

Idiopathic Inflammatory Myopathies (Myositis)

Idiopathic inflammatory myopathies are a group of disorders characterized by inflammation of the skeletal muscles involved in movement, and usually appear in adults between age 40-60 and in children age 5-15, but can occur at any age.

Idiopathic inflammatory myopathy manifests in several forms, including polymyositis (PM), dermatomyositis (DM), and sporadic inclusion body myositis (IBM). The primary symptom of all forms is muscle weakness that may develop gradually over a period of weeks, months, or years. Other symptoms include joint pain and fatigue.

Both PM and DM involve weakness of the proximal muscles, particularly the hips and thighs, upper arms, and neck. DM is distinguished by a red or purple rash on eyelids, elbows, knees, or hands. PM and DM are more common in women while sporadic IBM is more common in men and usually involves muscles of the wrist, fingers, and thigh.

Typical Testing Strategy

Initial Screening Tests

- Creatine kinase
- Erythrocyte sedimentation rate/C-reactive protein
- Thyroid-stimulating hormone: rule out thyroid disease as etiology for myopathy
- Metabolic profile
- Complete blood count
- Antinuclear antibodies

Antibody Testing

See Tests to Consider

Definitive Diagnosis

Muscle biopsy (which can be guided by magnetic resonance imaging [MRI]) is gold standard

Disease Overview

Incidence

4-10/million adults; rare in children

Age of Onset

Varies by disorder:

- DM is bimodal: childhood and 50-70 years
- PM: rare in childhood, typically >20 years

Tests to Consider

Dermatomyositis and Polymyositis Panel 3001783

Method: Qualitative Immunoprecipitation/Semi-Quantitative Multiplex Bead Assay/Qualitative Immunoblot

May be useful for evaluation of patients with progressive proximal muscle weakness and/or with cutaneous manifestations suggestive of dermatomyositis and/or associated connective tissue disease

Components

- Jo-1 antibody, IgG
- PL-7 (threonyl-tRNA synthetase) antibody
- PL-12 (alanyl-tRNA synthetase) antibody
- EJ (glycyl-tRNA synthetase) antibody
- SRP (signal recognition particle) antibody
- OJ (isoleucyl-tRNA synthetase) antibody
- Mi-2 (nuclear helicase protein) antibody
- P155/140 antibody
- SAE1 (SUMO activating enzyme) antibody
- MDA5 (CADM-140) antibody
- NXP-2 (nuclear matrix protein-2) antibody
- TIF1-gamma (TIF1-γ) antibody

Extended Myositis Panel 3001781

Method: Qualitative Immunoprecipitation/Semi-Quantitative Multiplex Bead Assay/Qualitative Immunoblot

May be useful for differential evaluation of polymyositis, dermatomyositis, necrotizing autoimmune myopathy, or overlap syndromes associated with connective tissue disease

Components:

- SSA-52 (Ro52) and SSA-60 (Ro60) (ENA) antibodies, IgG
- Smith/RNP (ribonucleic protein) (ENA) antibody, IgG
- Jo-1 antibody, IgG
- Mi-2 (nuclear helicase protein) antibody
- PL-7 (threonyl-tRNA synthetase) antibody
- PL-12 (alanyl-tRNA synthetase) antibody
- P155/140 antibody
- EJ (glycyl-tRNA synthetase) antibody
- Ku antibody
- SRP (signal recognition particle) antibody
- OJ (isoleucyl-tRNA synthetase) antibody
- SAE1 (SUMO activating enzyme) antibody
- MDA5 (CADM-140) antibody
- NXP-2 (nuclear matrix protein-2) antibody

- IBM: >50 years
- Necrotizing autoimmune myositis: primarily adults, often older

Syndromes

- DM: associated with cancer
- PM
- IBM
- Necrotizing autoimmune myositis
- Overlap syndrome
- Juvenile DM and PM

Symptoms

General Features

- Musculoskeletal: progressive muscle weakness (usually symmetrical and proximal)
 - Pharyngeal and neck flexion muscles frequently involved
- Arthralgias/arthritis: wrists, knees, small joints of hands
- Constitutional: fever, weight loss
- Pulmonary: fibrosing alveolitis, aspiration pneumonia
- Gastrointestinal: esophageal dysfunction, dysphagia
- Cardiovascular: myo-/pericarditis, valvular disease, rhythm disturbances
- Renal: rarely myoglobinuria, glomerulonephritis
- Dermatologic: Raynaud phenomenon, rashes, calcinosis over bony prominences

Antisynthetase Syndrome

- Found almost exclusively in middle-aged women with DM or PM
- Characterized by:
 - Low-grade fevers
 - Interstitial pneumonitis: major determinant of morbidity and mortality
 - Hyperkeratosis, cracking of lateral and palmar aspects of the fingers (mechanic's hands)
 - Raynaud phenomenon
 - Inflammatory polyarthritis, myalgias
- Presence of antinuclear antibodies known as antisynthetases

Dermatomyositis

- Characteristic photosensitive rash accompanied by symmetrical, subacute, proximal muscle weakness
 - Rash usually precedes muscle symptoms
 - Blue-purple rash: symmetrical distribution
 - Violaceous discoloration of upper eyelids with periorbital edema (heliotrope rash)
 - Erythema of metacarpophalangeal proximal and distal joints
 - Raised violaceous rash (Gottron sign) or scaly erythematous plaques over dorsal surface of bony prominences (Gottron papules): considered pathognomonic for DM
 - Macular erythema over the lower neck and upper chest in a V-distribution (V-sign), over upper back (Shawl sign), or over upper thighs (Holster sign)
 - Telangiectasias at base of fingernails, cuticular overgrowth and periungual erythema
 - Vasculitic skin changes
 - Subcutaneous nodules, periungual infarcts, digital ulcerations
- Cancer-associated myositis
 - Most commonly associated with DM, but can be found in PM

- TIF1-gamma (TIF1-γ) antibody
- Fibrillarin (U3 RNP) antibody, IgG
- PM/ScI-100 antibody, IgG by immunoblot

Polymyositis Panel 2013990

Method: Qualitative Immunoprecipitation/Semi-Quantitative Multiplex Bead Assay

May be useful for evaluation of patients with progressive proximal muscle weakness and antisynthetase syndrome

Components:

- Jo-1 antibody, IgG
- PL-7 (threonyl-tRNA synthetase) antibody
- PL-12 (alanyl-tRNA synthetase) antibody
- EJ (glycyl-tRNA synthetase) antibody
- SRP (signal recognition particle) antibody
- OJ (isoleucyl-tRNA synthetase) antibody

Dermatomyositis Autoantibody Panel 3001782

Method: Qualitative Immunoprecipitation/Qualitative Immunoblot

May be useful for evaluation of patients with characteristic cutaneous manifestations of dermatomyositis with or without muscle weakness

Components:

- Mi-2 (nuclear helicase protein) antibody
- P155/140 antibody
- SAE1 (SUMO activating enzyme) antibody
- MDA5 (CADM-140) antibody
- NXP-2 (nuclear matrix protein-2) antibody
- TIF1-gamma (TIF1-γ) antibody

Interstitial Lung Disease Autoantibody Panel 3001784

Method: Qualitative Immunoprecipitation/Semi-Quantitative Multiplex Bead Assay/Qualitative Immunoblot/Semi-Quantitative Enzyme-Linked Immunosorbent Assay/Quantitative Immunoturbidimetry

May be useful for evaluation of interstitial lung disease in the context of connective tissue disease

Components:

- SSA-52 (Ro52) and SSA-60 (Ro60) (ENA) antibodies, IgG
- Scleroderma (ScI-70) (ENA) antibody
- Jo-1 antibody, IgG
- PL-7 (threonyl-tRNA synthetase) antibody
- PL-12 (alanyl-tRNA synthetase) antibody
- EJ (glycyl-tRNA synthetase) antibody
- Ku antibody
- SRP (signal recognition particle) antibody
- OJ (isoleucyl-tRNA synthetase) antibody
- PM/ScI-100 antibody, IgG by immunoblot
- MDA5 (CADM-140) antibody
- NXP-2 (nuclear matrix protein-2 Ab)
- Rheumatoid factor

- May be diagnosed prior to, simultaneously with, or after myopathy
- Increased risk of malignancy (20-25%) of any of the following types (highest risk in first 2-3 years after diagnosis):
 - Ovarian, breast, melanoma, colorectal, non-Hodgkin lymphoma
- Amyopathic DM
 - Characteristic cutaneous findings of DM >6 months without muscle involvement
 - May progress to DM
 - Some risk for lung disease, malignancy
 - Electromyography may demonstrate subtle myopathy

Polymyositis

- Dominated by muscular presentation with no rash
- Usually subacute presentation
- May be associated with other autoimmune diseases
- Diagnosis of exclusion: must rule out the following:
 - Neuromuscular disease
 - Endocrinopathy
 - Muscular dystrophy
 - Known biochemical muscle disorder or familial biochemical disorder
 - Drug-induced myopathy

Inclusion Body Myositis

- Two types: sporadic, hereditary
- Muscle involvement
 - Muscle atrophy early in disease
 - Distal weakness is most common: deep finger flexors and foot extensors common
 - Asymmetric distribution is common
 - Proximal muscles less frequently involved
 - Specific muscles
 - Small muscles in hand frequently involved
 - Quadriceps involvement common: associated with frequent falls
 - Facial muscles frequently involved
- Extramuscular disease rare: dysphagia is the exception (>50% of patients)
- May be misdiagnosed as PM, adult-onset muscular dystrophy, or motor neuron disease
- Associated with other autoimmune diseases

Necrotizing Autoimmune Myositis

- Acute or subacute presentation
- Severe proximal muscle weakness: clinically indistinguishable from PM
- May occur in association with cancer, other CT diseases, or drug use (eg, statins)
- Diagnosis of exclusion

Overlap Syndrome

- Most common in DM but can occur with other inflammatory myopathies
- Myositis in conjunction with connective tissue disease
 - Most common: systemic sclerosis, mixed connective tissue disease, systemic lupus erythematosus
- Rash: faint or transient
- Frequent association with antisynthetase antibodies
- Myopathy varies from mild to dominant presentation

Juvenile Disease

Juvenile Dermatomyositis (JDM)

- ~85% of juvenile idiopathic inflammatory myopathy (JIIM)

- Cyclic citrullinated peptide (CCP) antibody, IgG
- Antinuclear antibody (ANA) with HEp-2 substrate, IgG by IFA
- RNA polymerase III antibody, IgG

3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase (HMGCR) Antibody, IgG 2013101

Method: Semi-Quantitative Enzyme-Linked Immunosorbent Assay

Differential diagnosis of myositis in patients with or without statin exposure

In addition to clinical evaluation for muscle strength and serum creatine kinase, may be useful to monitor response to treatment

See [3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase \(HMGCR\) Antibody, IgG Test Fact Sheet](#) for more information.

See [Related Tests](#)

- Symmetrical and proximal muscle weakness
- Gottron papules
- Heliotrope rash
- Periungual telangiectasia
- Vasculitis: more common than in adults
- Other organ/skeletal involvement: cardiac, joints, gastrointestinal, pulmonary
- May have family history of other autoimmune diseases
- Amyopathic (hypomyopathic form)
 - Inflammatory rashes without muscle weakness
 - ~25% develop full-blown dermatomyositis

Juvenile Polymyositis

- 4-8%
- Proximal and distal muscle weakness
- Frequent falling episodes
- Cardiac damage

Juvenile Connective Tissue Disease Myositis

- 6-11% of JIIM
- Occurs in conjunction with another connective tissue disease
- Raynaud phenomenon
- Arthritis
- Malar rash
- Interstitial lung disease

Diagnostic Issues

May be difficult to distinguish between myopathies

- Antibody testing in conjunction with clinical presentation and muscle biopsy help to confirm the diagnosis
- Differentiation may be important for therapy and prognosis

Antibody Testing

Usually associated with connective tissue disease/overlap syndrome

Categories of Myositis Antibodies	Clinical Subsets	Antibodies
Myositis-specific antibodies	Antisynthetase syndrome	Jo-1 (histidyl-tRNA synthetase) antibody
		PL-7 (threonyl-tRNA synthetase) antibody
		PL-12 (alanyl-tRNA synthetase) antibody
		EJ (glycyl-ts RNA synthetase) antibody
		OJ (isoleucyl-tRNA synthetase) antibody
		KS (asparaginyI tRNA synthetase)
		Ha (tyrosyl tRNA synthetase)
		Zo (phenylalanyl tRNA synthetase)

Categories of Myositis Antibodies	Clinical Subsets	Antibodies
	Dermatomyositis	NXP-2 (nuclear matrix protein-2) antibody
		MDA5 (CADM-140) antibody
		Mi-2 (nuclear helicase protein) antibody
		SAE1 (SUMO activating enzyme) antibody
		P155/140
		TIF1 gamma
		Necrotizing
	HMGR (3-hydroxy-3-methylglutaryl coenzyme A reductase) antibody	
Myositis-associated antibodies	Overlap syndromes	PM/SCI-100
		Smith/RNP
		Ku
		Ro52 (SSA-52)
		Ro60 (SSA-60)

Test Interpretation

Results

- Positive: as a single test, not diagnostic for inflammatory myopathy
- Negative: does not rule out inflammatory myopathy

Limitations

- Results by themselves are not diagnostic; strong clinical correlation is recommended
- Negative results do not rule out a diagnosis of inflammatory myopathy or overlap syndrome

Related Tests

[Creatine Kinase, Total, Serum or Plasma 0020010](#)

Method: Quantitative Enzymatic

[Antinuclear Antibodies \(ANA\), IgG by ELISA with Reflex to ANA, HEp-2 Substrate, IgG by IFA 0050080](#)

Method: Qualitative Enzyme-Linked Immunosorbent Assay/Semi-Quantitative Indirect Fluorescent Antibody

[SSA 52 and 60 \(Ro\) \(ENA\) Antibodies, IgG 2012074](#)

Method: Semi-Quantitative Multiplex Bead Assay

Jo-1 Antibody, IgG 0099592

Method: Semi-Quantitative Multiplex Bead Assay

Smith/RNP (ENA) Antibody, IgG 0050470

Method: Semi-Quantitative Multiplex Bead Assay

Signal Recognition Particle (SRP) Antibody 2002098

Method: Radioimmunoassay

PM/Sci-100 Antibody, IgG by Immunoblot 2003040

Method: Qualitative Immunoblot

Fibrillarin (U3 RNP) Antibody, IgG 2012173

Method: Qualitative Immunoblot

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