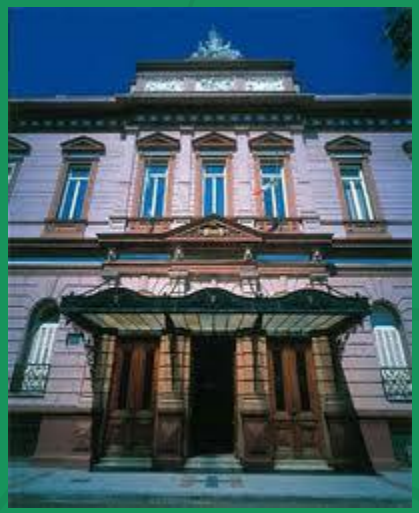

HOSPITAL ITALIANO
de Buenos Aires

Juvenile Dermatomyositis

PReS Latin America
Basic Pediatric Rheumatology Course 2015
Aguas de São Pedro, São Paulo, Brazil

Carmen L. De Cunto
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Departamento de Pediatría
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Objectives

- Which are the different clinical and autoantibody phenotypes?
- How can we assess activity and damage in children with myositis, in research settings and in clinical practice?
- What new therapies can be used for refractory disease?

Juvenile idiopathic inflammatory myopathies (JIIM)

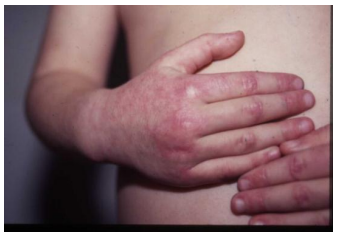
Rider L, et al. Rheum Dis Clin N Am 2013

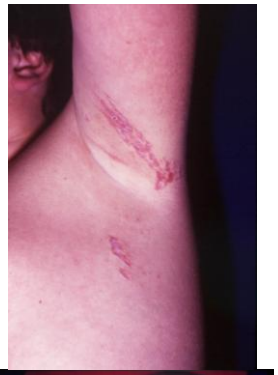
- Heterogeneous immune-mediated, and rare (2 to 4/1million) disorders, characterized by:
  Chronic muscle inflammation
  Skin rashes
  Involvement of other organs (vascular, pulmonary, gastrointestinal, and cardiac)

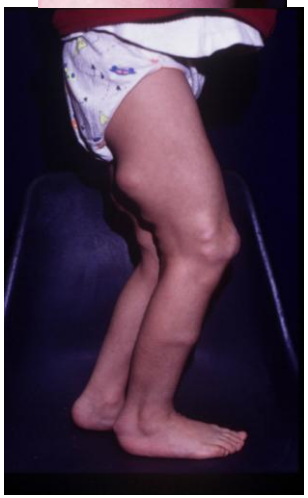
- Diagnosis *(Bohan & Peter, N Engl J Med 1975)*

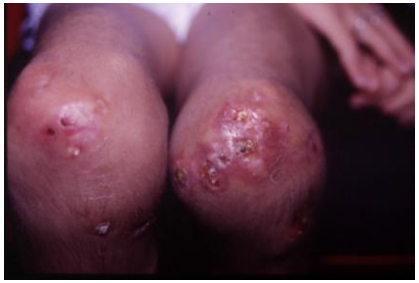
  Skin involvement + at least 3:

  Muscle weakness
  Elevated muscle enzymes
  Electromyography
  Muscle biopsy
  MRI findings * (modified by CARRA Registry investigators) *Rheumatology 2006*







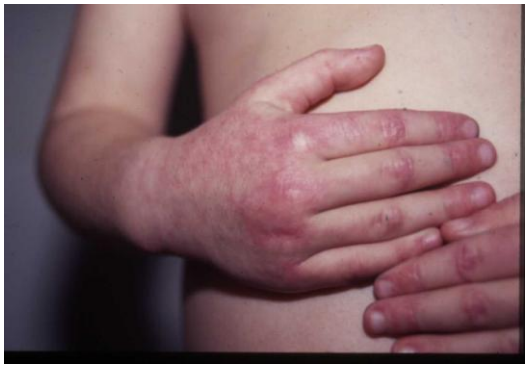


Patient´s case

- This was a four year old girl at the time of the first visit to the hospital. She developed a red rash on her cheeks, chin, elbows, knees and metacarpophalangeal, as well as proximal interphalangeal joints. Her initial diagnosis was atopic dermatitis. A few months later she became gradually weak and fatigue. She refused climbing stairs, getting up of the floor, dressing, and playing. She did not have nasal voice, nor problems to swallow or to breath.

  Blood tests showed: normal blood count and erythrocyte sedimentation rate, muscle enzymes (LDH, aldolase and CK) were moderately elevated with normal liver enzymes, ANA 1/640 speckled pattern, and negative anti DNA, Sm, Ro, La, anti RNP.
  Other tests: MRI (muscle edema), capillaroscopy (micro-hemorrhages, and dilated capillaries)

Gottron´s papules



Erythematous malar rash,
heliotrope rash, and periorbital edema

Magnetic resonance imaging (MRI)

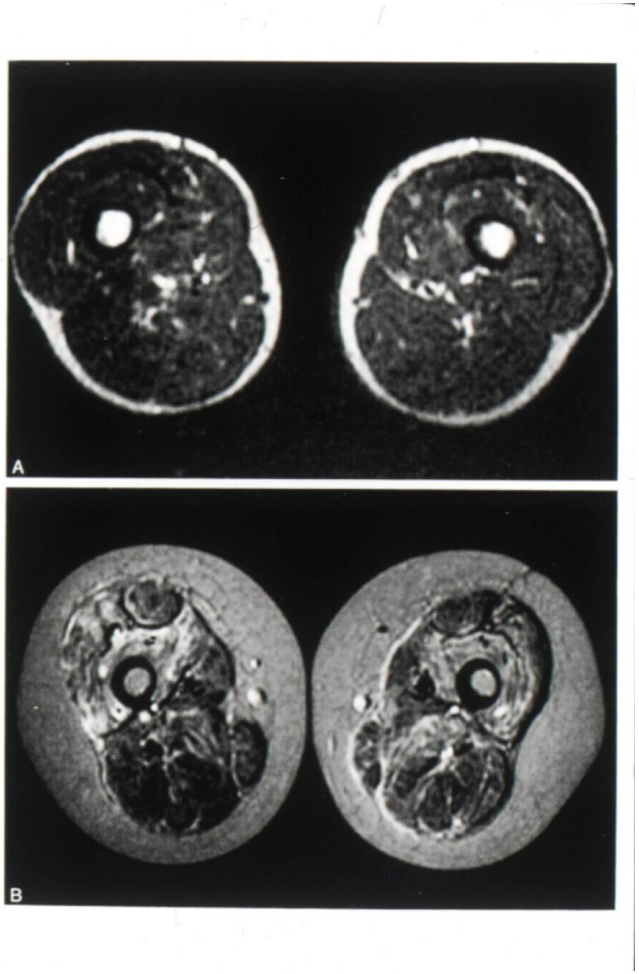
Provides additional evaluation to clinical exam

Represents a promising tool to estimate:
- total inflammatory burden (whole-body)
- tailor treatment
- monitor efficacy

Allows preoperative localization of muscle inflammation

Recognizes edema or inflammation in the skin, subcutaneous tissue, and fascia

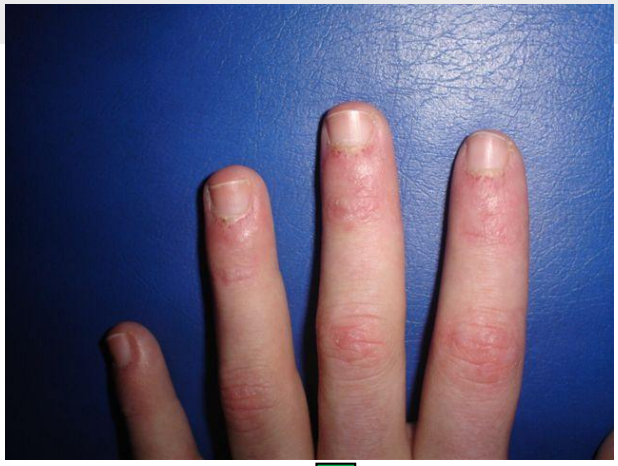
MRI-based scoring system (4 point scale) indicates degree of muscle inflammation

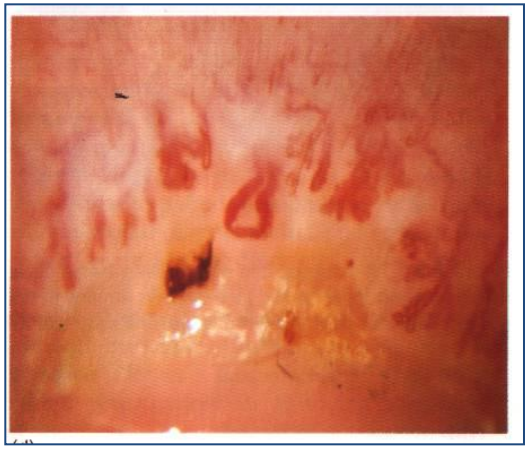


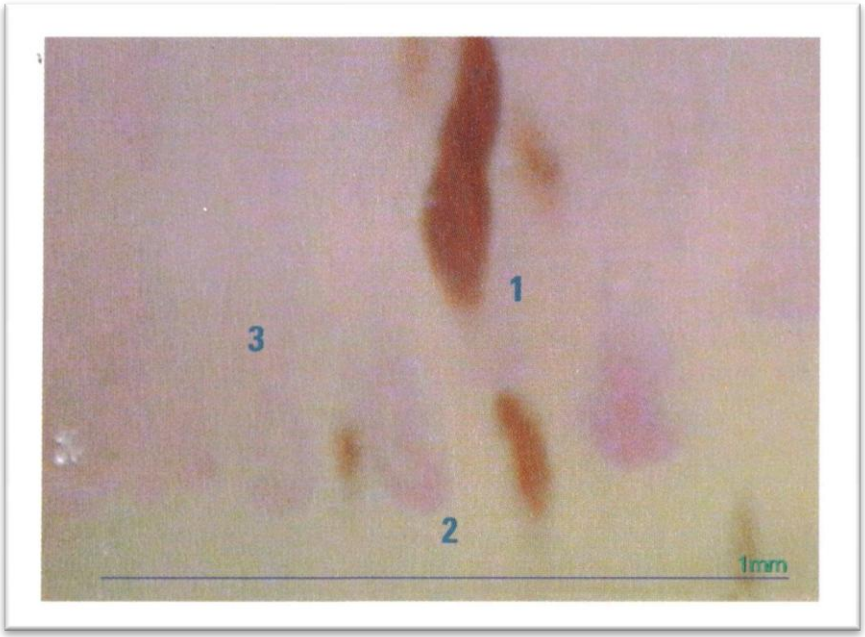
Malattia C, et al. Ann Rheum Dis 2014; 73(6):1083-90
Hilario Scand J Rheumatol 2014; 43(4):329-33
Tuen V, et al. Pediatric Rheumatology 2013; 11:15
Davis WR, et al. Rheumatology 2011; 50(12):2237-2244
Kimball A, et al. Arthritis Rheum 2000; 43(8):1866-1873

JDM nailfold findings

- 1. Micro-hemorrhages
  2. Dilated capillaries
  3. Dropout (decreased capillary density)







Capillaroscopic changes and disease activity

Table 3

Distribution of the patients with juvenile dermatomyositis according to capillaroscopic changes and disease activity

Capillaroscopic changes (mean)	Active disease (n = 26)	Inactive disease (n = 4)	P
N. micro-hemorrhages+	2.15	2.5	0.677
N. capillary dilation++	1.77	0.12	0.001*
N. megacapillaries++	0.18	0	0
N. bushy capillaries++	0.45	0.03	0.009*
Deletion score+++	2.06	0.5	0.004*

*Student *t* test. +Sum of the number of hemorrhages/number of fingers with hemorrhage; ++Sum of the number of changes/total number of fingers assessed; +++Sum of the deletion score/number of fingers with deletion.

Piotto, Len, Hilario, Terreri. Rev Bras Reumatol 2012, 52(5):722-732

Clinical phenotypes of JIIM

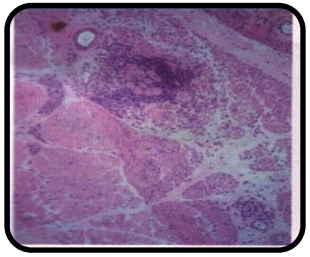
Juvenile Dermatomyositis

Most common (85%)

Gottron's sign, heliotrope rash, periungueal capillary changes, photosensitivity, calcinosis

Lowest CK

Lowest mortality

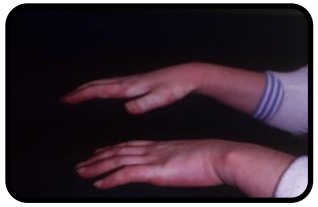


Juvenile polymyositis

Oldest, less frequent (4-8%)

Severe onset, weight loss, cardiac involvement

Highest CK, freq. wheelchair and hospitalizations



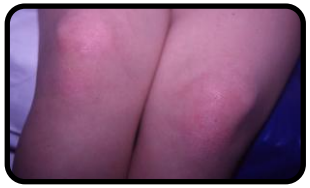
Overlap myositis

Less frequent (6-12%)

Malar rash, arthritis, Raynaud, sclerodactyly, intestitial lung disease

Intermediate CK

Highest mortality



Hypomyopathic JDM

Unfrequent (1%), JDM skin rashes

Subclinical or no muscle weakness

Mild elevation of muscle enzymes

Serologic classification of juvenile idiopathic inflammatory myositis

Table 1: Autoantibodies in JDM

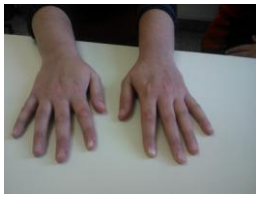
Antibody	Autoantigen target	Known frequency in patients with JDM (%)	Unique features
Antisynthetase Myositis Specific Antibodies			Associated with myositis, interstitial lung disease, polyarthritis, Raynaud's phenomenon, fever, and mechanic's hand
Anti-ARS	Aminoacyl-tRNA synthetases	1–5	
Anti-Jo-1	Histidyl-tRNA synthetase	2–5	
Anti-PL-12	Alanyl-tRNA synthetase	1–3	
Anti-PL-7	Theonyl-tRNA synthetase	<1	
Anti-EJ	Glycyl-tRNA synthetase	<1	
Anti-OJ	Isoleucyl-tRNA synthetase	<1	
Anti-KS	Asparagynyl-tRNA synthetase	Unknown	
Anti-HA	Tyrosyl-tRNA synthetase	Unknown	Skin rash in addition to above
Anti-Zo	Phenylalanyl-tRNA synthetase	Unknown	
Nonsynthetase Myositis Specific Antibodies			
Anti-Mi-2	DNA Helicase	4–10	Classic cutaneous skin lesions, including Gottron papules, heliotrope rash, periungual changes
Anti-p155/140	Transcriptional intermediary factor (TIF)–1 gamma protein	22–29	More severe skin disease, generalized lipodystrophy, and cancer in adults
Anti-p140 (Mj)	Nuclear matrix protein NXP2	13–23	Calcinosis and contractures
Anti-CADM140 or anti-MDA-5	Melanoma differentiation-associated gene 5	Reported in Japanese children with JDM, unknown elsewhere	Interstitial lung disease and elevated ferritin with concerns for macrophage activation
Anti-SRP	Signal recognition particle	1–3	Muscle fiber necrosis with minimal inflammatory cell infiltrate
Anti-SAE	Serum activating enzyme unit	Rare	Cutaneous manifestations and progressed to myositis with systemic features, including dysphagia
Anti-200/100		Unknown	Necrotizing myositis with statin exposure in adults
Myositis Associated Antibodies			
Anti-U1-RNP	U1 ribonucleoprotien (snRNP)	6	Features of sclerodermatous overlap
Anti-U3-RNP	U3 ribonucleoprotein (fibrillarin)	1	Features of sclerodermatous overlap
Anti-PM-Scl	Nucleolar multiprotein complex	5–7	Features of sclerodermatous overlap
Anti-Ro	52 or 60Kd ribonucleoproteins (hYRNA)	2	
Anti-La	Ribonucleoprotein	1	
Anti-Ku	P70/p80heterodimer, DNA-associated proteins	<1	
Anti-Topo	DNA topoisomerase I	Unknown	

Myositis specific antibodies (MSA)

Antisynthetase

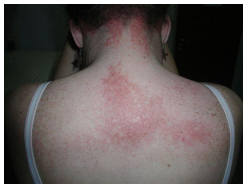
Anti-ARS (1-5%)

Anti-Jo-1 (2-5%)



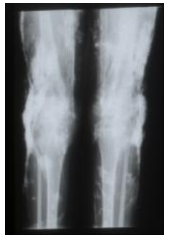
Nonsynthetase

Anti-Mi-2 (4-10%)



Anti-p155/140 (22-29%)

Anti-p140 MJ (13-23%)



Anti MDA-5 (38% in japanese children)

Myositis associated antibodies (MAA)

Anti -U1-RNP (6%)

Anti- PM-Scl (5-7%)

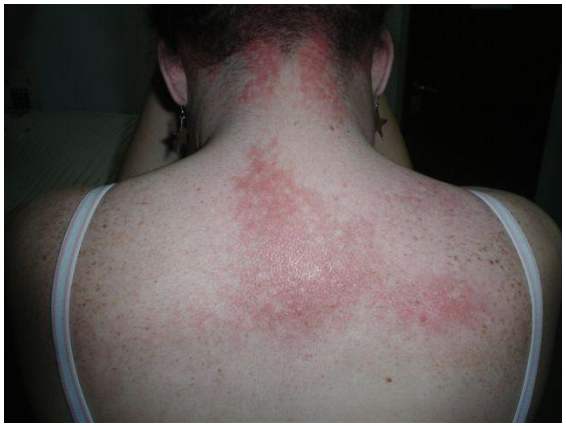
Rider L, et al. Medicine 2013; 92(4):223-243
Espada G, et al. J Rheumatol 2009; 36(11):2547-2551
Tansley S, et al. Arthritis Research & Therapy 2014,16:R138

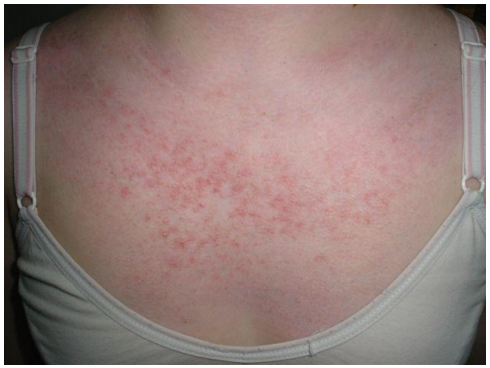
Patient´s case (continuation)

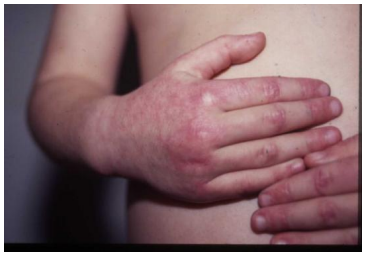
According to her clinical phenotype, she would probably had anti-p155/140.

During the evaluation she cried when muscle strength was assessed: MMT8 (Kendall Manual Muscle Testing) 40.
Her initial therapy included: oral prednisone (2mg/kg/day), methotrexate 15 mg/m^2 per week, and hidroxychloroquine.

She improved her muscle strength very quickly, however the skin involvement progressed, and an erythematous and pruritic rash appeared on her chest and her back.







Measures of disease activity, damage and patient reported outcomes in myositis

Rider L, et al. Arthritis Care Res 2011; 63(0 11):S157

Tools

Physician and Patient/Parent Global Activity (0-10 cm VAS)

Childhood Health Assessment Questionnaire (CHAQ)

Huber A, et al. J Rheumatol 2001; 28(5):1106-1111

The Child Health Questionnaire (CHQ)

MMT (Kendall Manual Muscle Testing)

Rider L, et al. Arthritis Care Res 2010; 62(4):465-472

CMAS (Childhood Myositis Assessment Scale)

Huber A, et al. Arthritis & Rheum 2004; 50(5):1595-1603

DAS (Disease Activity Score)

Bode RK, et al. Arthritis Rheum 2003; 49:7-15

MDAAT (Myositis Disease Activity Assessment Tool)

Isenberg DA, et al. Rheumatology (Oxford) 2004; 43(1):49-54

MDI (Myositis Damage Index)

Miller FW, et al. Rheumatology 2001; 40(11)1262-1273

CDASI (Cutaneous Dermatomyositis Disease Area and Severity Index)

Yassaee M, et al. Brit J Dermatol 2010; 162(3):669-673

CAT (Cutaneous Assessment Tool)

Huber AM, et al. Arthritis Rheum 2008; 59(2):214-221

DSSI (Dermatomyositis Skin Severity Index)

Carroll CL, et al. Brit J Dermatol 2008; 158(2):345-350

IMACS and PRINTO

- Core sets measures of response to therapy
- Definitions of improvement

Core sets of response to therapy

IMACS

(International Myositis Assessment and Clinical Studies Group)

Miller FW, et al. Rheumatology2001; 40(11):1262-73

- Global Activity (physician and parent) VAS
- Strength (MMT)
- Function (CMAS/CHAQ)
- Lab (2 enzymes)
- Extra-muscular

PRINTO

(Paediatric Rheumatology International Trials Organisation)

Ruperto N, et al. Arthritis Rheum 2008; 59(1):4-13
Ruperto N, et al. Rheumatology 2003;42(12):1452-59

- Global Activity (physician and parent) VAS
- Strength (MMT/CMAS)
- Function (CHAQ)
- Global disease (DAS/MYOACT) activity
- HRQoL

Two differences between IMACS and PRINTO core sets:
Inclusion of serum muscle enzymes
Health related QOL is not included

Rider L, et al. Arthritis Rheum 2004; 50(7):2281-2290

Definition of improvement (DOI)

IMACS

Rider L, et al. Arthritis Rheum 2004; 50(7):2281-2290

"3 of any 6 of core set measures improved by >20%, with no more than 2 worse by >25%, which could not include MMT"

PRINTO

Ruperto N, et al. Arthritis Care Res 2010; 62(11):1533-1541

"Any 3 among the 6 core set variables improved by at least 20% *vs*. baseline, with no more than 1 of the remaining variables worsening by more than 30%, which cannot be muscle strength"

Evaluation of clinically inactive disease (CID)

The PRINTO criteria

Lazarevic D, et al. Ann Rheum Dis 2013; 72:686-693

- MMT8 ≥ 78(0-80)
- Phy Glo (PGA) VAS ≤ 0.2
- CMAS ≥ 48
- CK ≤ 150 U/L

Definition of CID: 3 of 4 criteria

JDM Research Group (UK)

Almeida B, et al. Arthritis & Rheumatology. 2015 DOI10.1002/art.39200

Propose that PRINTO criteria require modification:

- Use of PGA as an essential criterion

or

- Adding items of skin disease activity

Where is the skin?

RESEARCH Open Access

Developing a provisional, international Minimal Dataset for Juvenile Dermatomyositis: for use in clinical practice to inform research

Liza J McCann[1*], Katie Arnold[2], Clarissa A Pilkington[2,4], Adam M Huber[5], Angelo Ravelli[6], Laura Beard[2], Michael W Beresford[1,7], Lucy R Wedderburn[2,3,4] and the UK Juvenile Dermatomyositis Research Group (JDRG)[4]

Provisional JDM Minimal Dataset, Form A - first data entry only

Instructions on use / definitions available as supplementary material.
- For variables that are not available at time of data entry, but will be available at a later date, mark 'not available', (so that they can be chased and added at a later date).
- For variables that have not been examined / investigated, mark 'not recorded'.

Patient ID Number*		**Patient Name***	
Patient Consultant / Lead Clinician? *		**Patient Hospital* and country**	

- Information to be completed or details omitted pending local ethics and legal considerations

Date of form completion	

A. Demographic Data

DOB*:		**Gender:**	Male / Female
Ethnicity (*Details to be further defined by consensus*)			

Family History (1st degree relative)

1. Neuromuscular disease	Yes	No	Not Known	Not Available
If yes, state disease				
2. Autoimmune disease	Yes	No	Not Known	Not Available
If yes, state disease				

B. Diagnostic Data

For definitions please refer to supplementary sheet

1. Disease type: JDM; JPM; JDM overlap with: Arthritis / Lupus / Scleroderma / Sjogren's / MCTD (RNP +ve) — *Mark all overlap features that apply*; Amyopathic JDM; Incomplete DM; Inclusion body myositis (IBM)

2. Date of first symptom (mm/yyyy)	____/____
3. Date of diagnosis (mm/yyyy)	____/____

4. Diagnostic Clinical Criteria

	Yes	No	Not Available (at time of data entry but can be completed later)	Not Done
Symmetrical proximal muscle weakness				

Dermatological features of JDM:				
Heliotrope rash	Yes	No	Not Available	Not Done
Gottron's papules or Gottron's sign	Yes	No	Not Available	Not Done
Nailfold capillary changes	Yes	No	Not Available	Not Done
Other characteristic JDM rash	Yes	No	Not Available	Not Done

Provisional JDM Minimal Dataset, Form B: prospective data entry

Instructions on use / definitions available as supplementary material.
- For variables that are not available at time of data entry, but will be available at a later date, mark 'not available' (so that they can be chased and added at a later date).
- For variables that have not been examined / investigated, mark 'not recorded'.

*Details of patient ID to be completed / omitted as per local ethics / legal requirements.

Patient ID Number*		**Patient Name***	
Patient Consultant / Lead Clinician		**Patient Hospital and country**	

Date of form completion	

A. Growth

Height (cm)		**Weight (kg)**	

B. Disease activity / damage (clinical features)

1. Active Muscle Disease

Proximal muscle weakness	Yes	No	Not Available	Not Done
Other muscle weakness	Yes	No	Not Available	Not Done
CMAS	Score _____		Not Available	Not Done
MMT8	Score _____		Not Available	Not Done

2. Active Skin Disease

Heliotrope rash	Yes	No	Not Available	Not Done
Gottron's Papules or Gottron's sign	Yes	No	Not Available	Not Done
Nailfold capillary changes	Yes	No	Not Available	Not Done
Lipodystrophy	Yes	No	Not Available	Not Done
Calcinosis	Yes	No	Not Available	Not Done
Cutaneous ulceration due to myositis	Yes	No	Not Available	Not Done
Subcutaneous oedema due to myositis				
Generalised	Yes	No	Not Available	Not Done
Peri-orbital	Yes	No	Not Available	Not Done
Other skin changes				
Malar / facial erythema due to myositis	Yes	No	Not Available	Not Done
Shawl sign / V sign due to myositis	Yes	No	Not Available	Not Done
Mechanic's hands	Yes	No	Not Available	Not Done
Alopecia due to myositis	Yes	No	Not Available	Not Done
Vasculopathic lesions due to myositis	Yes	No	Not Available	Not Done
Photosensitivity due to myositis	Yes	No	Not Available	Not Done
Livido reticularis due to myositis	Yes	No	Not Available	Not Done
Other erythema due to myositis	Yes	No	Not Available	Not Done
Panniculitis due to myositis	Yes	No	Not Available	Not Done

3. Major organ involvement due to myositis

Musculoskeletal involvement due to myositis	Yes	No	Not Available	Not Done
If yes: Arthritis	Yes	No	Not Available	Not Done
If yes: Contractures due to myositis	Yes	No	Not Available	Not Done
Gastrointestinal involvement due to myositis	Yes	No	Not Available	Not Done
If yes: Dysphagia	Yes	No	Not Available	Not Done
If yes: Dysphonia	Yes	No	Not Available	Not Done
If yes: Abdominal pain or GI ulceration due to myositis (exclude peptic ulcer disease)	Yes	No	Not Available	Not Done
Pulmonary involvement due to myositis – interstitial lung disease	Yes	No	Not Available	Not Done
Cardiac involvement due to myositis	Yes	No	Not Available	Not Done

4. Constitutional

Fever (>38°C) due to myositis	Yes	No	Not Available	Not Done
Weight loss (>5%) due to myositis	Yes	No	Not Available	Not Done
Fatigue due to myositis	Yes	No	Not Available	Not Done
Irritability due to myositis	Yes	No	Not Available	Not Done
Raynaud's phenomenon	Yes	No	Not Available	Not Done

5. Other

Malignancy	Yes	No	Not Available	Not Recorded

C. Is patient having on-going follow up at this centre after this date? Yes / No

If no, reason why:	**Death**	Yes	No
	Transfer to another geographical area	Yes	No
	Transfer to adult care	Yes	No
	Patient in stable remission	Yes	No

D. Global disease activity

1. Physician VAS – global activity (overall)	Not Available	Not Done
Value: _____ (range 0.0-10.0cm)		
2. Physician VAS – extra-muscular global activity	Not Available	Not Done
Value: _____ (range 0.0-10.0cm)		
3. Parental / patient VAS	Not Available	Not Done
Value: _____ (range 0.0-10.0cm)		

E. Health Questionnaires

CHAQ (range 0 - 3)	Not Available	Not Done	**Value**	_____

QoL Tool (*Exact tool to be determined by consensus*)

QoL Tool used	Yes	No	Not Available
Name of QoL Tool used		**Score**	

5. Diagnostic Investigations

Muscle biopsy evidence of myositis:	Yes	No	Not Available	Not Done
If yes, date of biopsy (dd/mm/yyyy): _____				
Elevation of muscle enzyme: CK	Yes	No	Not Available	Not Done
LDH	Yes	No	Not Available	Not Done
Aldolase	Yes	No	Not Available	Not Done
AST/SGOT	Yes	No	Not Available	Not Done
ALT/SGPT	Yes	No	Not Available	Not Done
EMG changes of myopathy	Yes	No	Not Available	Not Done
MRI Changes of Myositis	Yes	No	Not Available	Not Done
Auto-antibodies positive: ANA	Yes	No	Not Available	Not Done
Anti-p155/140	Yes	No	Not Available	Not Done
Anti-p140	Yes	No	Not Available	Not Done
Anti-Jo1	Yes	No	Not Available	Not Done
Anti-ARS	Yes	No	Not Available	Not Done
Anti-PL12	Yes	No	Not Available	Not Done
Anti-PL7	Yes	No	Not Available	Not Done
Anti-EJ	Yes	No	Not Available	Not Done
Anti-OJ	Yes	No	Not Available	Not Done
Anti-Mi2	Yes	No	Not Available	Not Done
Anti-SRP	Yes	No	Not Available	Not Done
Anti-U1-RNP	Yes	No	Not Available	Not Done
Anti-U3-RNP	Yes	No	Not Available	Not Done
Anti-PM-Scl 75	Yes	No	Not Available	Not Done
Anti-PM-Scl 100	Yes	No	Not Available	Not Done
Anti-Ro52	Yes	No	Not Available	Not Done
Anti-Ro60	Yes	No	Not Available	Not Done
Anti-La	Yes	No	Not Available	Not Done
Anti-Ku	Yes	No	Not Available	Not Done
Anti-Topo	Yes	No	Not Available	Not Done
Anti-SAE	Yes	No	Not Available	Not Done
Anti-Zo	Yes	No	Not Available	Not Done
Anti-CAM-140	Yes	No	Not Available	Not Done
Anti-K5	Yes	No	Not Available	Not Done
Anti-HA	Yes	No	Not Available	Not Done
Anti-ZA	Yes	No	Not Available	Not Done
Other MSA / MAA	Yes	No	Not Available	Not Done

C. Treatments

Medication given prior to diagnosis of myositis and registration into database: **Yes** / **No**

If yes, medications given:

Steroid	Yes	No	Not Available	Not Recorded
Methotrexate / other DMARD (*Disease modifying anti-rheumatic drug*)	Yes	No	Not Available	Not Recorded
Previous biologic	Yes	No	Not Available	Not Recorded
If yes to steroid:	Oral	Intravenous	Topical	Intramuscular

F. Investigations

1. Blood tests- muscle enzyme elevation

CK	Yes	No	Not Available	Not Done
LDH	Yes	No	Not Available	Not Done
Aldolase	Yes	No	Not Available	Not Done
AST/SGOT	Yes	No	Not Available	Not Done
ALT/SGPT	Yes	No	Not Available	Not Done

2. Abnormal investigation since last visit (consistent with flare of myositis)

MRI	Yes	No	Not Available	Not Done
Muscle biopsy	Yes	No	Not Available	Not Done
EMG	Yes	No	Not Available	Not Done
Lung function tests	Yes	No	Not Available	Not Done
ECG / ECHO	Yes	No	Not Available	Not Done

G. Treatment

1. Treatment start date (mm/yyyy)	____/____	Not Available	Not Recorded

2. Medication

Steroids	Yes	No	Not Available	Not Recorded
If yes to steroid:	Oral	Intravenous	Topical	Intramuscular
Methotrexate	Yes	No	Not Available	Not Recorded
Ciclosporin A	Yes	No	Not Available	Not Recorded
Mycophenolate Mofetil	Yes	No	Not Available	Not Recorded
Azathioprine	Yes	No	Not Available	Not Recorded
Hydroxychloroquine	Yes	No	Not Available	Not Recorded
Leflunamide	Yes	No	Not Available	Not Recorded
Cyclophosphamide	Yes	No	Not Available	Not Recorded
Rituximab	Yes	No	Not Available	Not Recorded
Etanercept	Yes	No	Not Available	Not Recorded
Infliximab	Yes	No	Not Available	Not Recorded
Adalimumab	Yes	No	Not Available	Not Recorded
IVIG	Yes	No	Not Available	Not Recorded
Plasmaphoresis	Yes	No	Not Available	Not Recorded
Topical steroid	Yes	No	Not Available	Not Recorded
Topical tacrolimus	Yes	No	Not Available	Not Recorded
Other Treatment:				

3. Physiotherapy Yes / No / Not Available / Not Recorded

McCann L, et al. Pediatric Rheumatology Online J. 2014;12:31

McCann *et al. Trials* (2015) 16:268
DOI 10.1186/s13063-015-0784-0

TRIALS

STUDY PROTOCOL Open Access

Development of an internationally agreed minimal dataset for juvenile dermatomyositis (JDM) for clinical and research use

Liza J. McCann[1*], Jamie J. Kirkham[2], Lucy R. Wedderburn[3,4,5], Clarissa Pilkington[4,5], Adam M. Huber[6], Angelo Ravelli[7], Duncan Appelbe[2], Paula R. Williamson[2] and Michael W. Beresford[1,8]

McCann L, et al, Trials 2015; 16:268

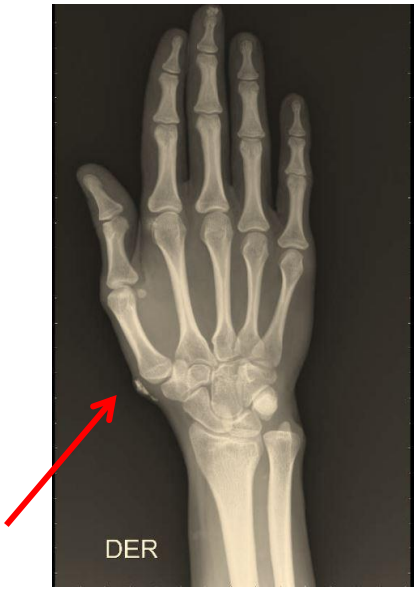
Long term outcome and prognostic factors

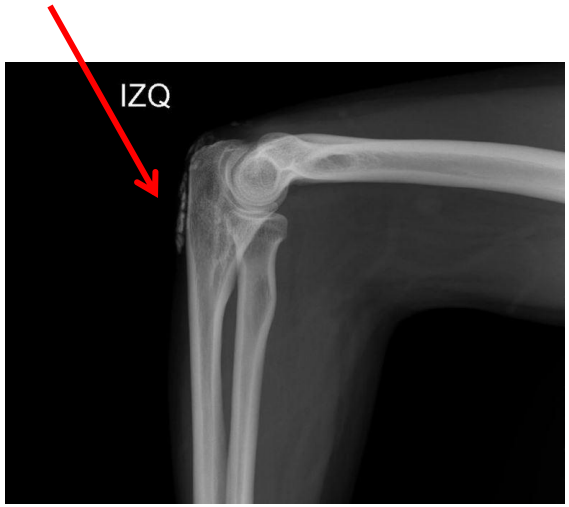
Patient´s case (continuation)

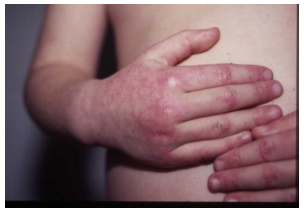
She improved her muscle strength very quickly, however the skin involvement progressed, and an erythematous and pruritic rash appeared on her chest and her back.

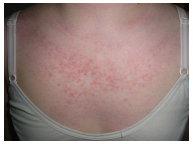
Five years after the diagnosis, she developed nodular calcinosis in her hands and elbows.

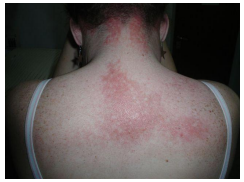
Due to the persistence of activity of cutaneous manifestations mycophenolate mofetil was indicated.











Long-term outcome and prognostic factors

Ravelli A, et al. Arthritis Care Res 2010; 62(1):63-72

- Mean disease duration: 8±5.2 years (Europe) and 7.4±4.6 years (Latin America)
- Reduced (mild) muscle strength (40%)
- Persistent active disease: DAS (60.5%) and MYOACT (41.2%) more frequently the skin
- Cumulative damage MDI (69%) skin, gastrointestinal (disphagia), skeletal (joint contractures), endocrine (growth failure 19.3%)
- Impaired physical function CHAQ (40.7%), severe (6.5%)
- Decreased HRQOL physical (10.5%) and psychosocial (12.8%) domains
- Outcome predictors: insidious onset, chronic course, calcinosis and lipodystrophy, and female patients

Sanner H, et al. Rheumatology 2014; 53:1578-1585

- At follow up (16.8 years), active disease (PRINTO criteria) 51%, (MYOACT total) 73%
- Predictors: age < 9 years at diagnosis, calcinosis, HLA-DRB1*0301

Huber A, et al. Arthritis Care Res 2014; 66(5):732-740

- Mortality: overall 4.2%, JDM 2.4%
- Causes: interstitial lung disease, gastrointestinal, multisystem
- Variables with the highest importance: clinical subgroup, severity at onset, older age at diagnosis, weight loss, and delay to diagnosis

What new therapies can be used for refractory disease?

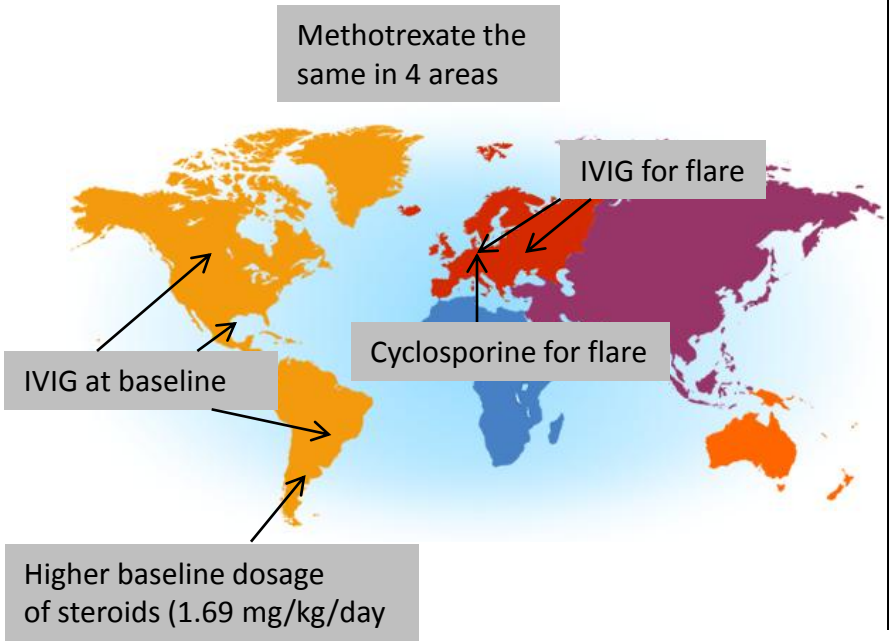
Therapeutic approaches

PRINTO study (n 294)

Hasija R, et al. Arthritis Rheum 2011; 63(11):3142-3152

Response to therapy: significant improvement during initial 6 months and continue up to month 12.

Differences among 4 main geographic areas (Western and Eastern Europe and South and Central America and North America)



CARRAnet JDM cohort (n 384)

Robinson A, et al. Arthritis Care Res 2014; 66(3):404-410

	Ever used %
Corticosteroids	95.7
Pulse corticosteroids	58.7
Methotrexate	92.5
Hydroxychloroquine	53
IV gammaglobulin	40.2
Mycophenolate mofetil	16.7
Cyclosporine	10.5
Rituximab	6.2
Etanercept	4.3
Infliximab	2.7
Adalimumab	1.6
Cyclophosphamide	1.4

Therapeutic approaches

CARRA Consensus Guidelines

Protocols for the initial treatment of moderately severe JDM

Huber AM, et al. Arthritis Care Res 2010; 62:219-225

Consensus treatments for moderate JDM: beyond the first two months

Huber AM, et al. Arthritis Care Res 2012; 64:546-553

Initial therapy: 3 options including steroids (oral and IV) + MTX (15mg/m^2)

PRINTO

A randomized trial in new onset JDM:

prednisone *vs.* prednisone + cyclosporine *vs.* prednisone + MTX

Ruperto N, et al. In press

n 139 pts.

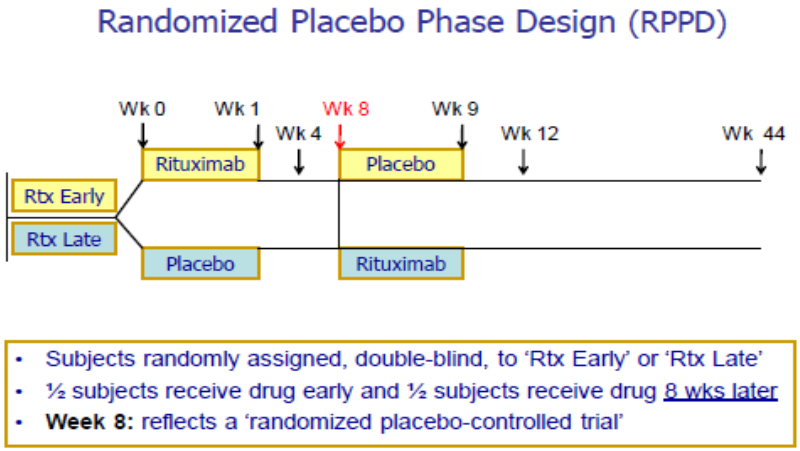
Results:

- Combination therapy (both) were superior than prednisone alone, at 6 months and after 24 months.
- Adverse events: cyclosporine (51%)>MTX (28%)

Rituximab

Rituximab in the treatment of refractory adult and juvenile dermatomyositis and adult polymyositis: a randomized, placebo-phase trial

Oddis C, et al. Arthritis Rheum 2013;65(2):314-324



Primary endpoint: time to DOI

Secondary endpoints:
•time to 20% improvement in the MMT8 on 2 consecutive visits.
•response rate or proportion of patients achieving DOI, at week 8.

Conclusion: although there were no significant differences in the two treatment arms for the primary and secondary endpoints, 83% of refractory adult and juvenile myositis patients met the DOI.

Rituximab

Predictors of clinical improvement in Rituximab treated refractory adult/JDM and adult PM

Aggarwal R, et al. Arthritis Rheumatol 2014; 66(3):740-749

1. Auto Abs (anti Jo-1, Mi-2)
2. Lower physician global assessment damage
3. Myositis subtype: juvenile better than adult

Novel assessment tools to evaluate clinical and laboratory responses in a subset of patients enrolled in the Rituximab in Myositis trial

Rider L, et al. Clinical Exp Rheumatol 2014; 32:689-696

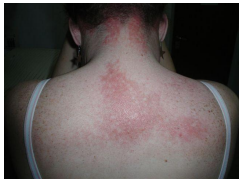
Additional assessments: MMT, CMAS, gait analysis, CDASI, DAS, SF-36, CHQ-PF50, PedsQL, 2 fatigue scales, Dermatology Life Quality Index (DLQI), CD20 counts, and MRI imaging

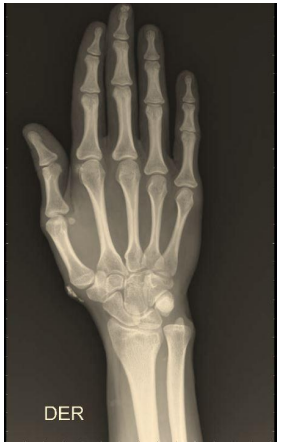
Results: muscle improvement (17-64%), cutaneous (43%) only DLQI (skin less sensitive to change than muscle). MRI improvement (20%), PedsQL (fatigue and sleep subscales) improved (25-75%).

Depletion of peripheral blood B cells did not correlate with clinical response.

Patient´s case (continuation)

Due to the persistence of activity of cutaneous manifestations mycophenolate mofetil was indicated, showing partial efficacy.
She consulted with a plastic surgeon for removal of the calcified nodules of her hands, although small, they were painful during daily activities.
She has a normal life (studying, dancing, going out with friends), however her HRQoL (psychosocial) is affected because of her skin involvement. She uses especial make up to cover the erythematous areas.
When I asked her to write about how she felt about her disease, she said:
“ I am waiting for a magic drug to make my skin clear”.
We worked together on a transition plan, and currently she is being followed by the adult team, who recently, put her on infliximab.





Muito Obrigada!

HOSPITAL ITALIANO
de Buenos Aires