Myositis 101

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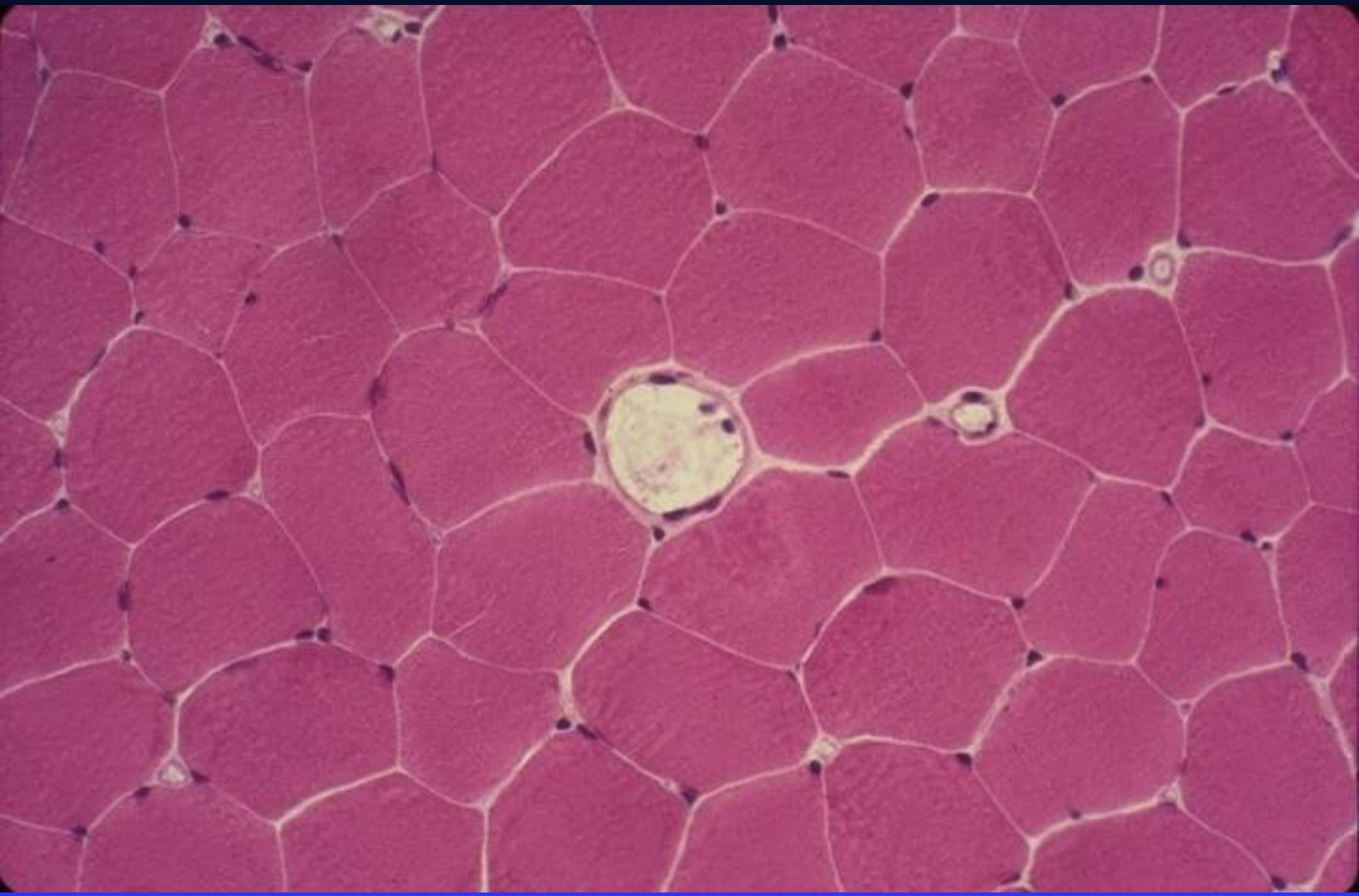
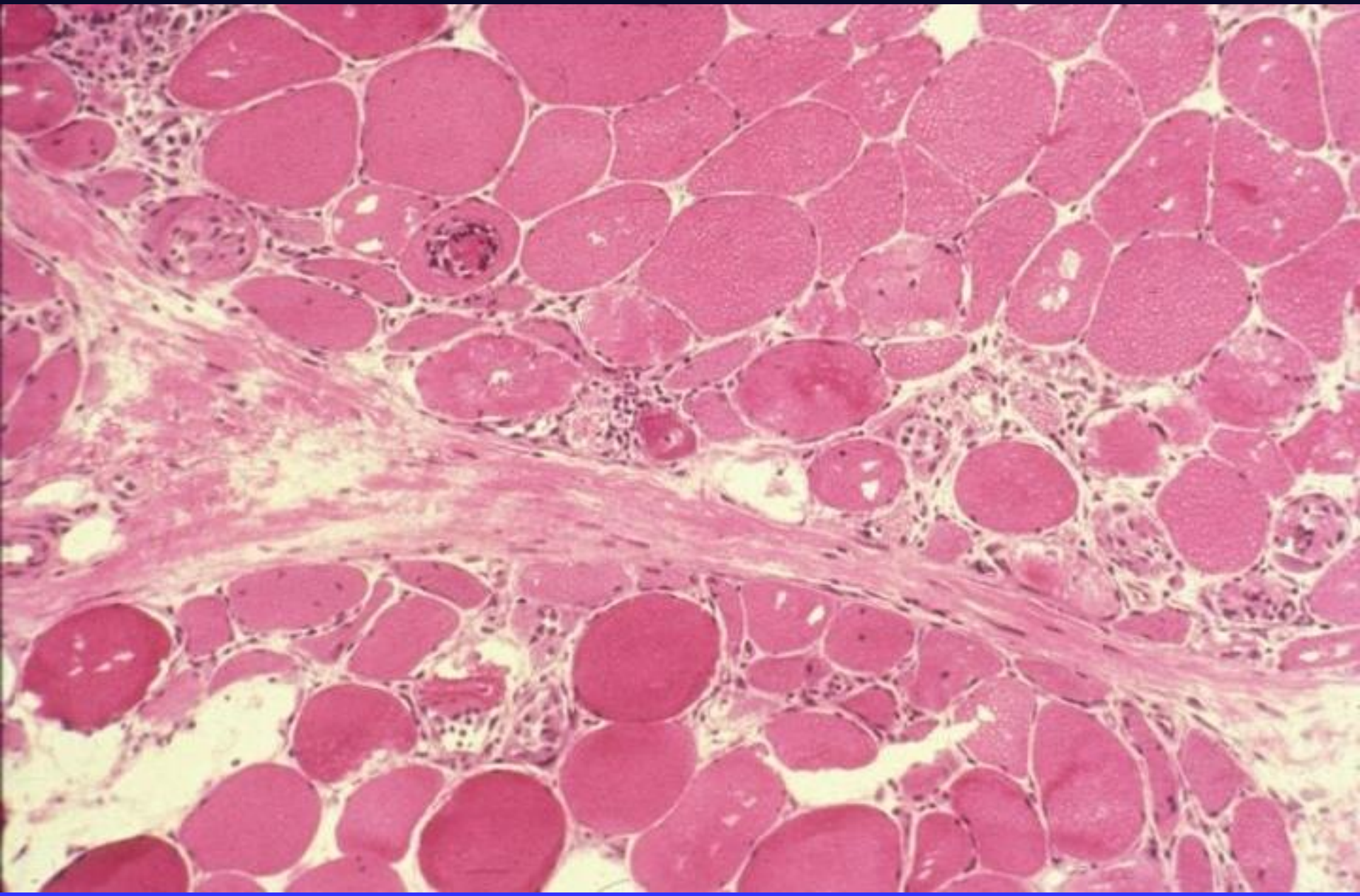
Criteria for Defining Polymyositis

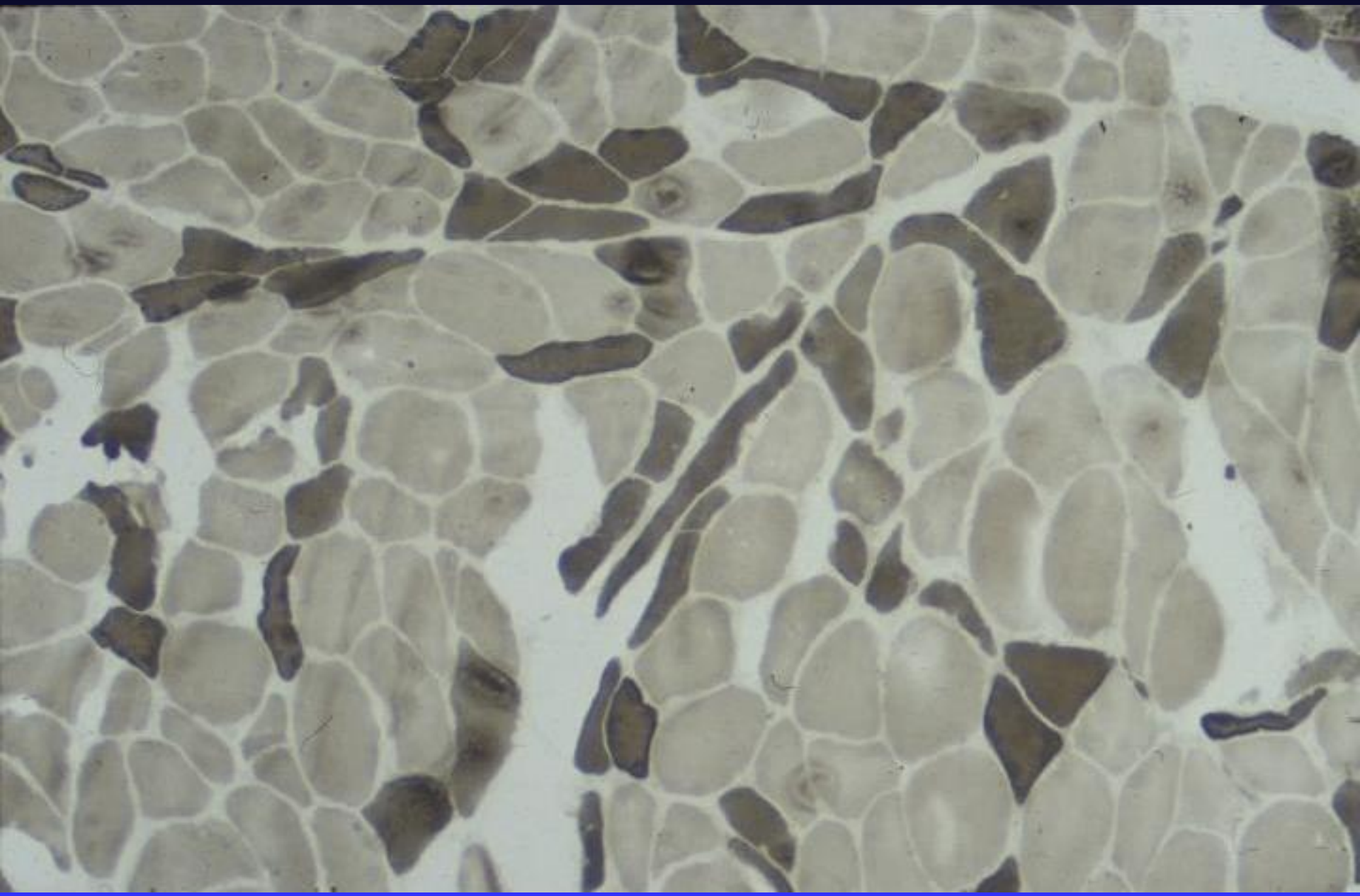
1. Symmetrical weakness of limb-girdle muscles and anterior neck flexors.
2. Muscle biopsy evidence of necrosis of Type I and II fibers, phagocytosis, regeneration, variation in fiber type with inflammatory exudation.
3. Elevation in serum or skeletal-muscle enzymes.
4. Electromyographic triad of short, small, polyphasia motor units, fibrillations and sharp waves; and bizarre, repetitive discharges.
5. Dermatologic features.

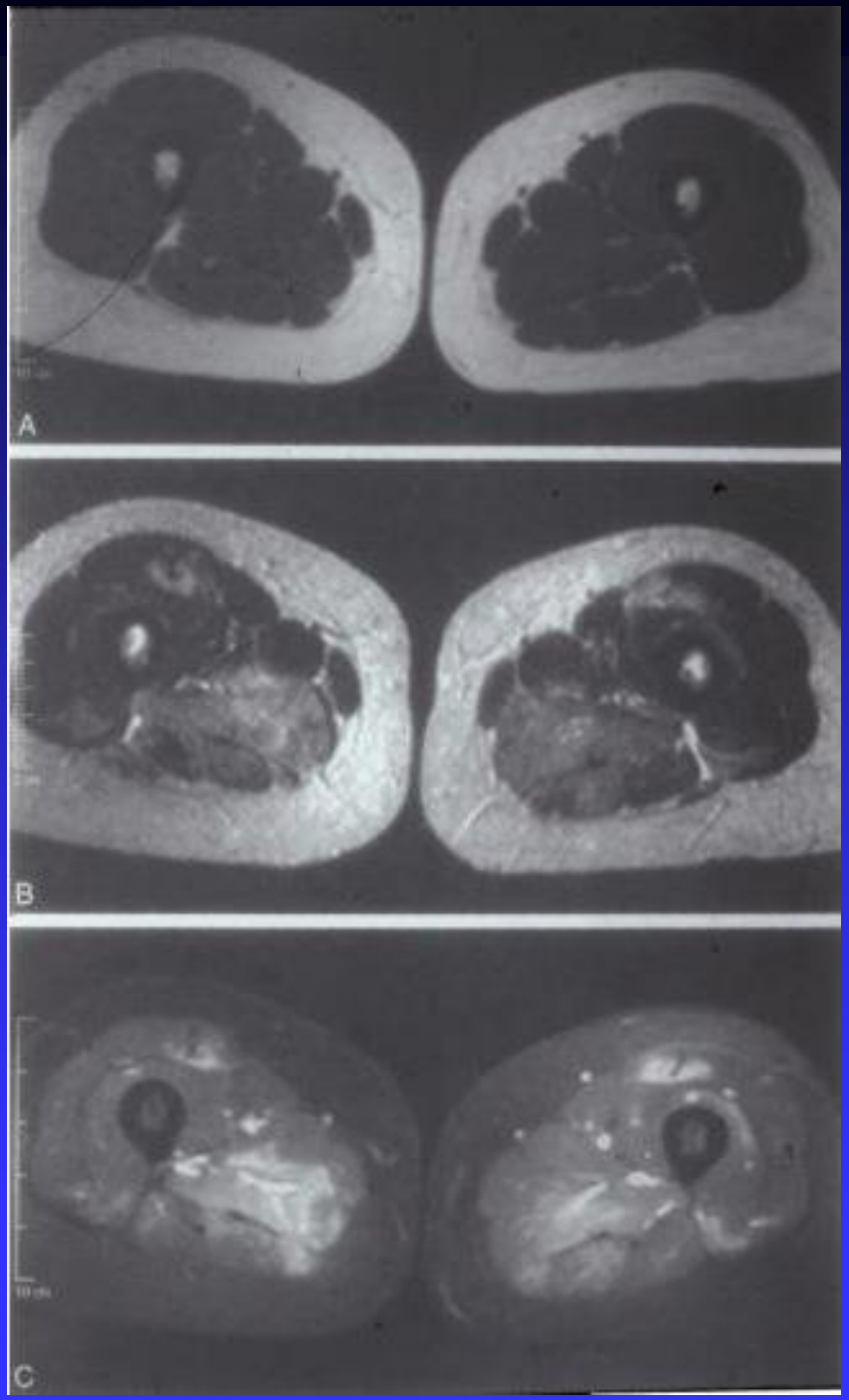
Bohan and Peter. *NEJM* 1975.

Nonsuppurative Inflammation of Muscle

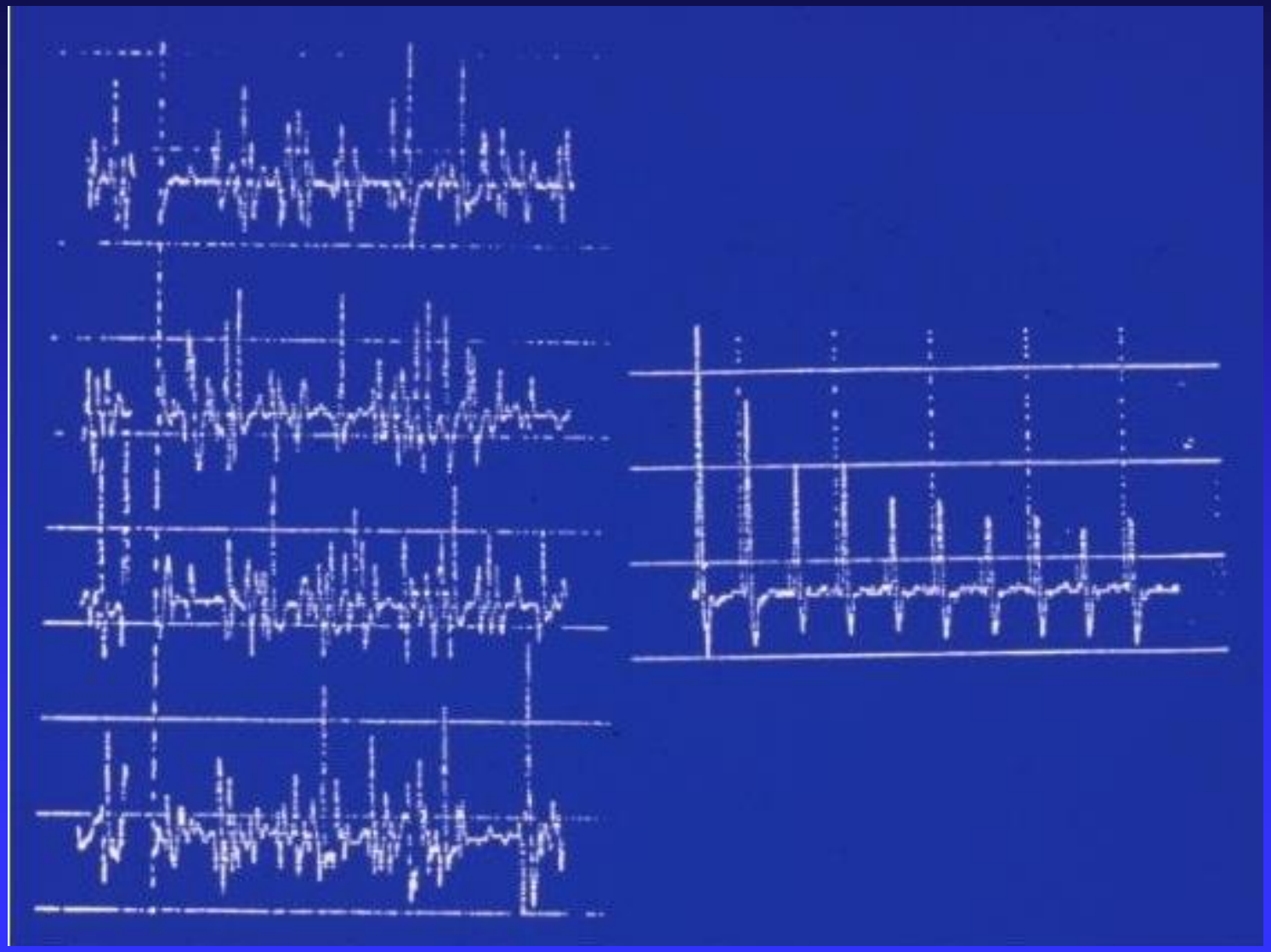







A
B
C

Electrodiagnostic Testing



Electrophysiologic Changes in Inflammatory Myopathy

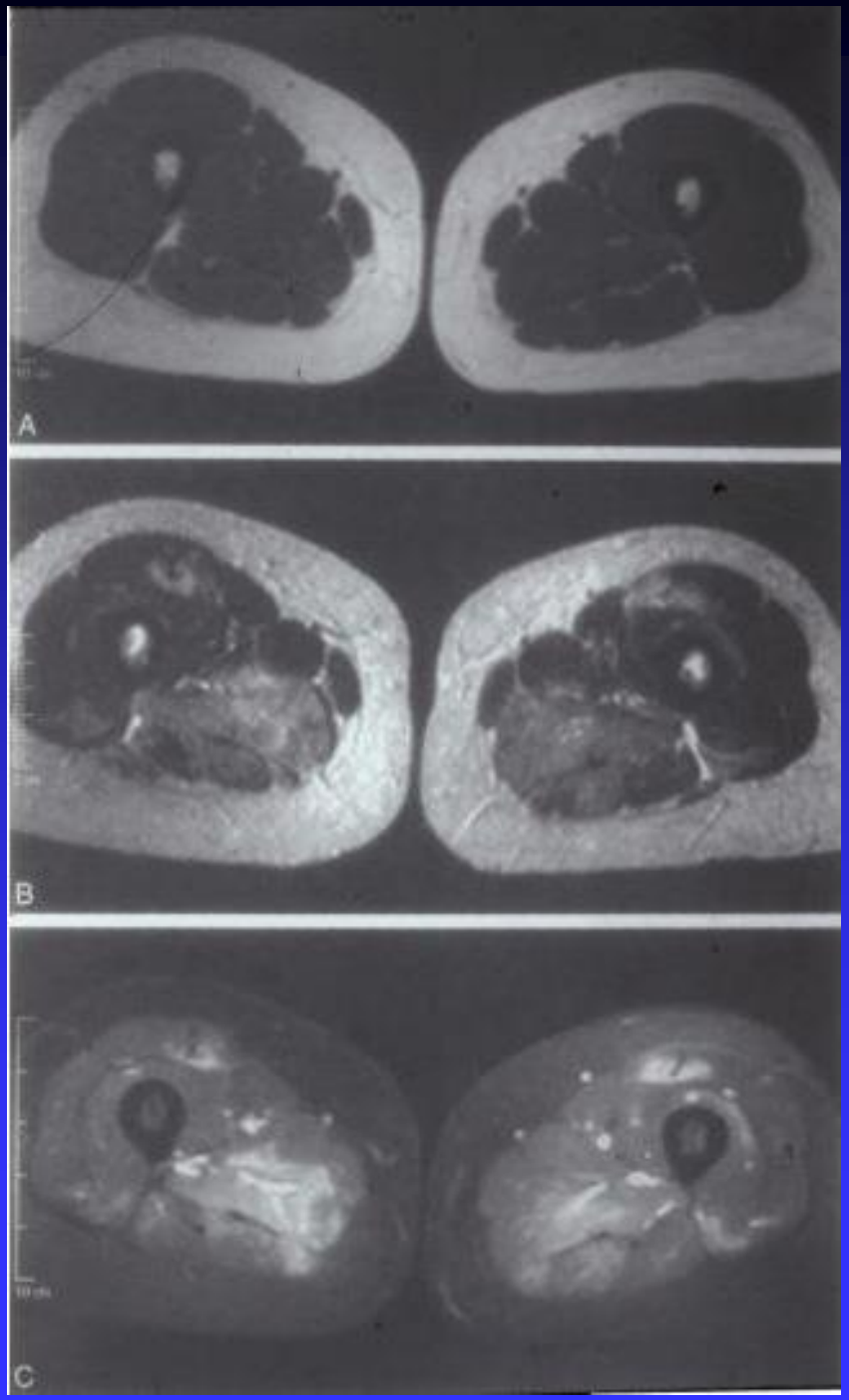
- Fibrillation at rest
- Increased insertional activity
- Bizarre high-frequency repetitive discharges
- Polyphasic potentials of short duration and low amplitude
- Spontaneous and positive sharp waves

EMG and Inflammatory Myopathies

- About 40% will have the classic triad
- EMGs are entirely normal in 10%
- Abnormalities may be limited to paraspinous muscles
- Neuropathic findings may also be seen in
  - Inclusion body myositis
  - Myositis with anti-SRP antibodies
  - Myositis and malignancy

EMG and Nerve Conduction

- Differentiate myopathic and neuropathic disorders and further localize the lesion.
- Identify appropriate site for biopsy.


A
B
C

Muscle Enzymes in IIM

- CPK, aldolase, AST, ALT, and LDH
- None of these enzymes may correlate well with disease activity
- Patients with an IIM may become completely asymptomatic, but continue to have elevated enzymes

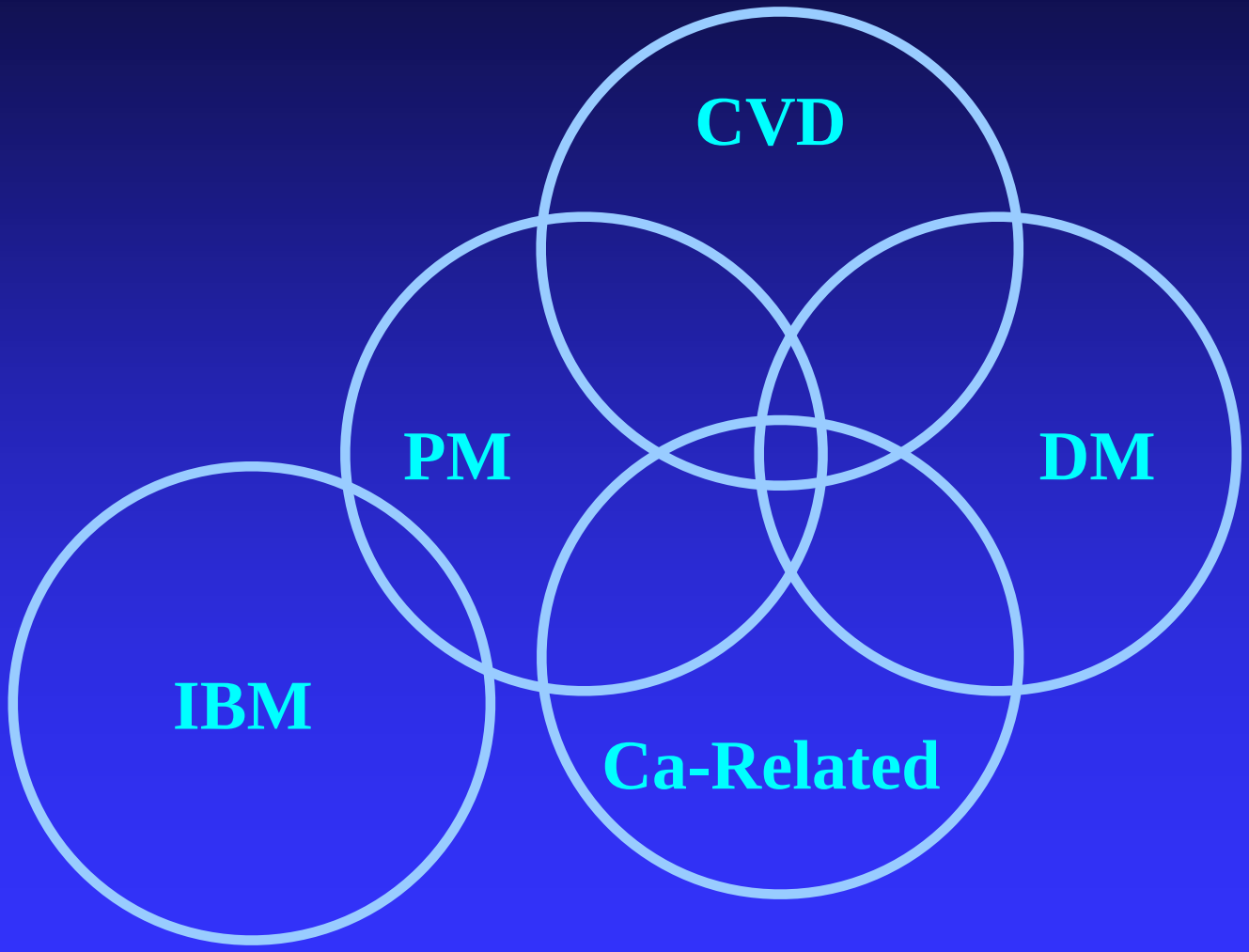
Not all High CK Levels are the due to Polymyositis! Other causes include:

- Racial differences
- Trauma
- Exercise
- Drugs/Toxins
- Carrier-states
- Pre-disease
- Benign (cause unknown)

Although the criteria are nonspecific, when occurring together, and without other explanations, the allow the diagnosis of an idiopathic inflammatory myopathy,

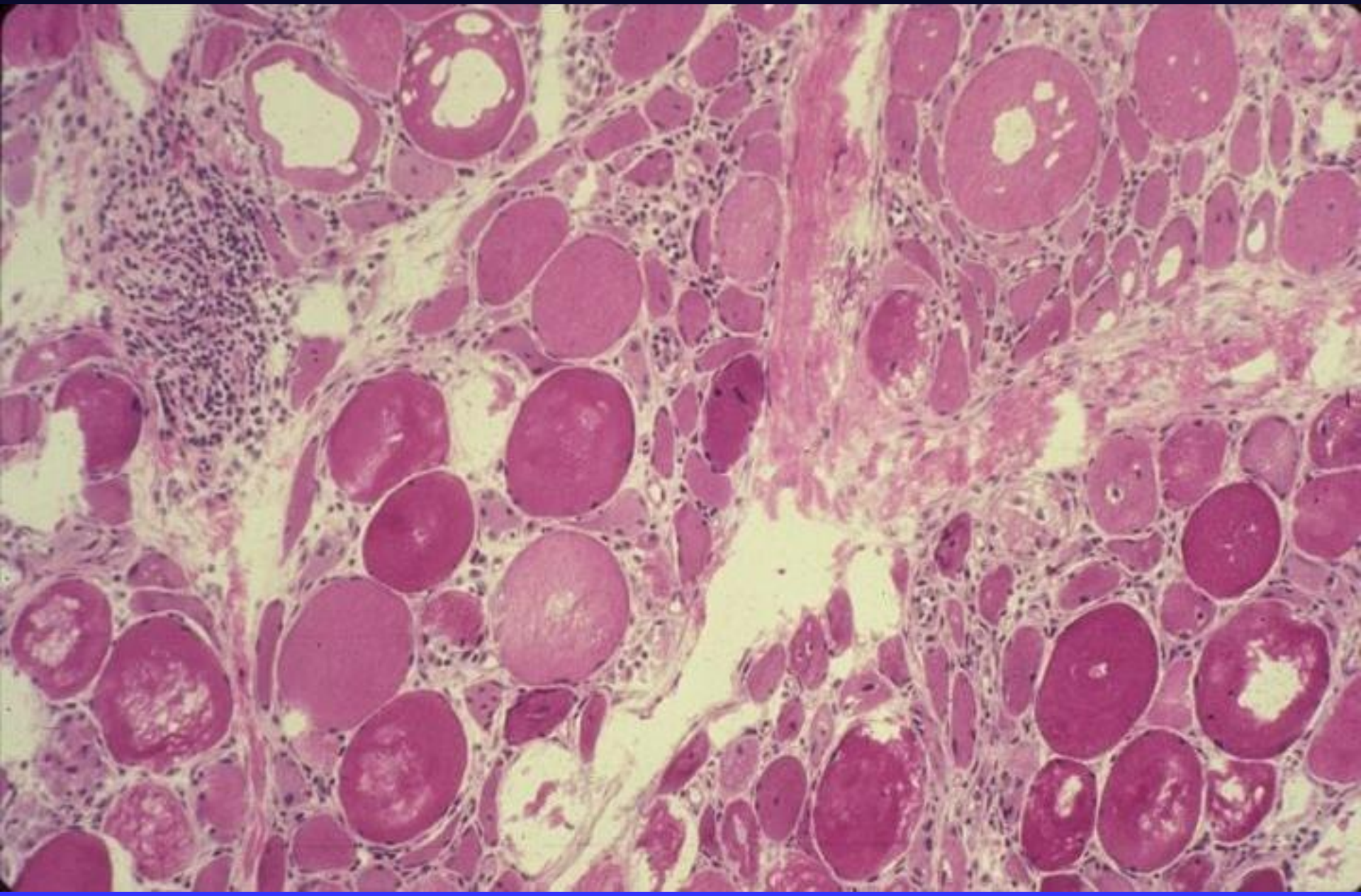
Idiopathic Inflammatory Myopathies

- Polymyositis
- Dermatomyositis
- Myositis with associated Collagen Vascular Disease
- Myositis with Malignancy
- Inclusion Body Myositis


CVD
PM
DM
IBM
Ca-Related

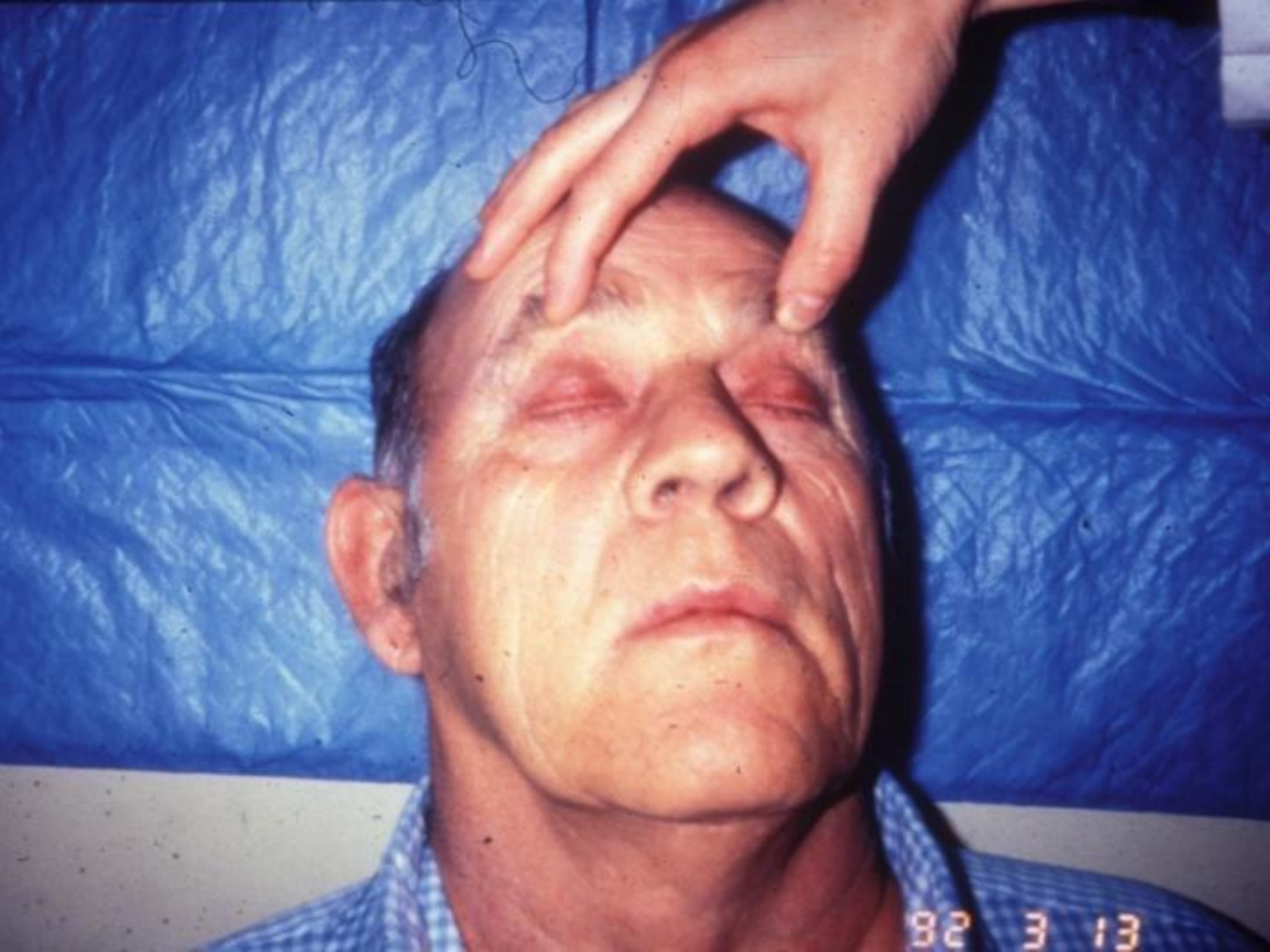
Polymyositis

- Proximal muscle weakness
- Elevated CPK
- Myopathic EMG
- Inflammation on histology



Dermatomyositis

- Polymyositis plus rash
- A different disease
- Different diseases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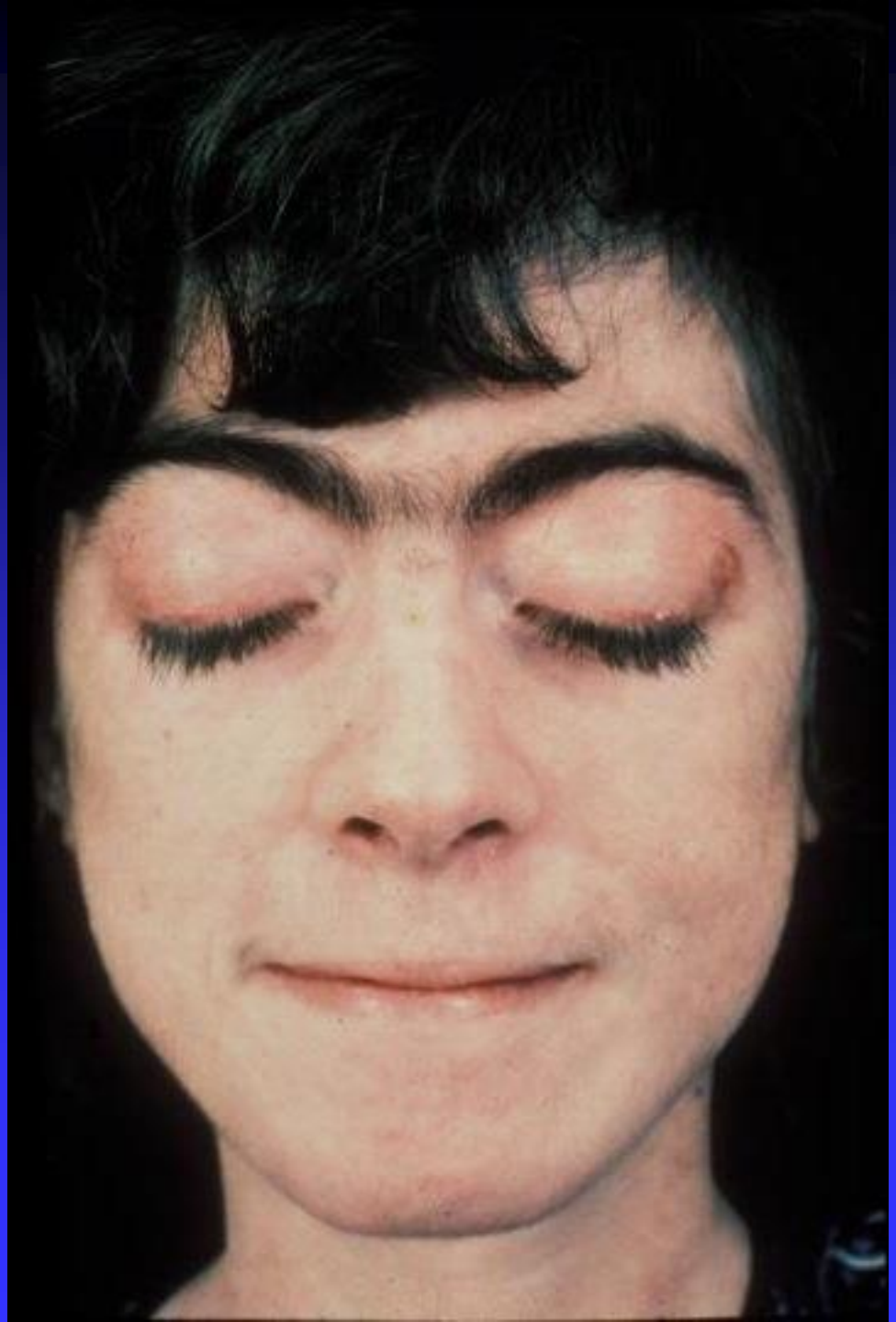
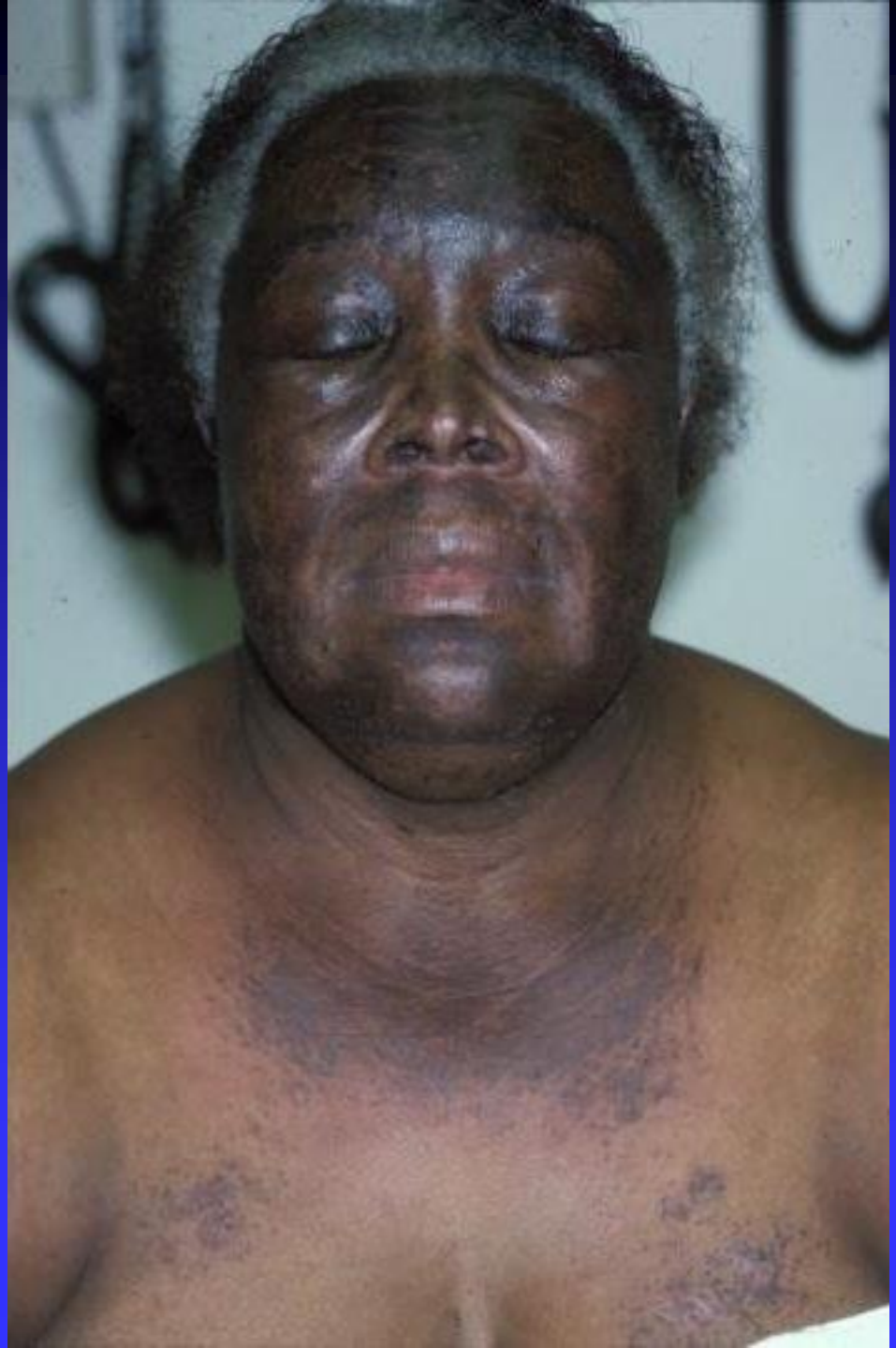
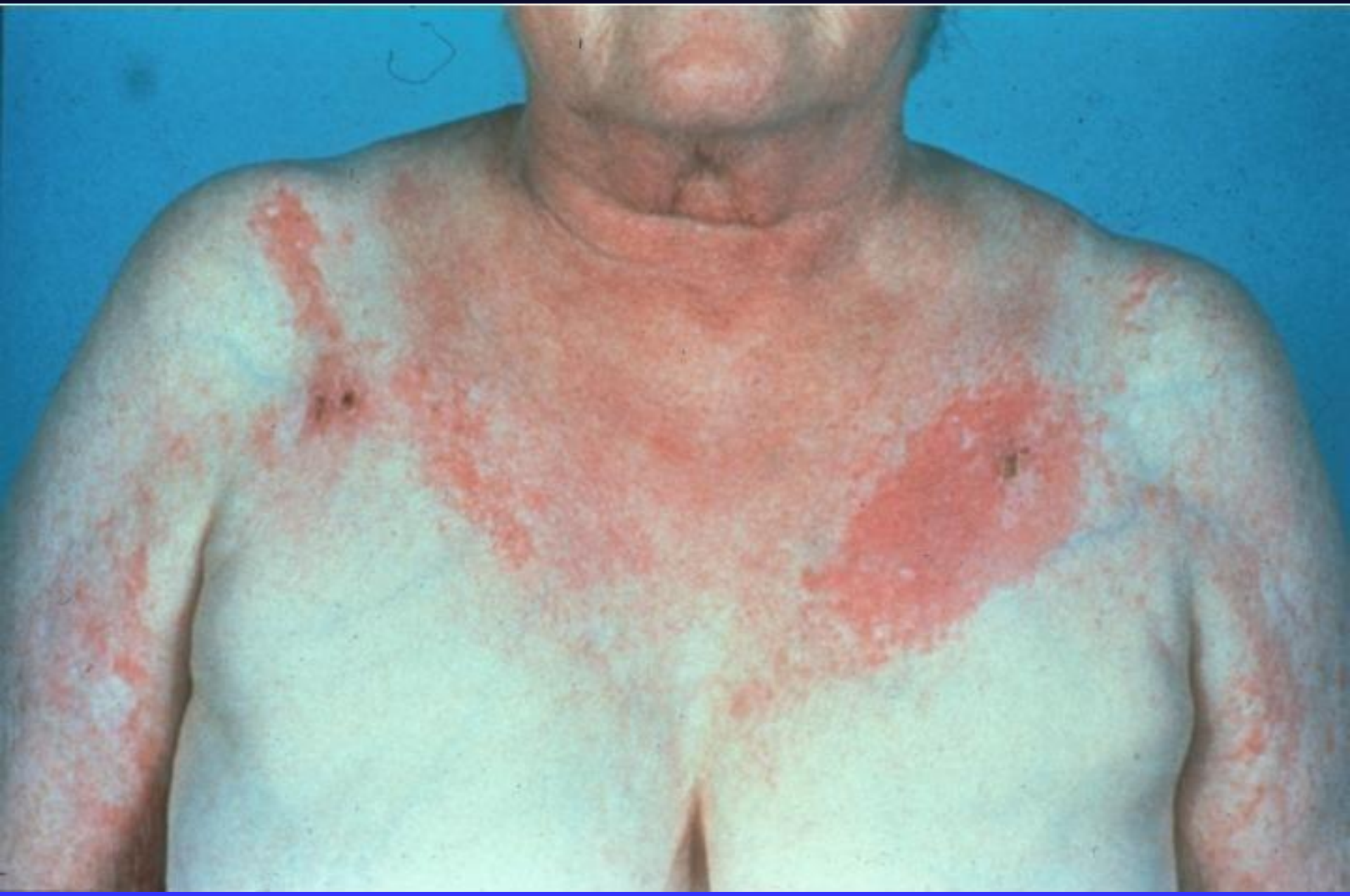
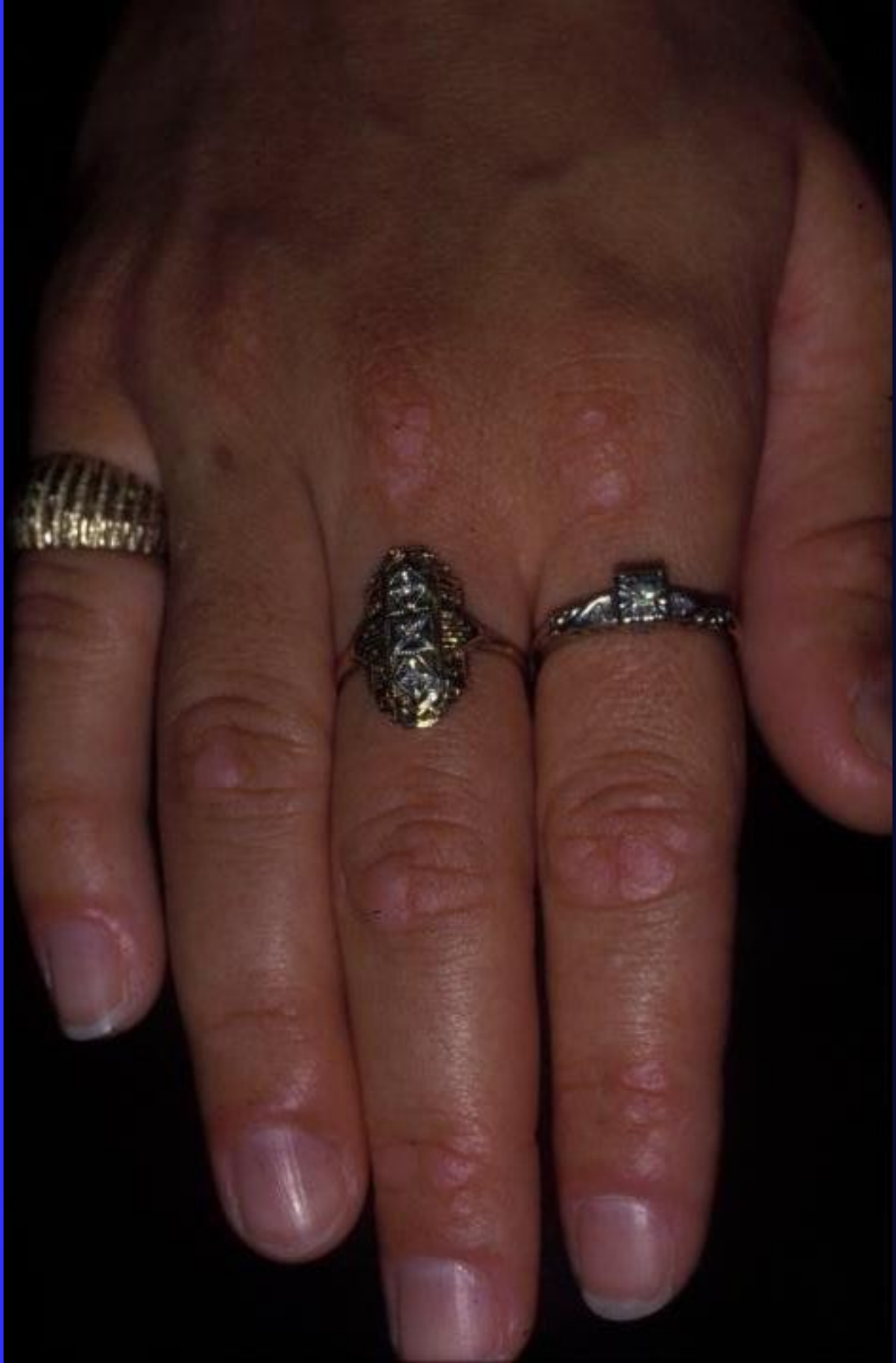
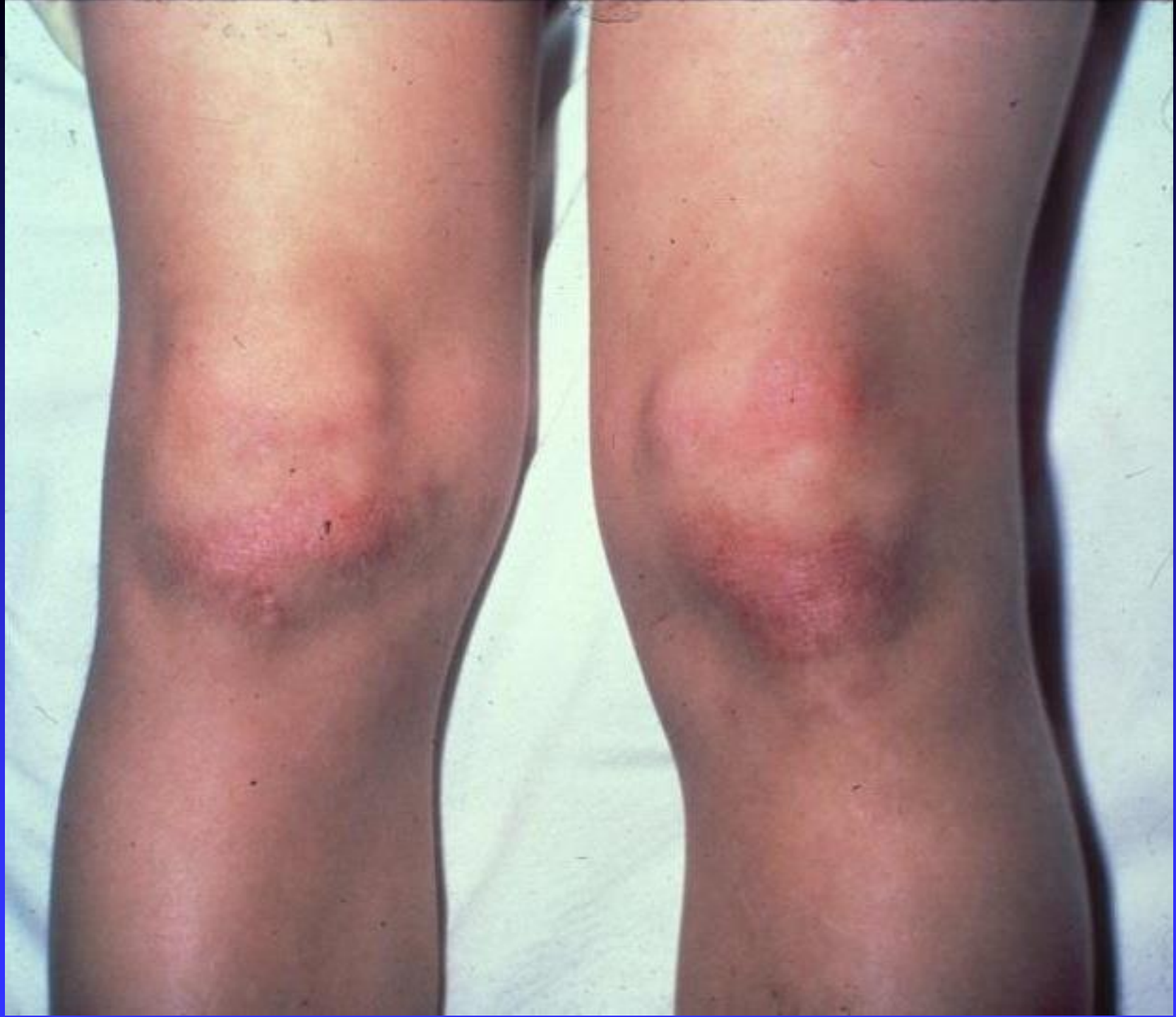
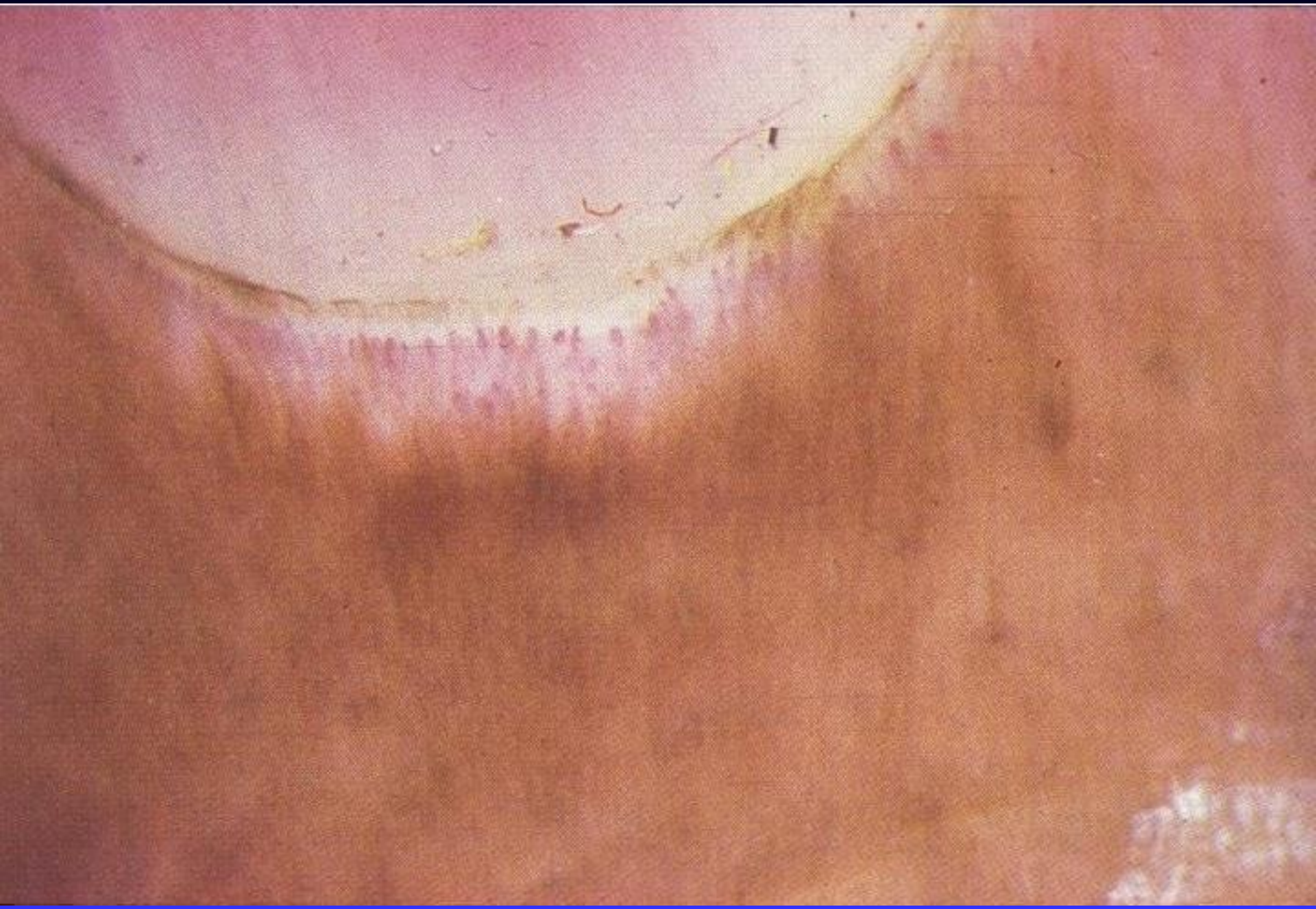


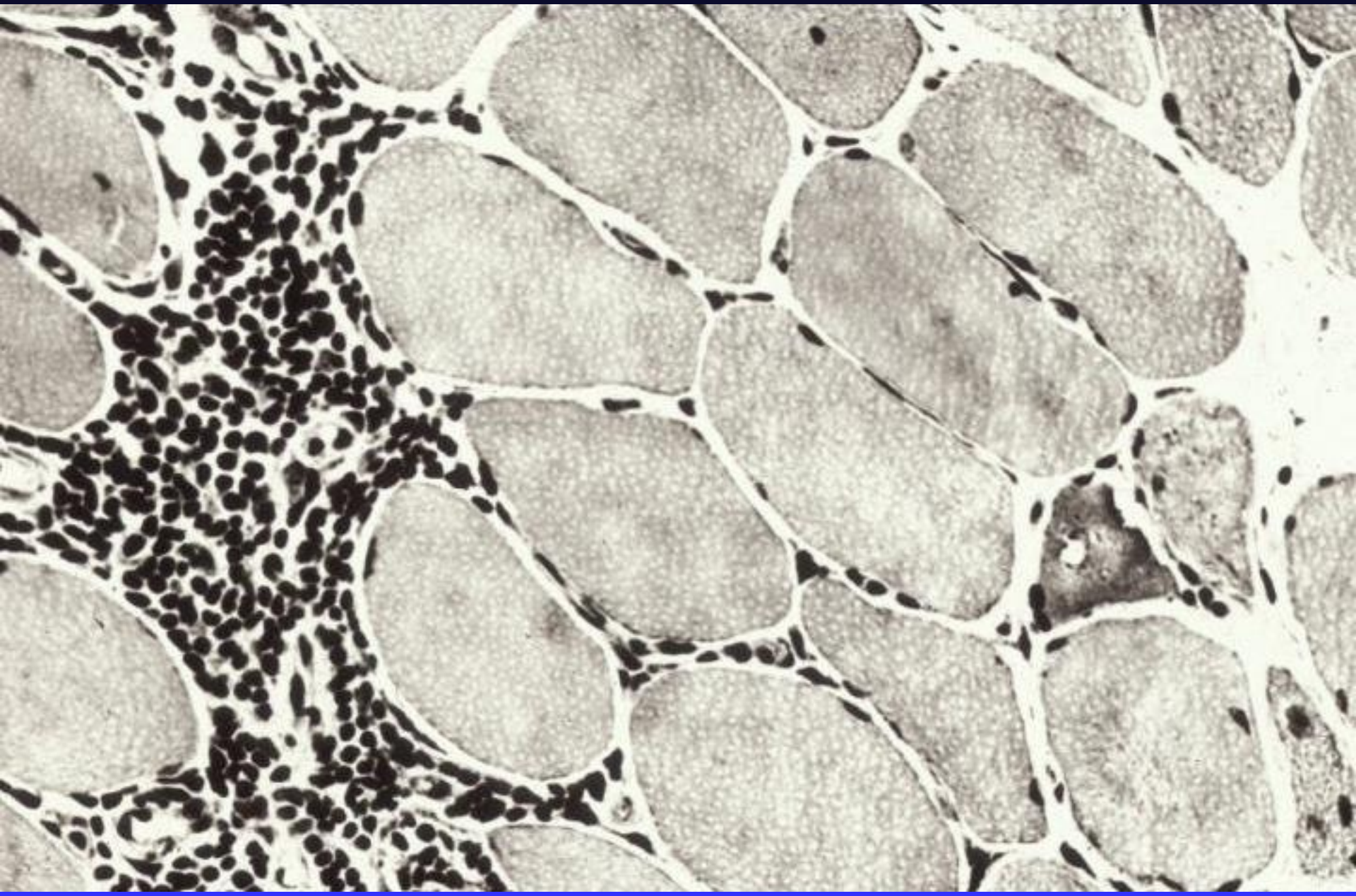


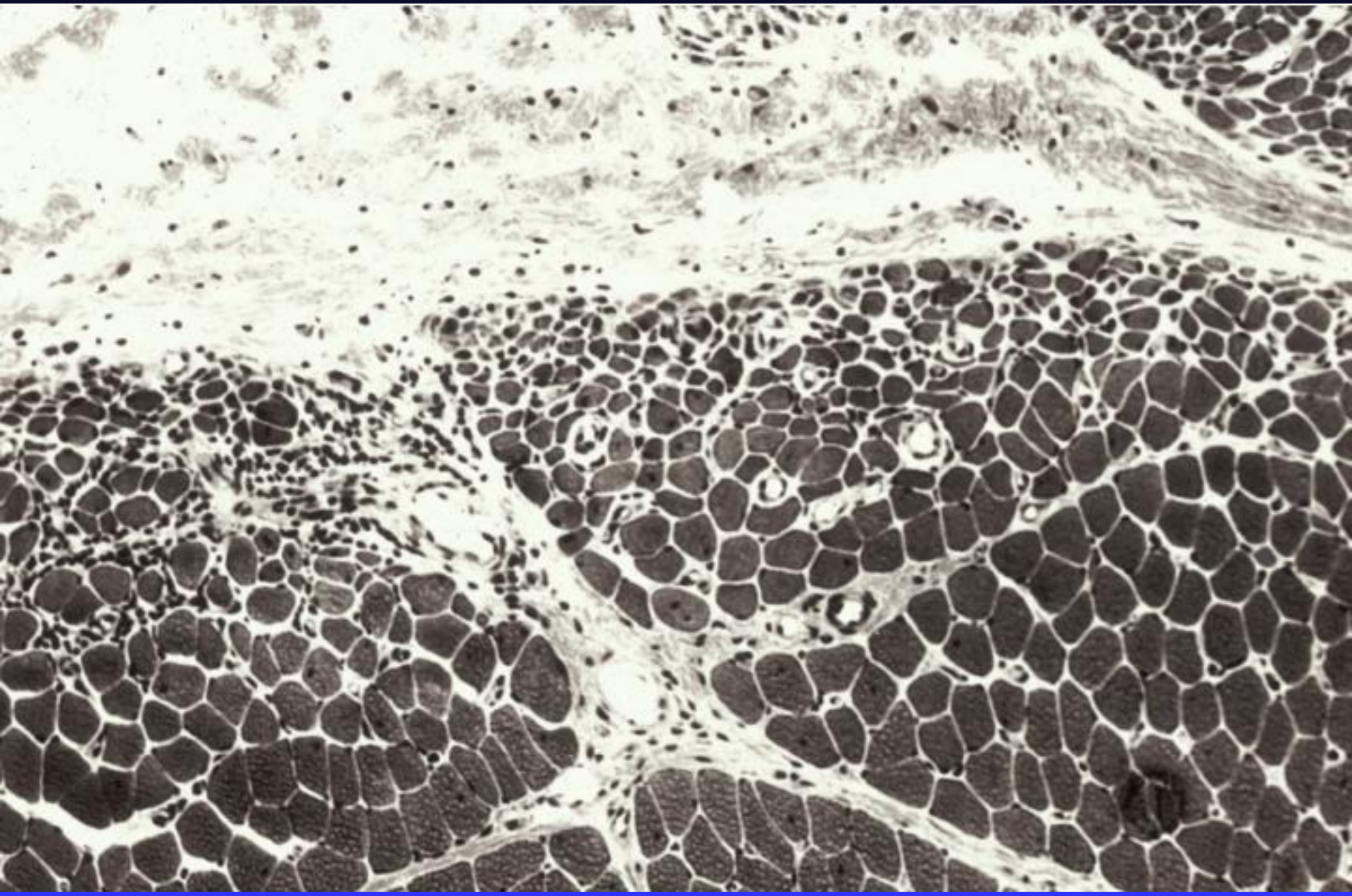






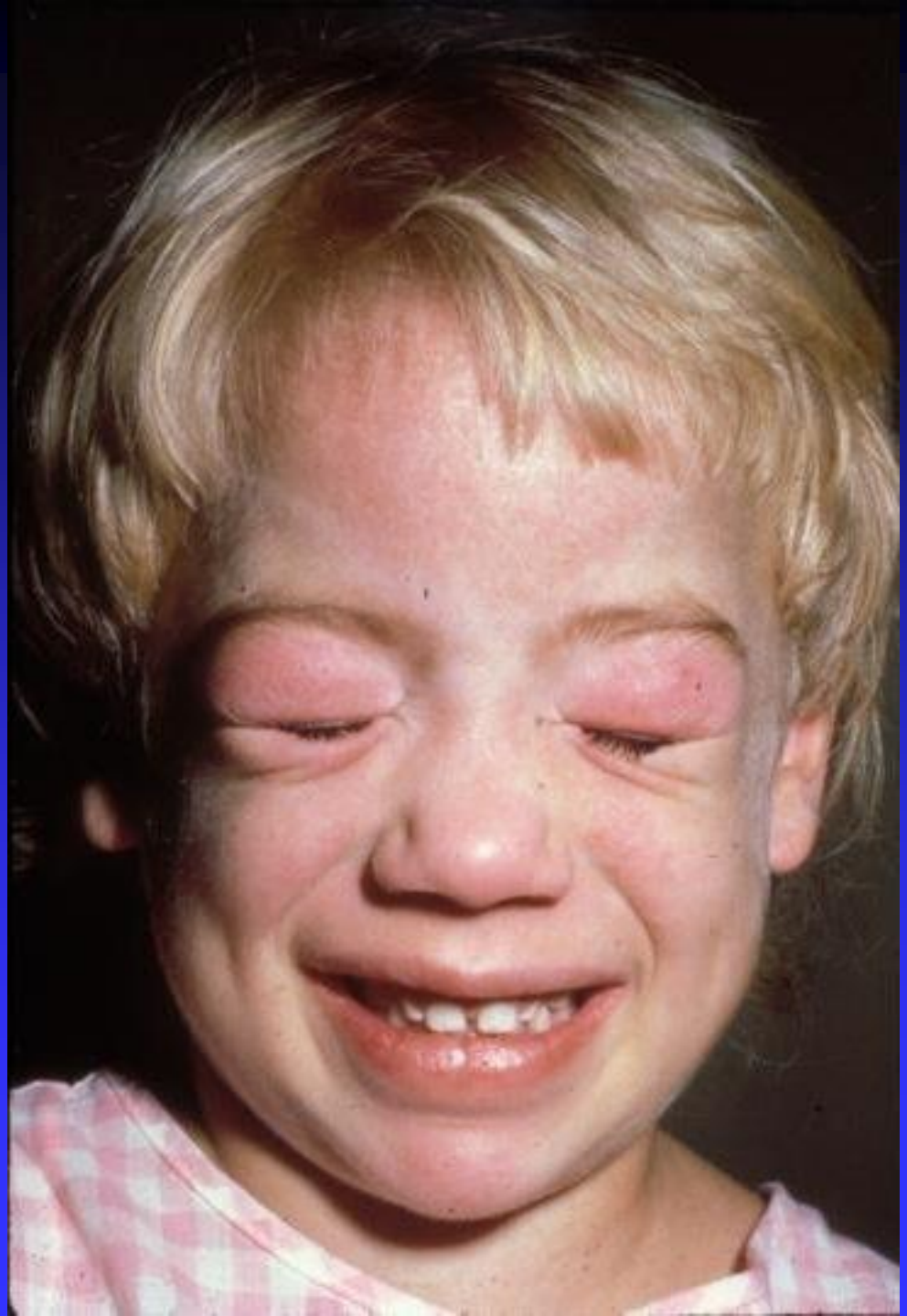


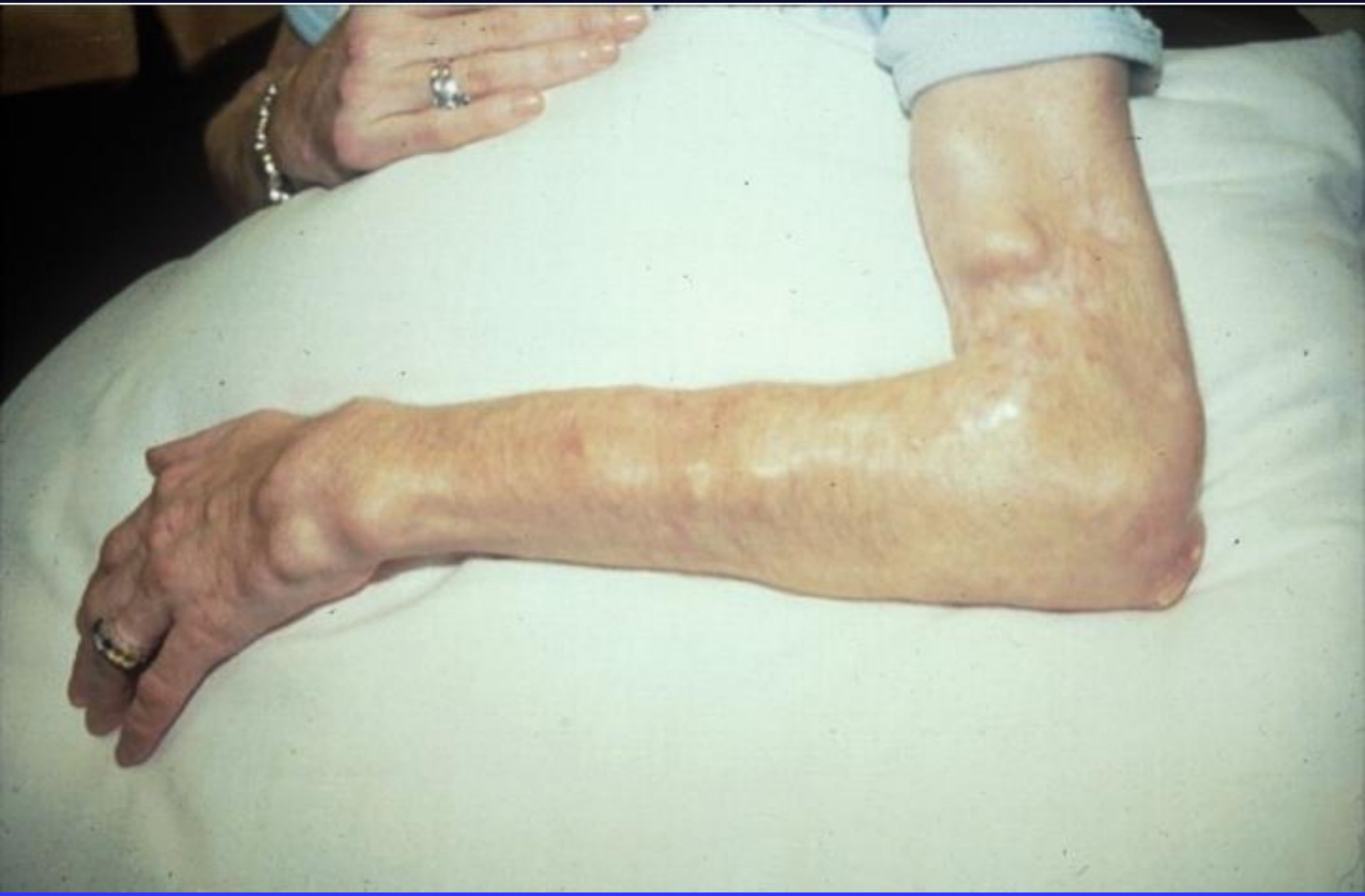


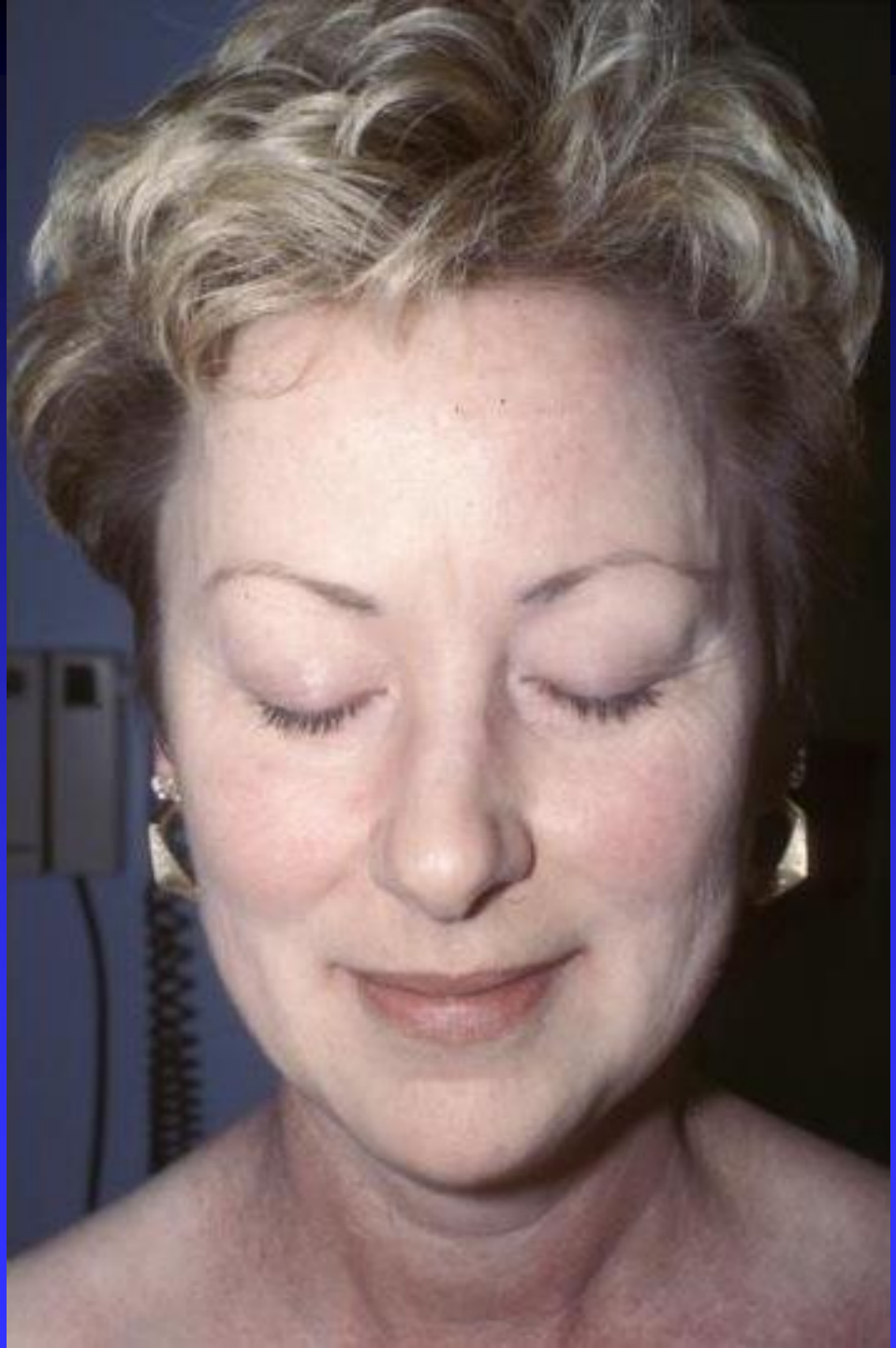


Dermatomyositis

- Subsets
  - Adult dermatomyositis
  - Juvenile dermatomyositis
  - Amyopathic dermatomyositis





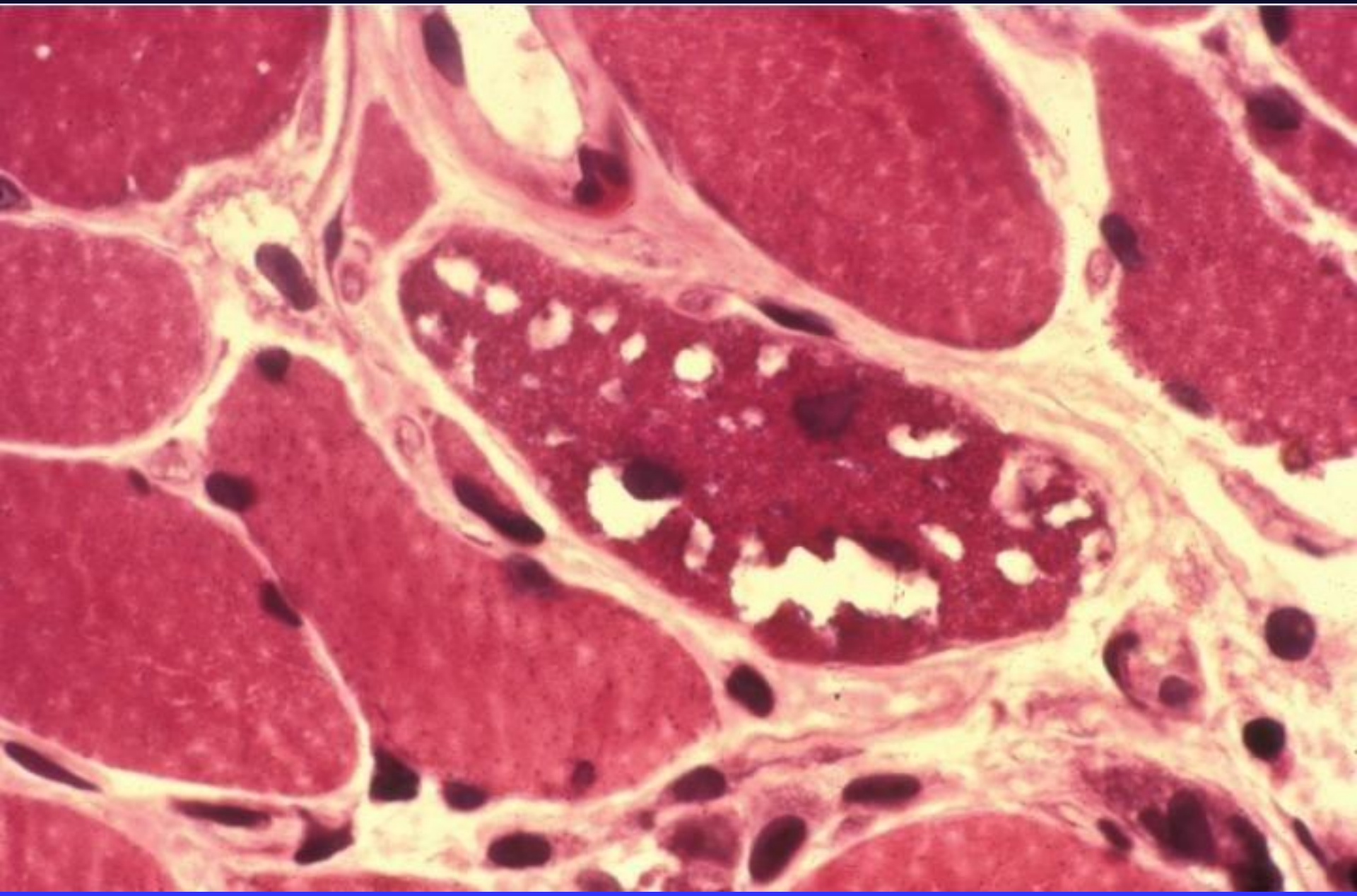


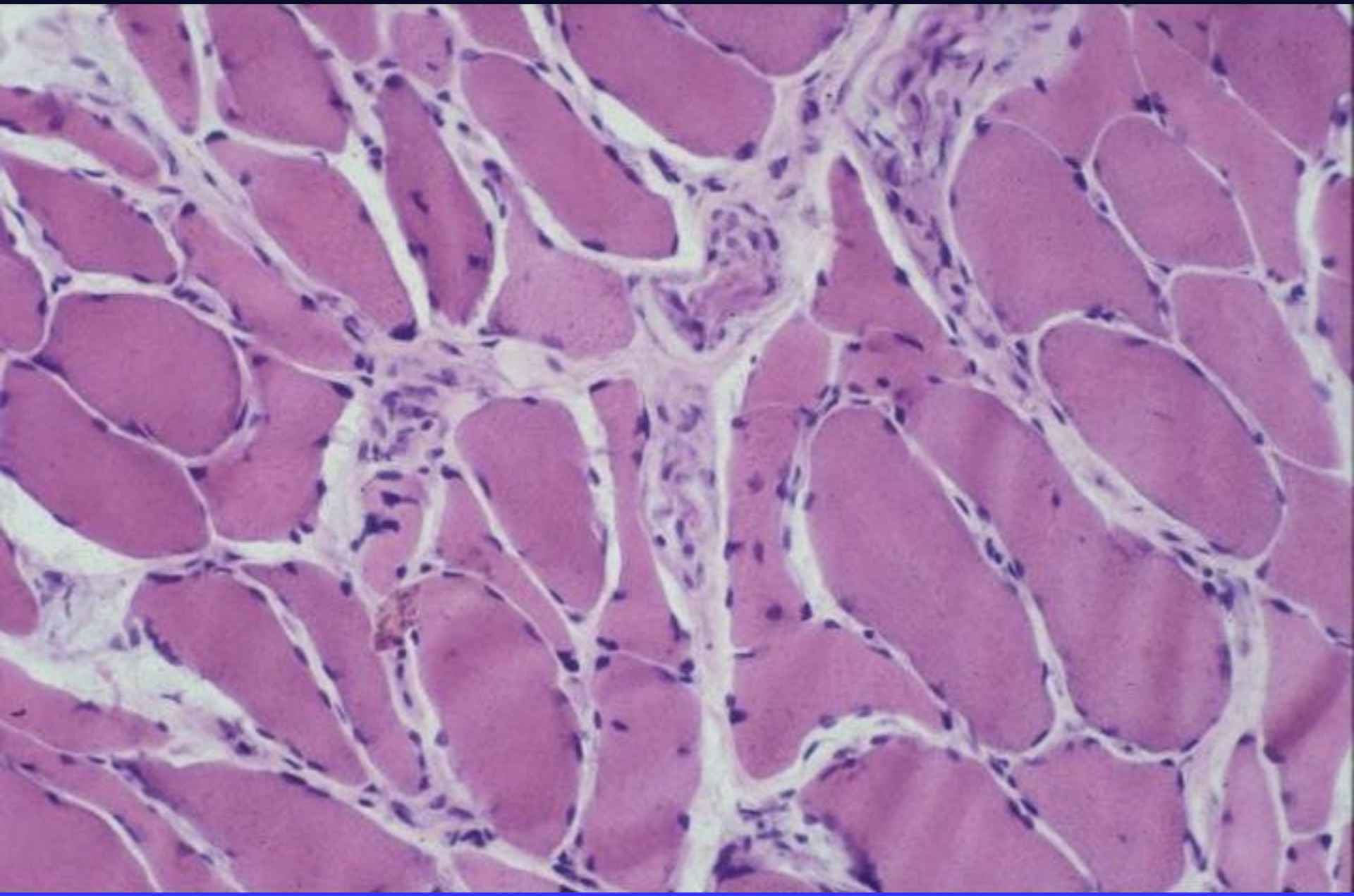
Inclusion Body Myositis – Clinical

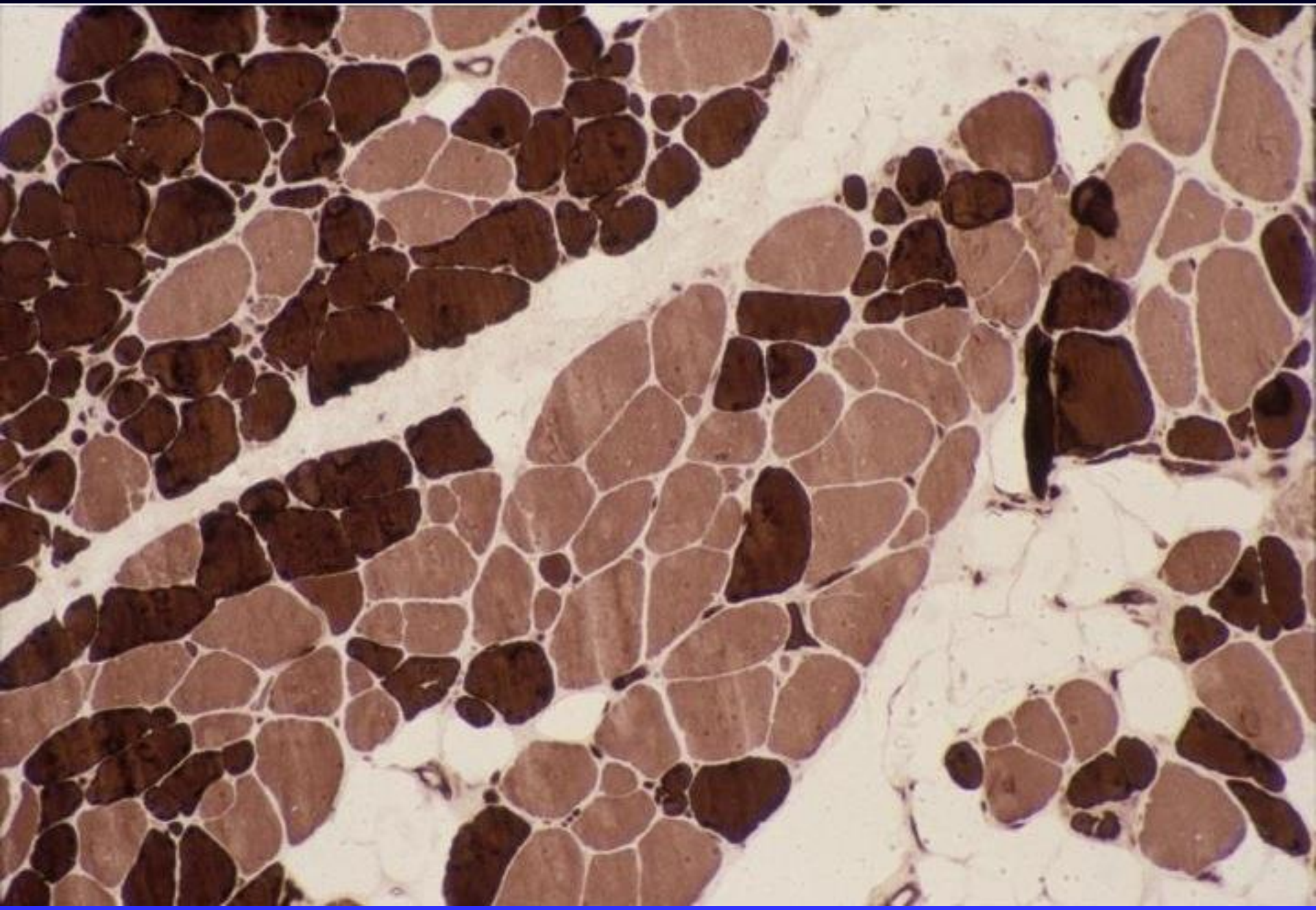
- Weakness
  - Proximal and symmetric
  - Distal
  - Asymmetric
- Response to Therapy
  - Poor if any

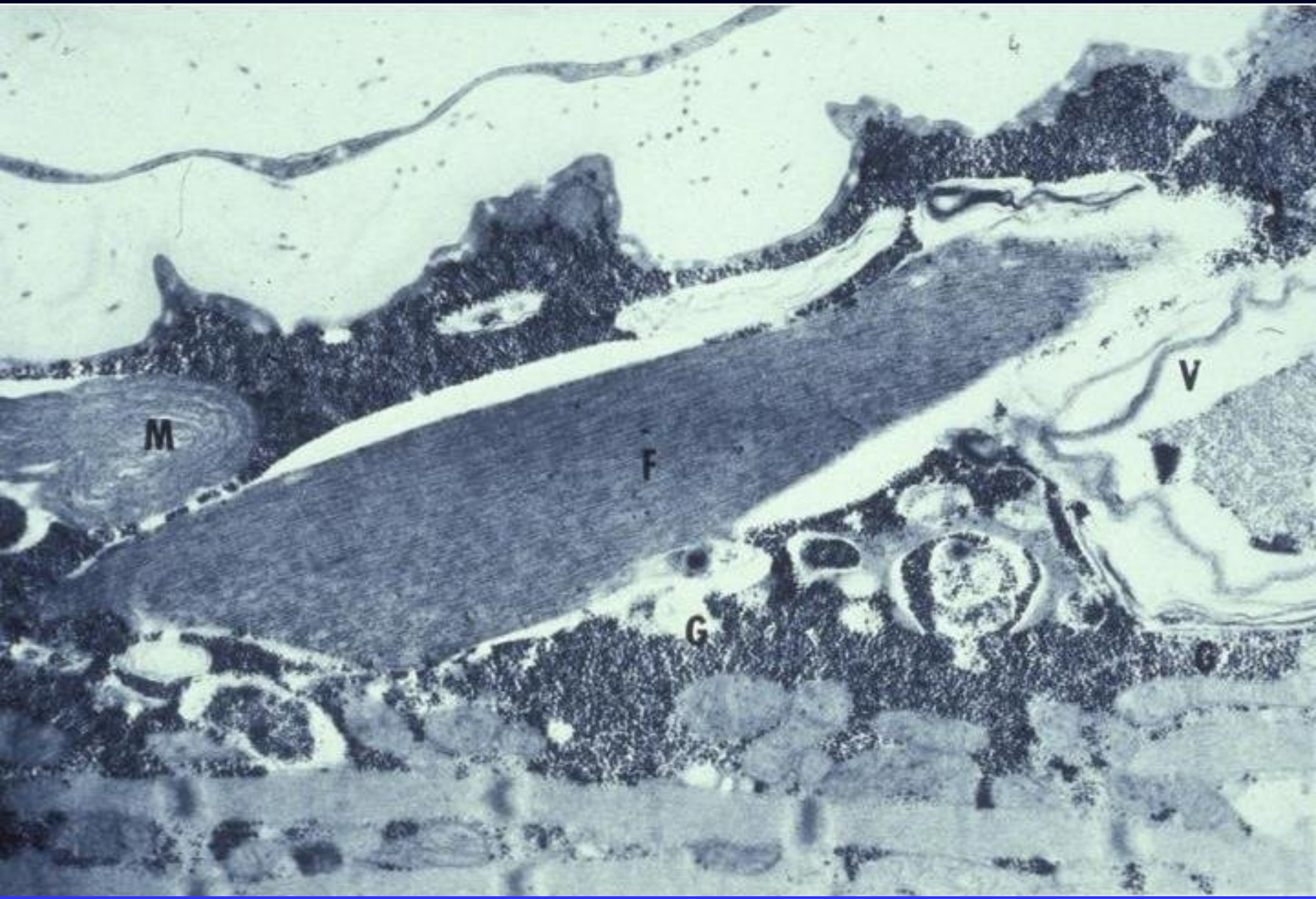
Inclusion Body Myositis

- Cellular infiltrate-like polymyositis but disappears
- Lined vacuoles
- Inclusions
- Amyloid deposits
- Mitochondrial abnormalities








M
F
V
G

Myositis and Connective Tissue Diseases

- Systemic lupus erythematosus
- Scleroderma
- Mixed connective tissue disease

Myositis and Cancer

- Increase risk with dermatomyositis
- Cancers are those most common for age and gender except for ovarian cancer
- Risk is greatest within one year of diagnosis
- Treatment of cancer often treats the myositis

Prognosis

- PM and DM
  - 55% do great
  - 35% have variable results
  - 10% do poorly
- IBM
  - Does not respond to drug therapy
  - Typically progresses slowly

Myositis Specific Autoantibodies

- May help predict outcomes

Anti-Synthetase Syndrome

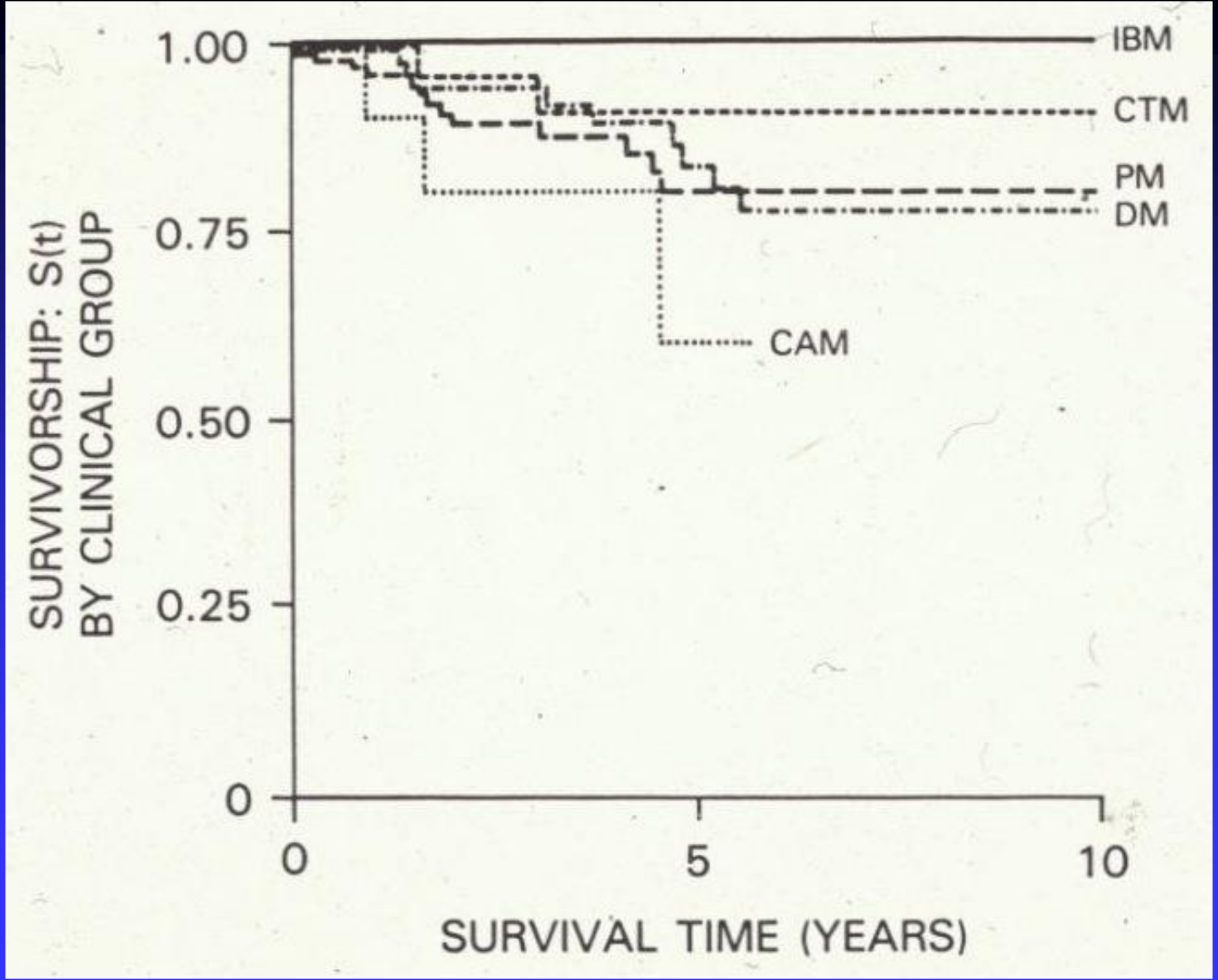
- Polymyositis > dermatomyositis
- Interstitial lung disease
- Fever
- Arthritis
- Raynaud's
- Mechanic's hands
- Difficult to treat

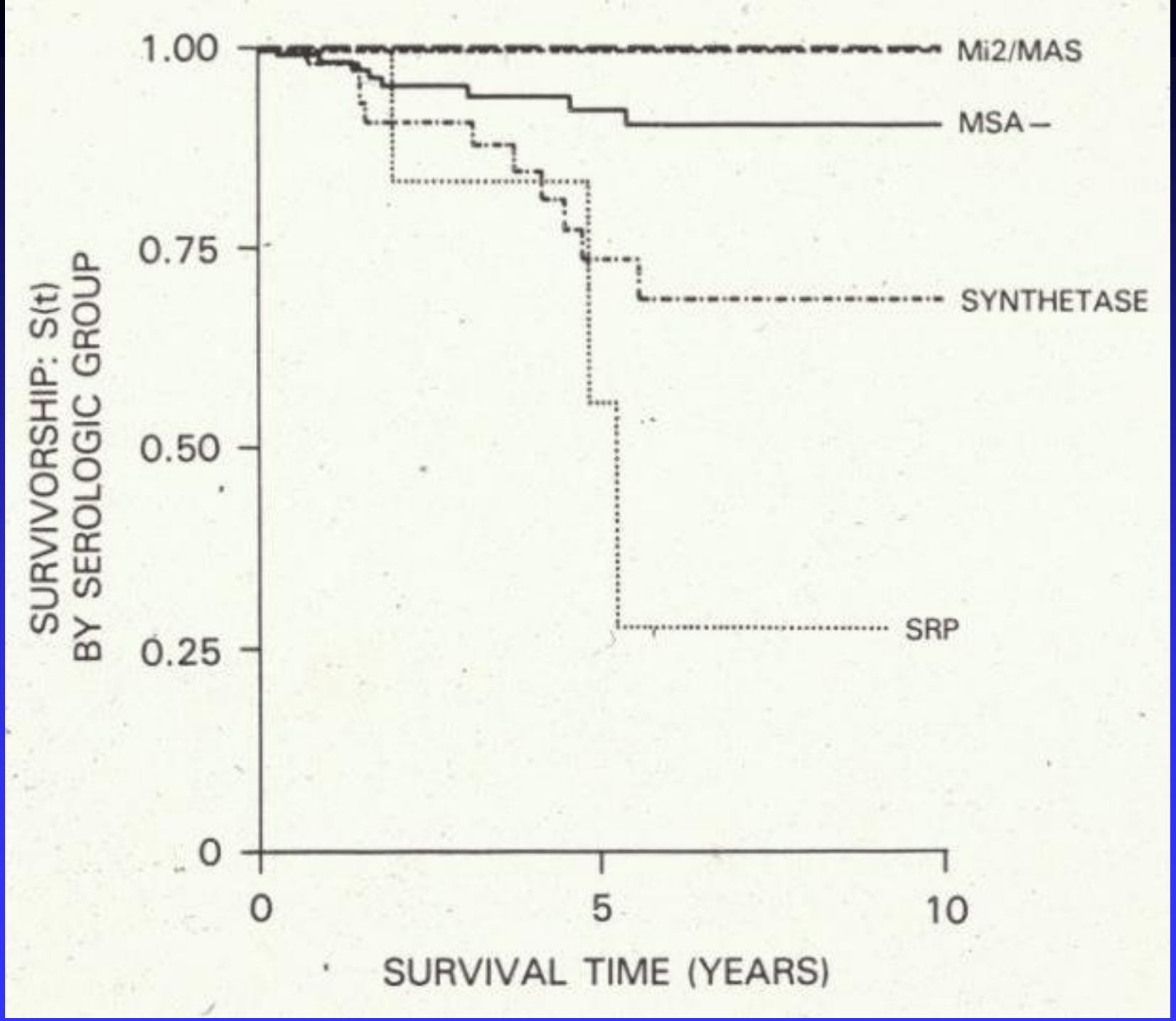
Anti-SRP

- Polymyositis >>> dermatomyositis
- Cardiomyopathy
- Distal weakness
- Very poor prognosis*

Anti-Mi 2

- Dermatomyositis
- Excellent prognosis*


1.00
0.75
0.50
0.25
0
SURVIVORSHIP: S(t)
BY CLINICAL GROUP
IBM
CTM
PM
DM
CAM
0
5
10
SURVIVAL TIME (YEARS)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SURVIVORSHIP: S(t)
BY SEROLOGIC GROUP
Mi2/MAS
MSA –
SYNTHETASE
SRP
0
5
10
SURVIVAL TIME (YEARS)

Although the criteria are nonspecific, when occurring together, and without other explanations, the allow the diagnosis of an idiopathic inflammatory myopathy,

Management of Inflammatory Myopathy

Impact of Cortisone on Polymyositis

- Changed the mortality form over 50% to less than 10%
- Steroid therapy may prove curative to 50%

Exercise is good!

- Aerobic
- Anaerobic

Both have been shown to improve strength and have anti-inflammatory effects

Controlled Trials

- Azathioprine + Prednisone
  - Bunch, 1981, 20 patients
- Plasma and leukophoresis
  - Miller, 1992, 39 (26) patients
- IV immune globulin
  - Dalakas, 1993, 15 patients
- Methotrexate/azathioprine – IV methotrexate
  - 30 patients
- Entanercept vs placebo
  - 16 patients

RIM Trial

- 202 subjects
  - 75 PM
  - 55DM
  - 52 JDM
- Negative results
- Regardless, over 80% of patients met the definition of improvement and average dose of prednisone dropped significantly

Others Used

- Cyclosporine
- Cyclophosphamide
- Chlorambucil
- Etanercept
- Infliximab
- Intravenous immune globulin
- Mycophenolate
- ACTH gel
- Rituximab
- Tacrolimus
- Stem cells

Treatment for IBM

- Exercise
- Immunosuppressives do not work
- Follistatin gene therapy
- Bimagrumab

Lack of Response

- Treatment insufficiency
  - (not enough drug prescribed or taken)
- Refractory disease
  - (IBM, interstitial lung disease, cancer, anti-SRP)
- Steroid toxicity
- Incorrect diagnosis