RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

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Juvenile Dermatomyositis

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- The speakers have no relevant financial relationships with any commercial interests.
- The speakers will be discussing off-label medication use.

Objectives

1. Review the epidemiology and clinical presentation of Juvenile dermatomyositis
2. Discuss diagnostics and diagnostic dilemmas specific to Juvenile dermatomyositis
3. Design an evidence-based pharmacotherapeutic regimen for a pediatric patient with Juvenile dermatomyositis

Overview

- Accounts for 80% of all children with Idiopathic Inflammatory Myopathies
- Typically affects skin and muscle
  - Most pronounced in proximal muscles
  - Disease manifestations are variable and can involve additional organ systems

Epidemiology

- Occurs in all regions of the world
- Estimated incidence rates in the United States
  - 1995 – 1998: 2.5 – 4.1 cases per million children per year
  - Similar rates among White, African American, non-Hispanics
  - Hispanics have a lower incidence rate
- Peak age of onset: 7 years
- F > M with ratio of 1.6 – 2.5:1

Causes

Etiology is unclear. It appears to be the result of genetic predisposition triggered by environmental factors.

Genetic Background	Environmental Factors
• Certain human leukocyte antigens (HLA) are associated and contribute to risk of disease (HLA DRB1*0301, DQA1*0301, DQA1*0501) • Non-HLA genes are also associated including genetic polymorphisms in tumor necrosis alpha (TNF-a-308A and TNF-a-238GG) and interleukin-1 receptor antagonist (IL-1-A1 and IL-1-A3)	• Unusual sun exposure • Nonsteroidal anti-inflammatory drug (NSAID) use in preceding 6 months • Hypertensive or psychiatric medications or HPV vaccine within 6 months • Infections: >50% with respiratory symptoms, 30% with GI symptoms in 3 months preceding

Clinical Manifestations

- Presentation is variable
- Almost all patients have some degree of muscle weakness
- Median duration from onset of symptoms to diagnosis: 3 – 7 months

Baseline Characteristics from CARRA Registry

Table 1 Demographics and diagnostic features ($N = 119$)

Age at diagnosis in years, median (IQR)	8 (4.0–11.5)
Age at disease onset in years, median (IQR)	7 (3.5–7.5)
Time to diagnosis in months, median (IQR)	3 (1–6.5)
Female, N (%)	76 (63.4)
Race or Ethnicity[a], N (%)	
White	86 (72.3)
Hispanic, Latino, or Spanish origin	22 (18.5)
Black, African American, African, or Afro-Caribbean	9(7.6)
Asian	7(5.9)
Native American, American Indian or Alaskan Native	3 (2.5)
Middle Eastern	3 (2.5)
Unknown[b]	3 (2.5)
Other[c]	4 (3.4)
Concomitant Medical History, N (%)[d]	22 (16.8)
Family History of Autoimmunity, N (%)[e]	25 (21)
Skin Predominant JDM, N (%)	38 (31.9)
History of, N (%)	
Proximal Muscle Weakness	86 (72.3)
Rash (Heliotrope or Gottron's)	110 (92.4)
Elevated muscle enzymes	99 (83.2)
EMG performed	4 (3.4)
Muscle Biopsy performed	19 (16)
MRI performed	81 (68.1)
Autoantibodies, proportion[f]	
ANA	75/96 (78.1%)
Myositis-specific antibodies	
Anti-MJ/NXP2	11/49 (22.4%)
Anti-p155/140/TIF1-γ	7/53 (13.2%)
Anti-Mi2	6/55 (10.9%)
Anti-MDA5	4/51 (7.8%)
Anti-Jo1	2/67 (3.0%)
Myositis-associated antibodies	
Anti-PM-Scl	3/43 (7.0%)
Anti-Smith	1/56 (1.7%)

CARRA = Childhood Arthritis and Rheumatology Research Alliance

Clinical Manifestations

Constitutional Symptoms:

- Fever, fatigue, anorexia, and weight loss
- Occasional lymphadenopathy

Musculoskeletal Disease:

- Typically symmetrical
- Limb-girdle musculature, anterior neck flexors, and trunk muscle
- Muscle pain
- Muscle tenderness and edema of overlying subcutaneous tissue of affected muscles
- Palatal and pharyngeal muscle involvement causing dysphagia, dysphonia, aspiration, and reflux
- Respiratory muscle weakness
- Arthritis and Tenosynovitis

Clinical Manifestations (Continued)

Mucocutaneous Disease:

- Heliotrope Rash
- Malar Rash
- Gottron papules
- Shawl Sign
- V Sign
- Skin Ulcerations
- Nailfold Capillary Change
  - Important diagnostic and prognostic roles
  - More normal nailfold capillary density is associated with shorter disease course
- Calcinosis: more common at pressure points
- Lipodystrophy: 3-10% Often associated with additional symptoms of metabolic abnormalities

Clinical Manifestations (Continued)

Clinical Manifestations (Continued)

Cardiopulmonary involvement:

- Cardiac involvement is rare
  - Typically asymptomatic
  - SHARE initiative recommends ECHO and EKG on all new JDM patients
- Interstitial lung disease is rare but one of the most serious complications
  - Symptoms can be mild or absent
    - PFT's including carbon monoxide diffusion are recommended at baseline
    - High resolution CT is recommended for confirmation
    - Typical HRCT findings in ILD: consolidation, reticulonodular infiltration, ground glass opacities, and peribronchovascular opacities. .Findings are typically symmetrical and in lower lobe
  - High association with anti-MDA5 antibodies

HRCT = high-resolution CT; ILD = interstitial lung disease; MDA5 = anti-melanoma differentiation-associated gene 5

Clinical Manifestations (Continued)

Gastrointestinal Disease

- Abdominal pain, ulceration, and hemorrhage
- Gut vasculopathy is rare but an important cause of death in JDM. Reports of perforation.
- Abdominal pain or change in stooling may be important clues to GI involvement

Rare Manifestations

- Neurological: seizures, pseudoseizures, sensory neuropathy, depression, fatal brainstem infarction
- Renal: more common in adults rare in pediatrics (should consider SLE with renal involvement)
- Eye and Eyelid: scarring and Blepharitis of eyelid, subcapsular cataract (corticosteroid use), retinopathy (rare)

Case Study: A.J.

Consult call from local pediatrician office:

3 y/o female with history of facial rash not responsive to typical atopic dermatitis treatment. MOC has noticed that she will scoot to furniture and use it to help get up off the floor. She is also rolling out of bed instead of sitting up. She continues to walk without abnormality. No changes in eating, drinking, or voice quality.

What is your differential diagnosis?

Clinical Manifestations (Continued)

Other Forms of Idiopathic Inflammatory Myopathies

- Amyopathic dermatomyositis
- Juvenile polymyositis
- Myositis with other connective tissue disease (overlap myositis)

Post Infectious Inflammatory Myopathies

- Bacterial: staphylococcal, streptococcal
- Viral: influenza, Coxsackievirus, HIV, adenovirus, Parvovirus B19, Dengue virus
- Fungal: candidiasis, cryptococcosis, histoplasmosis
- Parasitic: trichinosis, cysticercosis, toxoplasmosis

Clinical Manifestations (Continued)

Non-Inflammatory Myopathies

- Muscular dystrophies: Duchenne, Becker muscular dystrophy
- Metabolic myopathies: glycogen storage disease, lipid myopathies
- Endocrinological disorders: hypothyroidism, hyperthyroidism, hyperparathyroidism, diabetes
- Toxins
- Drug induced
- Malignancy associated dermatomyositis (rare in pediatrics)

Cutaneous Lesions without Muscle Involvement

- Psoriasis
- Flat warts
- Lichen planus
- Sarcoidosis
- Cutaneous T-cell lymphoma

Making the Diagnosis

Muscle enzymes: CK, LDH, AST, ALT, and aldolase

- Elevated in 80-96% of JDM patients

Other biomarkers

- CBC is often normal. Anemia or leukocytosis is sometimes found
- ESR and CRP may be elevated
- Von Willebrand factor may be increased – not sensitive or specific for active disease

Autoantibodies

- +ANA in 76% of patients – not specific or diagnostic
- Myositis Antibodies: anti-p155 and anti-p155/140
- Commonly associated with malignancy in adults not linked with malignancy in pediatrics

Making the Diagnosis (Continued)

Table 2 Overview of myositis specific antibodies and contribution to clinical decisions.

MSA	Criticality/comment	Relevance/criticality
HMGCoA reductase	The presence of anti-HMGCR antibodies predicts poor response to corticosteroid and immunosuppressant therapy. This anticipation is relevant for the clinician.	Relevant, not critical; however, false negative might lead to omission of biopsy
TIF1y	Strong association with malignancy in elderly patients. Extensive screening for malignancy is necessary prior to treatment of IIM.	Critical, false negative result might lead to delayed diagnosis of cancer
SRP	Associated with severe treatment resistant myopathy, leading to long term immunosuppressive therapy The presence of SRP antibodies predicts poor response to corticosteroid and immunosuppressant therapy. This anticipation is relevant for the clinician.	Relevant, not critical; however, false negative might lead to omission of biopsy
MDA5	Positive result should trigger screening for ILD and if confirmed more aggressive treatment and clinical vigilance	Critical, False negative result may lead to less intensive (respiratory) monitoring with a delay
PM/Scl	In general, associated with a milder disease course	Not critical, low relevance
Ku	Often associated with SLE and/or SSc. Requires monitoring and treatment to coexisting SLE and/or SSc, especially when other antibodies are present (eg, anti-dsDNA).[12]	Relevant, not critical
SAE	Severe cutaneous disease that classically precede DM with severe dysphagia and systemic symptoms.	Relevant, not critical
NXP2	Juvenile DM, diffused calcinosis. Cancer associated DM triggers consideration for screening for concurrent malignancy prior to treatment initiation.	Critical, similar to TIF1y, however, less pronounced
Mi-2	In general, associated with a milder disease course. If present without other MSA, reassures relatively mild disease phenotype.	Relevant, not critical; false positive can lead to a wrong perception of milder disease (no monitoring for ILD)
Jo-1, EJ, OJ, PL-7, PL-12	Positive result triggers the clinician to screen for ILD and to prospectively follow-up pulmonary function; often requires long-term immunosuppressive treatment ► Predicts better therapeutic response to rituximab[13] ► Influences patient management when pulmonologists identify these antibodies in patients with unexplained ILD ► Consider immunosuppressant strategies ► Follow-up for appearance of extra-pulmonary manifestations of the antisynthetase syndrome[14]	Relevant, not critical; False negative results might have a negative effect on optimal therapy choice in severe myositis (more arguments for rituximab) and patients with unexplained ILD (as single manifestation) might experience delay in diagnosis.

DM, dermatomyositis; IIM, idiopathic inflammatory myopathies; ILD, interstitial lung disease; MSA, myositis specific antibodies; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

Making the Diagnosis (Continued)

Muscle Biopsy

- Gold Standard
- Should always be considered especially in the absence of typical rash
- A muscle biopsy scoring tool has been developed and validated by International Juvenile Dermatomyositis Biopsy Consensus Group
  - Consists of four domains: inflammatory, vascular, muscle fiber, and connective tissue
  - Can be used on biceps and quadriceps muscle biopsy

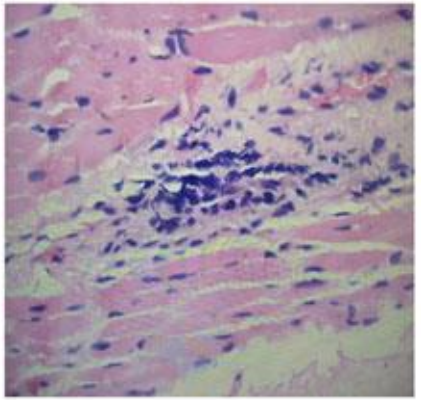
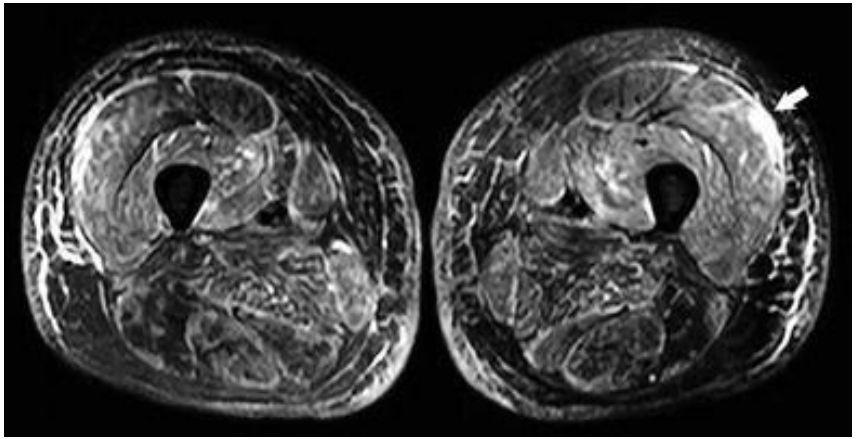


Fig. 2. Juvenile dermatomyositis: skeletal muscle biopsy with characteristic perivascular mononuclear cell infiltrate (HE, x400)

Making the Diagnosis (Continued)



Radiological Examination

- Plain radiographs: identifying and determining the extent of calcinosis, screening for pulmonary involvement
- MRI: important for diagnosing and monitoring myositis activity
  - IV contrast is not necessary
  - T2 weighted imaging and fat suppression reveal soft tissue edema and active disease
  - T1 weighted sequences detect muscle atrophy and fatty infiltration of chronic disease
  - STIR whole body sequences can also visualize subcutaneous tissue and myofascial tissue abnormalities in areas that are clinically undetected
- HRCT: used to diagnose ILD

Making the Diagnosis (and Monitoring Disease Activity)

- Muscle strength
  - Manual muscle testing (MMT8)
  - Childhood Myositis Scale (CMAS)
- Functional Ability: Childhood Health Assessment Questionnaire (CHAQ) = 30 item self report survey regarding activities of daily living
- Global Disease Activity: Physician (Provider) and Patient Global Assessments of Disease Activity

Making the Diagnosis (and Monitoring Disease Activity)

MMT-8 for RIM Trial

Muscle Groups	Right (0 – 10)	Left (0 – 10)	Axial (0 – 10)
Axial Muscles (0 – 10)			
Neck Flexors			0-10
Proximal Muscles			
Deltoid	0-10	0-10	
Biceps brachii	0-10	0-10	
Gluteus maximus	0-10	0-10	
Gluteus medius	0-10	0-10	
Quadriceps	0-10	0-10	
Distal Muscles (0 – 40)			
Wrist Extensors	0-10	0-10	
Ankle dorsiflexors	0-10	0-10	
MMT-8 score (0 – 150)	**0-70**	**0-70**	

MMT-8 is a set of 8 designated muscles with a potential score = 150

IMACS FORM 05c:
CHILDHOOD MYOSITIS ASSESSMENT SCALE (CMAS) SCORING SHEET

Subject's IMACS number _____
Assessor _____
Date of assessment (mm/dd/yy) _____
Assessment number _____

1. **HEAD LIFT:**
0 = Unable 3 = 30-59
1 = 1-9 sec 4 = 60-119 sec
2 = 10-29 5 = ≥ 2 min # of sec ____

2. **LEG RAISE/TOUCH OBJECT:**
0 = Unable to lift leg off table.
1 = Able to clear table, but cannot touch object (examiner's hand).
2 = Able to lift leg high enough to touch object (examiner's hand).

3. **STRAIGHT LEG LIFT/DURATION:**
0 = Unable 3 = 30-59 sec
1 = 1-9 sec 4 = 60-119 sec
2 = 10-29 sec 5 = ≥ 2 min #of sec ____

4. **SUPINE TO PRONE:**
0 = Unable. Has difficulty even turning onto side; able to pull right arm under torso only slightly or not at all.
1 = Turns onto side fairly easily, but cannot fully free right arm and is unable to fully assume a prone position.
2 = Easily turns onto side; has some difficulty freeing arm, but fully frees arm and fully assumes a prone position.
3 = Easily turns over, fully frees right arm with no difficulty.

5. **SITS-UPS:**
Hands on thighs, with counterbalance ____
Hands across chest, with counterbalance ____
Hands behind head, with counterbalance ____
Hands on thighs, without counterbalance ____
Hands across chest, without counterbalance ____
Hands behind head, without counterbalance ____
Total Sit-up Score (0-6) ____

6. **SUPINE TO SIT:**
0 = Unable by self.
1 = Much difficulty. Very slow, struggles greatly, barely makes it. Almost unable.
2 = Some difficulty. Able, but is somewhat slow, struggles some.
3 = No difficulty.

7. **ARM RAISE/STRAIGHTEN:**
0 = Cannot raise wrists up to the level of the A-C joint.
1 = Can raise wrists at least up to the level of the A-C joint, but not above top of head.
2 = Can raise wrists above top of head, but cannot raise arms straight above head so that elbows are in full extension.
3 = Can raise arms straight above head so that elbows are in full extension.

8. **ARM RAISE/DURATION:** Can maintain wrists above top of head for:
0 = Unable 3 = 30-59 sec
1 = 1-9 sec 4 = ≥ 60 sec
2 = 10-29 sec #of sec ____

9. **FLOOR SIT:** Going from a standing position to a sitting position on the floor.
0 = Unable. Afraid to even try, even if allowed to use a chair for support. Child fears that he/she will collapse, fall into a sit, or harm self.
1 = Much difficulty. Able, but needs to hold onto a chair for support during descent. Unable, or unwilling to try if not allowed to use a chair for support.
2 = Some difficulty. Can go from stand to sit without using a chair for support, but has at least some difficulty during descent. May need Gower's. Descends somewhat slowly and/or apprehensively; may not have full control or balance as maneuvers into a sit.
3 = No difficulty. Requires no compensatory maneuvering.

10. **ALL FOURS MANEUVER:**
0 = Unable to go from a prone to an all-fours position.
1 = Barely able to assume and maintain an all-fours position. Unable to raise head to look straight ahead.
2 = Can maintain all-fours position with back straight and head raised (so as to look straight ahead). But, cannot creep (crawl) forward.
3 = Can maintain all-fours, look straight ahead and creep (crawl) forward.
4 = Maintains balance while lifting and extending one leg.

11. **FLOOR RISE:** Going from a kneeling position on the floor to a standing position.
0 = Unable, even if allowed to use a chair for support.
1 = Much difficulty. Able, but needs to use a chair for support. (Unable if not allowed to use a chair.)
2 = Moderate difficulty. Able to get up without using a chair for support, but needs to place one or both hands on thighs/knees or floor. (Unable without using hands.)
3 = Mild difficulty. Does not need to place hands on knees, thighs or floor, but has at least some difficulty during ascent.
4 = No difficulty.

12. **CHAIR RISE:**
0 = Unable to rise up from chair, even if allowed to place hands on sides of chair seat.
1 = Much difficulty. Able, but needs to place hands on sides of seat. Unable if not allowed to place hands on sides of seat.
2 = Moderate difficulty. Able, but needs to place hands on knees/thighs. Does not need to place hands on sides of seat.
3 = Mild difficulty. Does not need to place hands on seat, knees or thighs but has at least some difficulty during ascent.
4 = No difficulty.

13. **STOOL STEP:**
0 = Unable.
1 = Much difficulty. Able, but needs to place one hand on exam table (or examiner's hand).
2 = Some difficulty. Able, does not need to use exam table for support, but needs to use hand on knee/thigh.
3 = Able. Does not need to use exam table or hand on knee/thigh.

14. **PICK-UP:**
0 = Unable to bend over and pick up pencil off floor.
1 = Much difficulty. Able, but relies heavily on support gained by placing hands on knees/thighs.
2 = Some difficulty. Has some difficulty (but not "much-difficulty"). Needs to at least minimally and briefly place hand(s) on knees/thighs for support. Is somewhat slow.
3 = No difficulty. No compensatory maneuver necessary.

The **maximum possible total score** for the 14 maneuvers is **52** (52 "points of muscle strength/function").

TOTAL CMAS SCORE: ____

Making the Diagnosis (and Monitoring Disease Activity)

IMACS FORM 05b: CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE

Subject's IMACS number
Person Completing: ___Mother ___Father ___Patient ___Other_____
Date of assessment (mm/dd/yy)
Assessment number

In this section we are interested in learning how your child's illness affects his/her ability to function in daily life. Please feel free to add any comments on the back of this page. In the following questions, please check the one response which best describes your child's usual activities (average over an entire day) **OVER THE PAST WEEK. ONLY NOTE THOSE DIFFICULTIES OR LIMITATIONS WHICH ARE DUE TO ILLNESS.** If most children at your child's age are not expected to do a certain activity, please mark "Not Applicable". For example, if your child has difficulty in doing a certain activity or is unable to do it because he/she is too young but **NOT** because he/she is **RESTRICTED BY ILLNESS**, please mark "Not Applicable".

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To do	NOT Applicable
DRESSING & GROOMING Is your child able to: -Dress, including tying shoelaces and doing buttons?					
-Shampoo his/her hair?					
-Remove socks?					
-Cut fingernails?					
ARISING Is your child able to: -Stand up from a low chair or floor?					
-Get in and out of bed or stand up in crib?					
EATING Is your child able to: -Cut his /her own meat?					
-Lift a cup or glass to mouth?					
-Open a new cereal box?					
WALKING Is your child able to: -Walk outdoors on flat ground?					
-Climb up five steps?					

*** Please check any AIDS or DEVICES that your child usually uses for any of the above activities:**

___ Cane
___ Walker
___ Crutches
___ Wheelchair
___ Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc)
___ Built up pencil or special utensils
___ Special or built up chair
___ Other (Specify:_____)

*** Please check any category for which your child usually needs help from another person BECAUSE OF ILLNESS:**

___ Dressing and Grooming
___ Arising
___ Eating
___ Walking

IMACS FORM 05b: CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To do	Not Applicable
HYGIENE Is your child able to: -Wash and dry entire body?					
-Take a tub bath (get in & out of tub)?					
-Get on and off the toilet or potty chair?					
-Brush teeth?					
-Comb/brush hair?					
REACH Is your child able to: -Reach and get down a heavy object such as a large game or books from just above his/her head?					
-Bend down to pick up clothing or a piece of paper from the floor?					
-Pull on a sweater over his/her head?					
-Turn neck to look back over shoulder?					
GRIP Is your child able to: -Write or scribble with pen or pencil?					
-Open car doors?					
-Open jars which have been previously opened?					
-Turn faucets on and off?					
-Push open a door when he/she to turn a door knob?					
ACTIVITIES Is your child able to: -Run errands and shop?					
-Get in and out of car or toy car or school?					
-Ride bike or tricycle?					
-Do household chores (eg, wash dishes, take out trash, vacuuming, yard work, make bed, clean room)?					
-Run and play?					

Please check any AIDS or DEVICES that your child usually uses for any of the above activities:

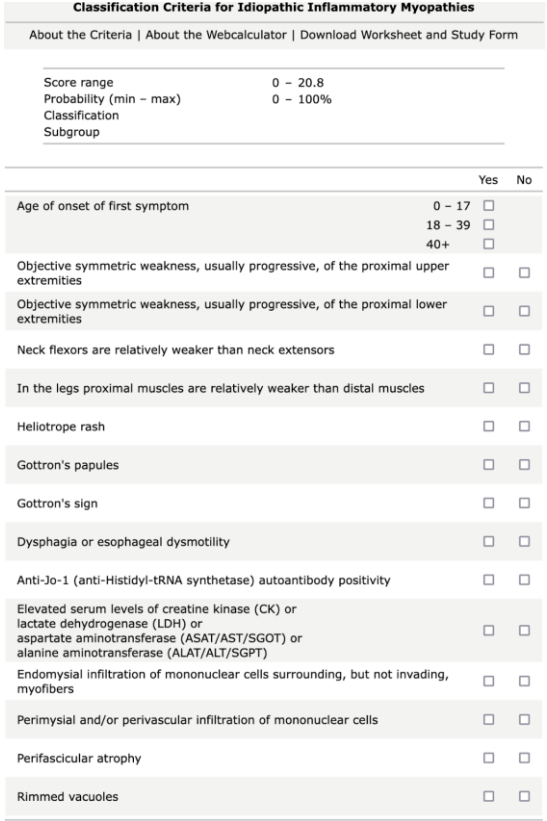
___ Raised toilet seat
___ Bathtub seat
___ Jar opener (for jars previously opened)
___ Bathtub bar
___ Long-handled appliances for Reach
___ Long-handled appliances in bathroom

Please check any categories for which your child usually needs help from another person BECAUSE OF ILLNESS?

___ Hygiene
___ Reach
___ Gripping and opening things
___ Errands and chores

IMACS FORM 05b: CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE

2017 EULAR/ACR Classification Criteria for Idiopathic Inflammatory Myopathies



Classification Criteria for Idiopathic Inflammatory Myopathies

About the Criteria | About the Webcalculator | Download Worksheet and Study Form

Score range	0 – 20.8
Probability (min – max)	0 – 100%
Classification	
Subgroup	

		Yes	No
Age of onset of first symptom	0 – 17	☐	
	18 – 39	☐	
	40+	☐	
Objective symmetric weakness, usually progressive, of the proximal upper extremities		☐	☐
Objective symmetric weakness, usually progressive, of the proximal lower extremities		☐	☐
Neck flexors are relatively weaker than neck extensors		☐	☐
In the legs proximal muscles are relatively weaker than distal muscles		☐	☐
Heliotrope rash		☐	☐
Gottron's papules		☐	☐
Gottron's sign		☐	☐
Dysphagia or esophageal dysmotility		☐	☐
Anti-Jo-1 (anti-Histidyl-tRNA synthetase) autoantibody positivity		☐	☐
Elevated serum levels of creatine kinase (CK) or lactate dehydrogenase (LDH) or aspartate aminotransferase (ASAT/AST/SGOT) or alanine aminotransferase (ALAT/ALT/SGPT)		☐	☐
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibers		☐	☐
Perimysial and/or perivascular infiltration of mononuclear cells		☐	☐
Perifascicular atrophy		☐	☐
Rimmed vacuoles		☐	☐

Classification	Probability	Score
Definite	> 90%	• > 7.5 without biopsy • > 8.7 with biopsy
Probable	55 – 90%	• 5.5 – 7.5 without biopsy • 6.7 – 8.7 with biopsy
Possible	50 – 55%	• <5.3 without biopsy • <6.5 with a biopsy

- Patients who meet criteria and have rash are classified as JDM
- Those <u>without</u> required rash criteria are classified as juvenile myositis other than JDM

Disease Course, Prognosis, and Outcome

Disease Course

- ⅓ of patient have a monocyclic course and reach remission without relapse
- 3 – 30% have polycyclic course
- 30 – 60% continue to have active disease despite treatment
- Median time to remission is 4.7 years
- MSK involvement typically resolves sooner than skin involvement

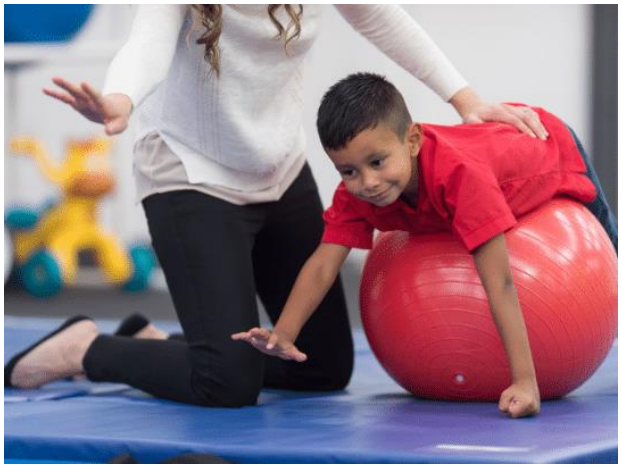
Prognosis and Outcomes

- Presence of rash 3 months after diagnosis and abnormal nailfold capillaries and rash at 6 months are predictor of longer time to remission
- Mortality rate has decreased from >30% to less than 5%
- Causes of death: GI vasculopathies, pulmonary disease, cardiovascular events, superimposed infections

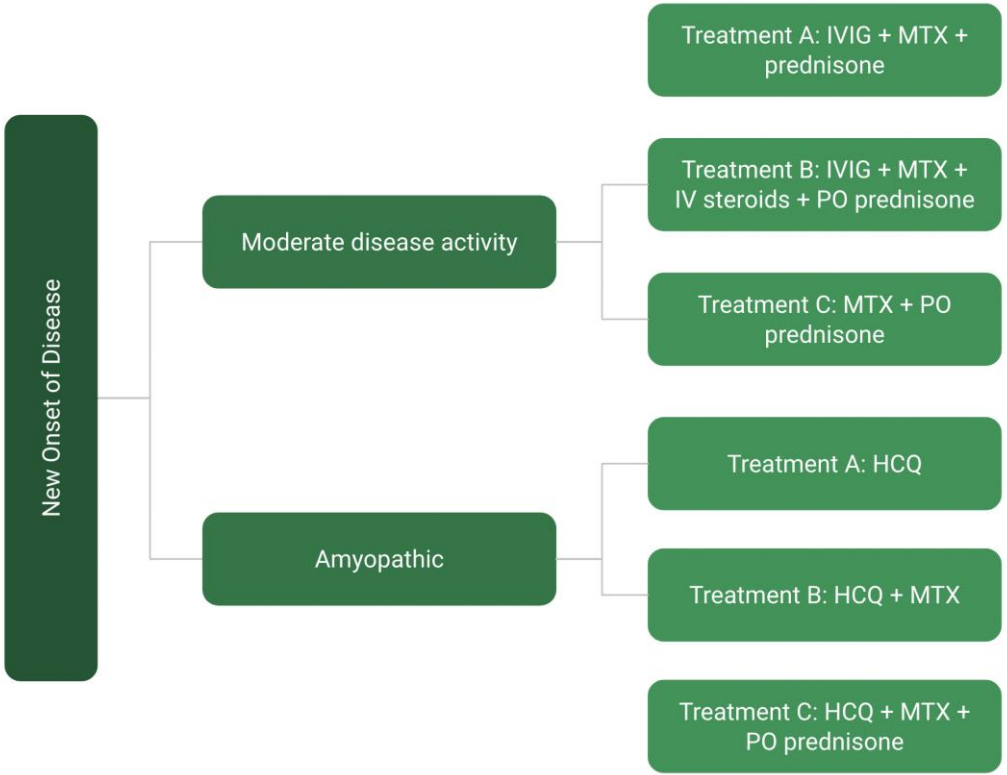
Sanner H. *Rheumatology (Oxford)*. 2014 Sep;53(9):1578-85.

Non – Pharmacological Treatment

- Sun avoidance
  - Sunscreen protective against UVA and UVB rays: SPF 30 or higher
  - Sun protective clothing
- Vitamin D and calcium Supplementation
- Physical Therapy and Occupational Therapy



Initial Treatment



MTX = methotrexate, IV = intravenous, PO = oral, HCQ = hydroxychloroquine

Huber AM. *Arthritis Care Res*. 2010 Feb;62(2):219-25
Kim S. *Pediatr Rheumatol Online J*. 2017 Jan 11;15(1):1.
Bellutti EF. *Ann Rheum Dis*. 2017 Feb;76(2):329-340.

Corticosteroid – Sparing Agents

Medication Name	Dosing	Clinical Pearls
IVIG	2 g/kg/dose (Max: 70 g) every 2 weeks x 3 doses, then monthly	• 2 g/kg/dose is typically given over a period of 2 days to minimize risk for infusion reaction and adverse effects • Adverse effects are typically associated with individual IVIG product
Mycophenolate mofetil	10 mg/kg/dose BID OR 600 mg/m^2/dose BID	• Used if patient is intolerant to MTX • Preferred agent for persistent skin disease
Cyclosporine	3 – 5 mg/kg/day BID	• Used if patient is intolerant to MTX • Therapeutic goal: no current consensus • Adverse effects: hypertrichosis, hypertension, hirsutism, abdominal pain
Rituximab	• BSA ≤1.5 m^2: 575 mg/m^2 • BSA > 1.5 m^2: 750 mg/m^2 (Max: 1 g/dose)	• Dosing frequency variable • Effects lasts ~ 6-9 months • Timing of vaccinations

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Kim S. *Pediatr Rheumatol Online J*. 2017 Jan 11;15(1):1.
Bellutti EF. *Ann Rheum Dis*. 2017 Feb;76(2):329-340.

Corticosteroid – Sparing Agents (Continued)

Medication Name	Dosing	Clinical Pearls
Cyclophosphamide	500 mg/m^2/dose (Max: 500 mg) IV every 2 weeks x 3, then 750 mg/m^2 (Max: 1.2 g) every 3 – 4 weeks	• Role in therapy: severe or refractory disease • Demonstrated to result in improvement in global disease, muscle disease, and skin disease activity
Hydroxychloroquine	5 mg/kg/day (Max: 400 mg)	Reserved for skin-predominant disease
Tacrolimus	Topical: Apply to affected area twice daily Oral: 3 – 5 mg/kg/day every 12 hours	• Topical: recalcitrant cutaneous lesions • Oral: aim for therapeutic trough goal of 5 – 15 mcg/mL
JAK inhibitors	Variable	• Agents: ruxolitinib, baricitinib, tofacitinib • Black Box Warning: increased risk of major cardiovascular events

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