MSS

DISEASES OF SKELETAL MUSCLE

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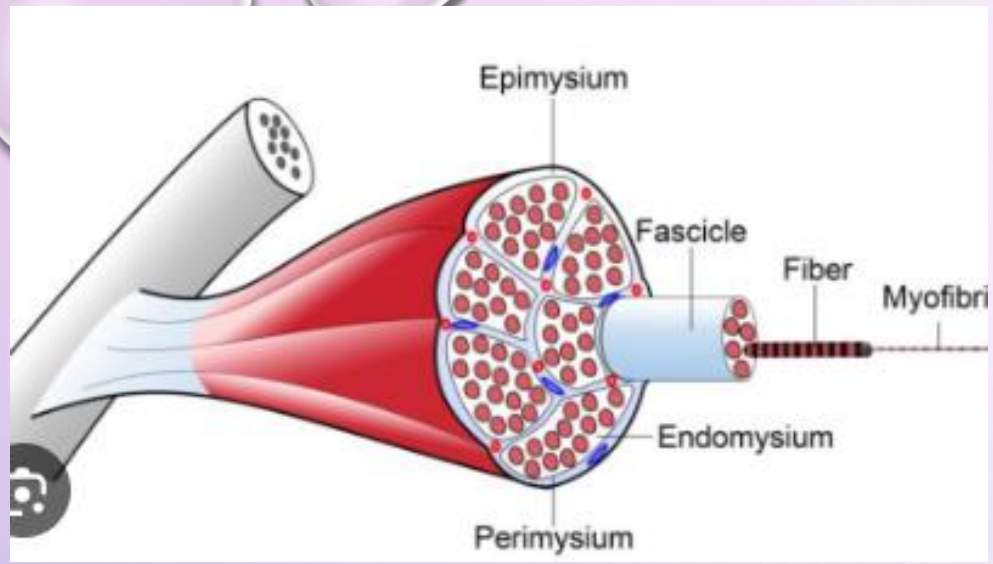
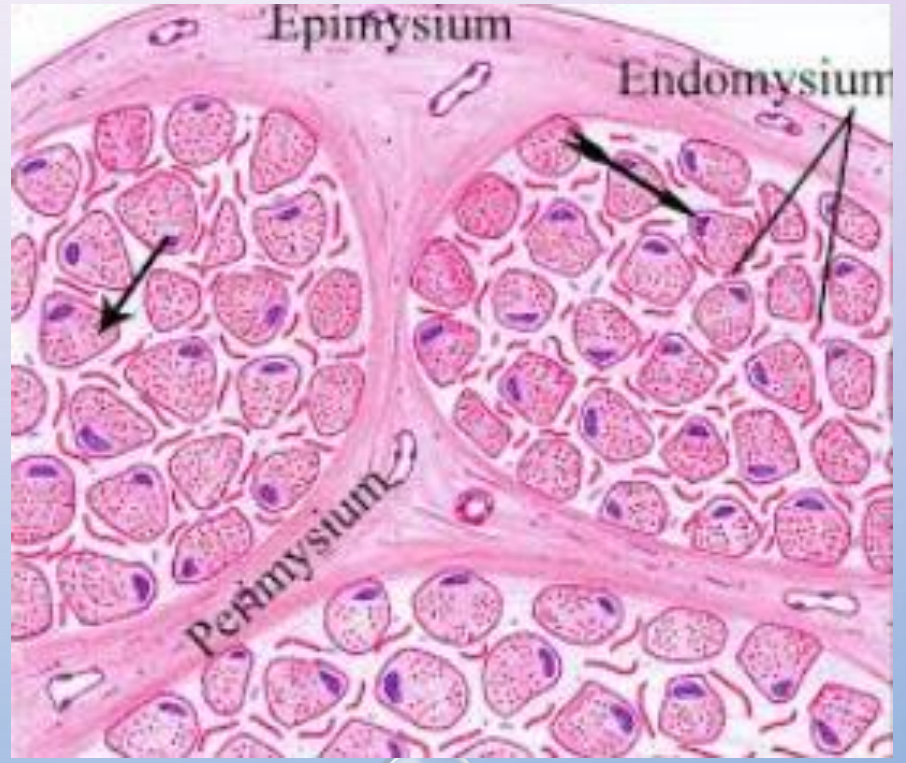

Epimysium
Fascicle
Fiber
Myofibri
Endomysium
Perimysium

Histology


Epimysium
Endomysium
Perimysium

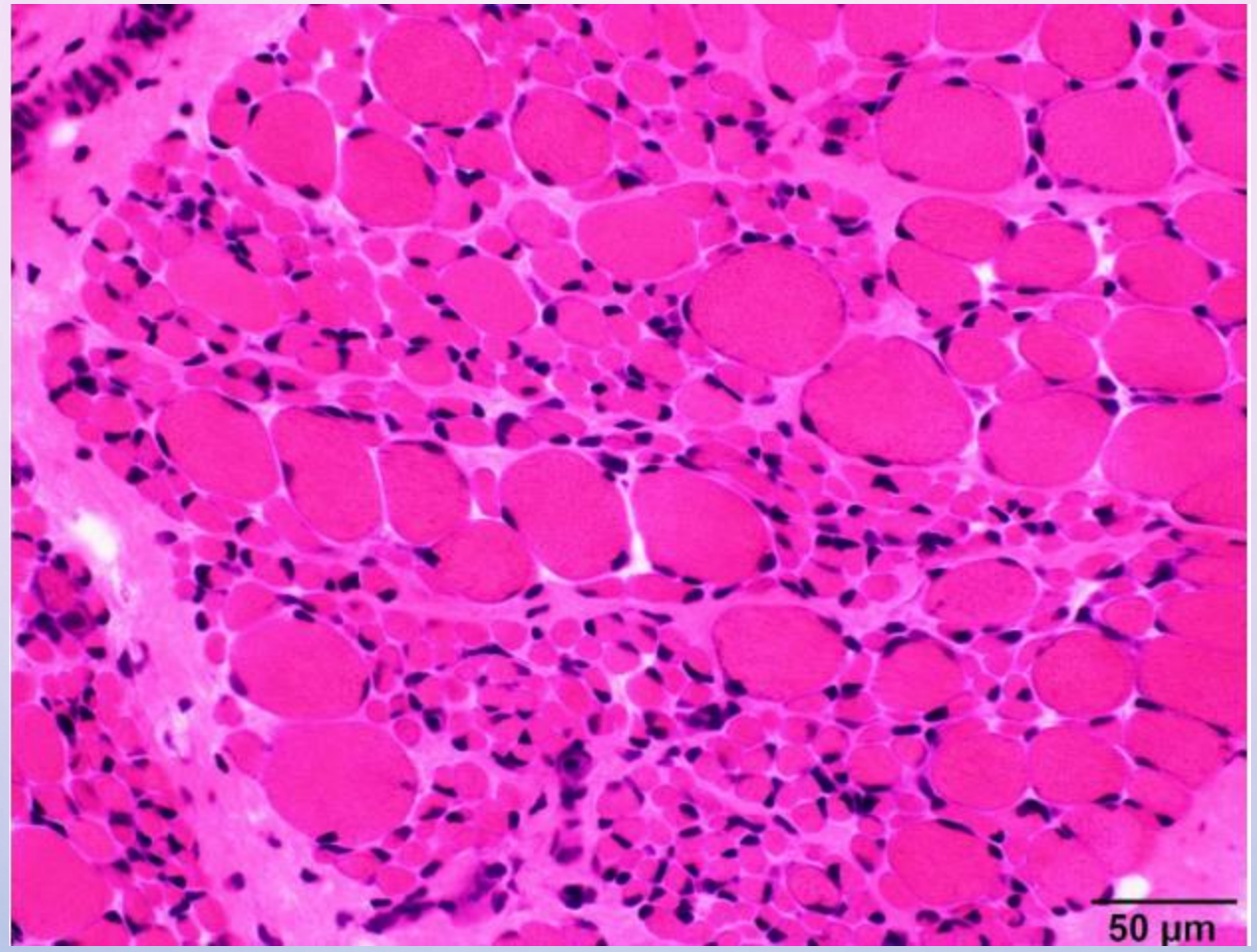
DENERVATION ATROPHY

- Denervation atrophy is the rapid loss of muscle mass (up to 80-90% in months) and strength caused by the loss of nerve supply, often resulting from peripheral neuropathy, spinal injuries, or motor neuron diseases

- 1. SPINAL MUSCULAR ATROPHY
  2. MUSCULAR DYSTROPHIES.
- 3. INFLAMMATORY MYOPATHIES

1. SPINAL MUSCULAR ATROPHY
SMA

- Autosomal recessive motor neuron diseases with onset in childhood or adolescence.
- All forms of sma are associated with mutations of the smn1 gene on chromosome 5.
- characterized by degeneration of alpha motor neurons in the anterior horn of the spinal cord, leading to progressive muscle weakness and atrophy



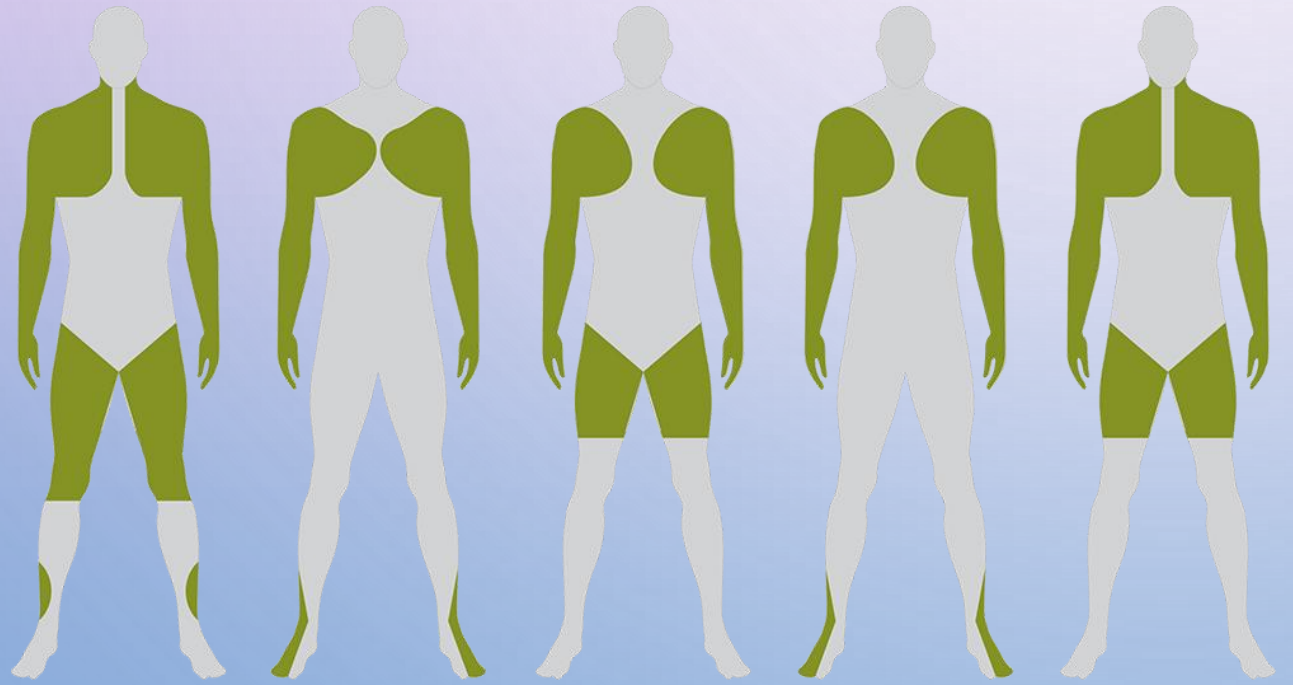
H&E shows an infantile denervation atrophy pattern. Small fibers are in groups (group atrophy) and round rather than angulated. Large fibers are hypertrophied. There is minimal interstitial fibrosis.

CLINICAL COURSE

- symmetric proximal muscle weakness (legs > arms)
- hypotonia and areflexia.
- cognition and sensation are typically normal

MUSCULAR DYSTROPHIES

- these are a heterogeneous group of inherited disorders, often beginning in childhood and characterized clinically by progressive muscular weakness and wasting.



X-Linked Muscular Dystrophy

Duchenne muscular dystrophy (DMD) :

- Is the most severe and most common form of muscular dystrophy.

- It is clinically manifest by age 5 years; and patients are wheelchair bound by age 10 to 12 years.
- The disease will progresses until death in the early 20s.

Becker muscular dystrophy (BMD)

- Involves the same genetic locus but is less common and less severe.
- Characterized by later onset and a slower rate of progression.

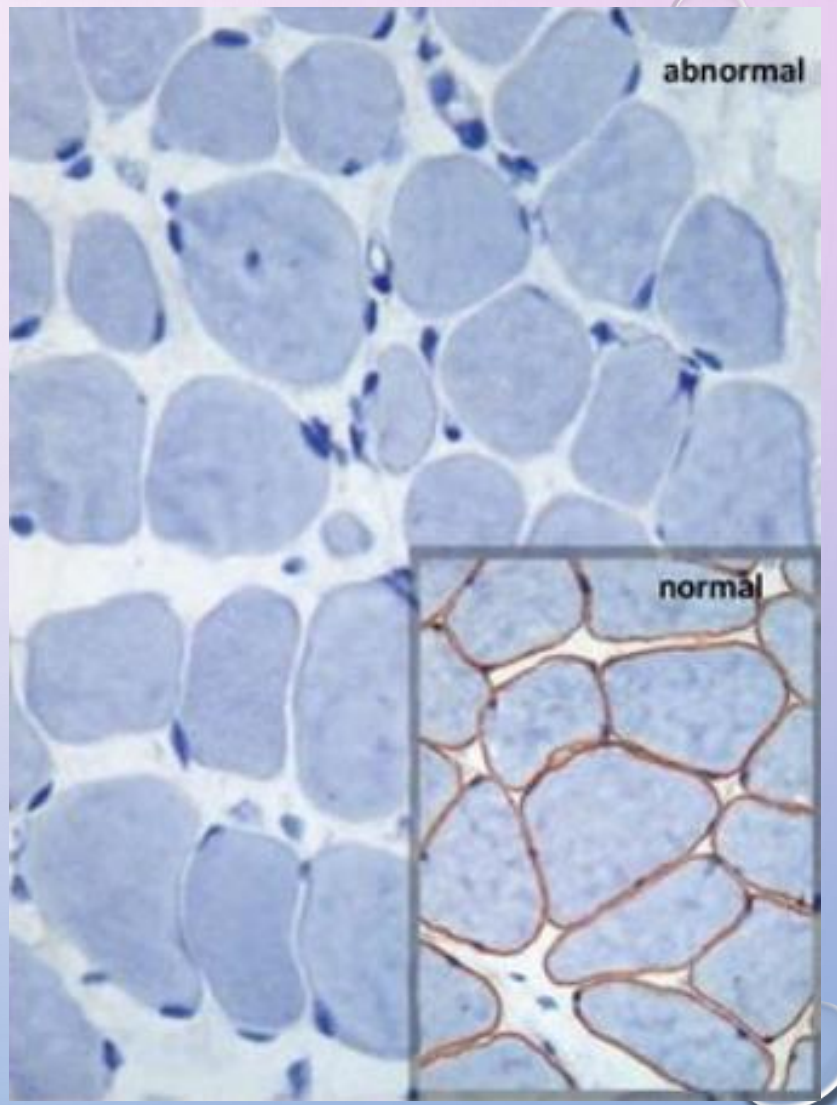
PATHOGENESIS

- Both condition characterized by abnormal dystrophin gene ????
- dystrophin protein is a product of DMD gene at xp21….responsible for transducing contractile forces from the intracellular sarcomeres to the extracellular matrix.
- Muscle from DMD patients has almost no detectable dystrophin; muscle from BMD patients has diminished amounts of dystrophin.

- Most mutations are deletions, with frameshift and point mutations accounting for the rest.

MORPHOLOGY

- Variation in myofiber diameter, with both small and giant fibers?
- increased numbers of internalized nuclei degeneration, necrosis, and phagocytosis of muscle fibers
- regeneration of muscle fibers
- proliferation of endomysial connective tissue
- in late stages, muscles are entirely replaced by fat and connective tissue



CLINICAL COURSE

- weakness: begins in the pelvic girdle muscles, extending to the shoulder girdle;
- heart: failure and arrhythmia

  - female carriers and affected males are at risk for developing dilated cardiomyopathy.

- cognitive impairment is a component of the disease.

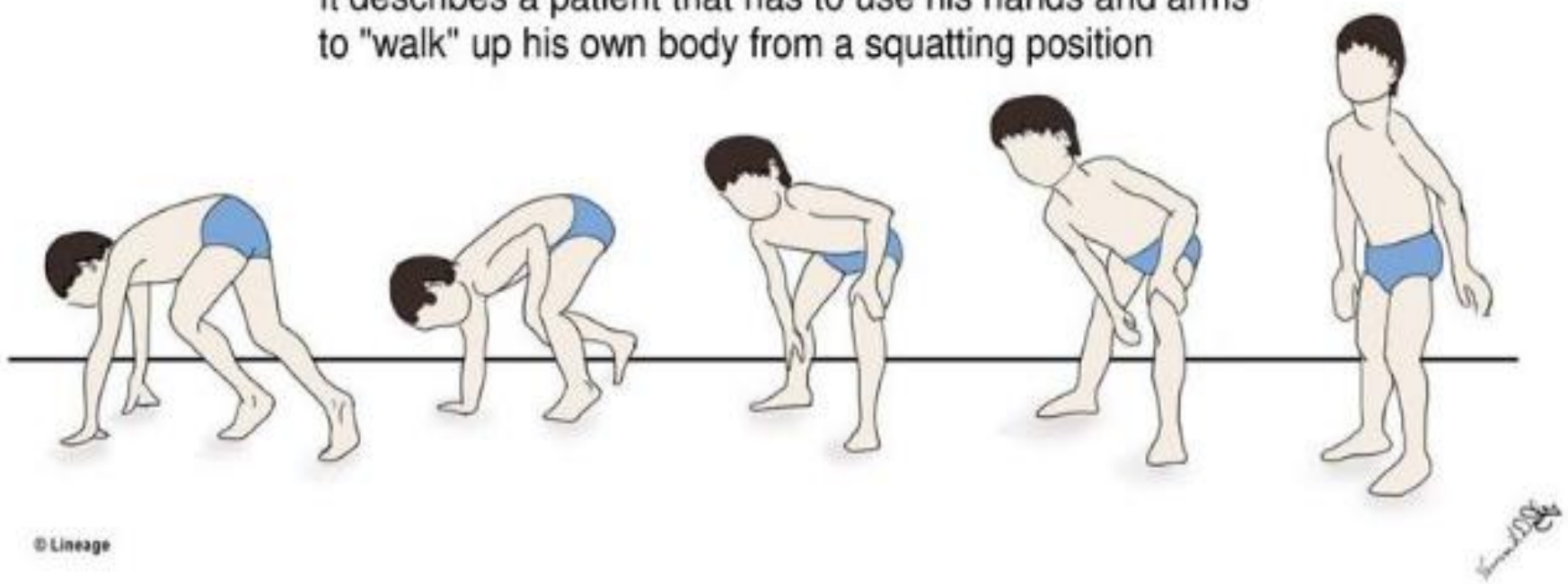
- death results from respiratory insufficiency, pulmonary infection, and cardiac decompensation.

Positive Gower sign in Duchenne and Becker muscular dystrophy

...due to proximal lower limb muscle weakness
...not only in Duchenne & Becker

Gower Sign

It describes a patient that has to use his hands and arms to "walk" up his own body from a squatting position

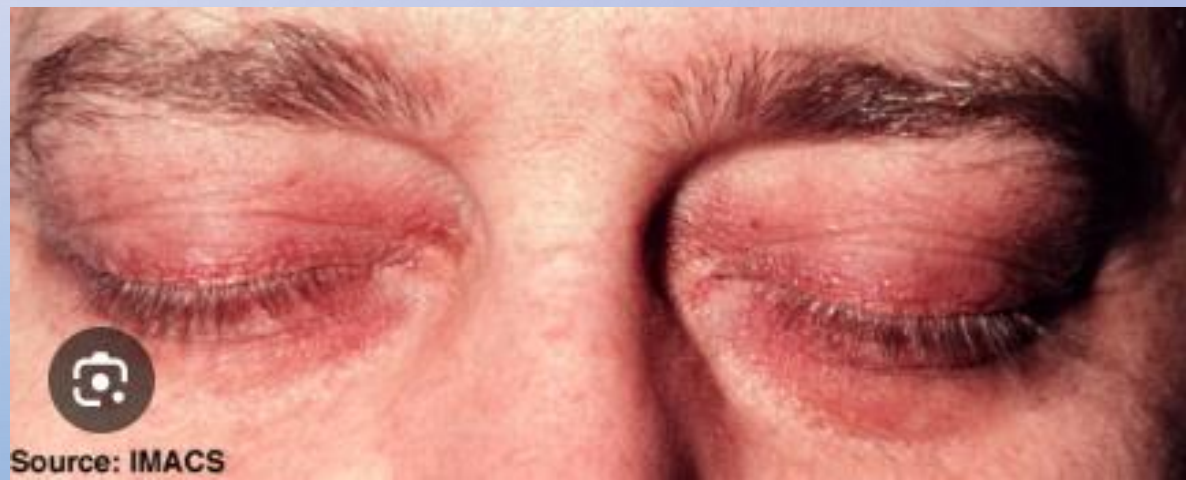


INFLAMMATORY MYOPATHIES

- Noninfectious inflammatory myopathies are a heterogeneous group of immune-mediated disorders characterized by skeletal muscle inflammation and injury.

DERMATOMYOSITIS

- Idiopathic process that leads to an inflammatory myopathy with skin manifestations.
- Dermatomyositis is thought to be caused by a microangiopathy affecting skin and muscle.
- myositis with perifascicular muscle fiber atrophy and generally inflammatory infiltrates around intramuscular vessels

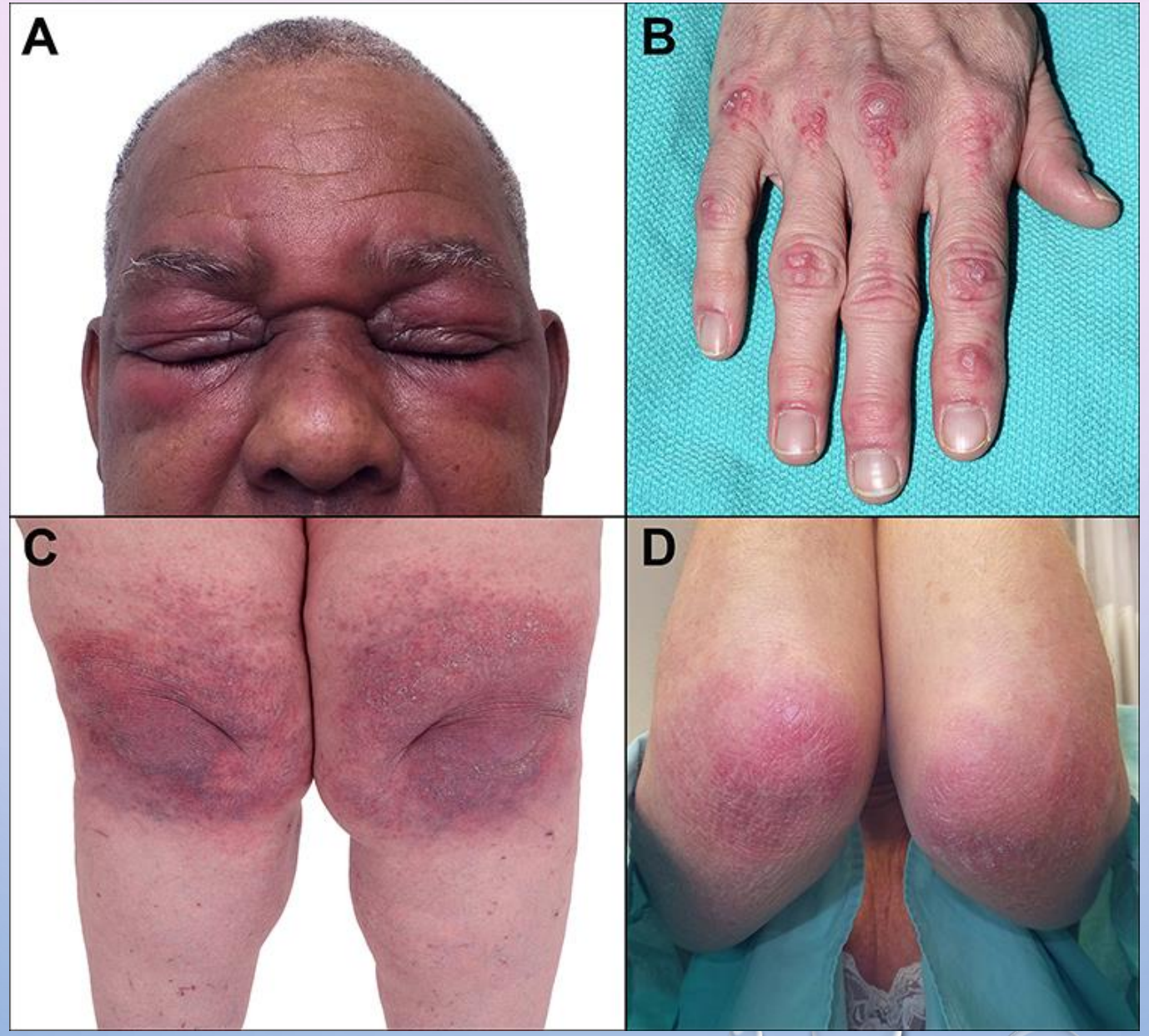


PATHOPHYSIOLOGY

- The primary process is attack on the endothelium of the capillaries of myofibers, with deposition of complement on the vessel walls and eventual formation of membrane attack complex .
- This causes perivascular inflammation and can eventually reduce the number of intramuscular small vessels

DERMATOMYOSITIS CLINICALLY

- Discoloration of upper eyelids and periorbital edema accompanies or precedes weakness; scaling, erythematous patches are also present over knuckles, elbows, and knees (grotton lesions).
- muscle weakness is slow in onset and bilaterally symmetric, affecting proximal muscles first; dysphagia occurs in a third of patients.
- interstitial lung disease, vasculitis, and myocarditis can also be present.
- immune suppressive therapy is beneficial.


A
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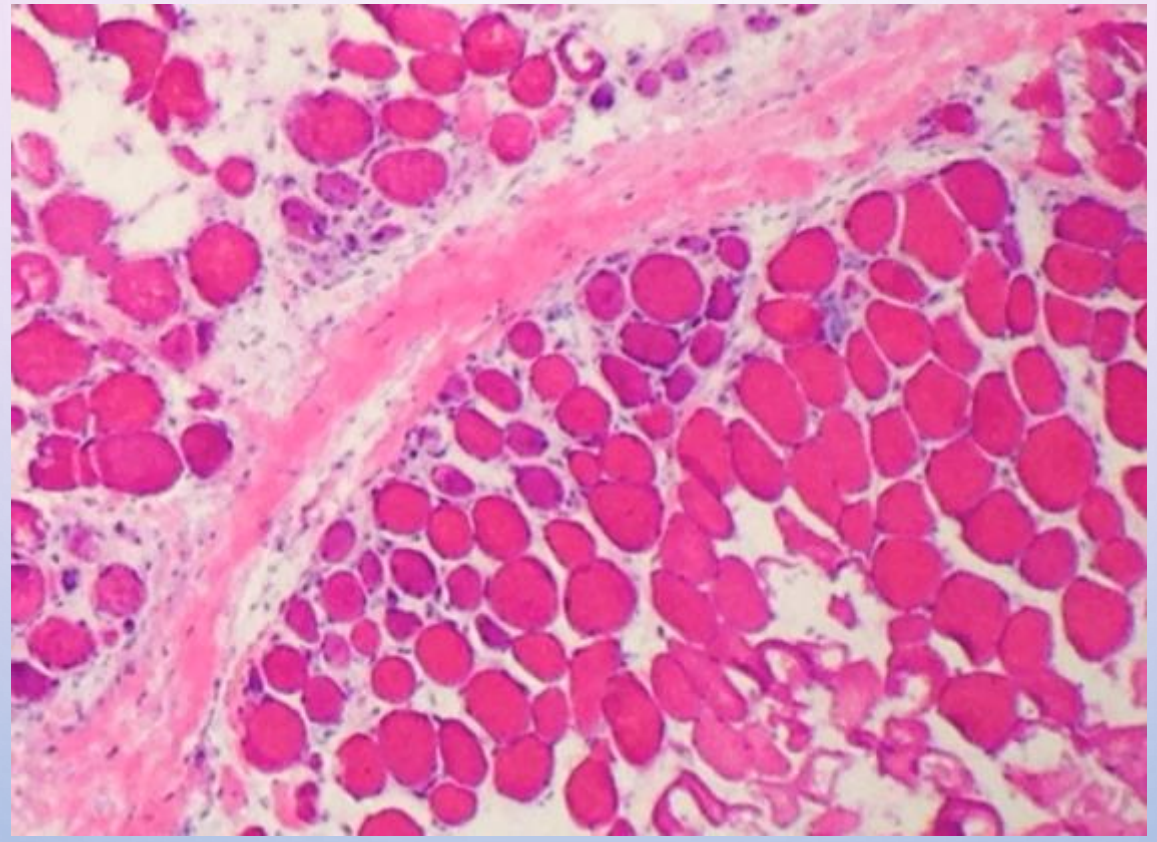
MORPHOLOGY



Perifascicular atrophy is the hallmark of dermatomyositis

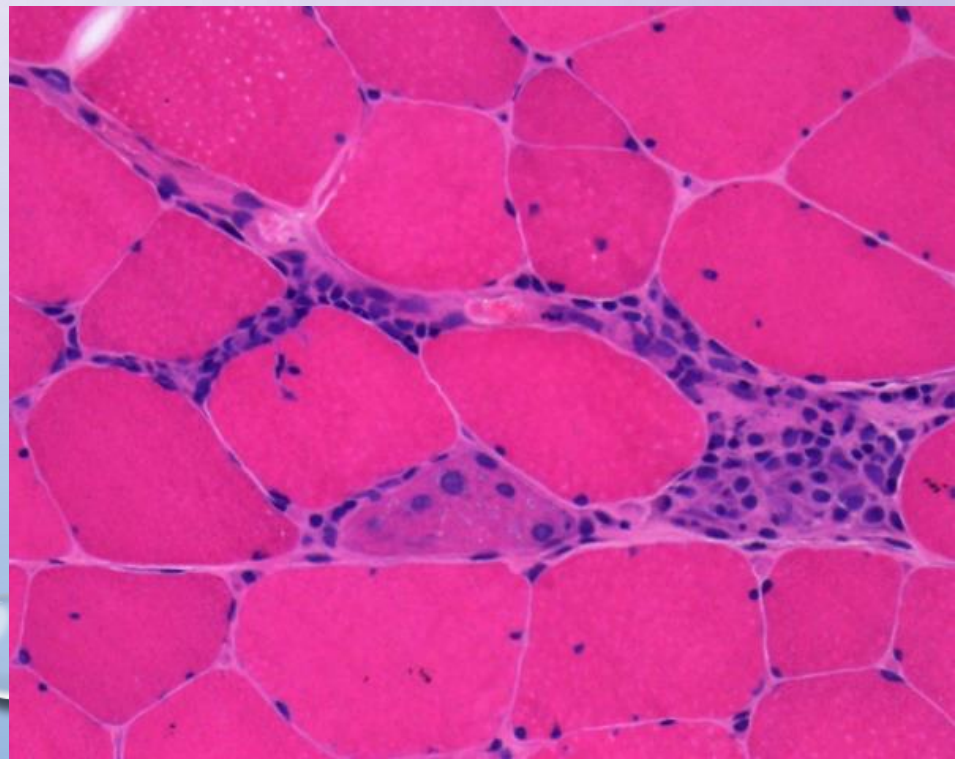
POLYMYOSITIS

lit is similar to dermatomyositis but lacks cutaneous involvement; it occurs primarily in adults.

- The pathogenesis involves cytotoxic t-cell–driven myocyte damage; various autoantibodies against trna synthetases are also present.
- immune suppressive therapy is beneficial.

MORPHOLOGY

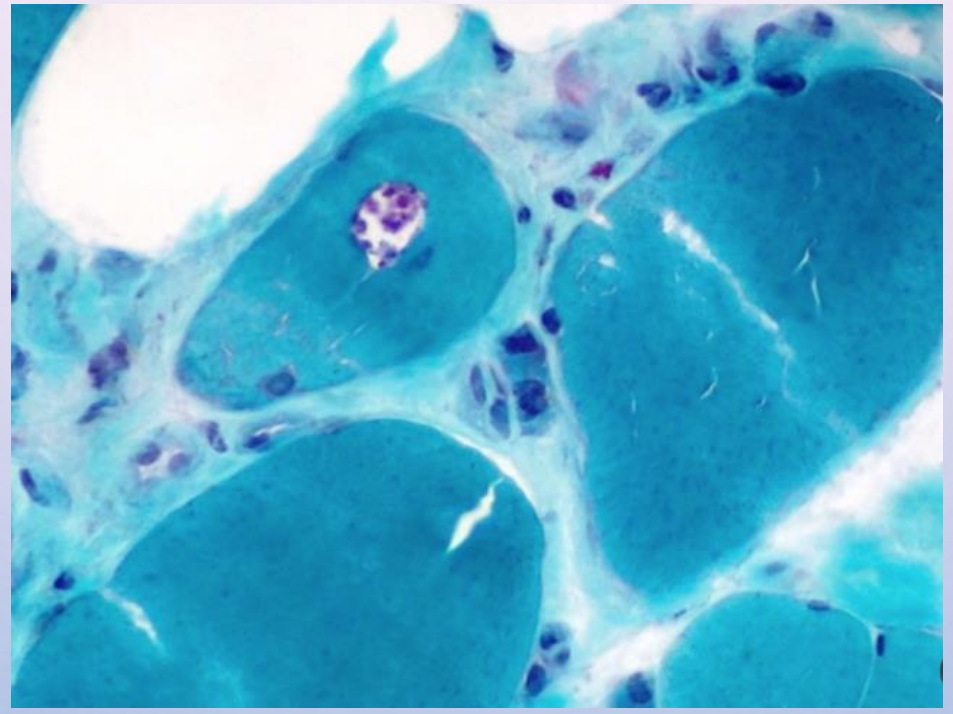
- lymphocytic infiltrate may be accompanied by macrophages
- myopathic changes including myofiber size variation with small rounded myofibers and increased internalized nuclei



INCLUSION BODY MYOSITIS

- An inflammatory myopathy of predominantly skeletal muscle usually seen in ages 50+
- The main histologic finding is rimmed vacuoles with accumulation of specific proteins of autophagy (intracellular depositions of b-amyloid protein and hyperphosphorylated tau proteins suggest abnormal protein folding as an etiology.
- begins with distal muscle involvement, especially extensors of the knee and flexors of the wrists, and can be asymmetric.

MORPHOLOGY



Inclusion body myositis. This section is stained with a Gomori Trichrome stain. In the center of the myofiber, there is a 'rimmed vacuole' which is a classic feature of inclusion body myositis.