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Sex differences among patients with different forms of autoimmune muscle disease

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Disclosures

- I have patented an anti-HMGCR autoantibody test, but do not receive compensation for this
- I will discuss off-label treatments for myositis

Overview

- Describe the four major types of autoimmune muscle disease
- Review sex differences among the different types
- Do a deeper dive in one type

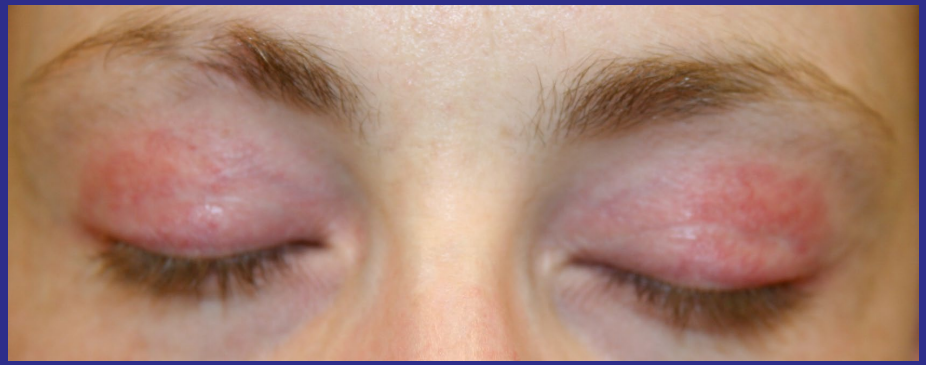
Four major types of autoimmune muscle disease

- Dermatomyositis
- Antisynthetase syndrome
- Immune-mediated necrotizing myopathy
- Inclusion body myositis

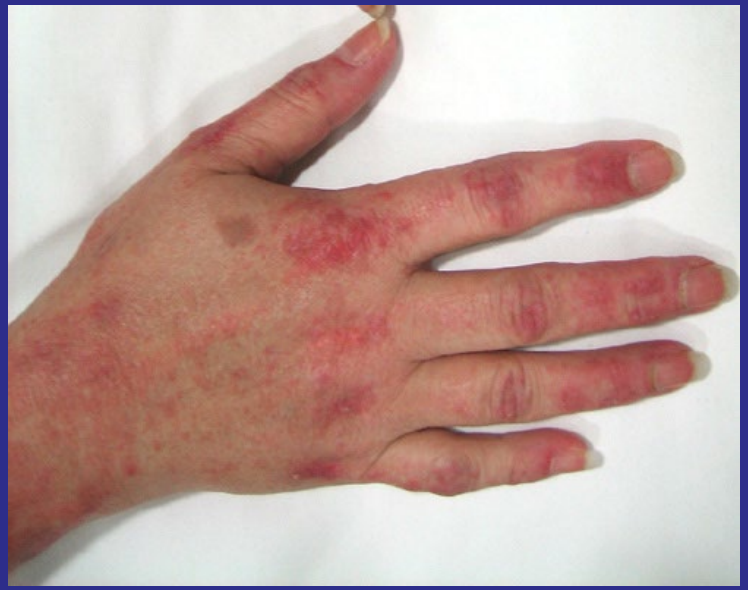
Dermatomyositis

- Symmetric proximal muscle weakness progressing over weeks or months
- Typical skin rash progressing over weeks or months
- Elevated muscle enzyme levels
- Autoantibodies
- Myopathic electromyography
- Abnormal muscle biopsy

Dermatomyositis skin rashes

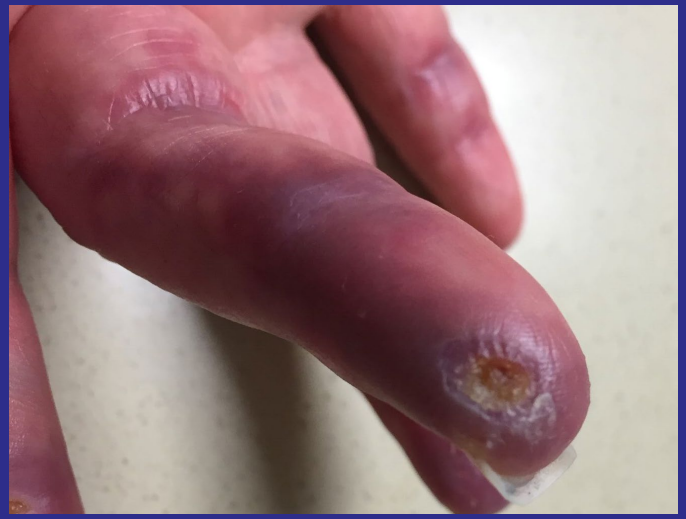


Heliotrope rash

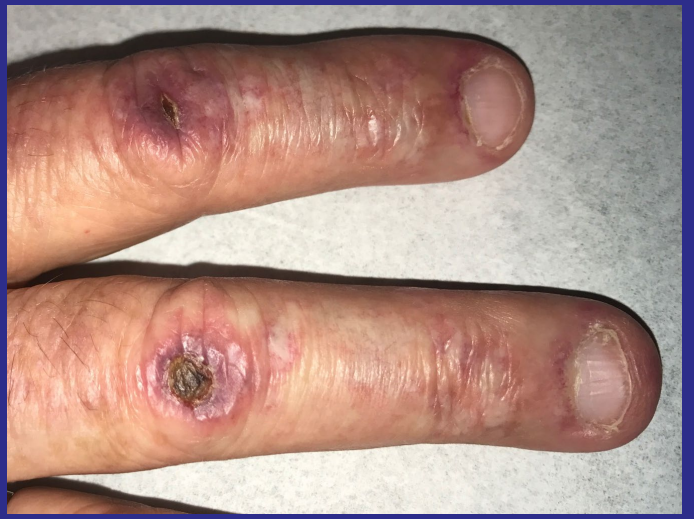


Gottron’s papules

Dermatomyositis skin rashes

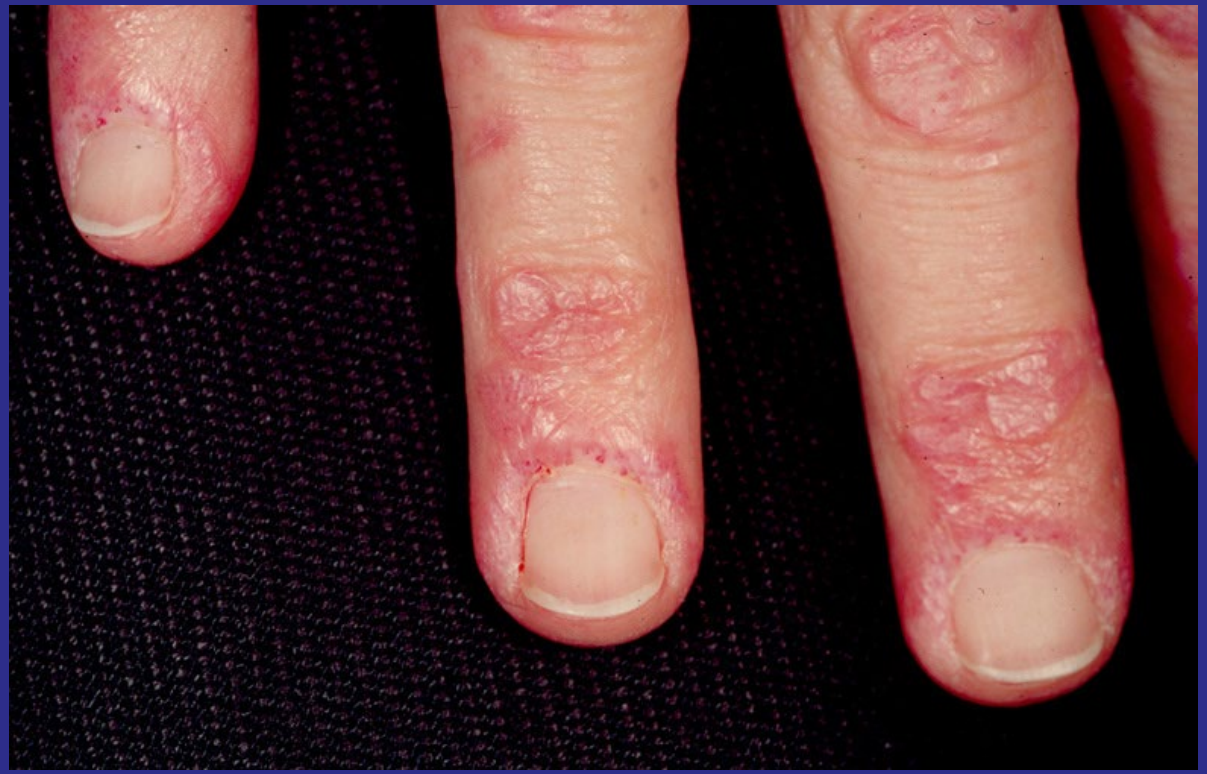


Ulcerating lesion



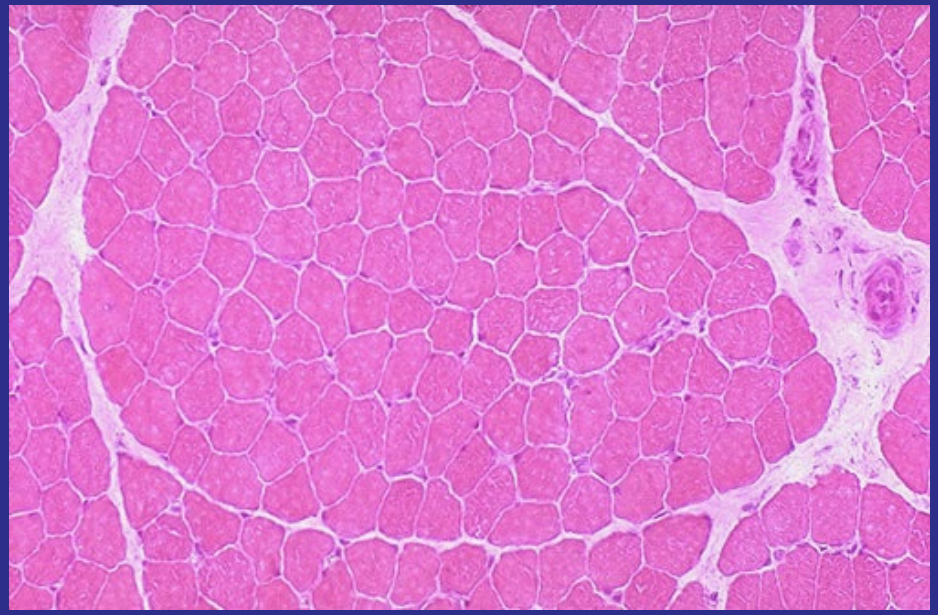
Ulcerating Gottron's papules

Dermatomyositis skin rashes

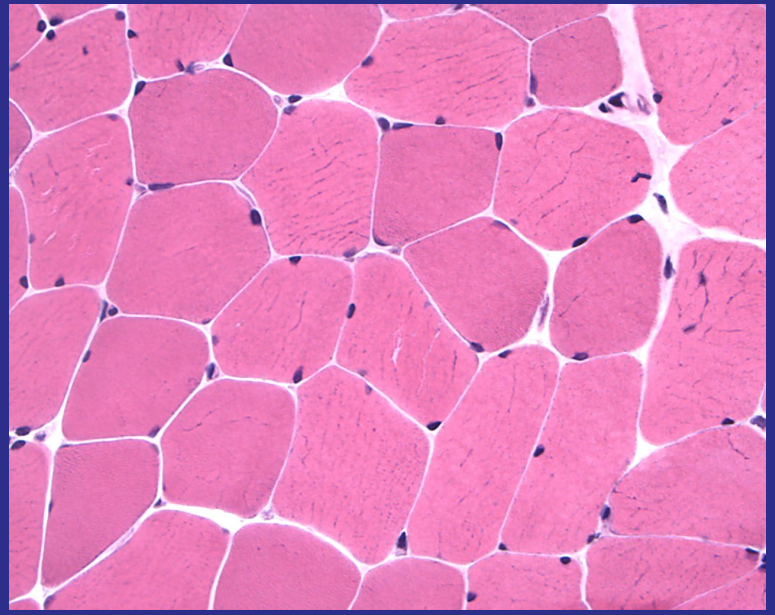


Nailbed changes

Normal muscle biopsy

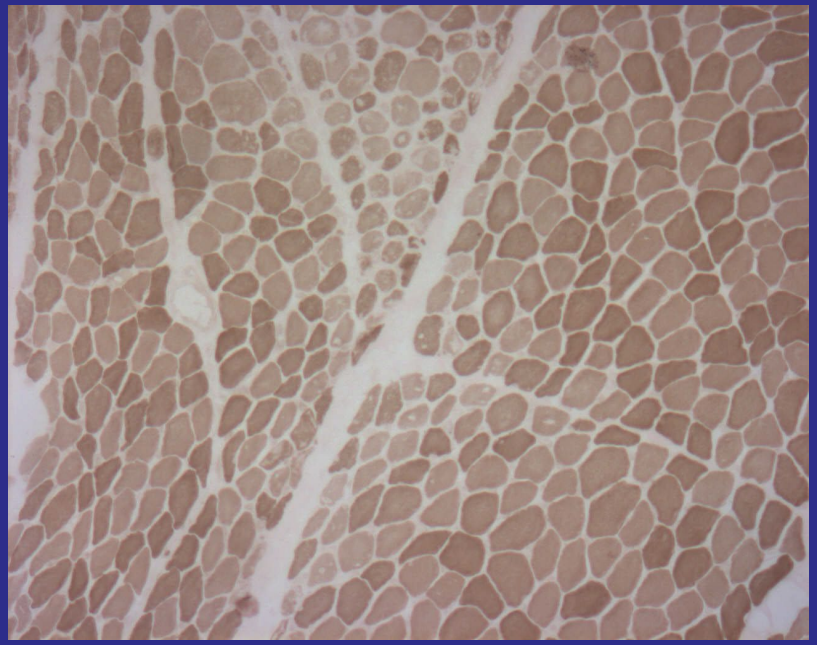


Low power

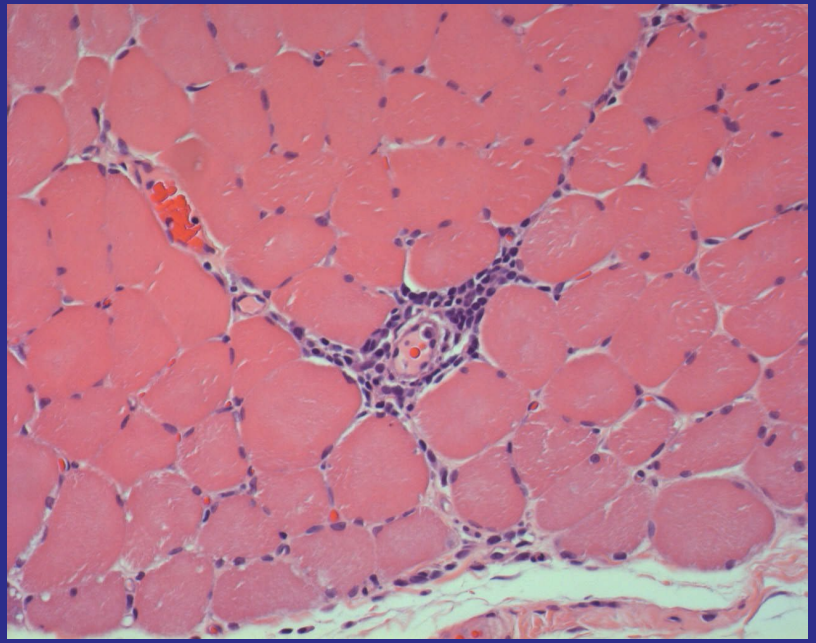


Higher power

Dermatomyositis muscle biopsy



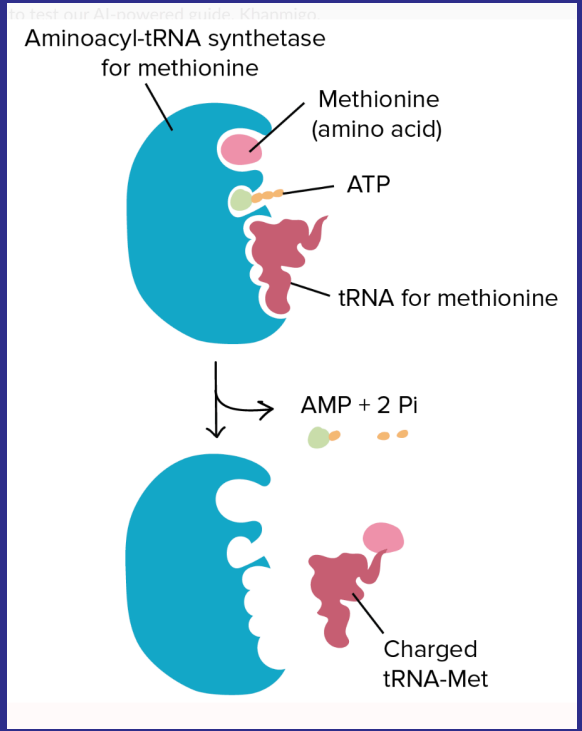
Perifascicular Atrophy



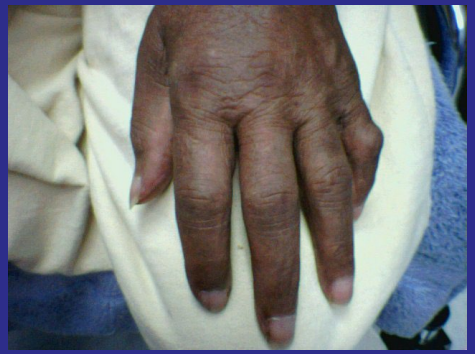
Perivascular Inflammation

The antisynthetase syndrome

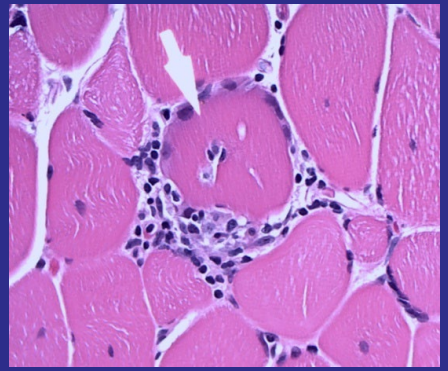
- Autoantibodies recognizing one of the aminoacyl-tRNA synthetases
  - Histidyl-tRNA synthetase (Jo1)
  - Alanyl-tRNA synthetase (PL12)
  - Threonyl-tRNA synthetase (PL7)
  - Glycyl-tRNA synthetase (EJ)
  - Isoleucyl-tRNA synthetase (OJ)



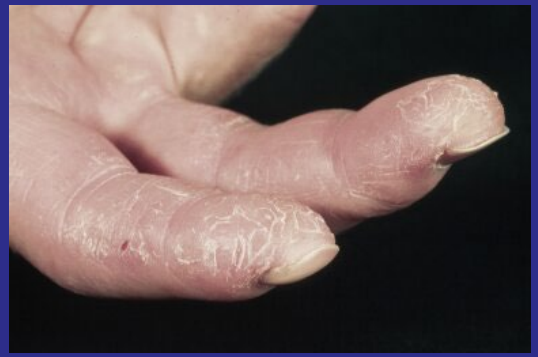
The antisynthetase syndrome



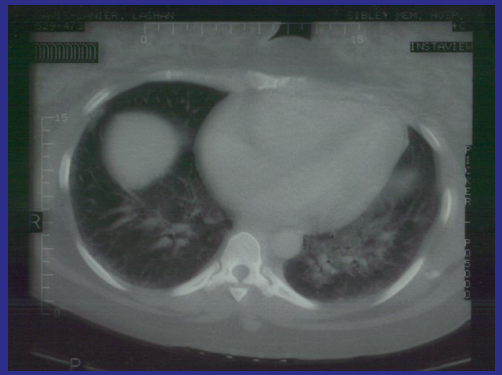
Arthritis



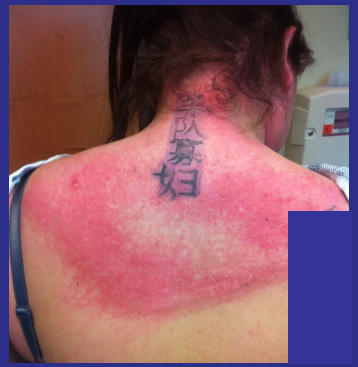
Myositis



Mechanic's Hands



Interstitial Lung Disease

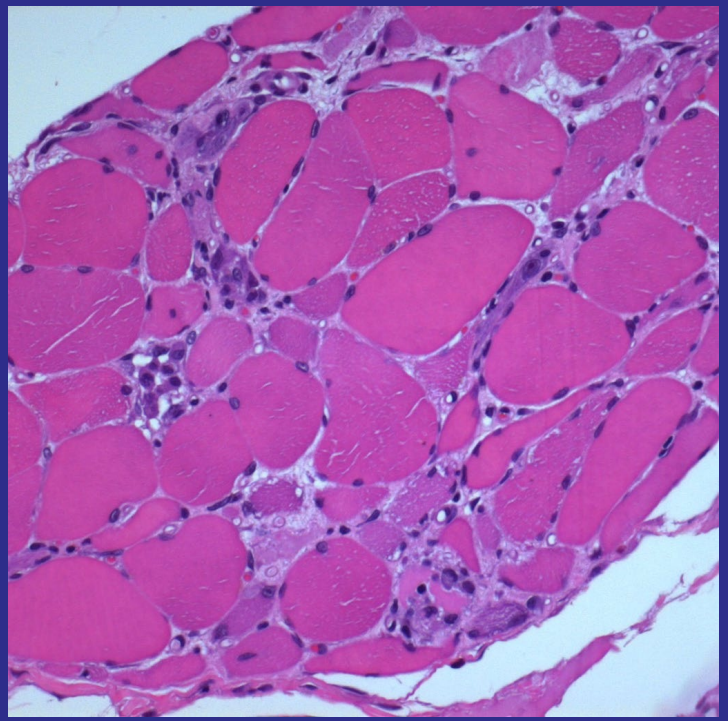


Rash

Raynaud's Phenomenon

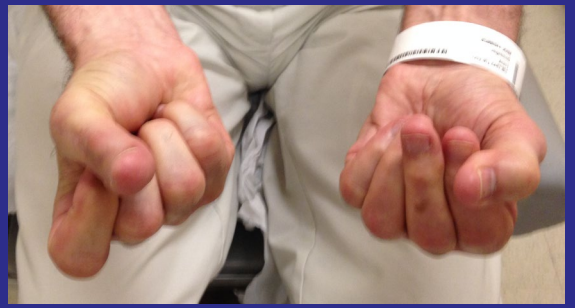
Immune-mediated necrotizing myopathy

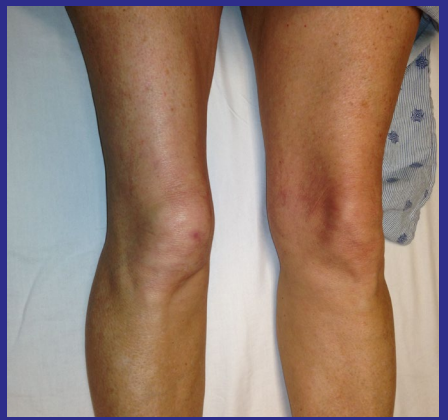
- Muscle biopsy: myofiber necrosis
- Autoantibodies targeting…
  - Signal recognition particle
  - HMG-CoA reductase
- Rapidly progressive
- Severe weakness
- Minimal extra-muscular involvement
- Often difficult to treat



Inclusion Body Myositis

- The most common myopathy in patients over 50 years old
- Insidious onset
- Asymmetric weakness
  - Quadriceps
  - Distal finger flexors
  - Wrist flexors
  - Ankle dorsiflexors
  - Obicularis occuli
- Dysphagia common





Inclusion body myositis muscle biopsy

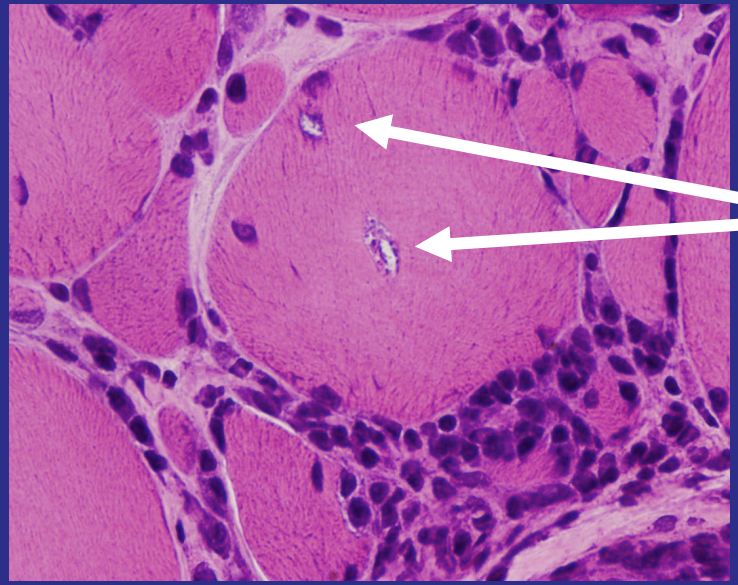


Figure courtesy of
Dr. Anthony Amato

Rimmed vacuoles and invasion of myofibers by CD8+ T cells

Most forms of myositis preferentially effect women

	% Female
Dermatomyositis	70%
Antsynthetase syndrome	69%
IMNM	64%
IBM	39%

Inclusion Body Myositis

- Slowly progressive
- Poor response to therapy
- Clinical heterogeneity may influence treatment responsiveness
- Data regarding heterogeneity (e.g., sex differences) are limited

Methods

- Clinical, histologic, radiologic, and electrophysiologic data analyzed for all patients with IBM and other forms of myositis enrolled at The Johns Hopkins Myositis Center from 2003 to 2018
- Univariate, multivariate, and graphical analyses were used to identify prognostic factors in IBM
- The evolution of creatine kinase and muscle strength was studied using multilevel linear regression models. Nonmodifiable risk factors (sex, race, disease duration, and age at the onset of first symptoms) were used as adjusting covariates for the regression analyses

Results I

- 335 patients with IBM included
- 64% were male
- Average age of disease = 58.7 years
- Average delay to diagnosis = 5.2 years
- Initial misdiagnosis (52%) was common
- Black patients had significantly weaker arm abductors, hip flexors, and knee flexors compared with non-Black patients

Results II

- Compared to males, females had*
  - stronger knee extensors
  - stronger finger flexors
  - increased prevalence of dysphagia (OR 1.8)
  - slower rate of strength decline
  - less spontaneous activity on EMG
  - increased rate of misdiagnosis and mistreatment
  - a longer time to correct diagnosis (6.2 vs. 4.7 years)

*Using multilevel regression models including time from onset

Implications for women with IBM

- Female IBM patients have a distinct clinical phenotype and trajectory compared to men
- These unrecognized differences may have contributed to delay of correct diagnosis in women
- Women may have different responses to therapies, which may influence the design of future clinical trials in IBM

Thank you!