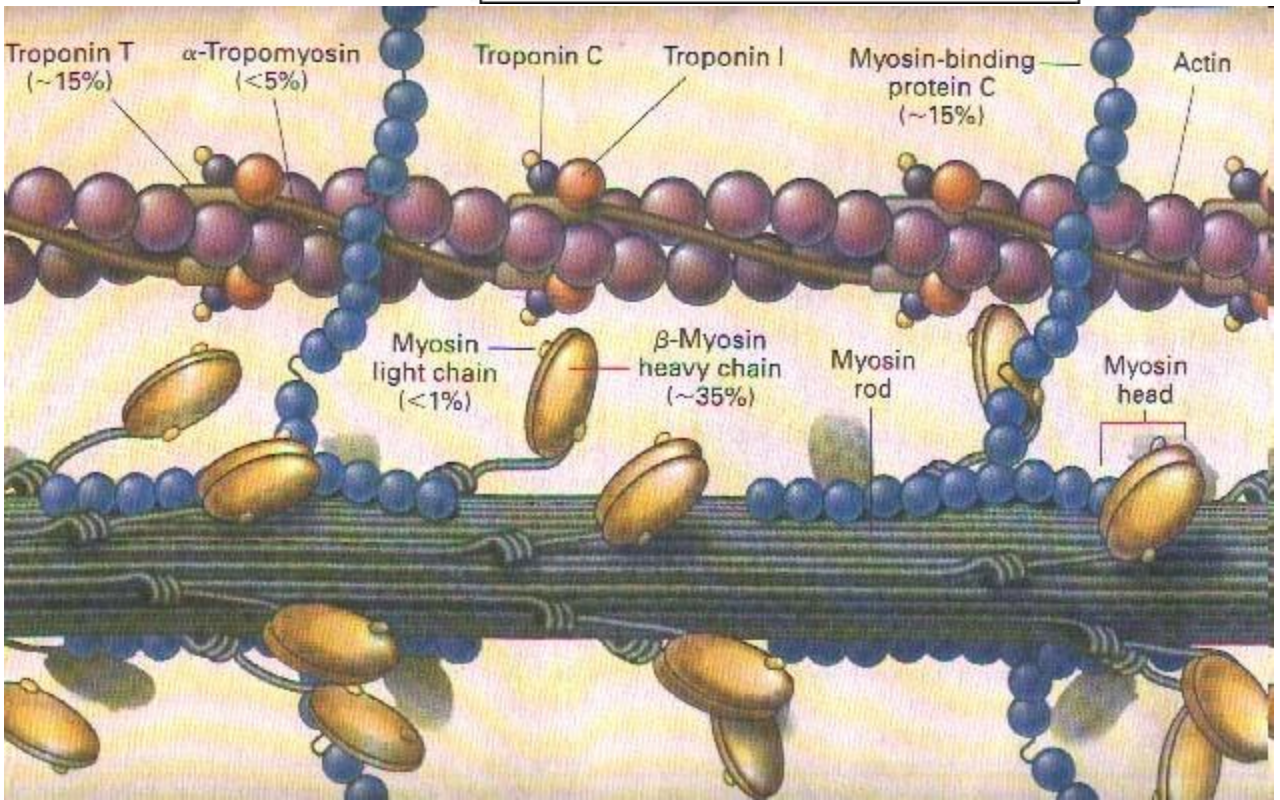


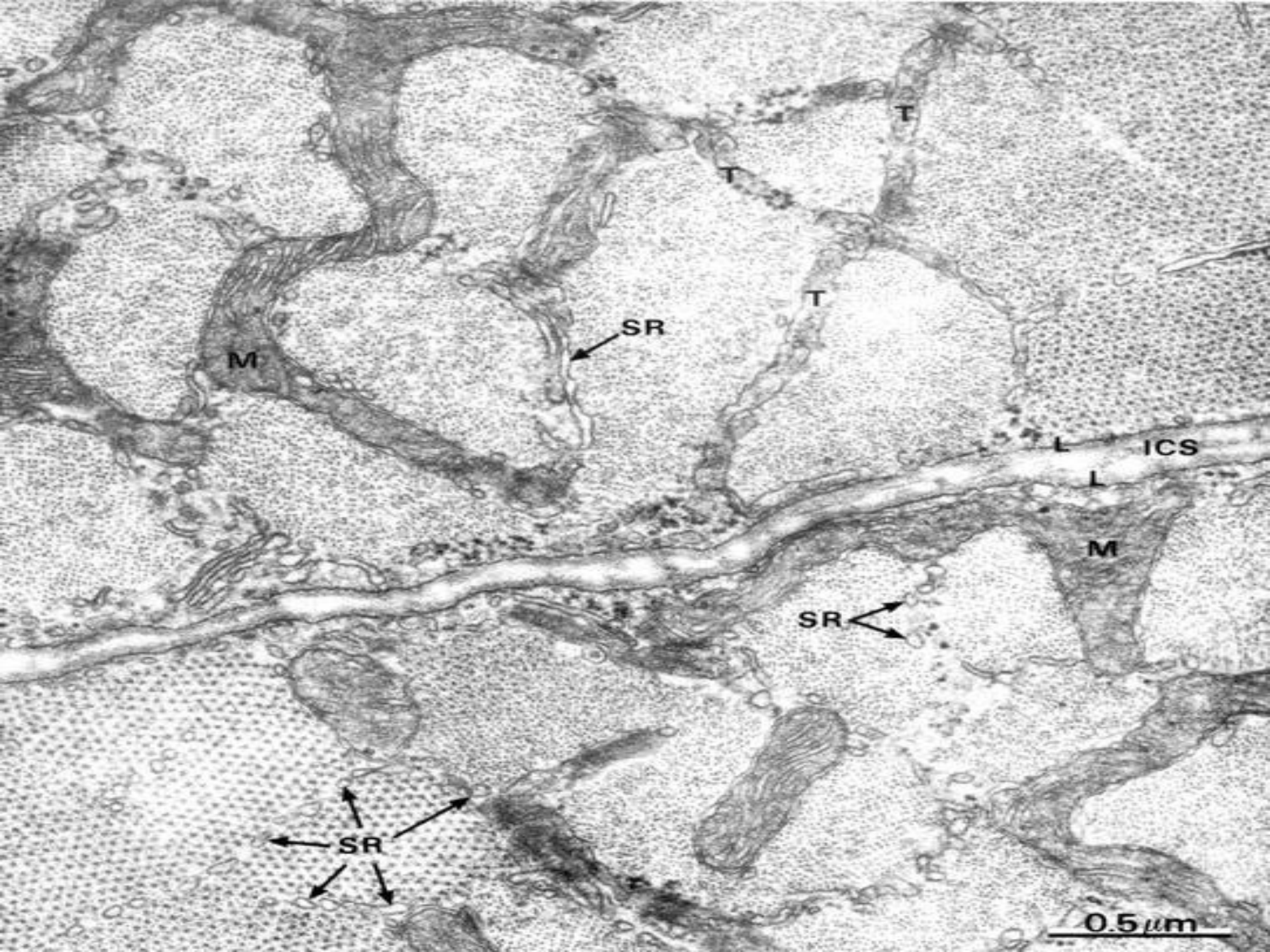



G
I
A
Z
M
S
Z
S
Mi
H


I Band
H Band
I Band
CapZ
Titin
Z-disk
Myosin head
Myosin tail
Relaxed
Contracted
Actin filament
M-line

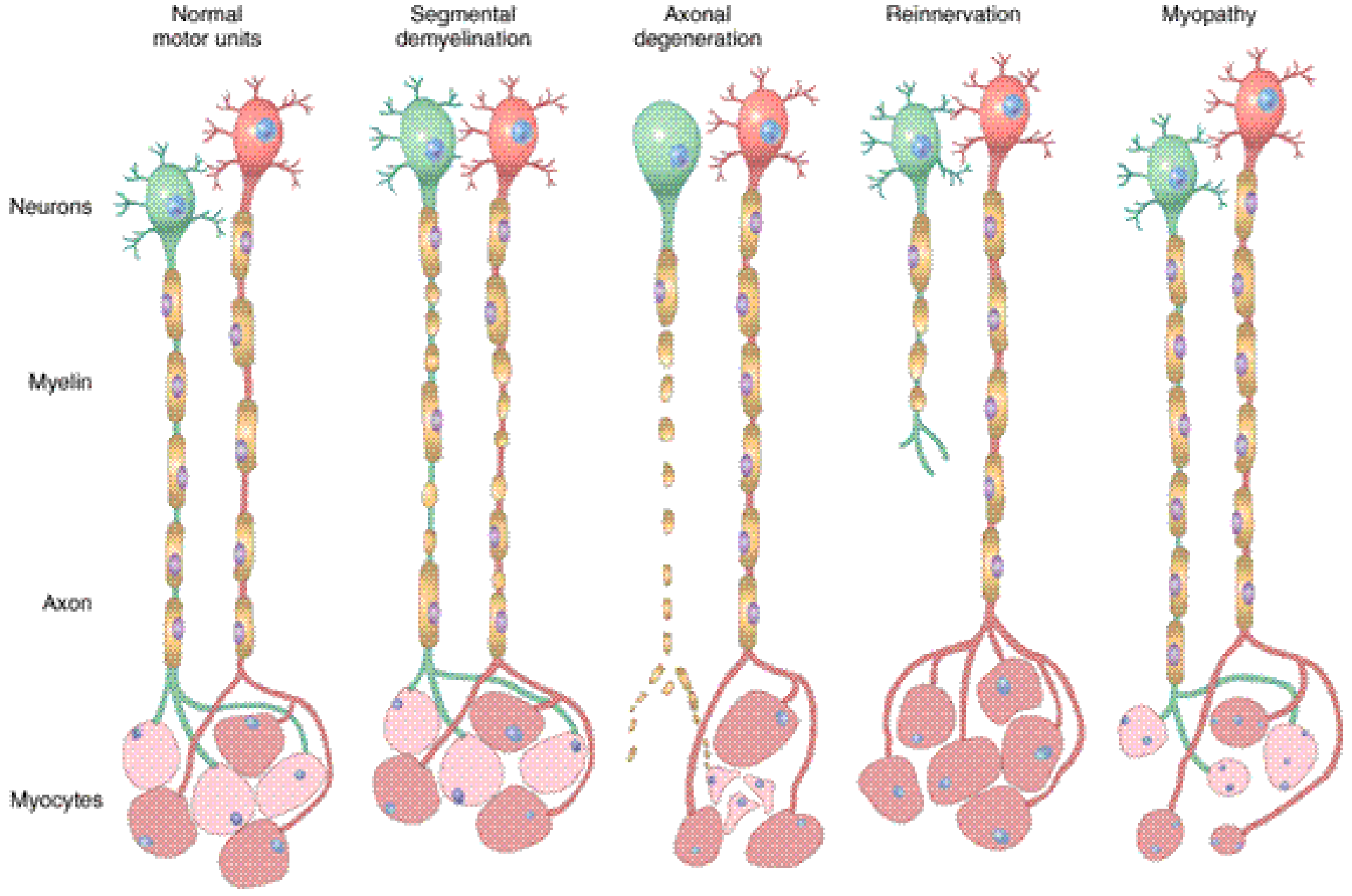

To surface of fibre
To adjoining SR
0.001 mm
Tubule around a myofibril
T
SR
SR
Filaments
Sarcomere


Troponin T (~15%)
α-Tropomyosin (<5%)
Troponin C
Troponin I
Myosin-binding protein C (~15%)
Actin
Myosin light chain (<1%)
β-Myosin heavy chain (~35%)
Myosin rod
Myosin head

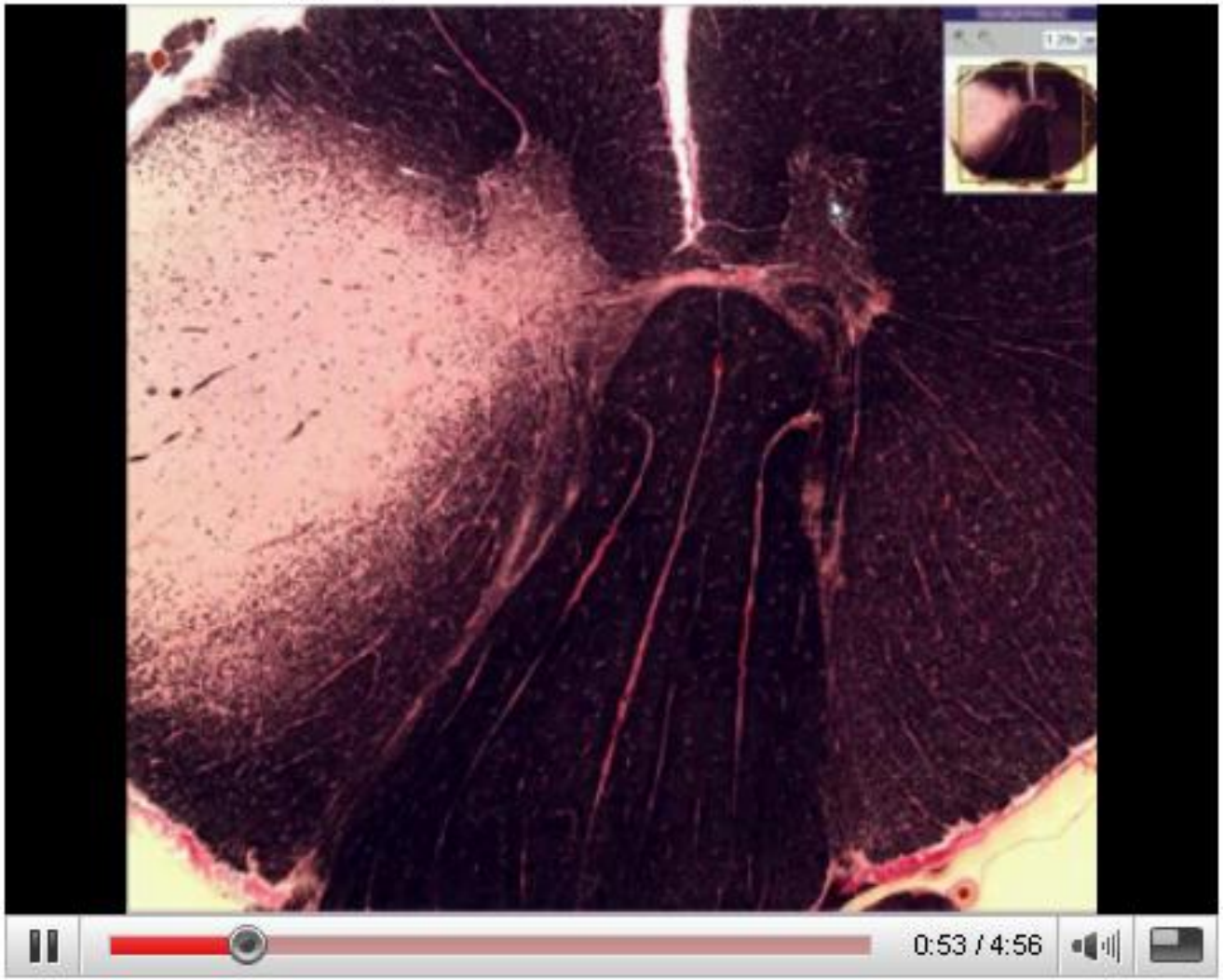

T
T
T
SR
M
L
ICS
L
M
SR
SR
0.5 μm

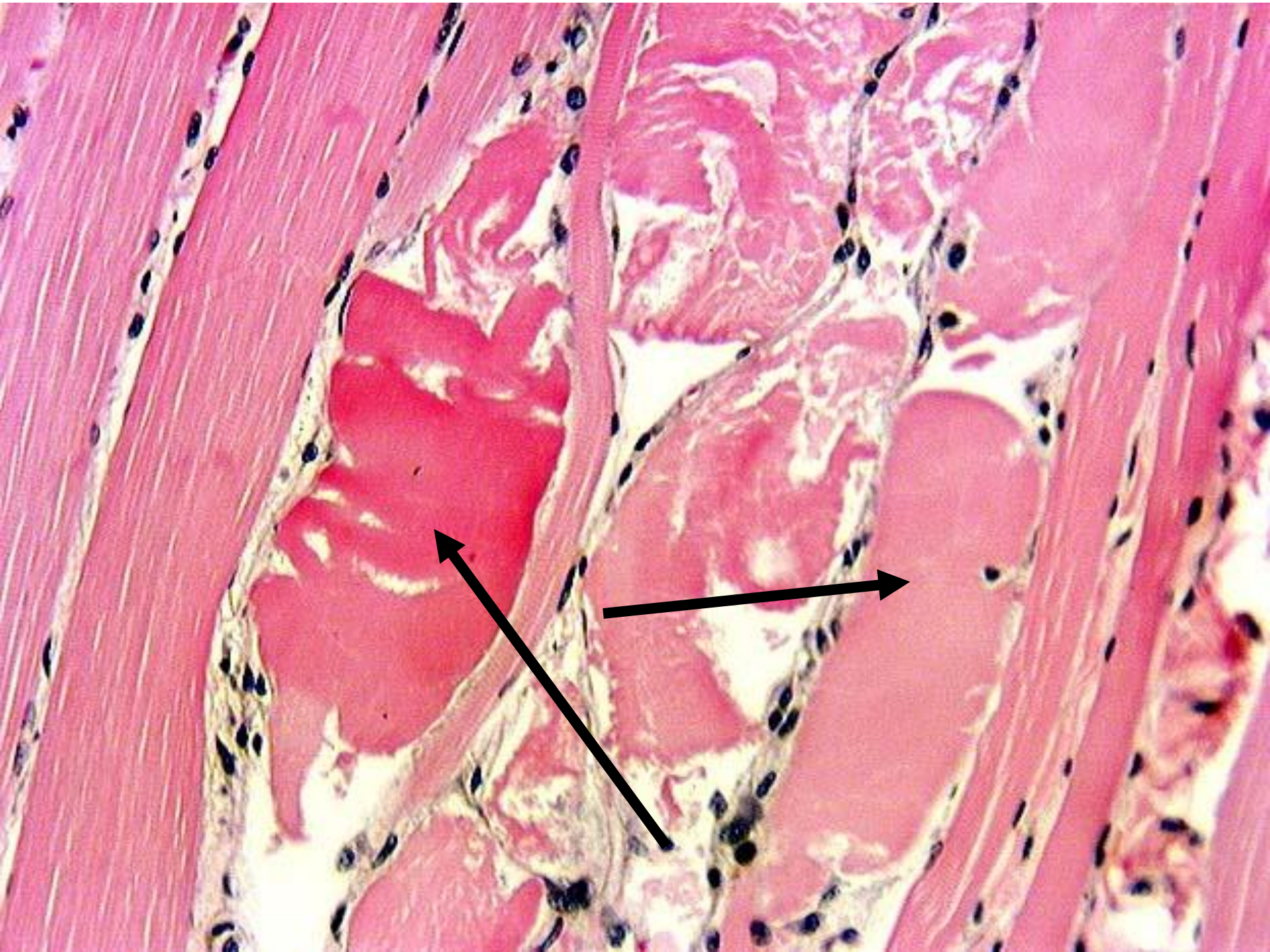
GENERAL Reactions

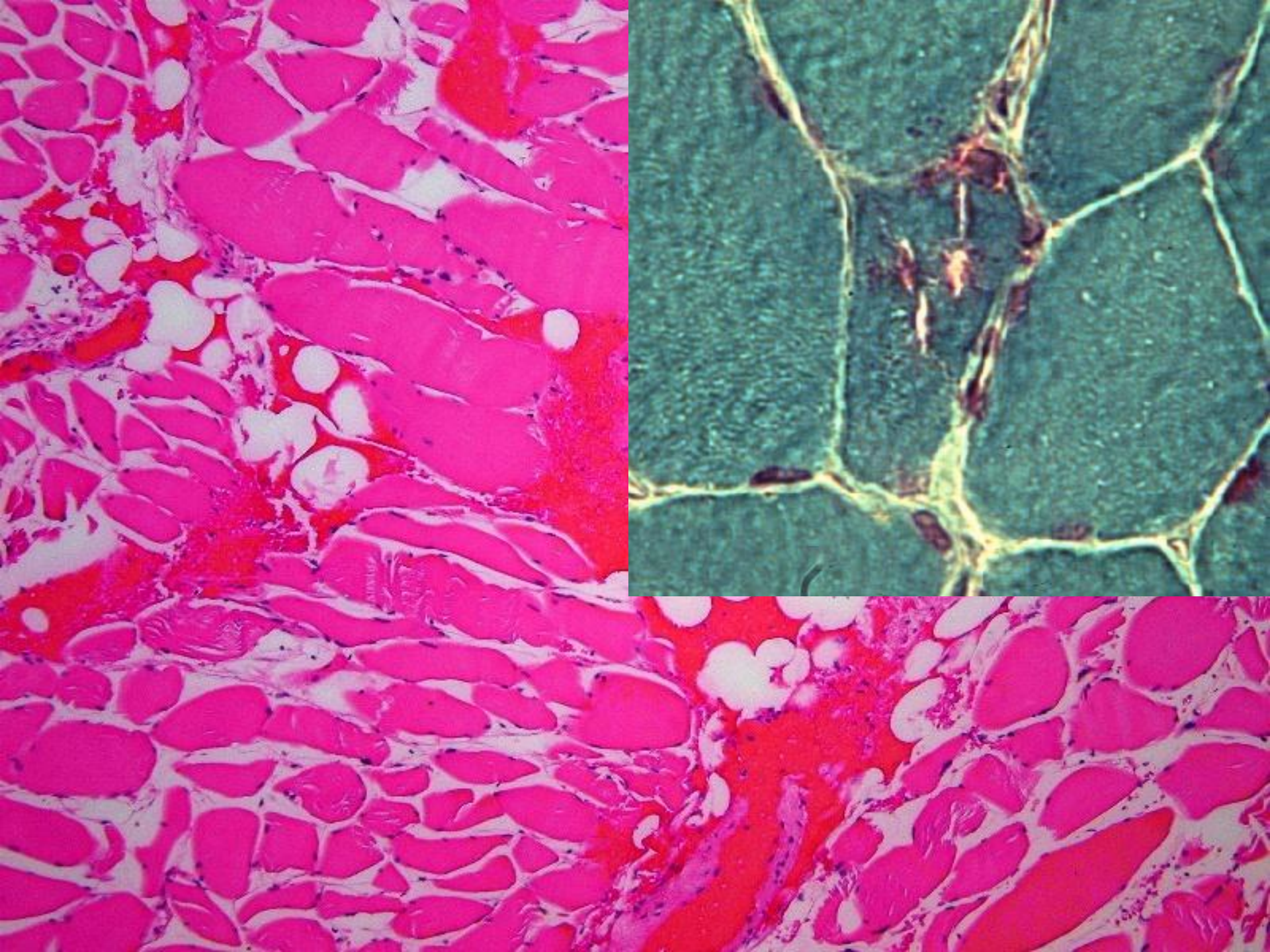
- **NERVE**
  - DEMYELINATION (segmental)
  - AXONAL DEGENERATION
  - NERVE REGENERATION
  - REINNERVATION
- **MUSCLE FIBER**
  - NECROSIS
  - VACUOLIZATION
  - REGENERATION
  - ATROPHY
  - HYPERTROPHY

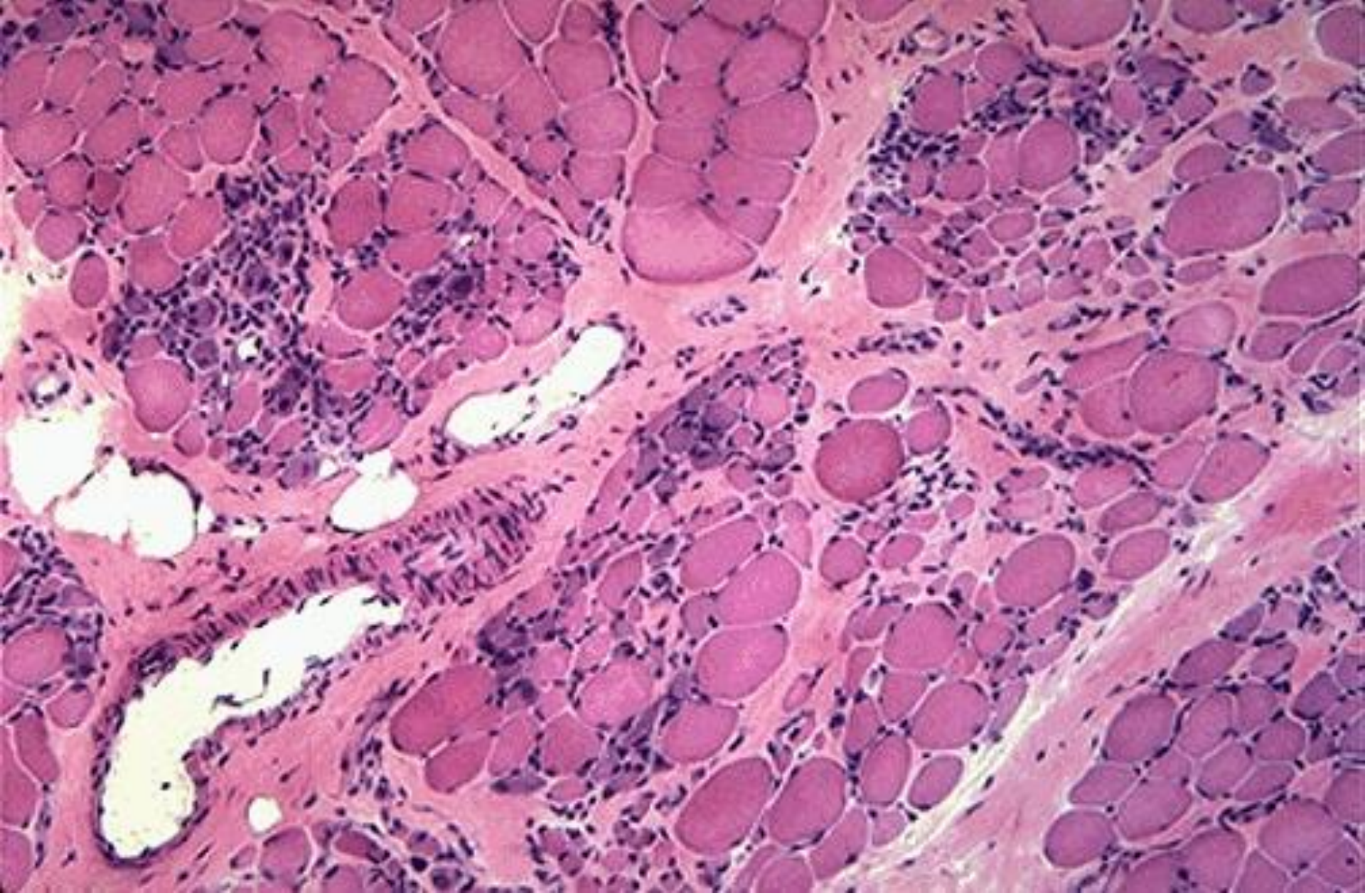

Normal motor units
Segmental demyelination
Axonal degeneration
Reinnervation
Myopathy
Neurons
Myelin
Axon
Myocytes

Histopathology Spinal cord--Multiple sclerosis









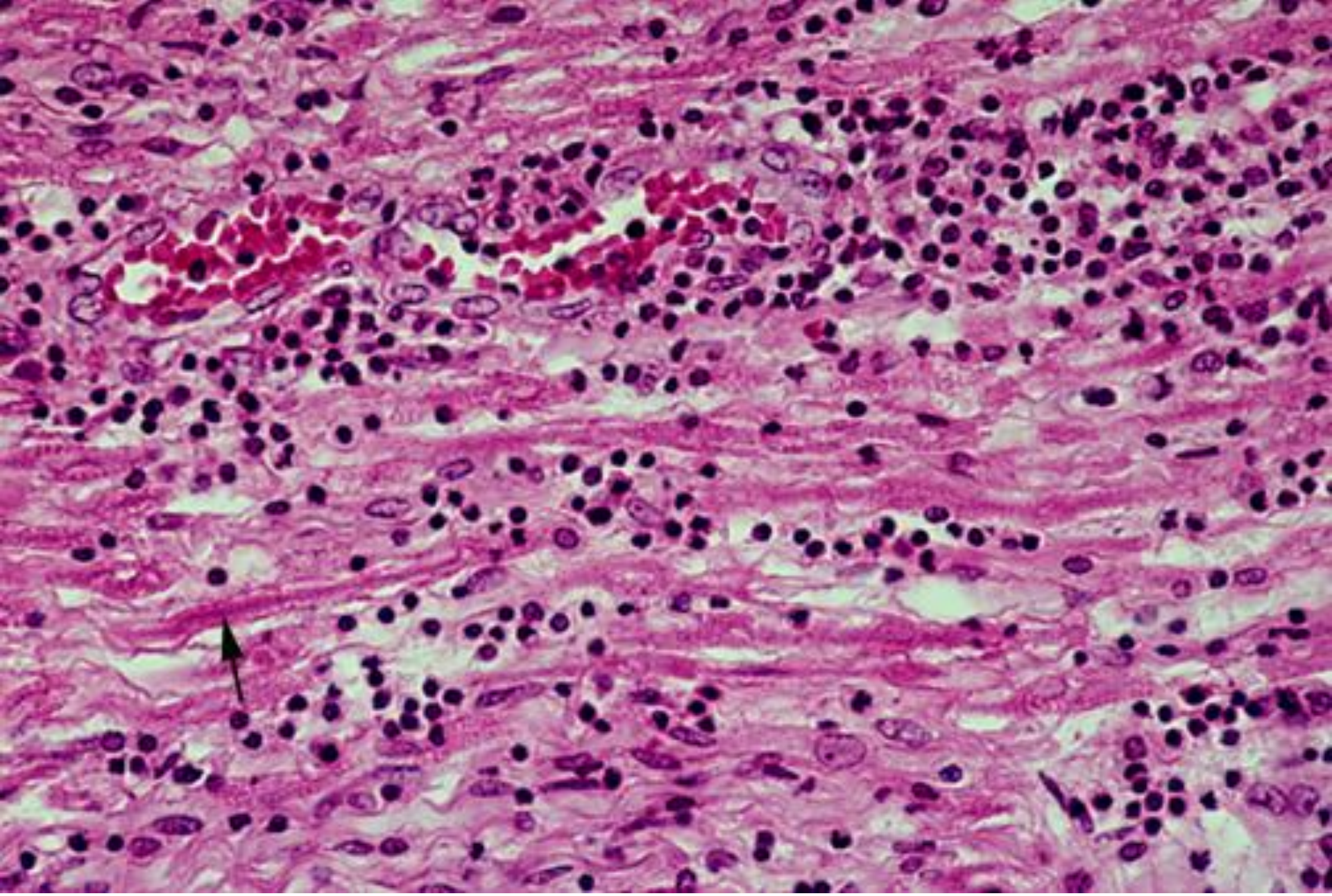
HYPERTROPHY, ATROPHY

NEUROPATHIES, MYOPATHIES

- **NEUROPATHIES (7)**
  - Inflammatory
  - Infectious
  - Hereditary (HMSN-I HMSN-II, HMSN-III)
  - Acquired Toxic/Metabolic
  - Traumatic
  - Neoplasms
- **MYOPATHIES (9)**
  - Denervation
  - Dystrophies
  - Ion Channel
  - Congenital
  - Genetic Metabolic
  - Inflammatory
  - Toxic
  - NeuroMuscular Junction
  - Neoplasms

NEUROPATHY, Inflammatory

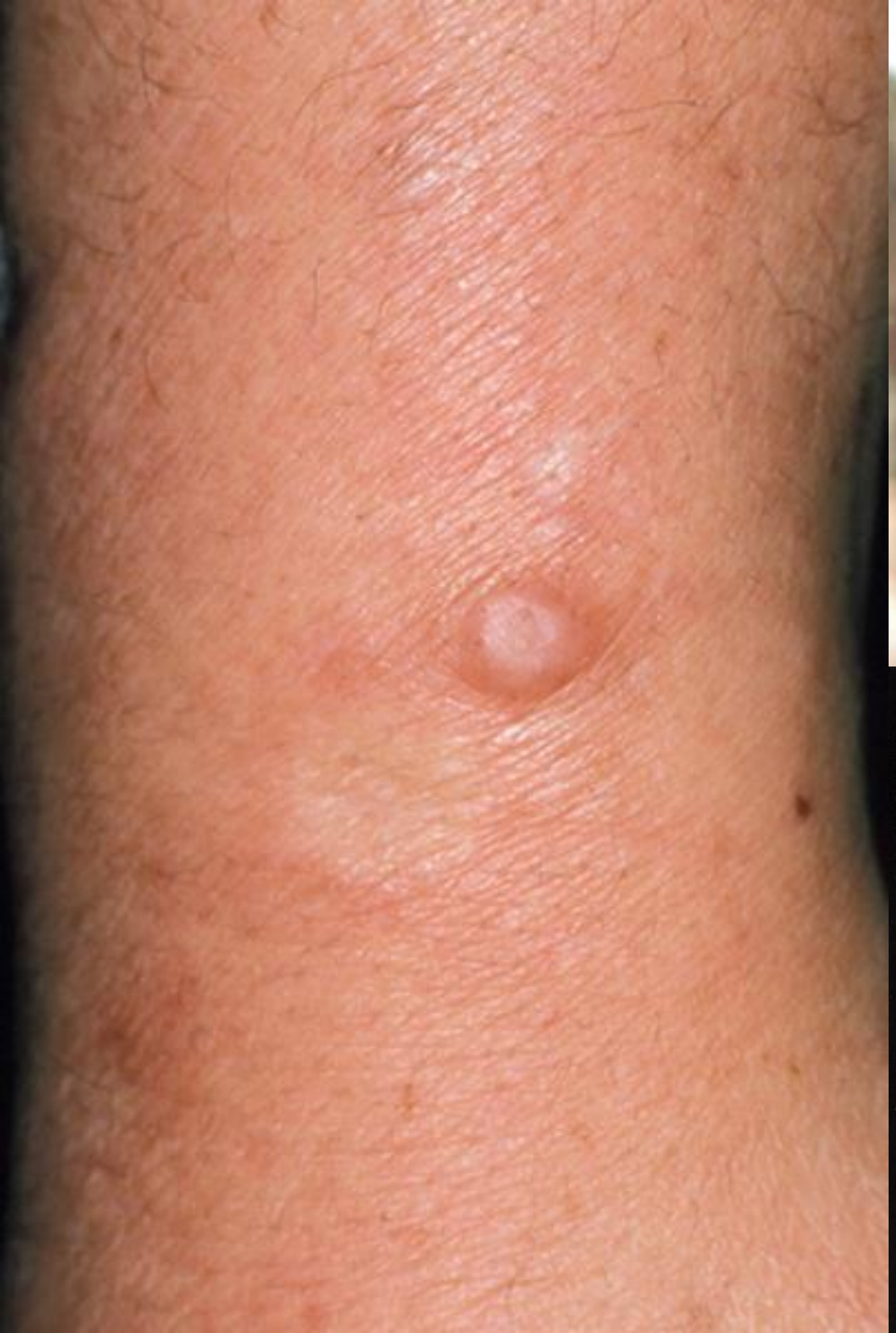
- **Guillain-Barré**
  - Preceded by “influenza”-like illness
  - NO actual specific etiologic agent isolated, autoimmune disease to myelin gangliosides most likely
  - Inflammation of a peripheral nerve
  - DEMYELINATION
  - “ASCENDING*” paralysis (*LOWER extremities before UPPER extremities)

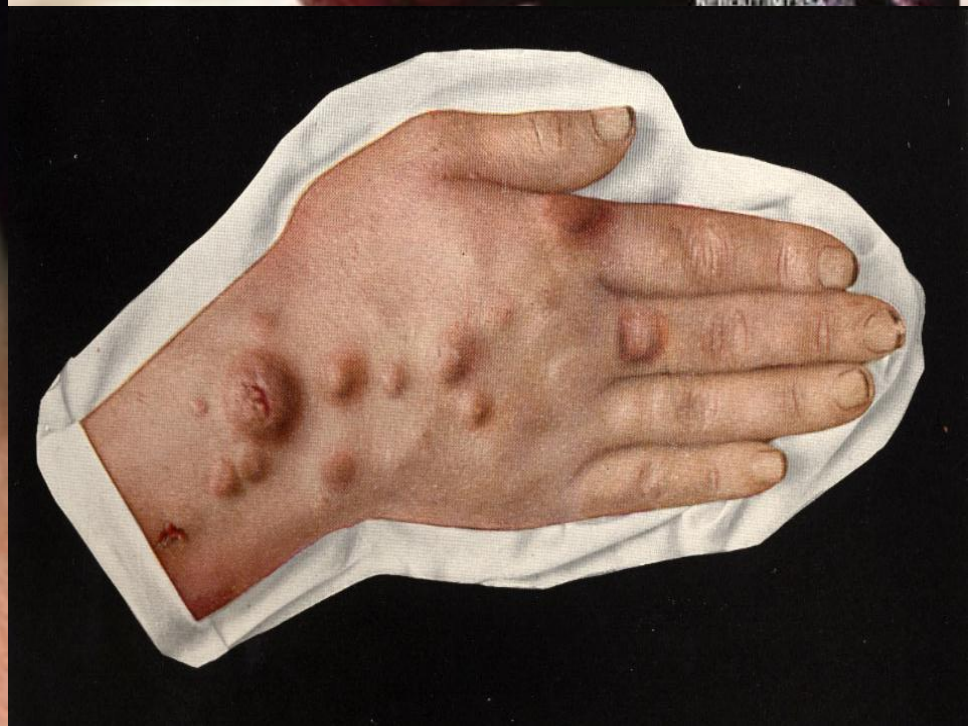


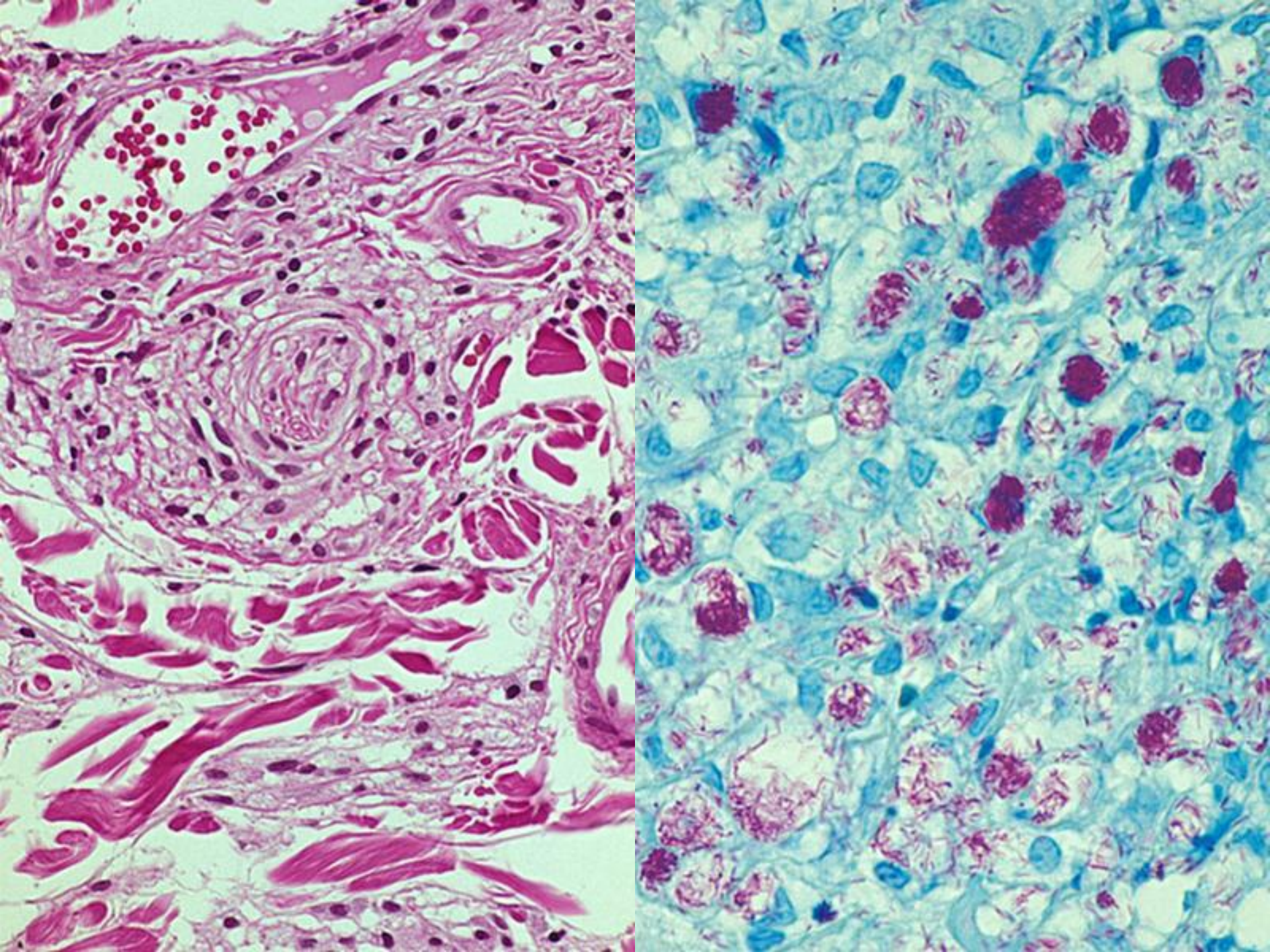
Guillain-Barré, (AIDP), Acute Inflammatory Demyelinating Polyneuropathy

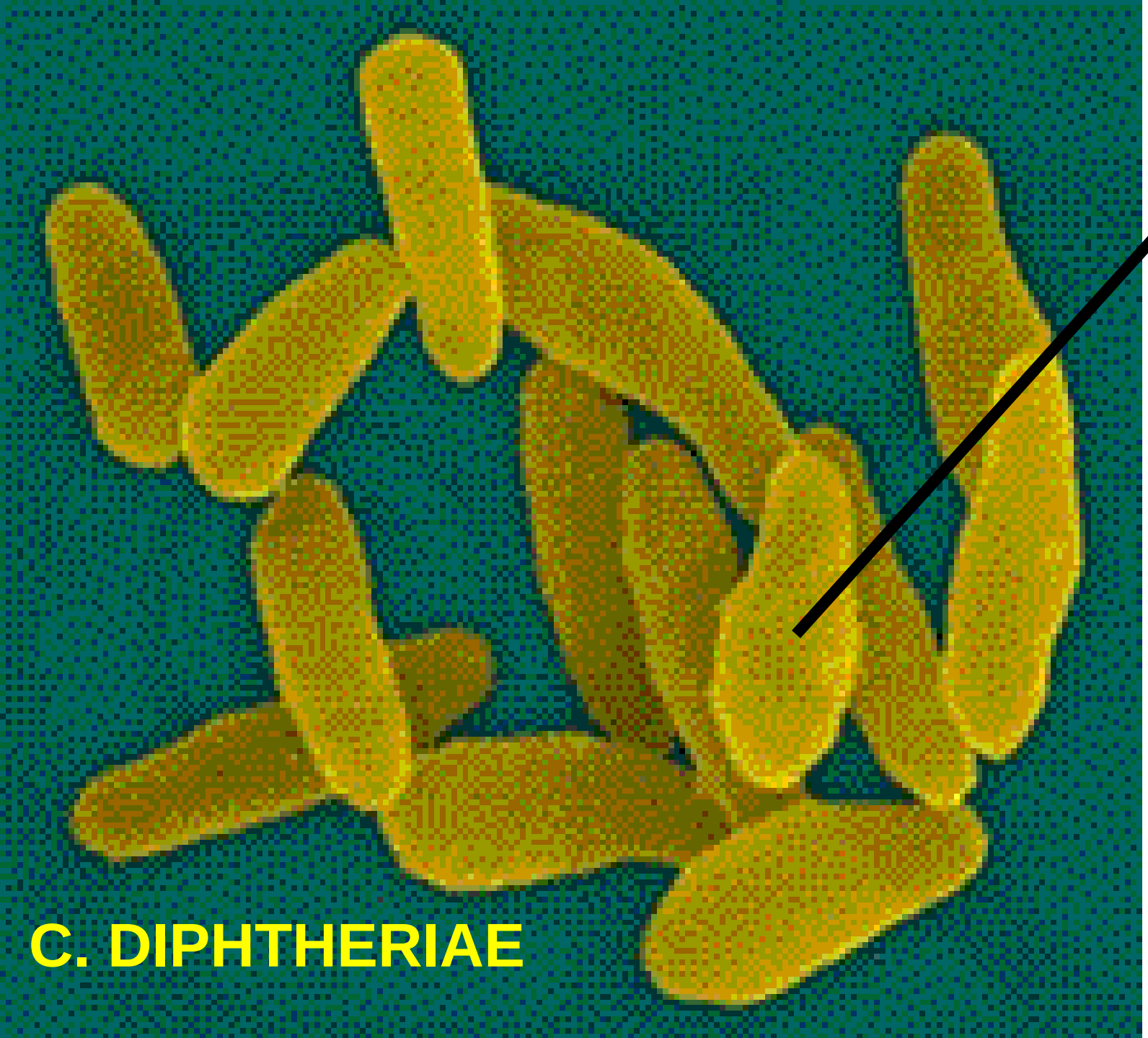
NEUROPATHY, Infectious

- Leprosy
- Diphtheria
- V/Z (Varicella-Zoster)

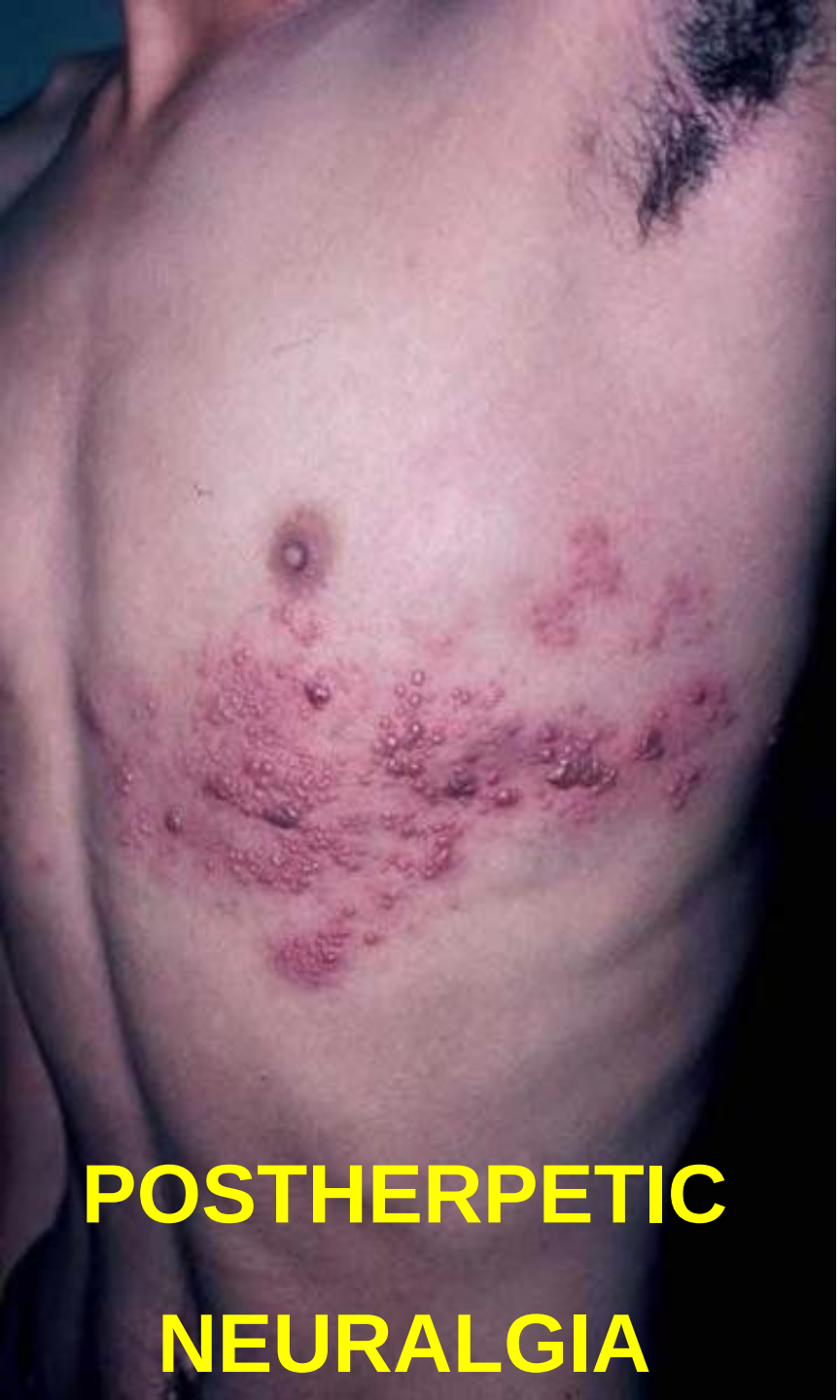






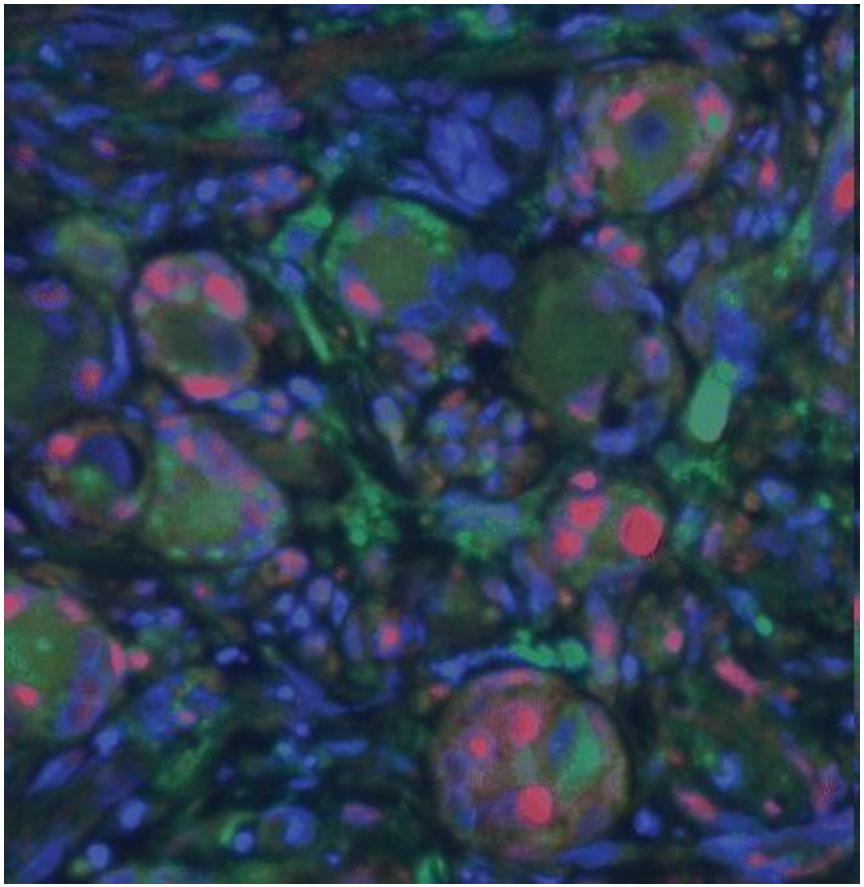


NEUROTOXIN



POSTHERPETIC

NEURALGIA



ZOSTER in DRG

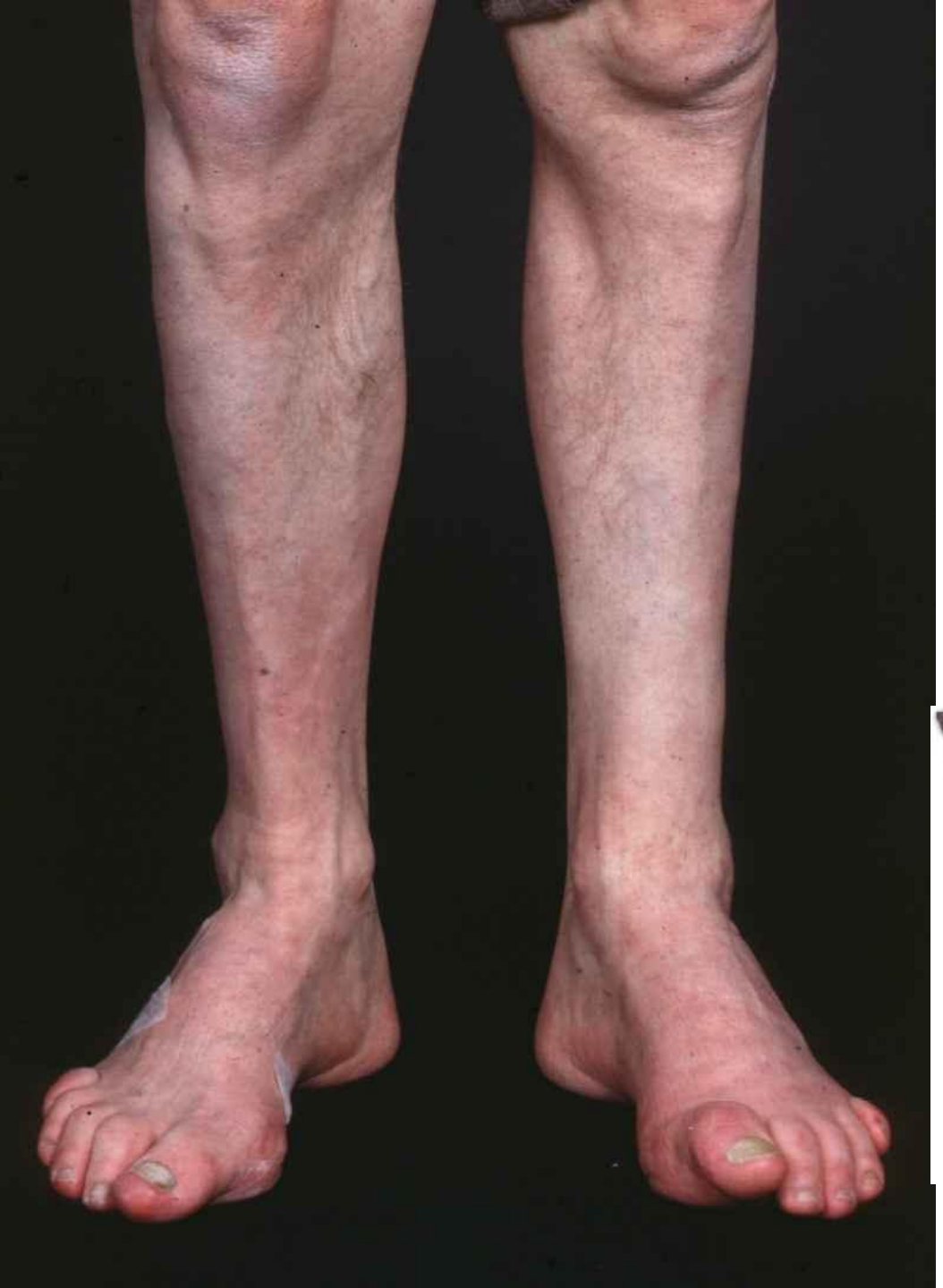
ZOSTER

NEUROPATHY, Hereditary (defective myelination)

(Hereditary Motor and Sensory Neuropathy)

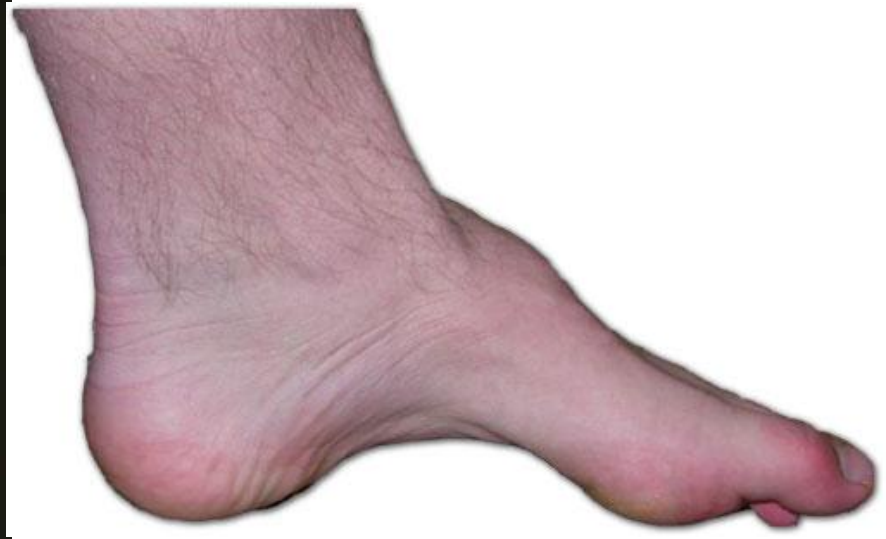
- **HMSN-I (Charcot-Marie-Tooth,**

  duplication of large region of Chromosome #17, p12 region, 80% of time!)
- **HMSN-II (Like CMT of the neurons)**
- **HMSN-III (Palpable Nerves) (aka, Dejerine-Sottas)**



PES CAVUM(S),

in CMT



NEUROPATHY,
Toxic/Metabolic

Symmetric, Asymmetric

Sensory, Sensorimotor

Somatic, Autonomic

Focal, Multifocal

(Adjectives of neuropathy in general!)

NEUROPATHY,
Toxic/Metabolic

Diabetes Mellitus

Vitamin Deficiencies (many Bs, E)

Heavy Metals, Pb, As, etc.

Organic Compounds

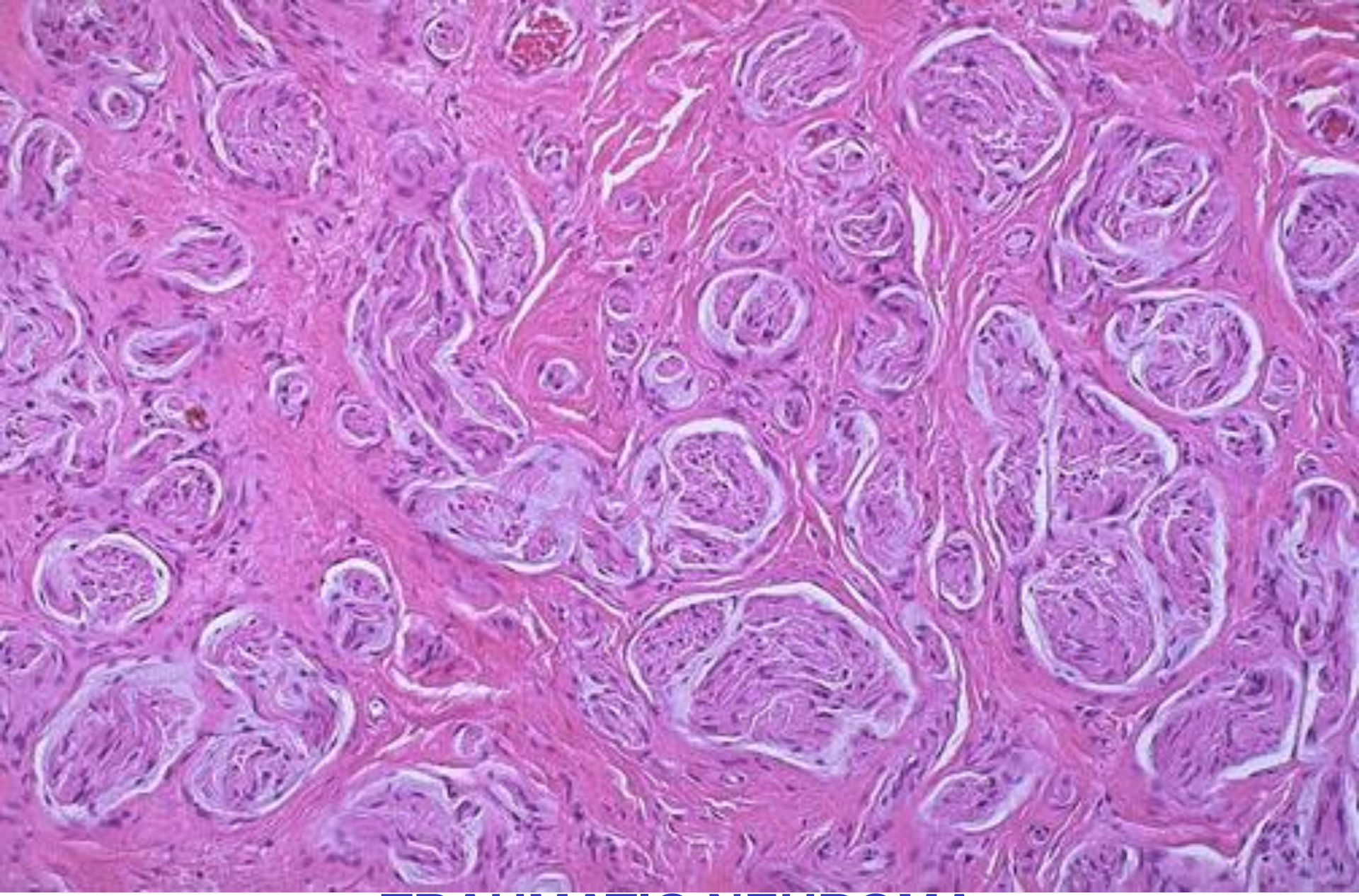
CHEMO

A diabetic ulcer is JUST AS MUCH related to NEUROPATHY as ISCHEMIA!!!

DEMYELINATION

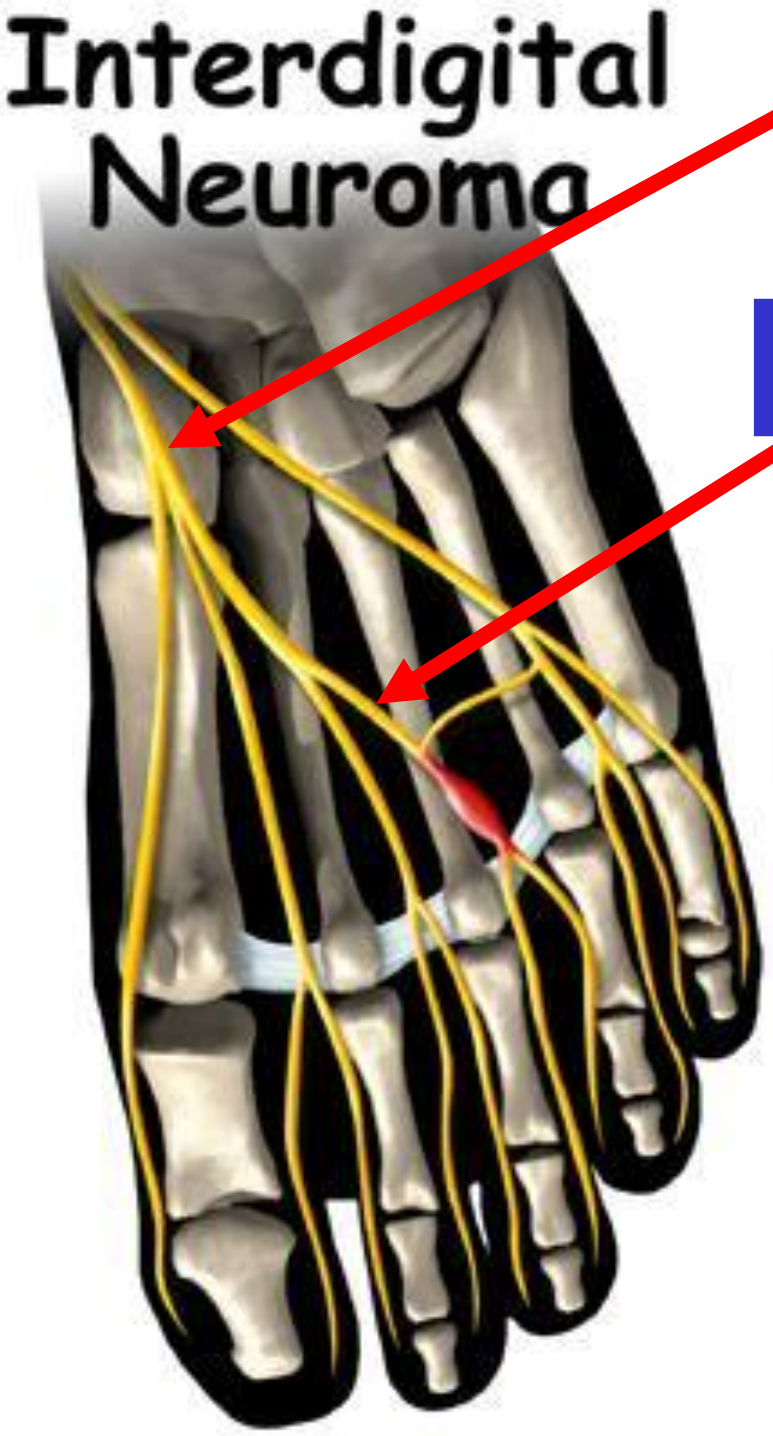
NEUROPATHY, Traumatic

- **Laceration** regeneration rate = 1mm/day or 1 in/mo.
- **Avulsion**
- **Carpal Tunnel**
- **Traumatic (amputation) “Neuroma”**
- **“Saturday Night” Palsy (radial n.)**
- **Morton “Neuroma”**



TRAUMATIC NEUROMA

“Regenerating Axons and Glia (Schwann Cells), but with no direction”



MEDIAL Plantar Nerve

3rd COMMON digital branch
of MEDIAL plantar nerve

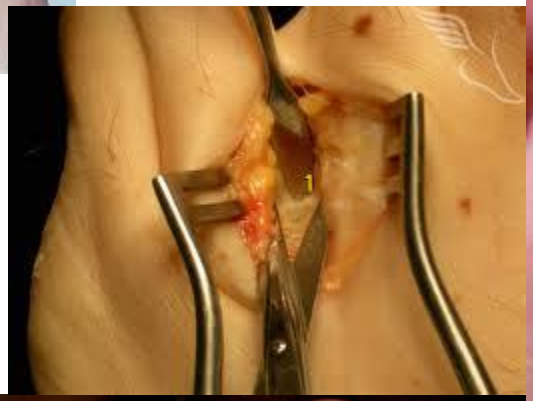
MORTON'S NEUROMA

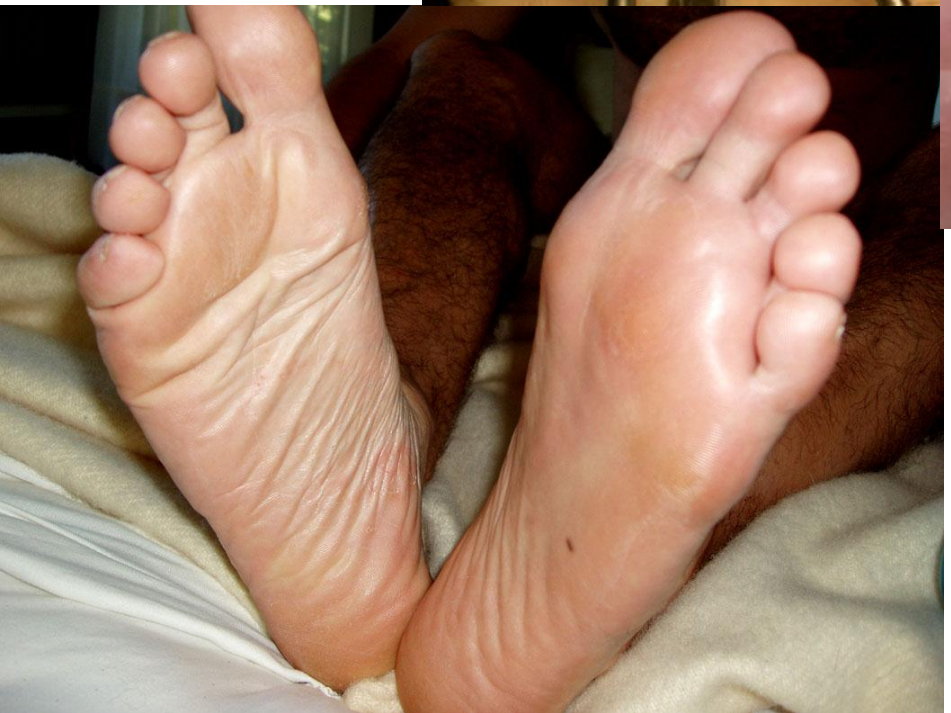
Traumatic Compression

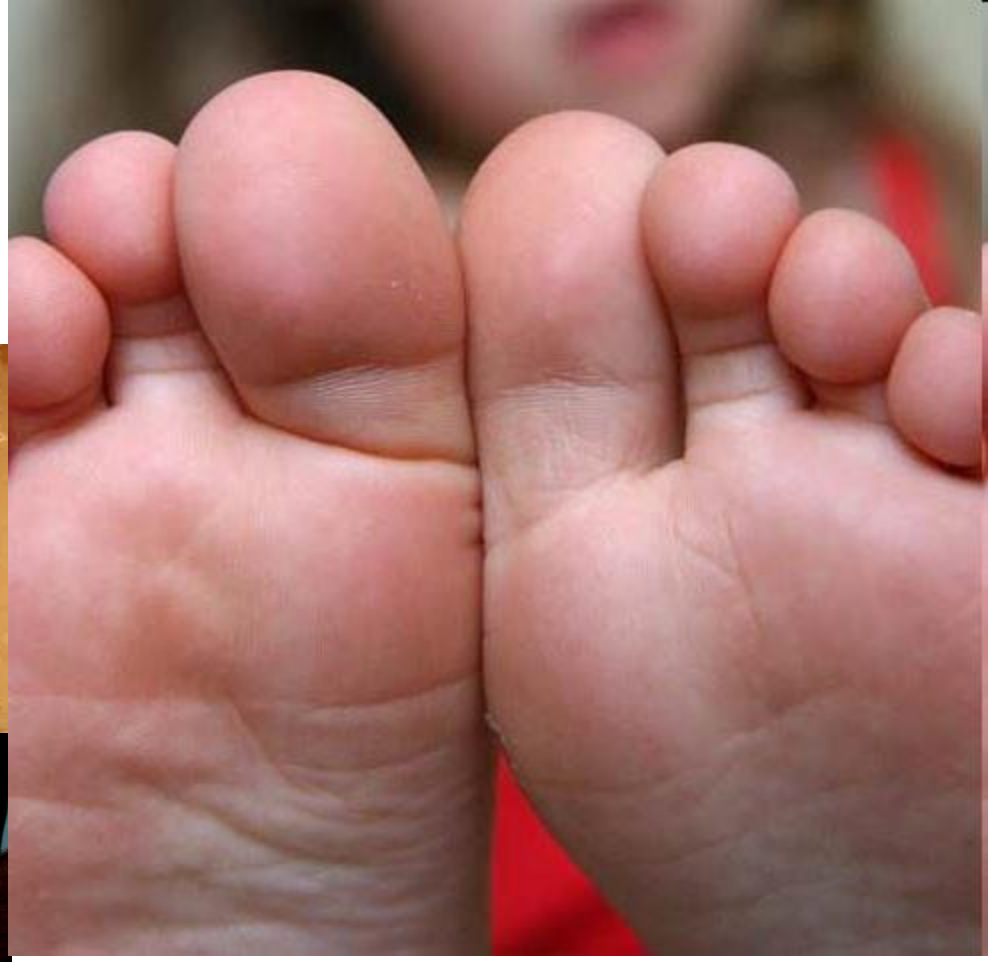
F>M

Interdigital

Intermetatarsal





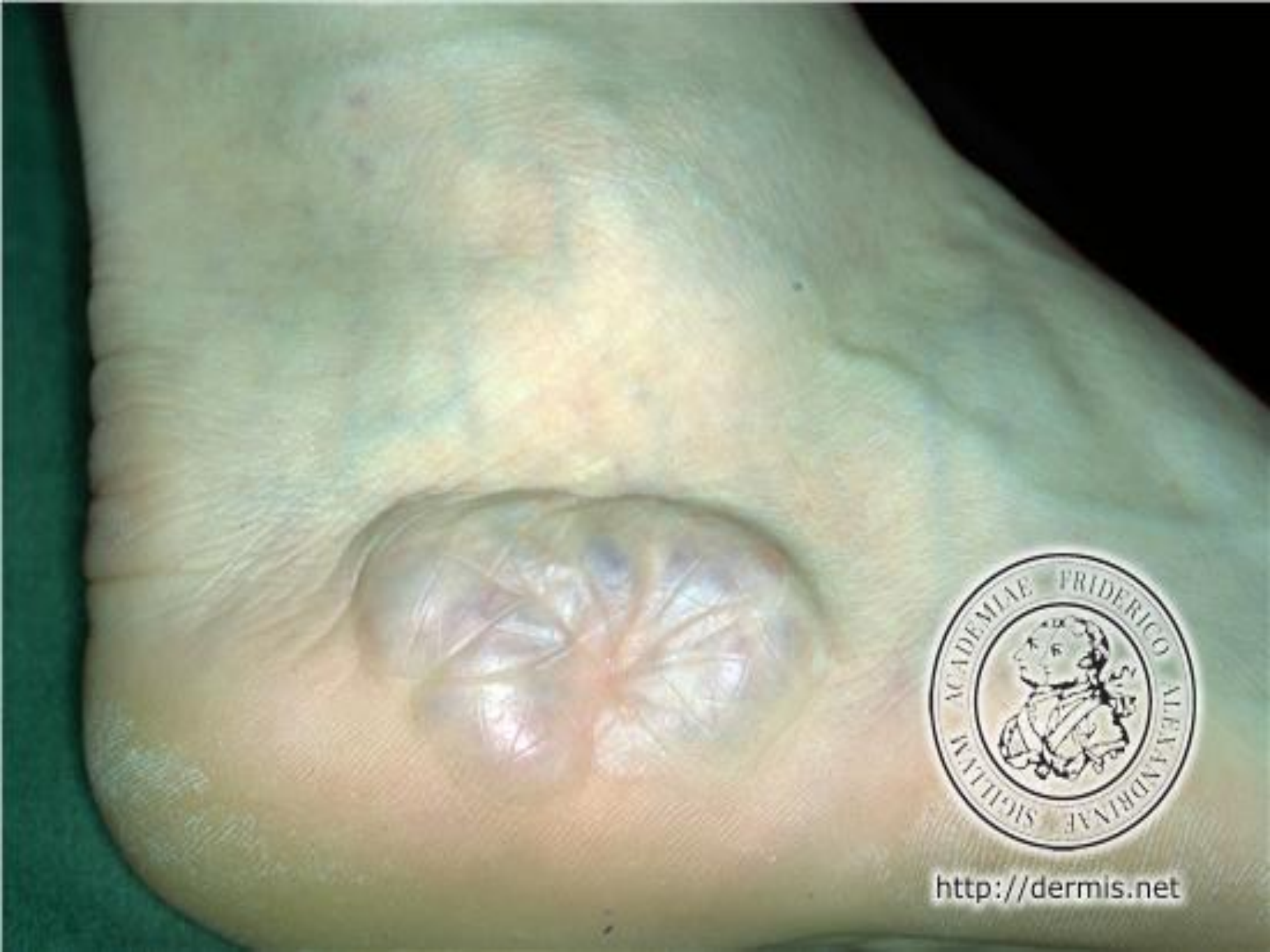


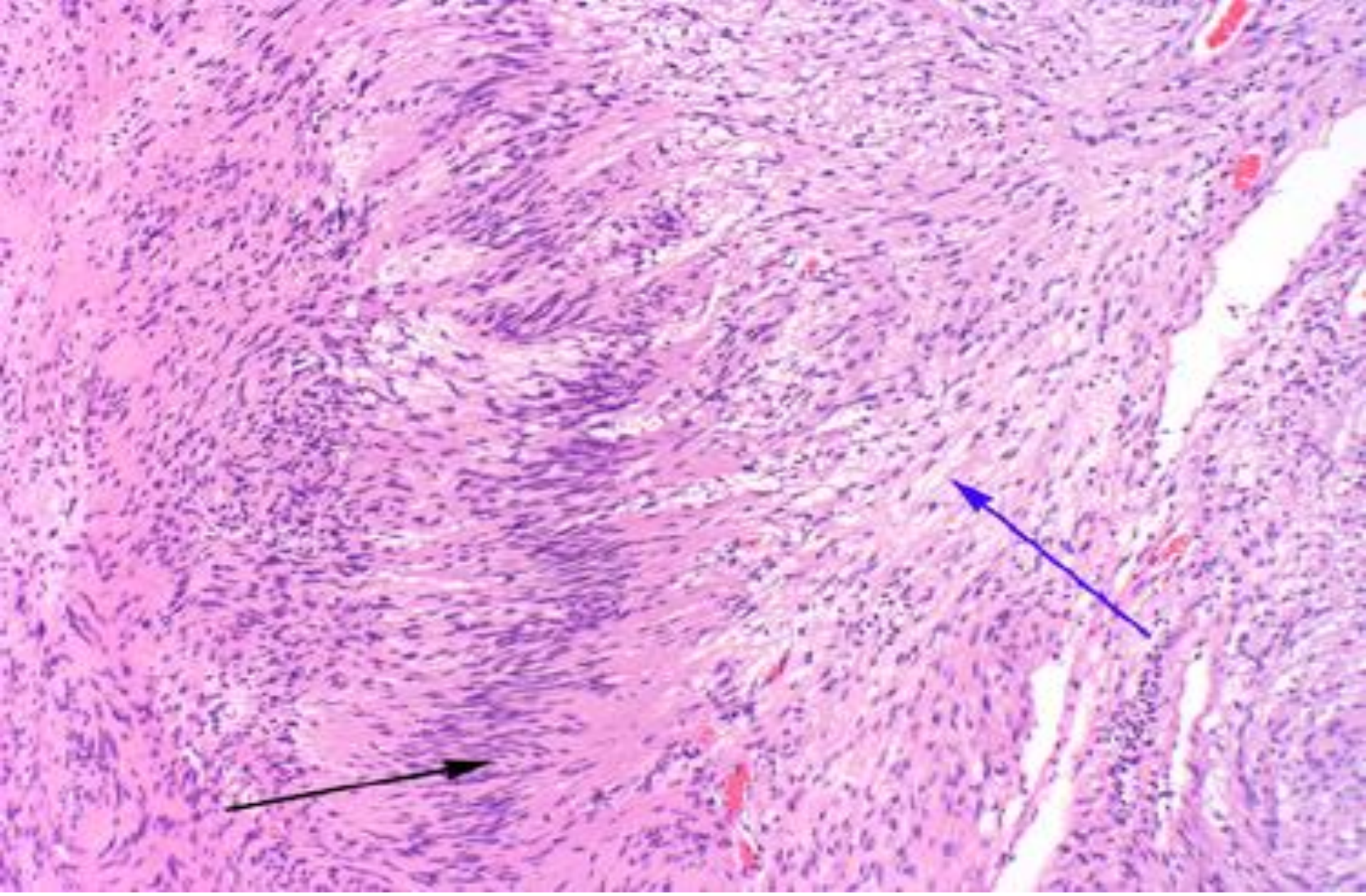
http://www.google.com/search?hl=en&sugexp=gsishc&xhr=t&q=morton's+neuroma&cp=14&bav=on.2,or.r_gc.r_pw.&um=1&ie=UTF-8&tbm=isch&source=og&sa=N&tab=wi&biw=1366&bih=705

NEUROPATHY, Neoplastic

Benign: Schwannoma

Malignant: Malignant Schwannoma

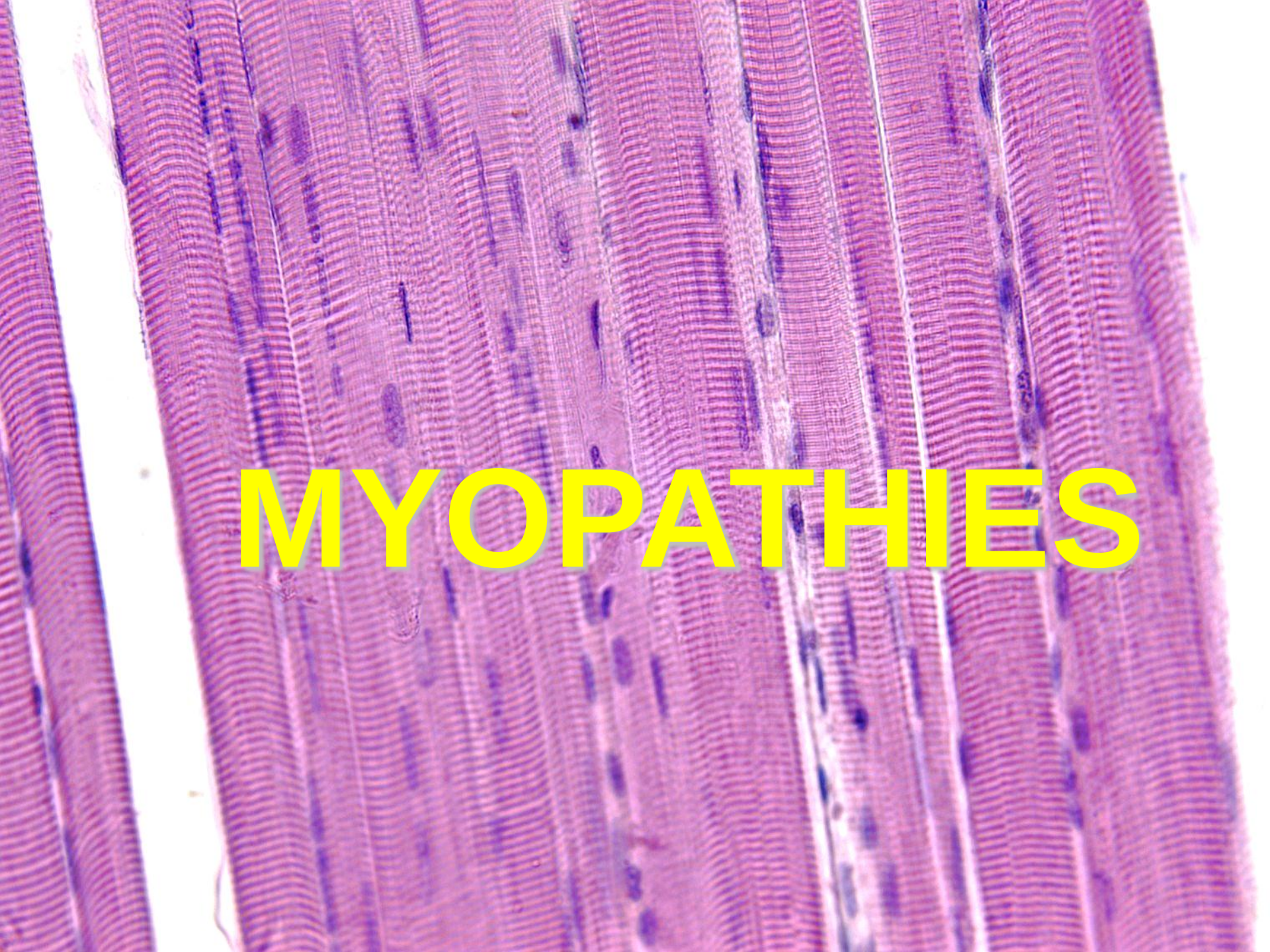

ACADEMIAE FRIDERICO ALEXANDRINAE SICILIAVE
http://dermis.net



Antoni A: “Palisaded” Antoni B: NON-Palisaded

QUIZ:

- Why are Schwannomas the ONLY tumors of peripheral nerve?


MYOPATHIES

NEUROPATHIES, MYOPATHIES

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  - Inflammatory
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  - Hereditary (HMSN-I)
  - HMSN-II, HMSN-III
  - Acquired Toxic/Metabolic
  - Traumatic
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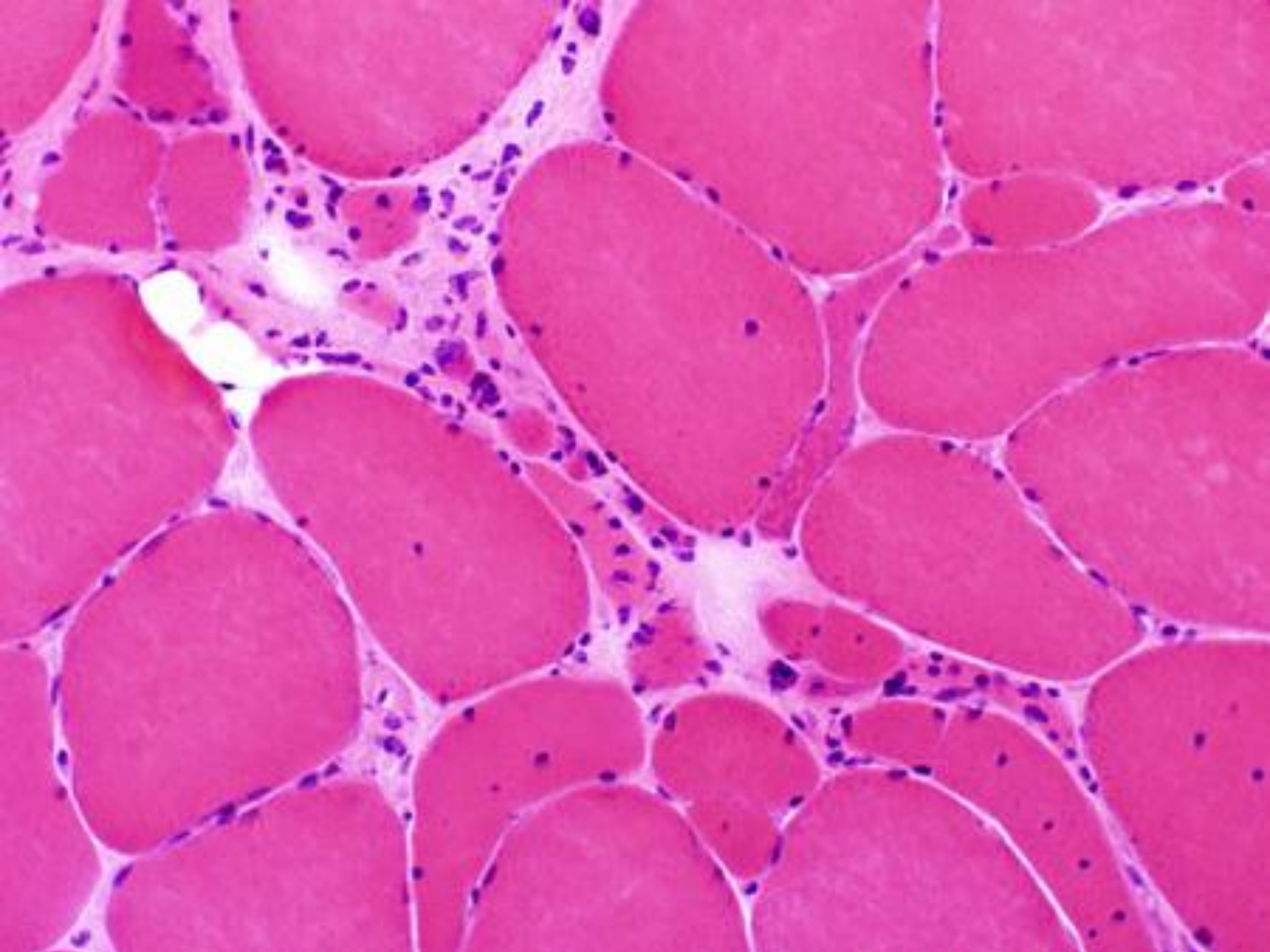
- **MYOPATHIES (9)**
  - Denervation (SMA)
  - Dystrophies
  - Ion Channel
  - Congenital
  - Genetic Metabolic
  - Inflammatory
  - Toxic
  - NeuroMuscular Junction
  - Neoplasms

MYOPATHY, Denervation

MUSCLE FIBERS **CANNOT** SURVIVE UNLESS THEY ARE INNERVATED

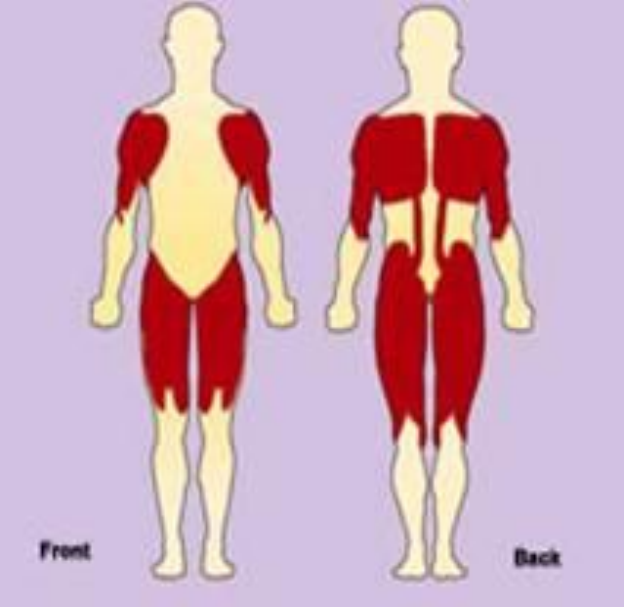
PERIPHERAL NERVE PATHOLOGY

ANTERIOR (ventral) HORN CELL PATHOLOGY



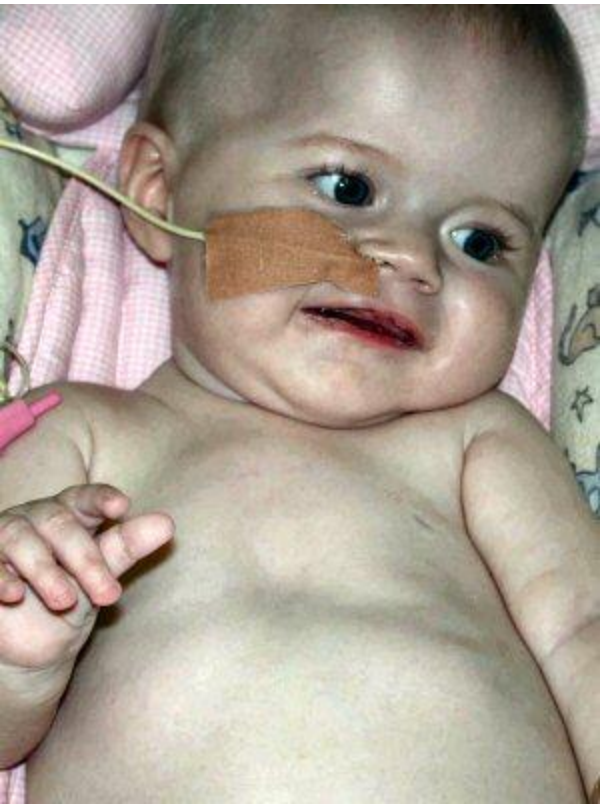
SPINAL MUSCULAR ATROPHY

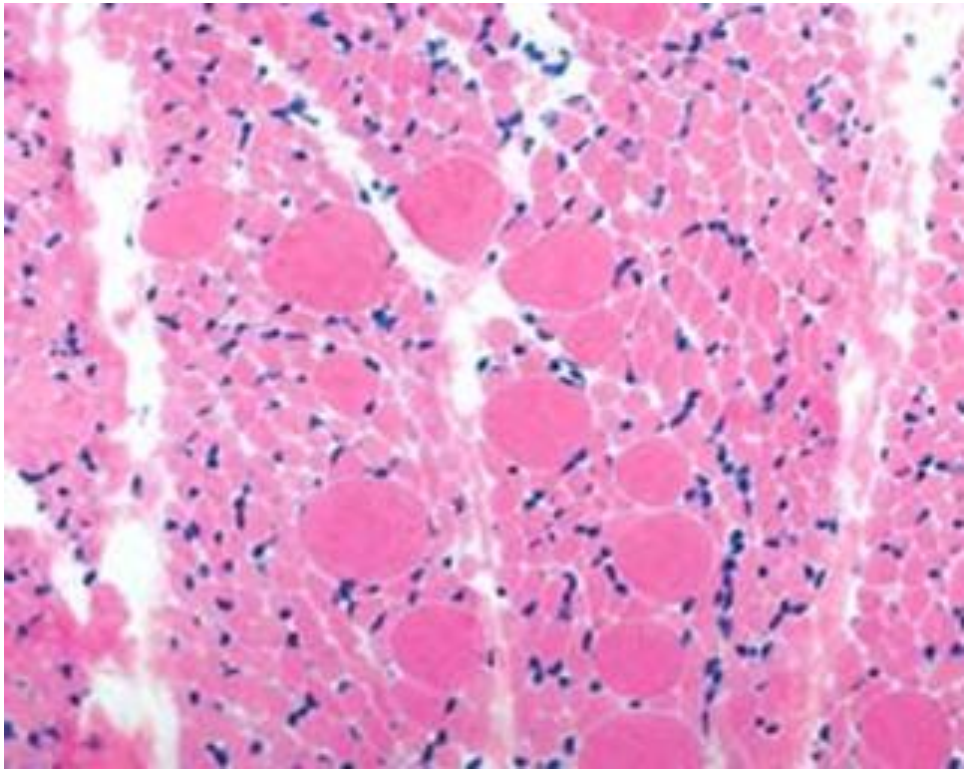
- **Childhood diseases**
- **Chromosome #5 that harbors the survival motor neuron gene (*SMN1*)**
- **Anterior Horn Cells**
- **Often PAN-fascicular**
- **Shoulder, hip muscles**



Madison Reed

Devon Stants

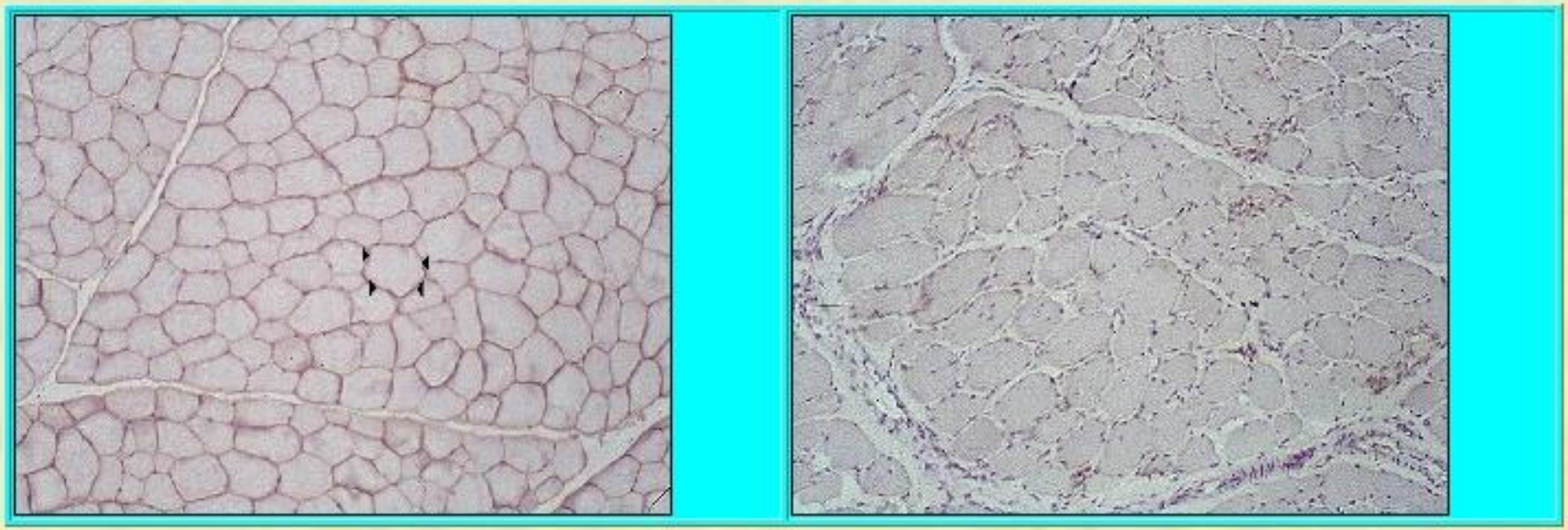




MYOPATHY, "Dystrophic"

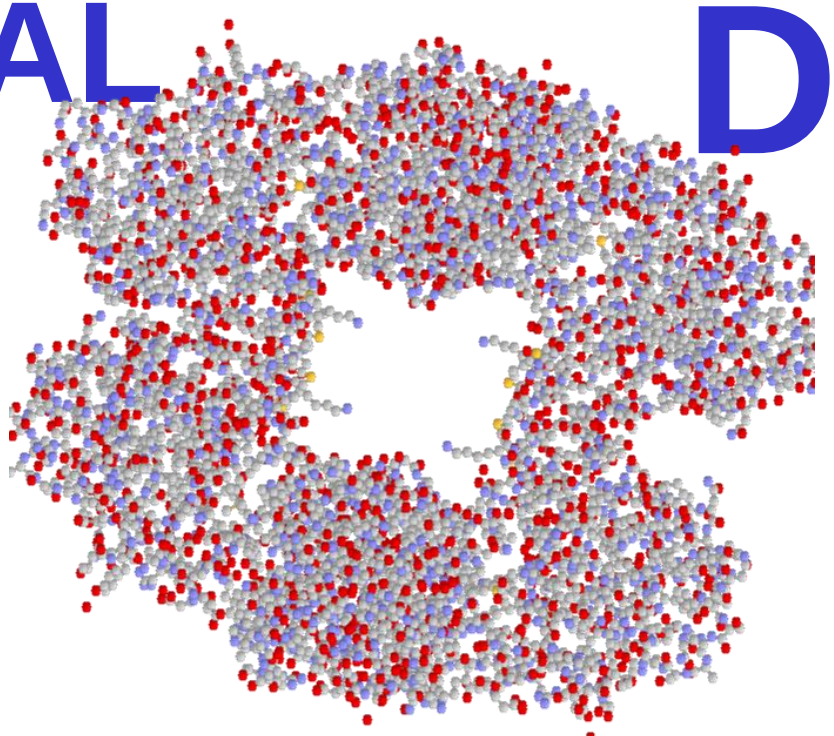
- Jerry's kids, no "DYSTROPHIN"
- **DUCHENNE (DMD)**, x-linked
- **BECKER (BMD)** (less common, less severe, same chromosome)
- Many others also, all of which have complex genetic patterns which have all been precisely defined
- **MYOTONIA*** is a common feature

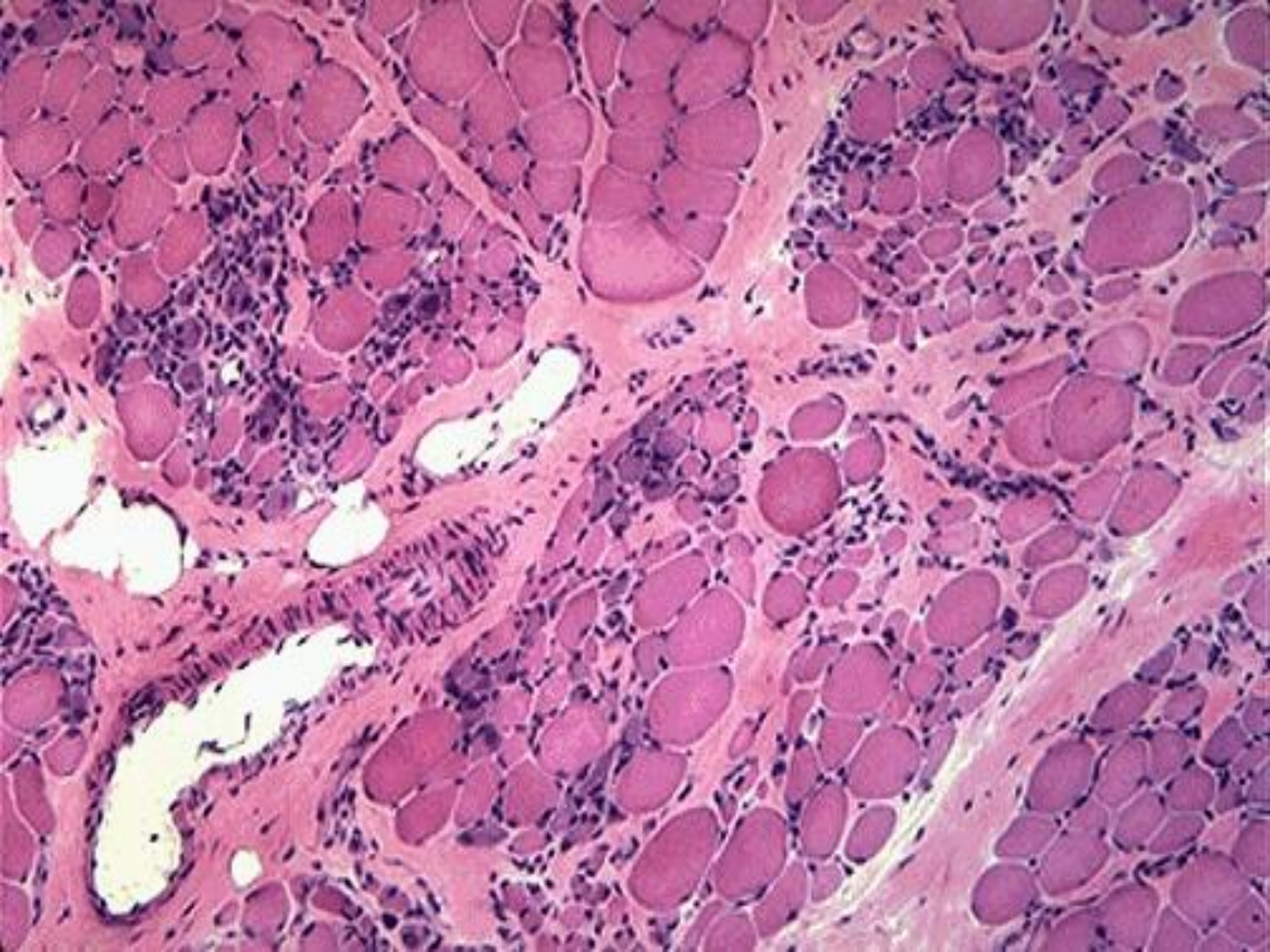
*spasm,rigid

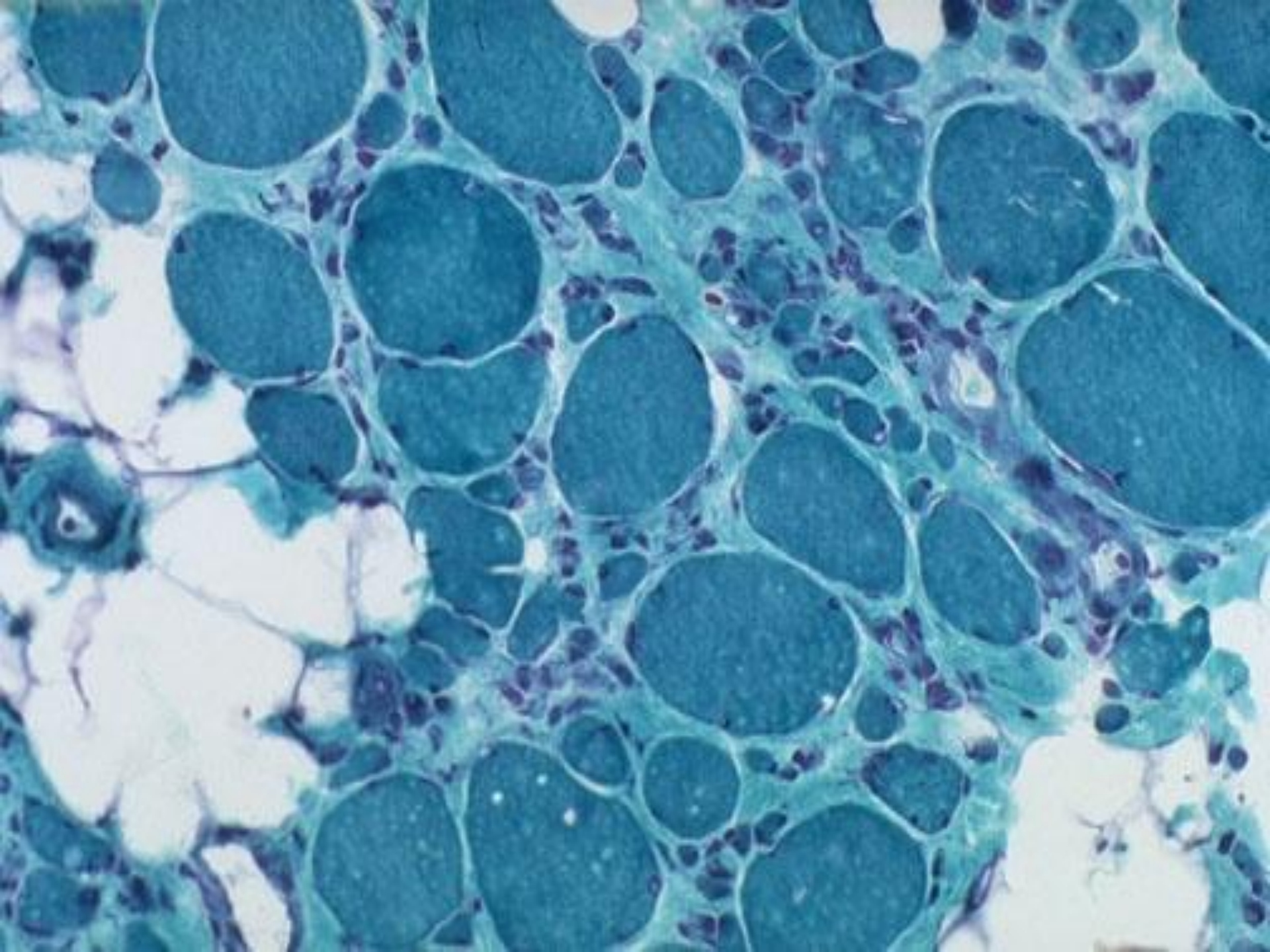


NORMAL

DMD





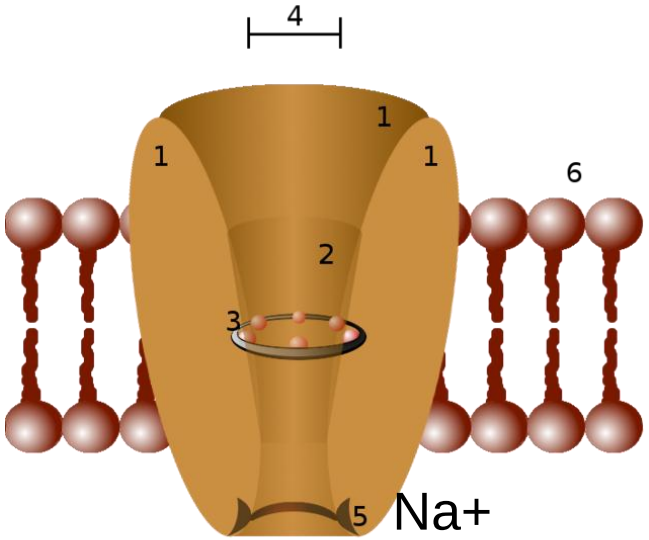


Limb Girdle Muscular Dystrophies

	Inheritance	Locus	Gene	Clinicopathologic Features
1A	Autosomal-dominant	5q31	Myotilin	Onset in adult life with slow progression of limb weakness, but sparing of facial muscles; dysarthric speech
1B	Autosomal-dominant	1q21	Lamin A/C	Onset before the age of 20 years in lower limbs, progression during many years with cardiac involvement
1C	Autosomal-dominant	3p25	Caveolin-3 (M-caveolin)	Onset before the age of 20, clinically similar to type 1B
1D	Autosomal-dominant	7p	Unknown	Limb girdle muscle weakness, adult onset
2A	Autosomal-recessive	15q15.1-21.1	Calpain 3	Onset in late childhood to middle age; slow progression during 20–30 years
2B	Autosomal-recessive	2p13.3-q13.1	Dysferlin	Mild clinical course with onset in early adulthood
2C	Autosomal-recessive	13q12	γ-Sarcoglycan	Severe weakness during childhood, rapid progression; dystrophic myopathy on muscle biopsy
2D	Autosomal-recessive	17q21	α-Sarcoglycan (adhalin)	Severe weakness during childhood, rapid progression; dystrophic myopathy on muscle biopsy
2E	Autosomal-recessive	4q12	β-Sarcoglycan	Onset in early childhood, with Duchenne-like clinical course
2F	Autosomal-recessive	5q33	δ-Sarcoglycan	Early onset and severe myopathy; dystrophic myopathy on muscle biopsy
2G	Autosomal-recessive	17q11-q12	Telethonin	Distal weakness with limb-girdle weakness in late childhood to adulthood; rimmed vacuoles in muscle cells
2H	Autosomal-recessive	9q31-q34.1	Tripartite motif-containing protein 32 (TRIM32)	Limb-girdle and facial weakness with onset in childhood, mild, slowly progressive course

MYOPATHY, Ion Channel "Channelopathies"

- **MYOTONIA/HYPOTONIC PARALYSIS**
- **FAMILIAL, (genetic) DISEASES**
- **TRIGGERED BY:**
  - **Exercise**
  - **Cold**
  - **Carb Intake**
- **Classified by K+, ↑K+, ↓K+**
- **MALIGNANT HYPERTHERMIA can be triggered off by anesthetic halogenated inhalation agents in some of these patients!!!**



Na+
K+
Cl^-
Voltage

Cong.
Acq.
Mutations
Ab's

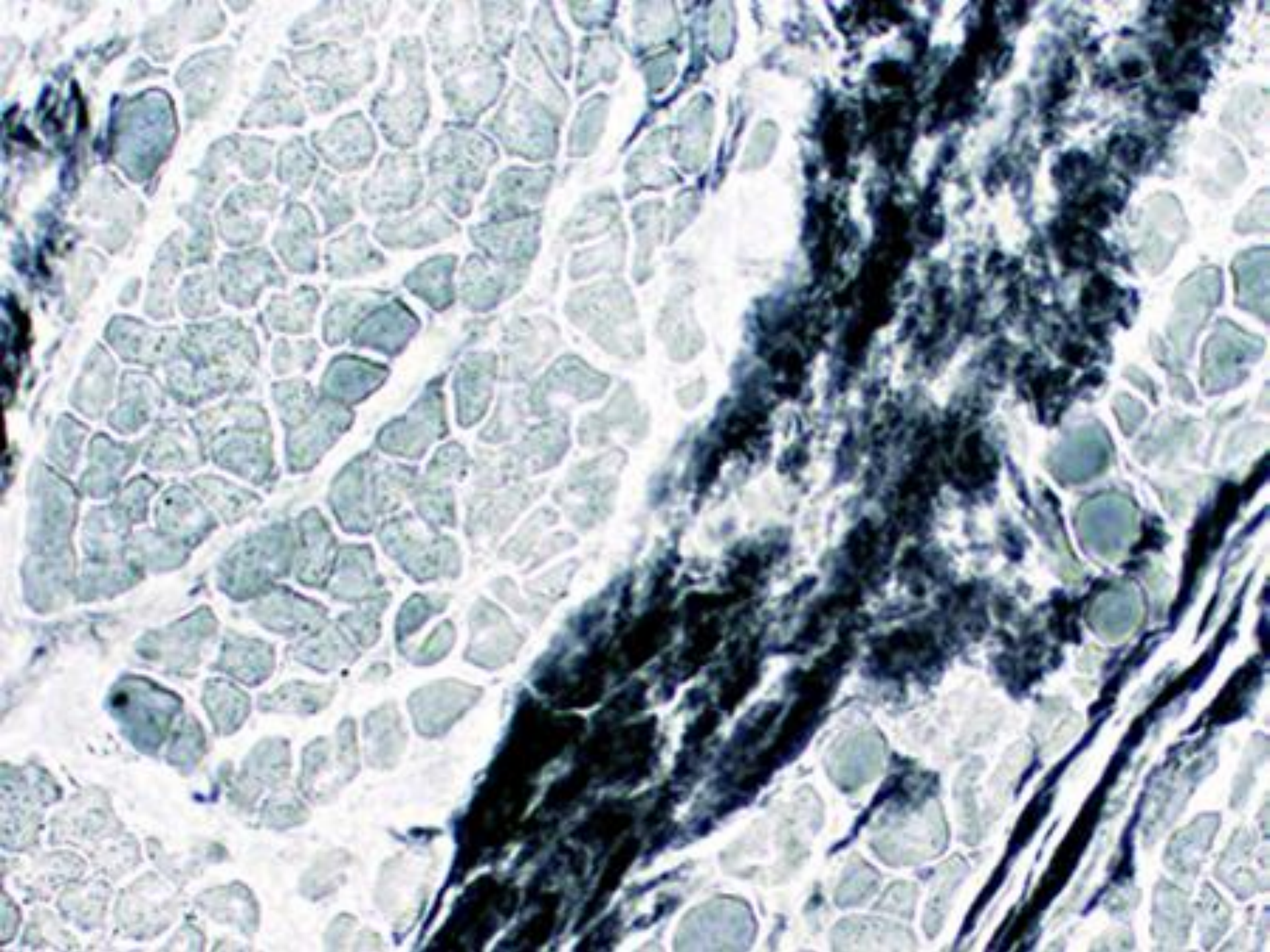
MYOPATHY, Congenital "Floppy Babies"

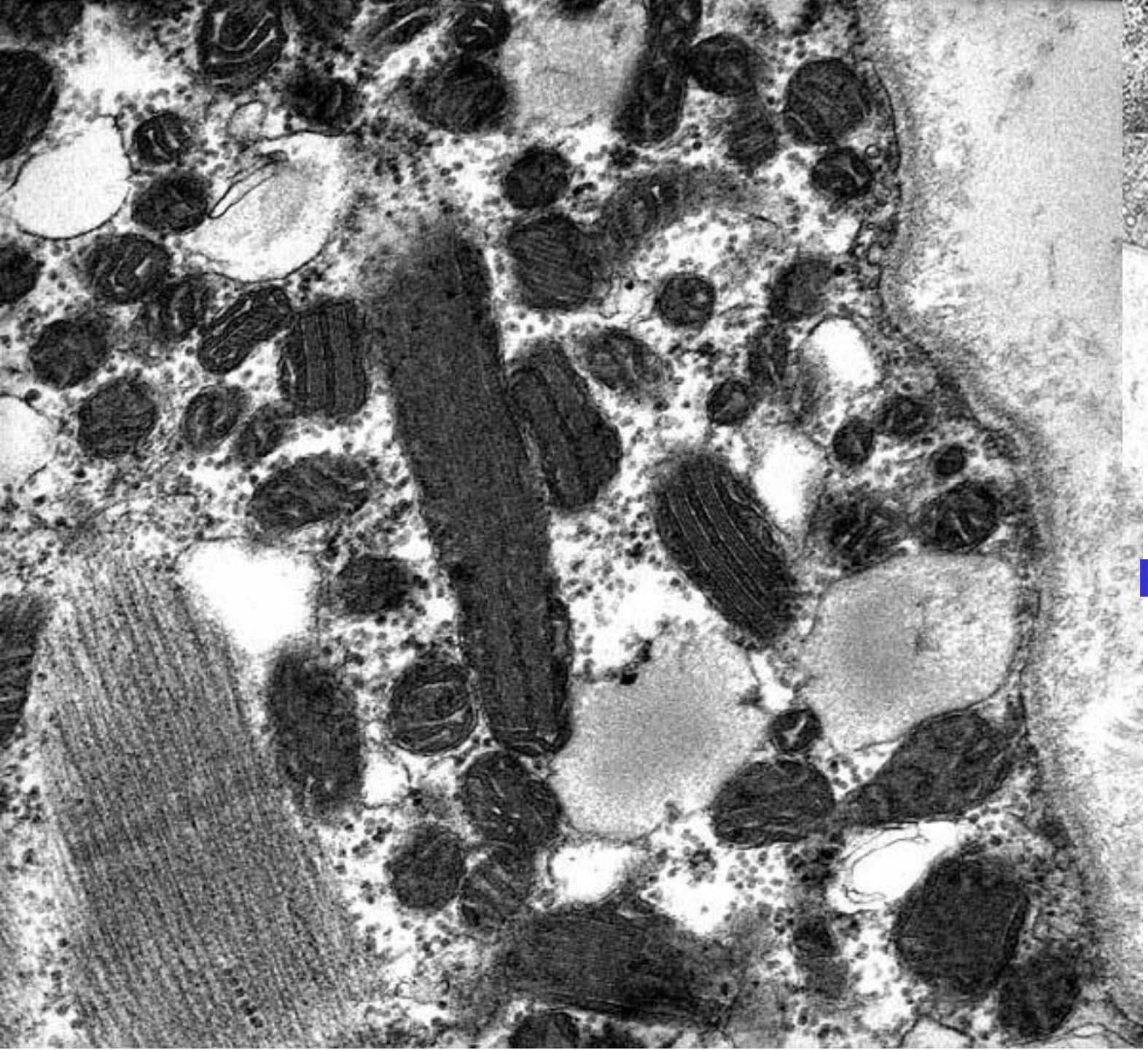
- **HYPOTONIC**
- **FAMILIAL, (genetic) DISEASES**
- **MANY TYPES, in most of which the precise genetic defects have been identified**

MYOPATHY, Metabolic (genetic also)

- **LIPID**
  - **Mitoch. Enz. Def.→ LIPID ACCUMULATION**
- **MITOCHONDRIAL**
  - **"PARKING LOT" mitochondria**

Metabolic myopathies involve **MITOCHONDRIA!**





PARKING

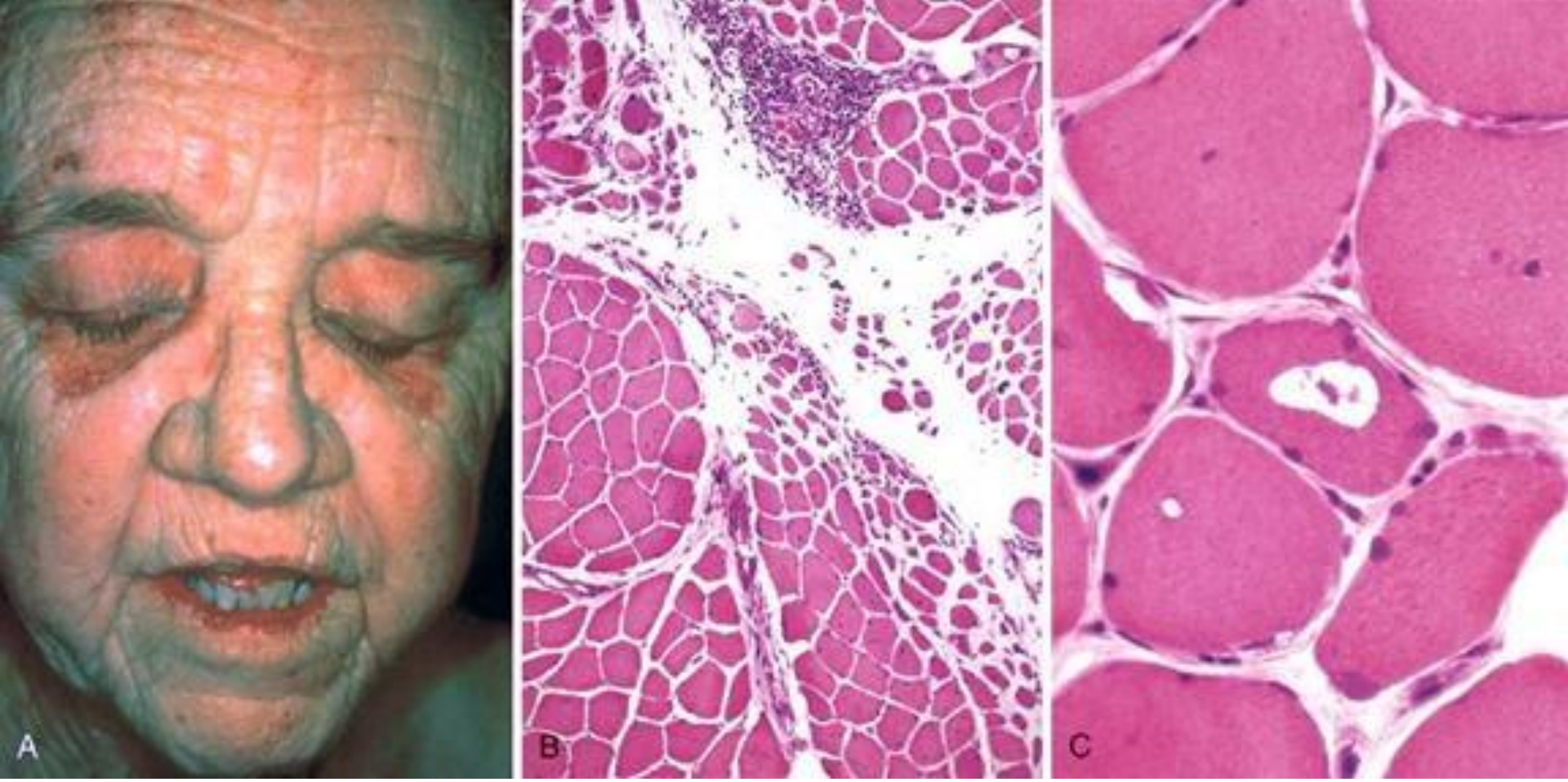
LOT

MITOCH.

MYOPATHY, Inflammatory

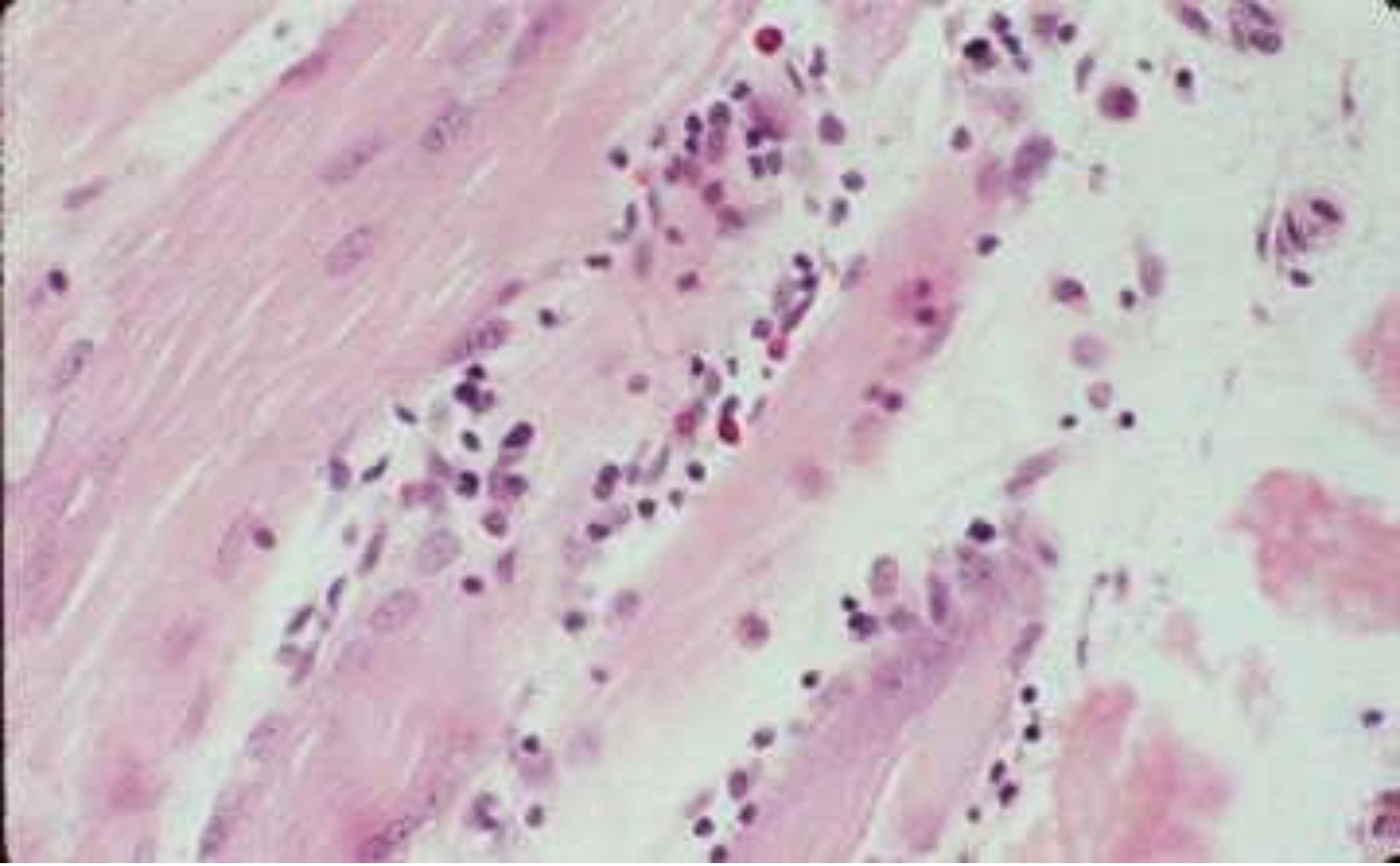
- DERMATOMYOSITIS
- POLYMYOSITIS
- INCLUSION BODY MYOSITIS

- ALL HAVE UNCLEAR ETIOLOGIES



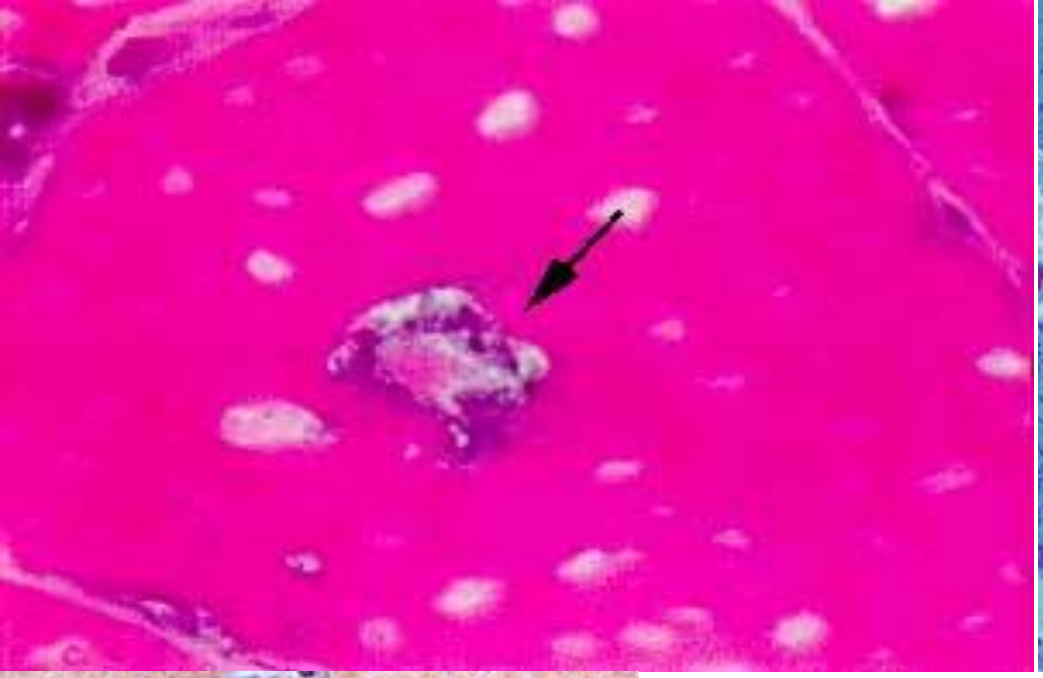
DERMATOMYOSITIS

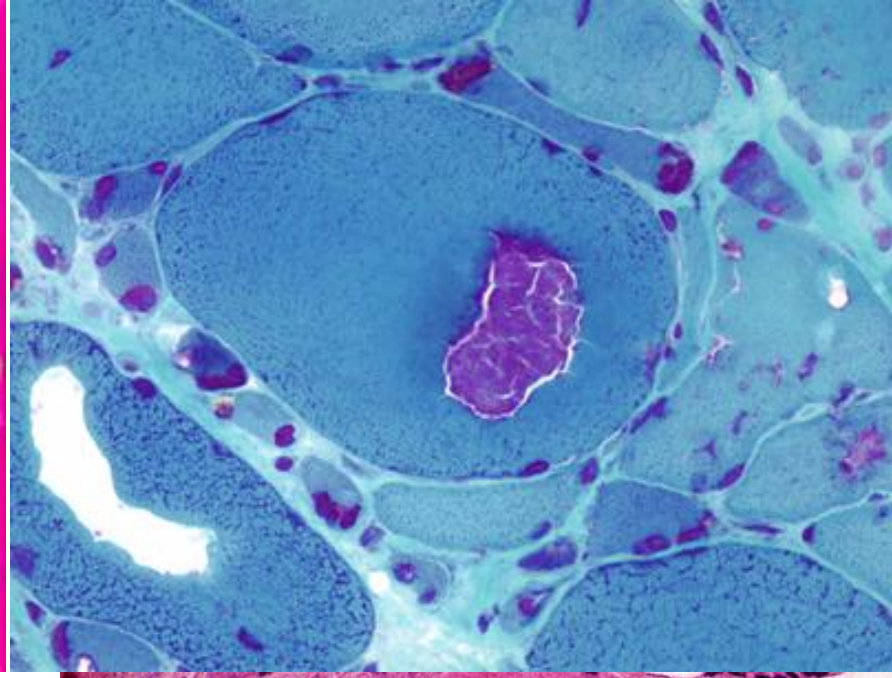
(often peri-vascular, half have cancer, often young)

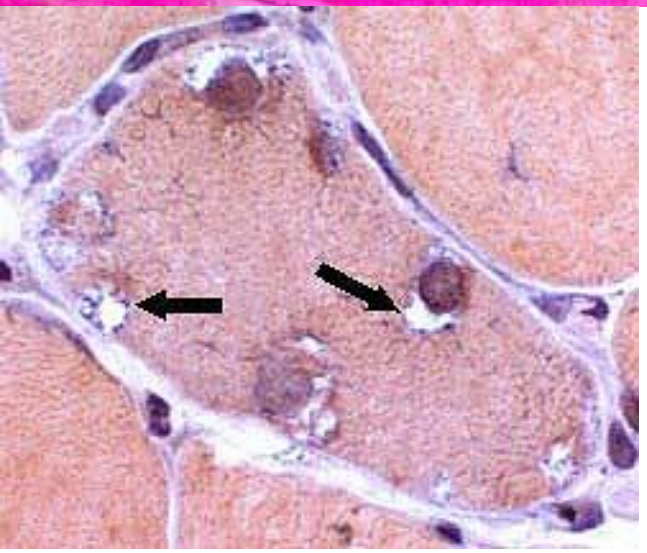


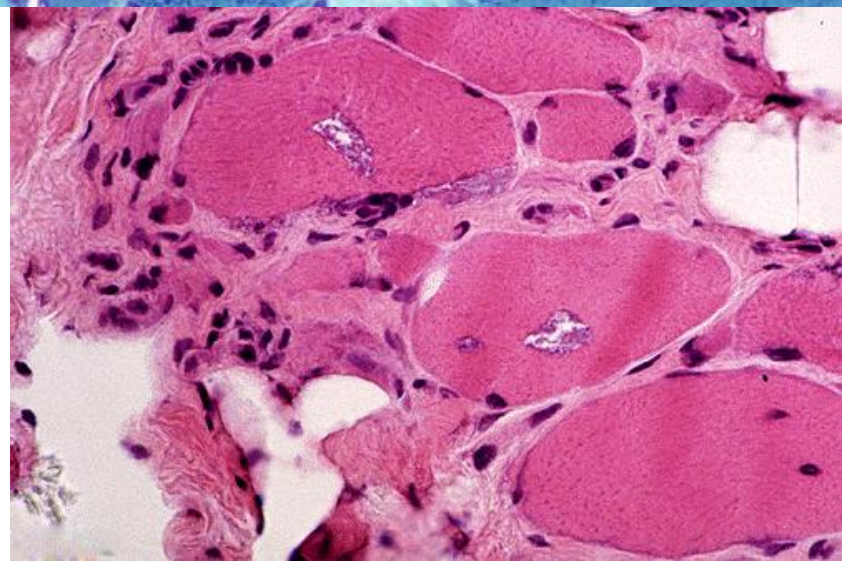
POLYMYOSITIS, usually endo-myseal

CCP:Weakness, muscle atrophy, proximal musculature









INCLUSION BODY MYOSITIS, “rimmed” vacuoles

Autoimmune? Many cases hereditary, dysphagia?

MYOPATHY, Toxic

- THYROTOXICOSIS
- ETHANOL
- DRUGS (steroids, chloroquine)
- DRUGS (MANY MANY others)

MYOPATHY, NeuroMuscular Junction

- **Myasthenia Gravis**
  - Associated with thymomas
  - Thymectomies often useful Rx:
  - AUTOIMMUNE DISEASE, CLEARLY
  - Ab's to ANTI-CHOLINESTERASE RECEPTORS
  - Anticholinesterase test is very diagnostic (edrophonium)
  - YOUNG WOMEN WITH EYE MUSCLE:
    - Ptosis →
    - Diplopia→
    - General Weakness
- **Lambert-Eaton Syndrome** (paraneoplastic), 60% have malignancies, auto-antibodies against NMJx

MYOPATHY, Neoplastic

- **Benign**
  - **Rhabdomyoma**
- **Malignant**
  - **Rhabdomyosarcoma**