


# Approach to the Patient with Myopathy

November 7, 2026

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# Disclosures

- Clinical Trial Support
  - Fate Therapeutics
  - GSK
  - Sanofi
  - Astra Zeneca

# OUTLINE

- *Definition*
- *Epidemiology*
- *Pathophysiology*
- *Classification; diagnosis*
- *Clinical Features*
- *Special myopathic cases*
- *Treatment*



# Idiopathic Inflammatory Myopathy

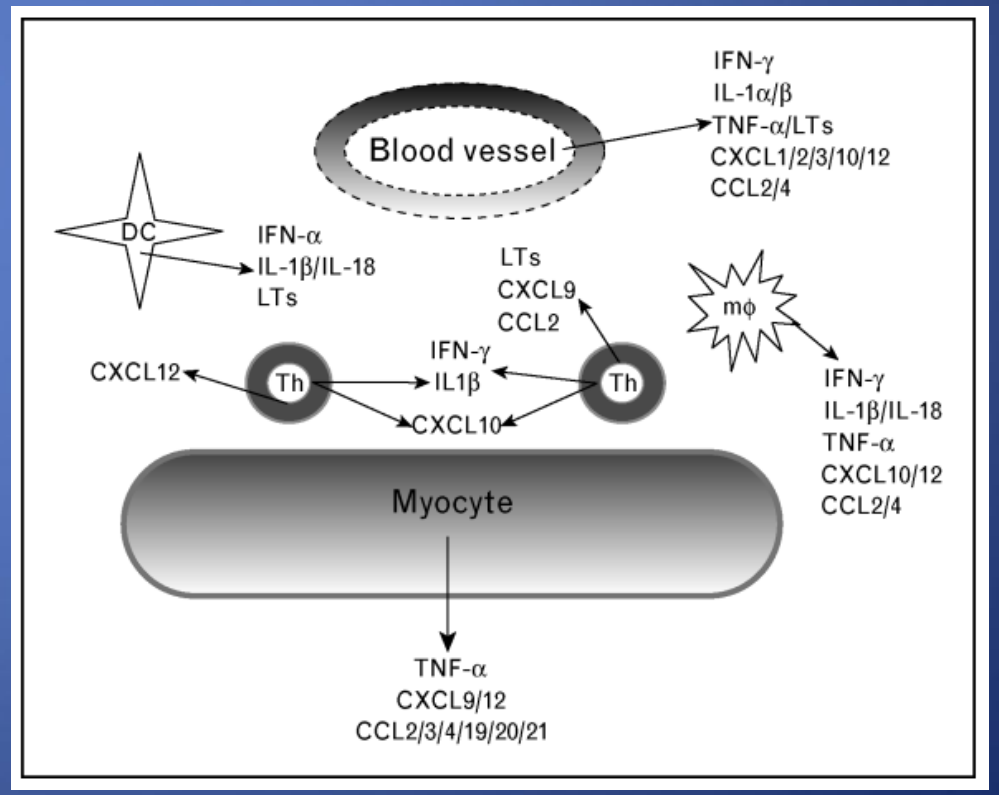
- Uncommon heterogeneous inflammatory muscle disorders featuring proximal muscle weakness
  - Adult Polymyositis
  - Adult Dermatomyositis
  - Special Cases:
    - Childhood DM
    - PM/DM associated with other CTD
    - Immune mediated necrotizing myopathy (anti-HMGCoA)

# Epidemiology

- Rare: incidence from 2 - 10 new cases/ million persons (underestimate?)
- Bimodal: 10-15 yrs, 45-55 yrs
- 3-4:1 African-American to White
- F:M 2-3:1
- Overlap syndromes:
  - Scleroderma
  - lupus, MCTD

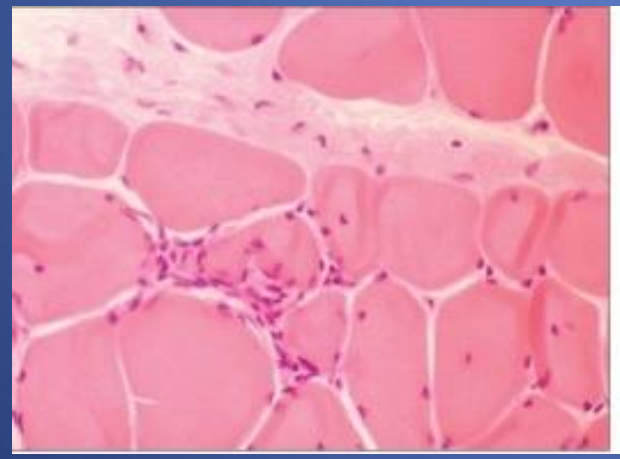
# Common Pathophysiology

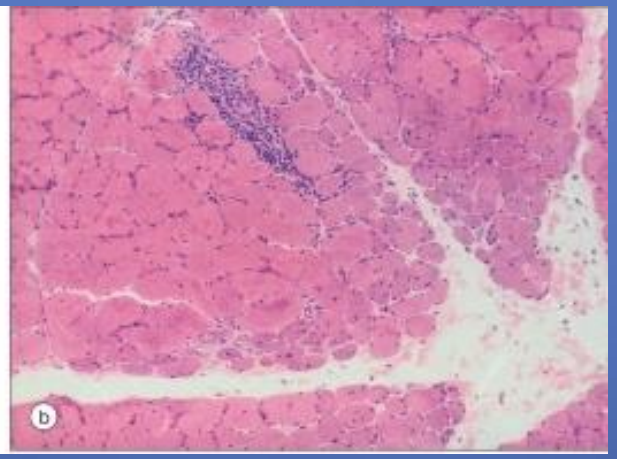
- B lymphocytes (myositis specific auto-Ab)
- Cytotoxic CD8+T cells for polymyositis
- CD4+T cells for dermatomyositis
- Pro-inflammatory cascade:
  - chemokines
  - complement activation
  - IL-1 and TNF
  - focal inflammation
  - death, repair

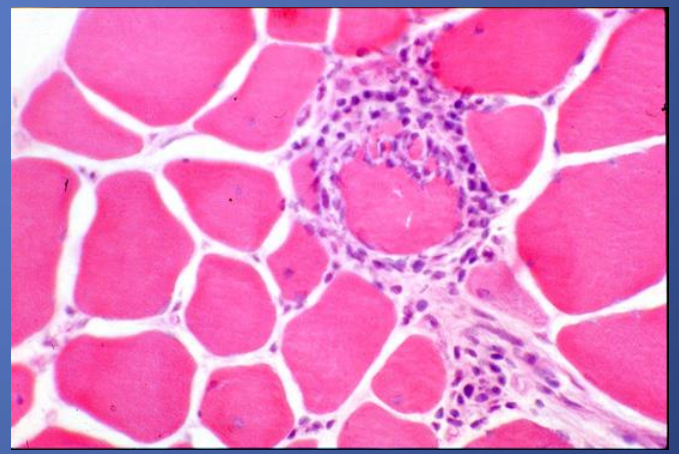


# Difference between PM and DM

- **Polymyositis**
  - Inflammatory infiltrate within fascicle.
  - Scattered/isolated necrotic fibers.
  - Target= myofiber.
- **Dermatomyositis**
  - Perivascular infiltrate around fascicles.
  - Necrotic fibers in group.
  - Target= blood vessels.

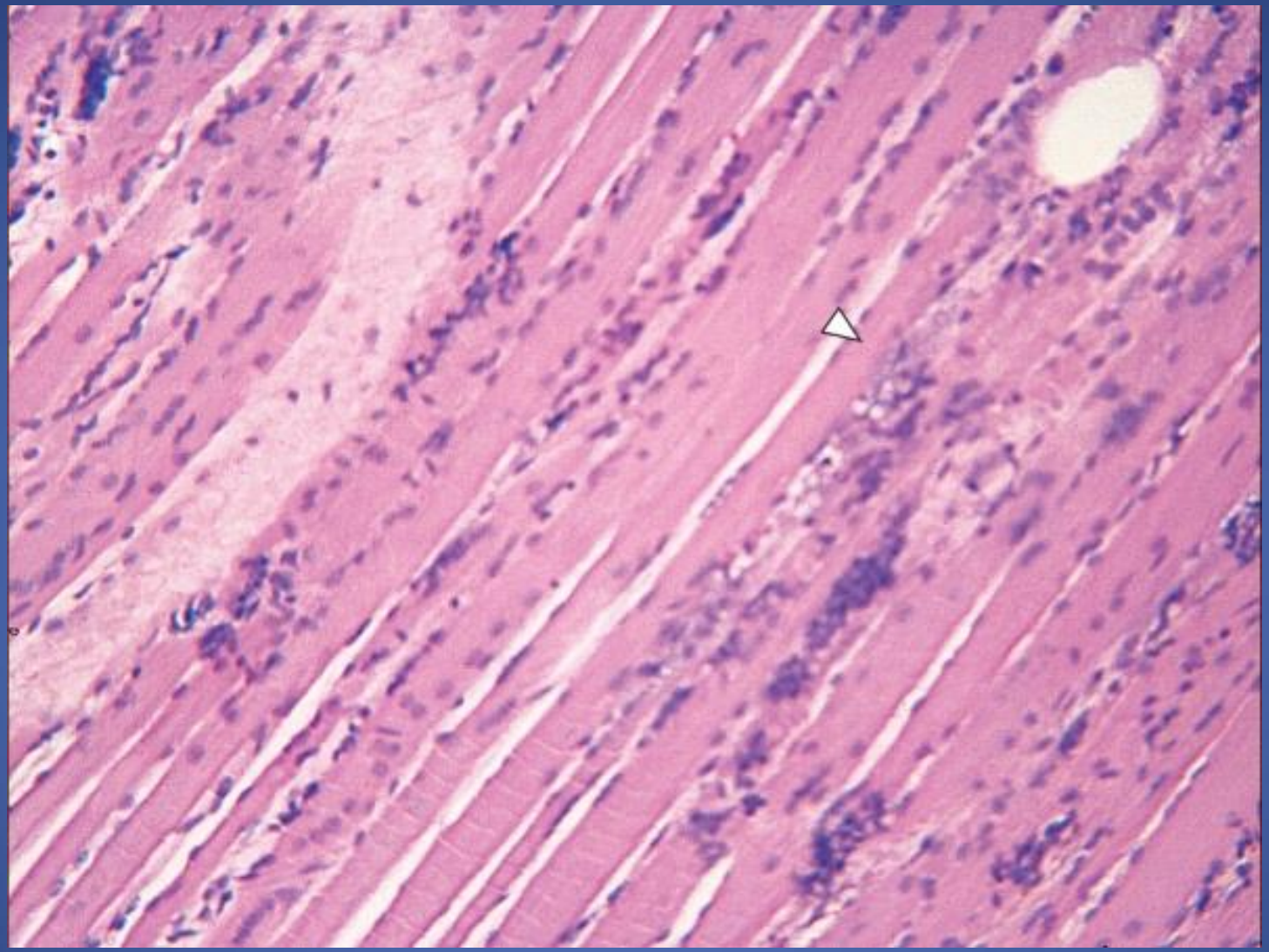




- Hematoxylin and Eosin cross-section of polymyositis:
- necrosis, regeneration and inflammation
- lymphocytic infiltration

# Polymyositis: longitudinal



myofiber destruction; areas of degeneration and necrosis of myofibers in association with interstitial lymphocytic infiltration

# Bohan and Peter Classification (1975)

1. Symmetrical proximal muscle weakness

   insidious and proximal muscles
2. Muscle biopsy evidence of myositis

   necrosis, phagocytosis, regeneration, atrophy, perivasc infiltrate
3. Increase in serum skeletal muscle enzymes

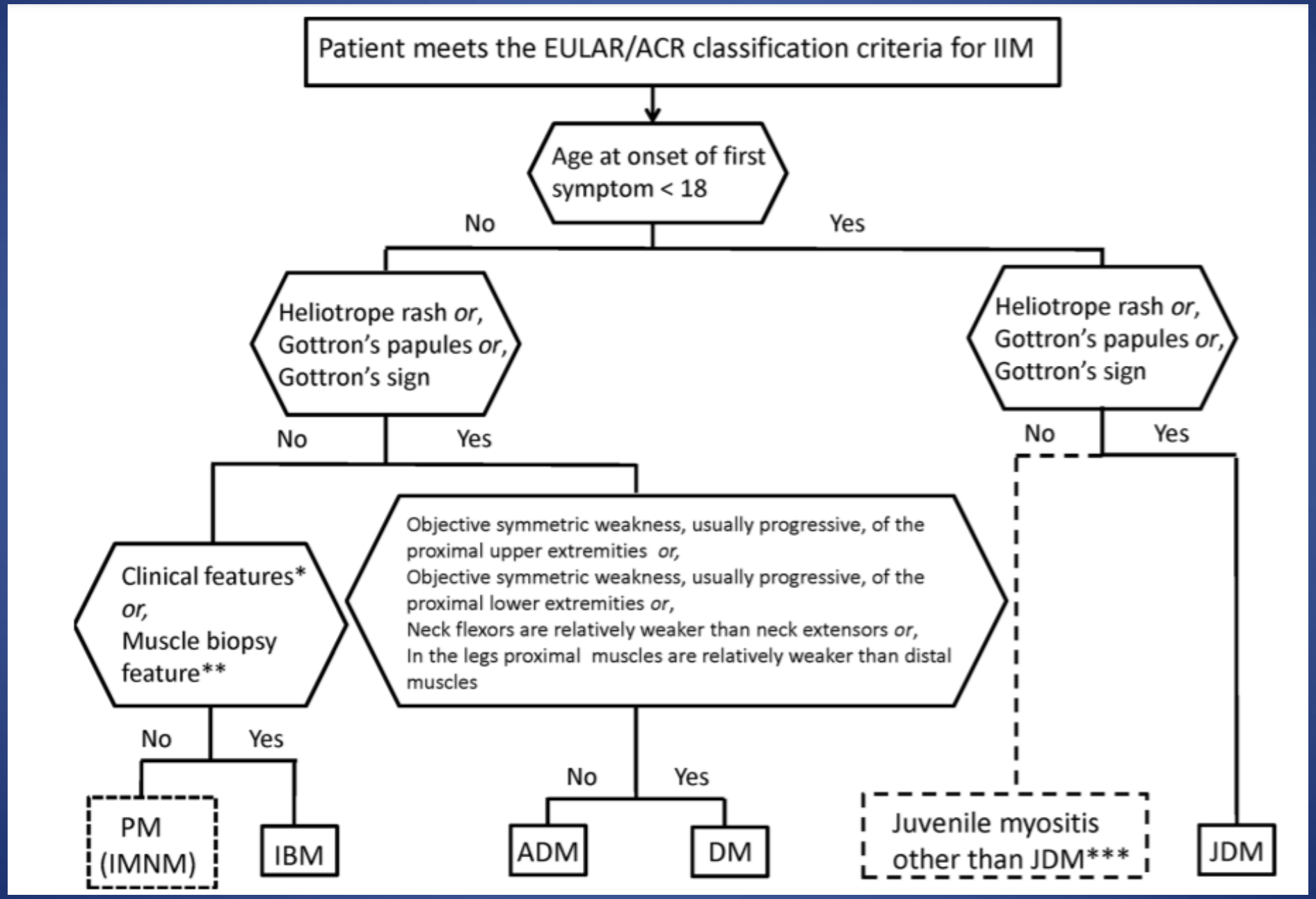
   CPK, aldolase, LDH, AST, ALT
4. Characteristic electromyographic pattern

   short polyphasic motor units, fibrillations, irritability and repetitive dc's
5. Typical rash of dermatomyositis
   heliotrope, gottrons, shawl, v neck

Polymyositis:
Definite: all of 1-4
Probable: any 3 of 1-4
Possible: any 2 of 1-4

Dermatomyositis:
Definite: 5 plus any 3 of 1-4
Probable: 5 plus any 2 of 1-4
Possible: 5 plus any 1 of 1-4

# 2017 ACR/EULAR Criteria for Immune Mediated Myopathy



# Case 1

A 67 year-old female presents to her internal medicine physician with complaints of a rash on her face, in particular the eyelids. She states it is aggravated when she is in the sunlight.

Also, she reports of muscle aches and weakness. She has the most difficulty when climbing the stairs or standing up from a seated position.

Physical examination is remarkable for a rash that is purple in color and located on the eyelids. She also appears to have a papular rash affecting the knuckles. Lastly, she has weakness of the hip girdle muscles, with the motor strength of bilateral hip flexors and extensors being 3/5.

Which muscle enzyme is most sensitive for the detection of this condition?

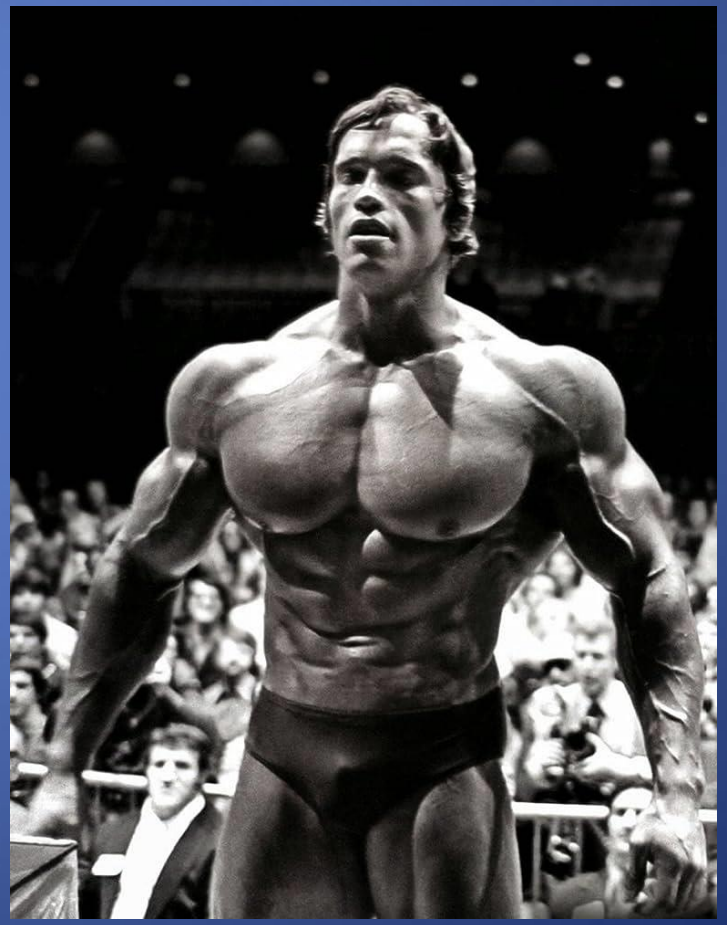


A. Creatine phosphokinase (CPK)
B. Lactate dehydrogenase (LDH)
C. Aldolase
D. AST
E. ALT

# Diagnosis: Muscle Enzymes

- Diagnosis; monitoring
  - Enzymes leak
- Sensitivity: CPK>aldolase>ALT/AST>LDH
- LDH may be most treatment specific

- Variations:
  - Muscle mass
  - Genetics
  - Kidney function



# Diagnosis: Muscle Biopsy

- Gold standard for confirmation
- Pitfalls:
  - patchy disease and sampling error
  - Most myopathic muscle has highest yield
  - Biopsy the contralateral muscle to EMG
- Role of MRI mapping?

# Clinical Features - Muscle

- Nonspecific fatigue, fevers, weight loss (constitutional, malignancy)
- Usually painless symmetrical muscle weakness
  - proximal>distal
  - stairs, toileting, abduction, neck flexion
  - gait abnormalities
- Dysphagia, nasal regurgitation of liquids
- Hoarseness or dysphonia (nasal voice)
- Ocular or facial weakness→ uncommon
  - consideration of another diagnosis

# Clinical Features - Skin

- May precede, develop simultaneously or subsequently
  - Heliotrope rash
  - Shawl sign
  - V neck sign
  - Gottron's papules
    - scaly, erythematous or violaceous papules/plaques over hand IP joints
  - Holster sign
  - Samitz sign








# Heliotrope rash

Erythematous/violaceous rash over the eyelids, face with/without perioribital edema

# Clinical Features: Skin

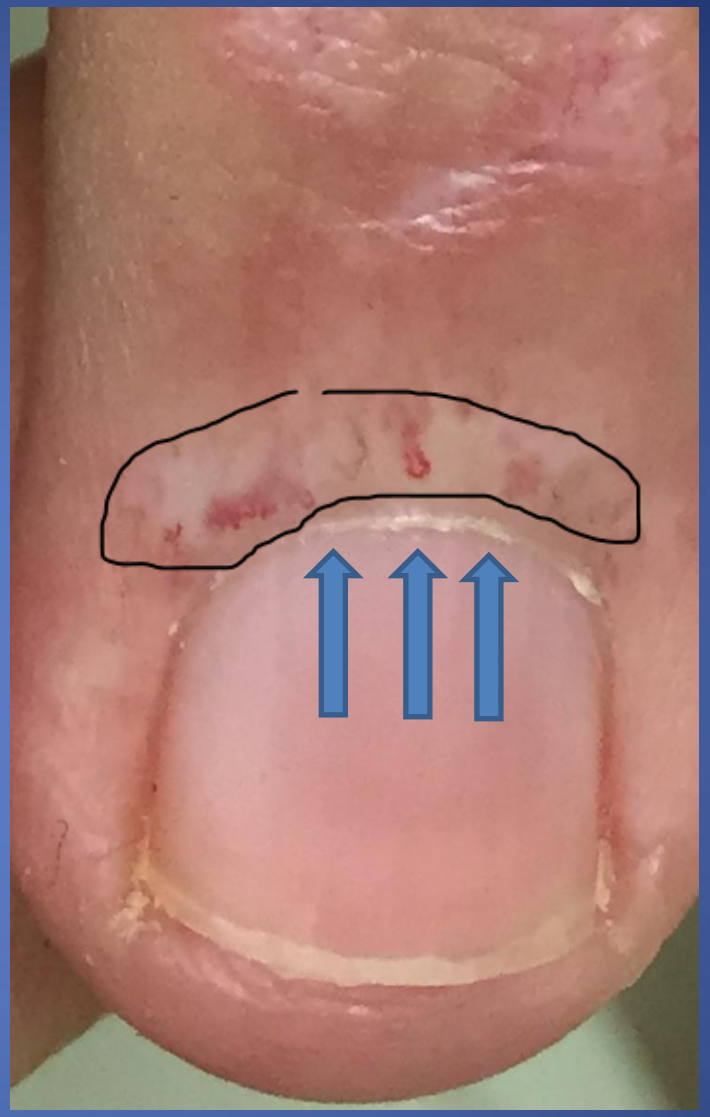












Gottron’s papules
dilated capillary nailfold loops
Samitz sign

# Special Myopathic Syndromes: Amyopathic Dermatomyositis

- Classical cutaneous DM
- No clinically apparent myopathy
- May herald future myopathy (50%)

# Special Myopathic Syndromes: Autoantibodies

| Autoantibodies | Clinical features |
|---|---|
| Anti-ARS (antisynthetase) | AS syndrome with moderate-to-serve muscle weakness with high muscle enzyme levels, RP, mechanic's hands, fever, arthritis, and ILD |
| Anti-Jo-1 | Chronic continuous disease course, with clinical symptoms for >two years after diagnosis; mean five-year survival rate = 65%, usually due to ILD; AS syndrome features |
| Anti-PL-7 | AS syndrome with higher frequency of ILD |
| Anti-PL-12 | AS syndrome with higher frequency of ILD |
| Anti-EJ | Dermatomyositis and ILD |
| Anti-OJ | Myositis and ILD |
| Anti-KS | ILD with less myositis |
| Anti-Ha | NA |
| Anti-Zo | Myositis and ILD |
| Anti-SRP | Acute onset NM with severe weakness, high CK, cardiac involvement; refractory to treatment |
| Anti-Mi-2 | Adult DM and JDM with hallmark cutaneous disease, milder myositis with good response to treatment |
| Anti-TIF1-γ (anti-p155/140) | CAM in adult DM; severe cutaneous disease in adult DM and JDM |
| Anti-SAE | Adult DM; may present with CADM first |
| Anti-MDAs (anti-CADM140) | CADM; rapidly progressive ILD |
| Anti-NXP-2 | Predominantly JDM with subcutaneous edema, calcinosis, and servere muscle disease with contractures; increased risk of cancer in some adult DM studies |
| Anti-HMGCR | NM; associated with statin use in adults; severe proximal muscle weakness; partially responsive to immunosuppressive medications; better response to IVIg |

# Case 2:

cc: diffuse muscle soreness

HPI: 24 yo African American man with 10 lb wt gain. He usually lifts weights regularly but is just not lifting quite as many pounds as before but there is no definite weakness on exam.

CPK:

What do you do next?

- urgent muscle biopsy
- EMG
- TSH
- urine for myoglobin
- aldolase

| Latest Ref Rng | 15 - 190 IU/L |
|---|---|
| 9/30/2011 | 2276 (H) |
| 10/8/2011 | 2438 (H) |
| 10/17/2011 | 1982 (H) |

| Component | CK | TSH | REPORT |
|---|---|---|---|
| Latest Ref Rng | 15 - 190 IU/L | 0.35 - 4.00 uIU/mL | < OR = 8.1 U/L |
| 9/30/2011 | 2276 (H) | | |
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| 1/23/2012 | | >100 (H) | Aldolase: 10.7 (H) |

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| 1/23/2012 | | >100 (H) | Aldolase: 10.7 (H) |
| 9/8/2012 | 130 | 11.58 (H) | |

# Case 3

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| Component | CK |
| --- | --- |
| Latest Ref R | <=398 U/L |

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|---|---|
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| 2/12/2013 | **498651 (H)** |

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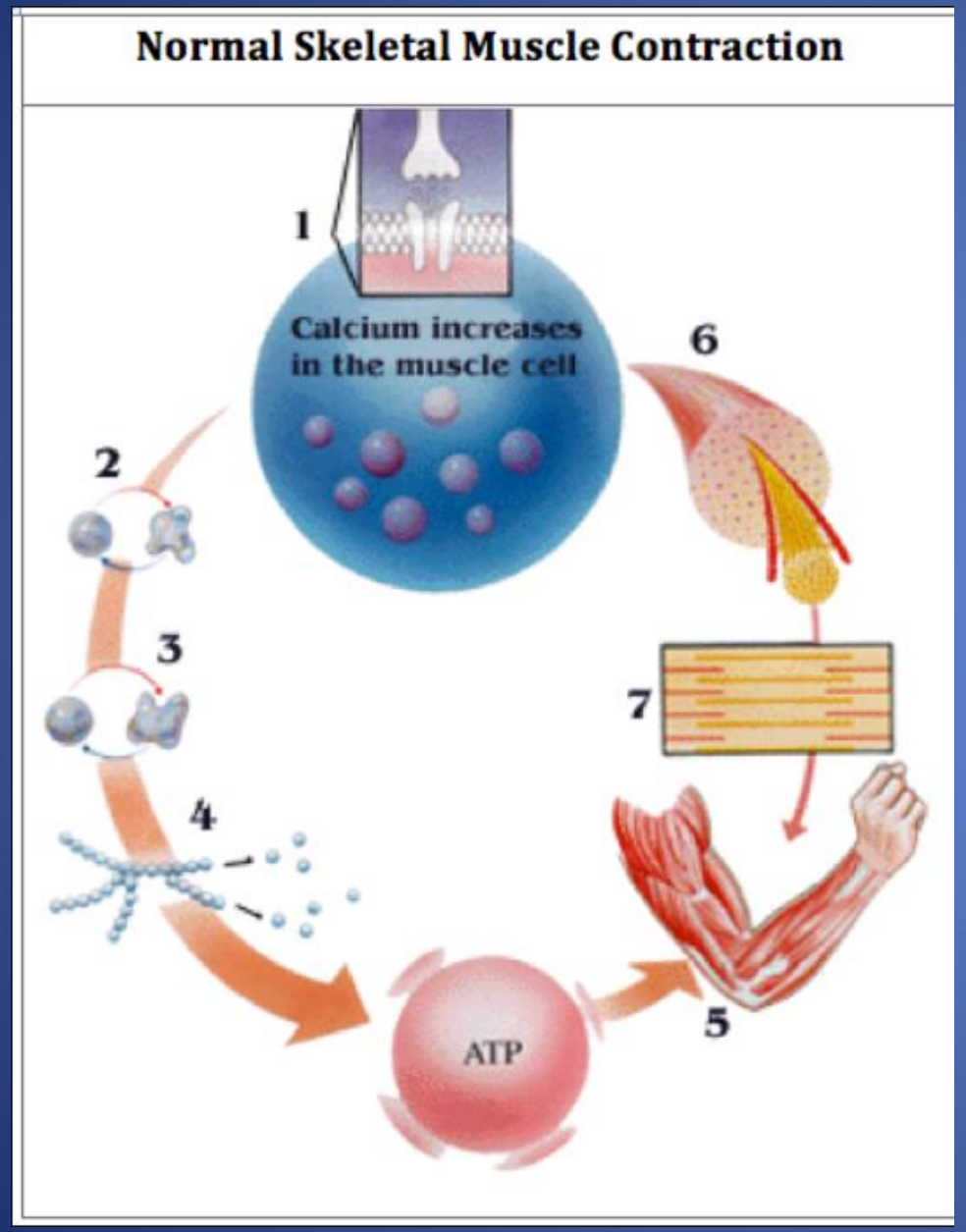
| Component | CK |
|---|---|
| Latest Ref R | <=398 U/L |
| 2/12/2013 | **498651 (H)** |
| 2/13/2013 | **368800 (H)** |
| 2/19/2015 | **31,161 (H)** |
| 4/22/2015 | 301 |

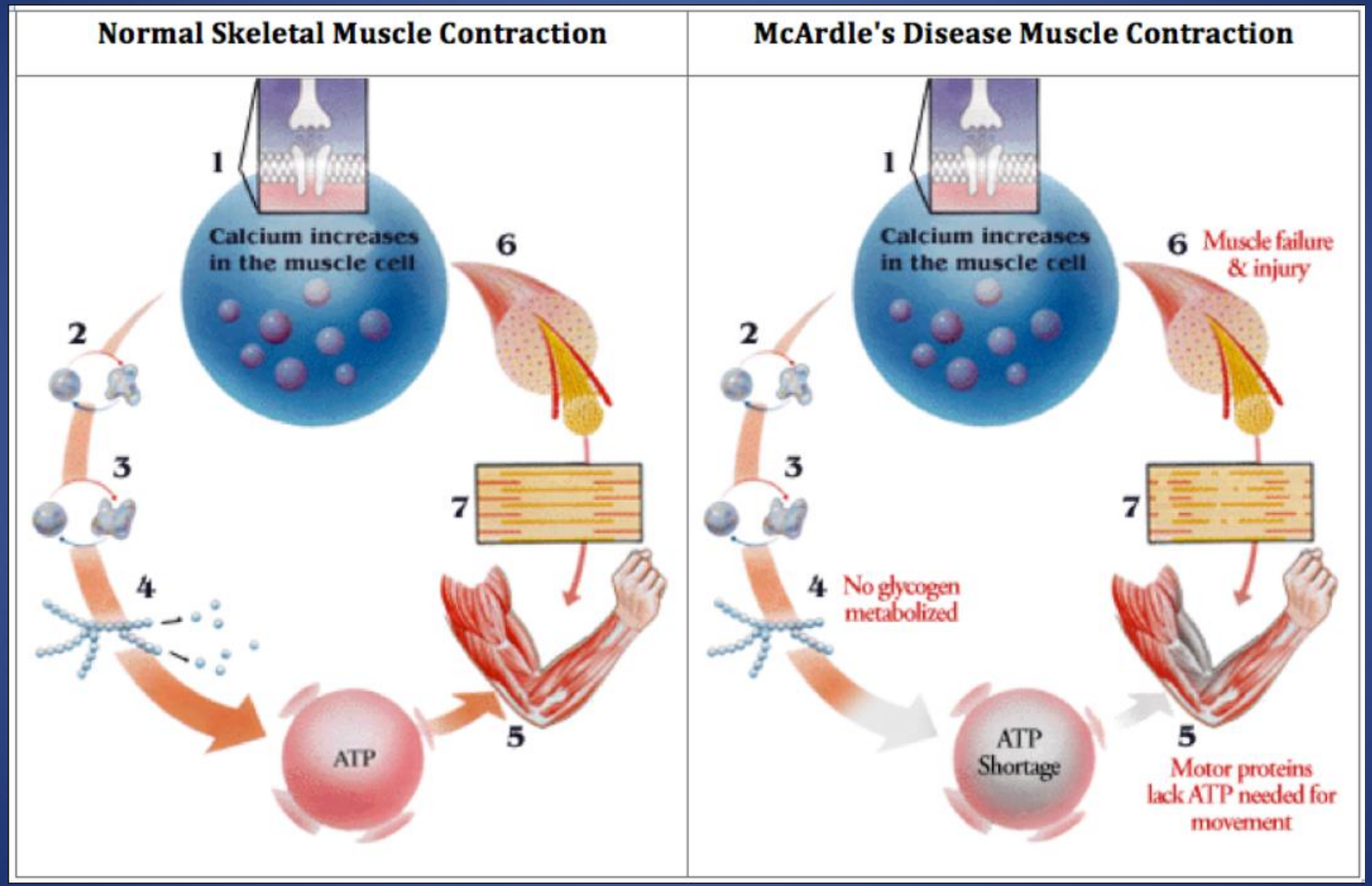
What is this condition?

- Muscle infarction
- ✓ Metabolic myopathy
- Polymyositis
- Muscular dystrophy

What was the treatment?

- glucocorticoids
- hemodialysis
- infliximab
- plasmapheresis
- ✓ cautious monitoring and diet and exercise counseling


Normal Skeletal Muscle Contraction
1
Calcium increases in the muscle cell
2
3
4
ATP
5
6
7


Normal Skeletal Muscle Contraction
McArdle's Disease Muscle Contraction
1
Calcium increases in the muscle cell
2
3
4
ATP
5
6
7
1
Calcium increases in the muscle cell
2
3
4
No glycogen metabolized
ATP Shortage
5
Motor proteins lack ATP needed for movement
6
Muscle failure & injury
7

# Differential Diagnosis

- ‘tiredness’ vs ‘fatigue’ vs ‘low energy’
- clinical weakness
  - motor task (muscle weakness)
  - repetitive performance (fatigue)
- ROS (constitutional, ENT, skin, pulmonary)
- Neurological
  - Guillain barre
  - Myasthenia gravis
  - Amyotrophic lateral sclerosis
- Rheumatic
  - Lupus, vasculitis
- Other
  - Neoplastic, metastatic disease
  - Endocrine

| General type | Subtypes/examples |
| --- | --- |
| Denervating conditions | Spinal muscular atrophies, amyotrophic lateral sclerosis |
| Sarcoidosis | |
| Neuromuscular disorders | Eaton–Lambert syndrome, myasthenia gravis |
| Genetic muscular dystrophies | Duchenne's facioscapulohumeral, limb girdle, Becker's, Emery–Dreifuss type, distal, ocular |
| Glycogen storage diseases | Adult-onset acid maltase deficiency, McArdle's disease |
| Lipid storage myopathies | Carnitine deficiency, carnitine palmityltransferase deficiency |
| Endocrine myopathies | Hypothyroidism, hyperthyroidism, acromegaly, Cushing's disease, Addison's disease, hyperparathyroidism, hypoparathyroidism, vitamin D deficiency myopathy, hypokalemia, hypocalcemia |
| Metabolic myopathies | Uremia, hepatic failure |
| Toxic myopathies | Acute and chronic alcoholism, drugs including penicillamine, clofibrate, chloroquine, emetine, statins, niacin, colchicine, checkpoint inhibitors |
| Nutritional myopathies | Vitamin E deficiency, malabsorption |
| Acute rhabdomyolysis | |
| Proximal neuropathies | Guillain–Barré syndrome, acute intermittent porphyria, diabetic lower-limb chronic plexopathies, chronic autoimmune polyneuropathy |
| Septic myositis | Including Staphylococcus, Streptococcus, *Clostridium perfringens (welchii)* and leprosy |

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

# Statin-Associated Autoimmune Myopathy

Andrew L. Mammen, M.D., Ph.D.

From the National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, and the Johns Hopkins University School of Medicine, Baltimore — both in Maryland. Address reprint requests to Dr. Mammen at the Muscle Disease Unit, Laboratory of Muscle Stem Cells and Gene Expression, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, 50 South Dr., Rm. 1146, Bldg. 50, MSC-8024, Bethesda, MD 20892, or at andrew.mammen@nih.gov.

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STATINS SIGNIFICANTLY REDUCE THE INCIDENCE OF CARDIOVASCULAR disease, are generally safe, and have an acceptable side-effect profile. Indeed, a recent meta-analysis confirmed that mild musculoskeletal problems, such as myalgia, occur in approximately equal numbers of persons treated with statins and those given placebo.[1] Only in rare cases, in approximately 1 of 10,000 treated persons per year,[2] do statins cause serious muscle damage, with weakness and elevated levels of creatine kinase. In the majority of such cases, the patients recover spontaneously after the statin treatment is discontinued.[3,4] It is now recognized, however, that in very rare cases, an autoimmune myopathy develops in patients treated with statins; this disorder is characterized by muscle weakness, evidence of muscle-cell necrosis on biopsy, and the presence of autoantibodies against 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase.[5-16] In contrast to most patients who have side effects from statin therapy, those with statin-associated autoimmune myopathy may have progressive weakness that must be controlled with immunosuppressive therapy. This review describes the clinical characteristics, diagnosis, proposed pathologic mechanisms, and treatment of statin-associated autoimmune myopathy.

| REMARKS | REFERRING PHYSICIAN | REPORTED 10/26/2017 11:53 |
|---|---|---|
| | LEE | STATUS FINAL |

| TEST | RESULT (* = OUT OF RANGE) | UNITS | REFERENCE RANGE |
|---|---|---|---|
| TEST NAME: | SEE BELOW | | |
| ANTI-HMGCR AB, (EIA) | | | |
| RESULT: | SEE BELOW | | |
| | >200* | Units | |
| NORMAL RANGE: | <20 | | |

NEGATIVE. . . . . .<20
WEAK POSITIVE. . . . .20-39
MODERATE POSITIVE. . .40-59
STRONG POSITIVE. . . .>=60

ANTI-HMGCR ANTIBODIES ARE USUALLY FOUND IN ASSOCIATION WITH NECROTIZING MYOPATHY RELATED TO STATIN THERAPY. HOWEVER, ABOUT 30% OF ANTI-HMGCR ANTIBODY POSITIVE PATIENTS WITH NECROTIZING MYOPATHY HAVE NEVER BEEN EXPOSED TO STATINS. THE LITERATURE SUGGESTS THAT FALSE POSITIVES ARE EXTREMELY RARE.

# Treatment: Medications/non-drug

- Glucocorticoids:
  - high dose prednisone 1 mg/kg/day
  - taper gradually after 4 weeks

- Immunosuppressants:
  - Azathioprine
  - Methotrexate (unless ILD)
  - Mycophenolate mofetil
  - Tacrolimus
  - Brepocitinib (FDA approved 2026 – TYK2, JAK1)

- IVIg – monthly x 6 (FDA approved 2021)

- B cell depletion:
  - Rituximab

- Rehabilitation: muscle reserves
  - passive/active assisted ROM exercises
  - Strengthening/hypertrophy of reserves

**FDA Approves Octapharma's Octagam® 10% for Adult Dermatomyositis**



August 23, 2021
Category: In The News

**The U.S. Food and Drug Administration (FDA) has granted approval to Octapharma USA for Octagam® 10% the first and only intravenous immunoglobulin (IVIg) to be indicated for the treatment of adult dermatomyositis!**

MAY IS
**MYOSITIS**
AWARENESS
MONTH

On August 27, 2026, the FDA approved Lisraya (brepocitinib) for adults with dermatomyositis.
It is the first oral treatment ever approved specifically for this rare autoimmune disease.

| Component | CK | REPORT | LDH |
| --- | --- | --- | --- |
| Latest Ref Rng | 15 - 170 IU/L | < OR = 8.1 | 91 - 180 IU/L |
| 10/15/2009 | 6902 (H) | Aldolase: 75.2 (H) | 1340 (H) |

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| 10/23/2009 | | | |
| 10/30/2009 | 5370 (H) | | 1319 (H) |
| 11/2/2009 | | | |
| 11/6/2009 | 7420 (H) | Aldolase: 101.1 (H) | 1449 (H) |
| 11/7/2009 | | | |
| 11/30/2009 | 4024 (H) | Aldolase: 82.6 (H) | 1053 (H) |
| 12/11/2009 | 3314 (H) | Aldolase: 67.8 (H) | 772 (H) |
| 1/5/2010 | 2418 (H) | Aldolase: 50.4 (H) | 664 (H) |
| 1/22/2010 | 251 (H) | | 459 (H) |
| 2/17/2010 | 2459 (H) | | 519 (H) |
| 3/18/2010 | 913 (H) | Aldolase: 17.8 (H) | 345 (H) |
| 4/27/2010 | 571 (H) | Aldolase: 10.0 (H) | 249 (H) |
| 6/3/2010 | 252 (H) | Aldolase: 4.5 | 183 (H) |
| 8/11/2010 | 150 | Aldolase: 4.0 | 175 |

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| 8/11/2010 | 150 | Aldolase: 4.0 | 175 |
| 12/27/2010 | 181 (H) | Aldolase: 4.7 | 190 (H) |
| 1/19/2011 | 132 | Aldolase: 5.9 | 182 (H) |
| 3/30/2011 | 312 (H) | Aldolase: 6.0 | 202 (H) |
| 5/5/2011 | 733 (H) | | 281 (H) |

# Prognosis

- Dermatomyositis and Polymyositis
  - 5 year survival is 95%
  - 10 year survival is 84%

- Mortality:
  - pulmonary or systemic complications
  - malignancy
  - medications, infections

- Poor markers:
  - older age at diagnosis
  - delayed treatment
  - cardiac and pulmonary involvement

# Conclusions

- Recognize proximal muscle weakness
- Broad differential diagnoses: CPK, weakness
- 2017 myopathy guidelines
- Skin, vascular changes
- Auto antibody work up; medication effects
- Treatments and complications