MUSCULOSKELETAL GALAXY

JUNE 5 – 9, 2024 | PORTLAND, OR

AAPA American Academy of Physician Associates | AAOS American Academy of Orthopaedic Surgeons

But I hurt!
Autoimmunity Pearls

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Disclosures

- I have no relevant relationships with ineligible companies to disclose within the past 24 months.

Objectives

- Review patient cases and pick out features that should catch your attention for further autoimmune work up
- Identify inflammatory features on exam and x ray
  - Differential diagnosis for joint pains
  - Differential diagnosis for muscle pains
- List basic work up with labs and limitations

A good history and physical exam are key!

Joint Pain

Case 1

- A 21 year old male cross country runner comes to you with bothersome plantar fasciitis. He has been wearing shoes with inserts, he has been icing the plantar fasciae, and he even has met with physical therapy to learn proper stretching before he goes for his runs.
- His only other complaint is low back pain, which wakes him up from sleep. He attributes this to a bad mattress, as he is sleeping in the college dorms.
- PMH: Near sighted (wears contacts), mild scalp psoriasis treated with topical coal tar shampoo

What's odd?

- Young male
- Persistent enthesial inflammation
- Inflammatory low back pain
- Psoriasis

Extra-articular symptoms are key for diagnosis!

Spondyloarthritis includes AS, IBD arthritis, PsA, ReA

Inflammatory Low Back Pain

- Must be differentiated from mechanical back pain (>95% of patients with chronic low back pain have mechanical LBP)
- Characteristics
  - Onset at age <40
  - Insidious onset
  - Better with exercise
  - Not better with rest
  - Pain in the 2nd half of the night
  - Alternating buttock pain

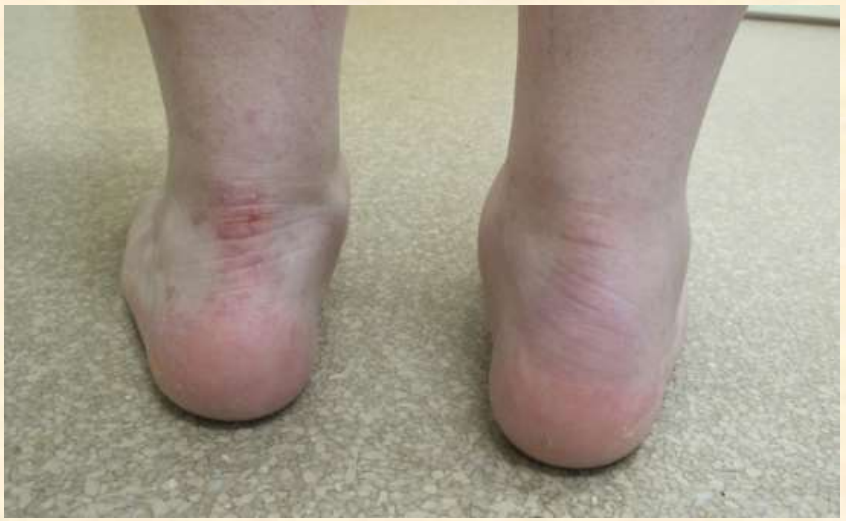
Rheum Dis Clin North Am. 2012 Aug;38(3):501-12.
Ann Rheum Dis. 2009 Jun;68(6):784-8.

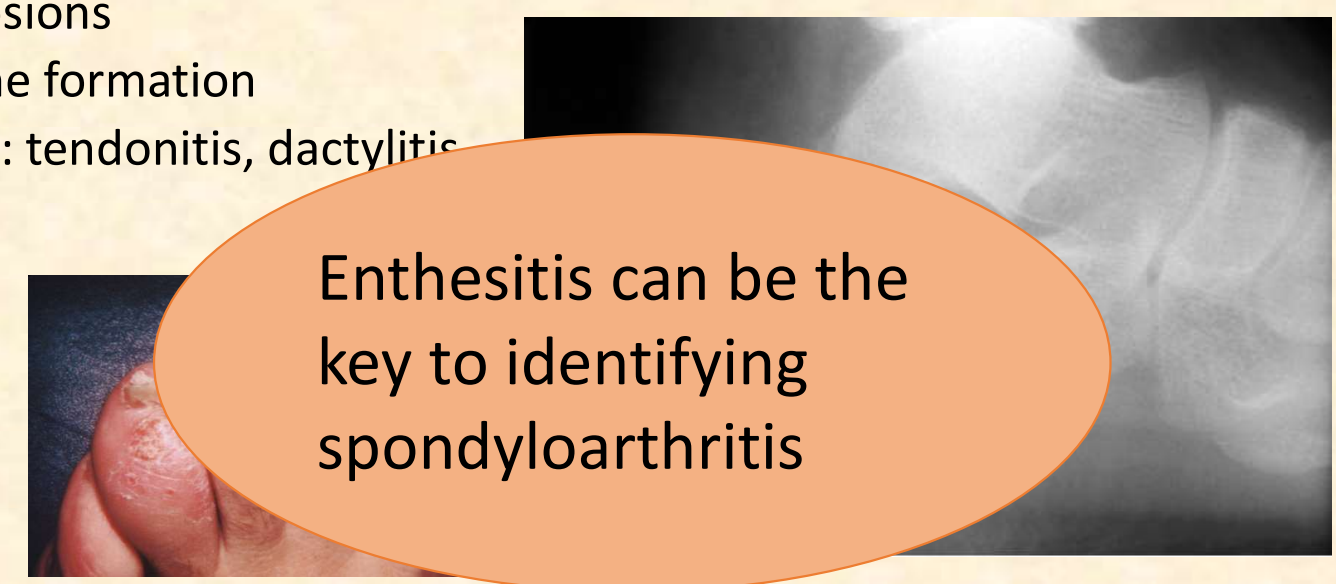
Spondyloarthropathies

- Affected musculoskeletal structures
  - Entheses: Insertion of tendons, ligaments, and fascia onto fibrocartilage > ENTHESITIS
  - Axial skeleton: Sacroiliac, vertebral bodies, and axial joints > SACROILIITIS/SPONDYLITIS
  - Peripheral joints: Predominantly lower extremity and large joints > SYNOVITIS

Enthesitis

- Inflammation at the insertion of the tendon, ligament, or articular capsule onto the bone
- Bony erosions
- New bone formation
- Clinically: tendonitis, dactylitis





Enthesitis can be the key to identifying spondyloarthritis

Image credit: American College of Rheumatology Image Bank, Copyright 2023

Sacroiliitis

- Subchondral inflammation
- Erosion of cartilage
- Bone plate blurring
- Reactive sclerosis
- Fibrous ankylosis
- Bony obliteration of SI joint

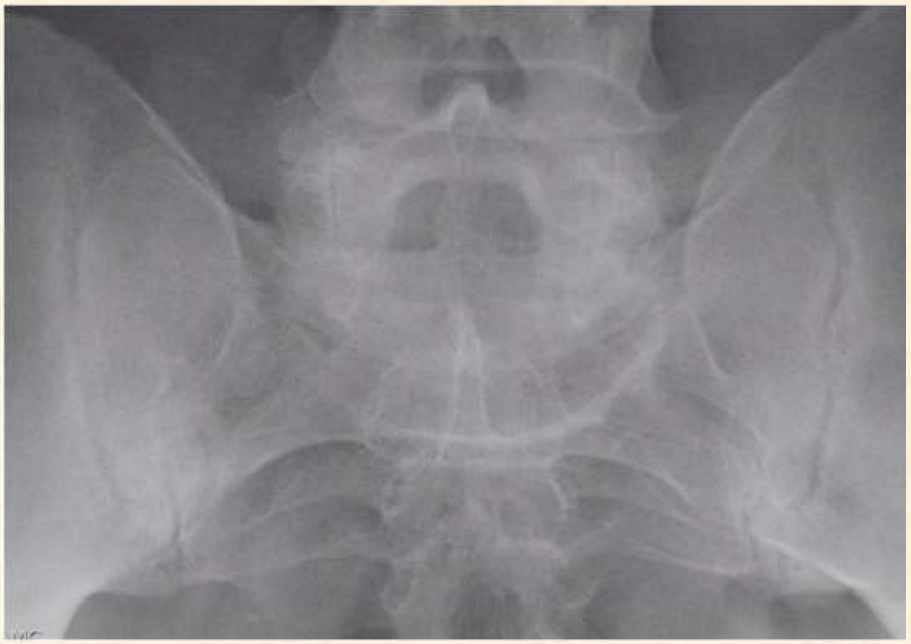
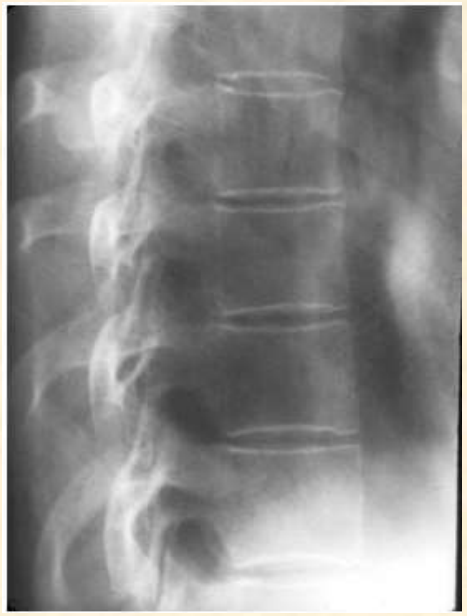
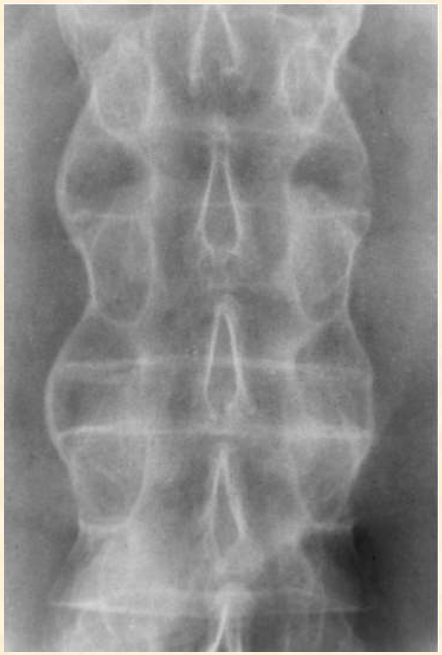


Image credit: American College of Rheumatology Image Bank, Copyright 2023

Spondylitis

- Vertebral body
  - Inflammation and erosions of the bone in contact with Sharpey's fibers (outer fibers of the annulus fibrosis of the disc)
  - Prominent neovascularization
  - New bone formation
- Zygoapophyseal (facet) joints
  - Synovial joint inflammation
  - Neovascularization, erosions
  - New bone formation, ankylosis (fusion)





Spondyloarthritis: Genetics and Labs

- Strong familial aggregation (50-70% have a family history of spondyloarthritis)
  - High identical twin concordance
  - Complex pattern of inheritance
- Associated with HLA-B27 (Class I MHC allele)
  - Strongest association with AS: 90% HLA-B27+
  - Spondylitic psoriatic arthritis (60%) and reactive arthritis (50%)
- HLA-B27 increases the risk of AS
  - Risk for AS in HLA-B27+ individuals is 2-5%
  - Risk of AS in an HLA-B27+ individual with a first degree relative with AS is 10-20%

Comparison

Spondyloarthritis	
Population	M>F 2:1
Symptoms	Inflammatory low back pain, enthesitis, large and small joint inflammatory arthritis
Comorbidities	Psoriasis Inflammatory Bowel Disease (Crohn's disease, ulcerative colitis) Uveitis
Exam	Limited forward flexion (Schober test)
Labs	HLA B27 positive in 90% of AS patient cases

Case 2

- A 34 year old female without a significant past medical history comes to you for evaluation of right wrist pain. She fell onto her wrist after she tripped over a side walk.
- She was evaluated at an urgent care when she injured the wrist, and was told to use rest, ice, elevation, and ibuprofen.
- This injury was three months ago. When you see her in clinic, you observe right wrist fullness, warmth, and limitation in ROM, as well as R 2nd MCP fullness.
- PMH: Prior metatarsalgia

What's odd?

- Young healthy female with a non-healing joint injury
- Pattern of repeated joint problems
- Three months of symptoms failing conservative therapy
- What work up now?

Inflammatory arthritis has joint warmth, swelling (effusion), and limited ROM

Imaging- Rheumatoid Arthritis

- Early on (within first year) radiographs are often normal
- Later we can see small erosions from the inflammation

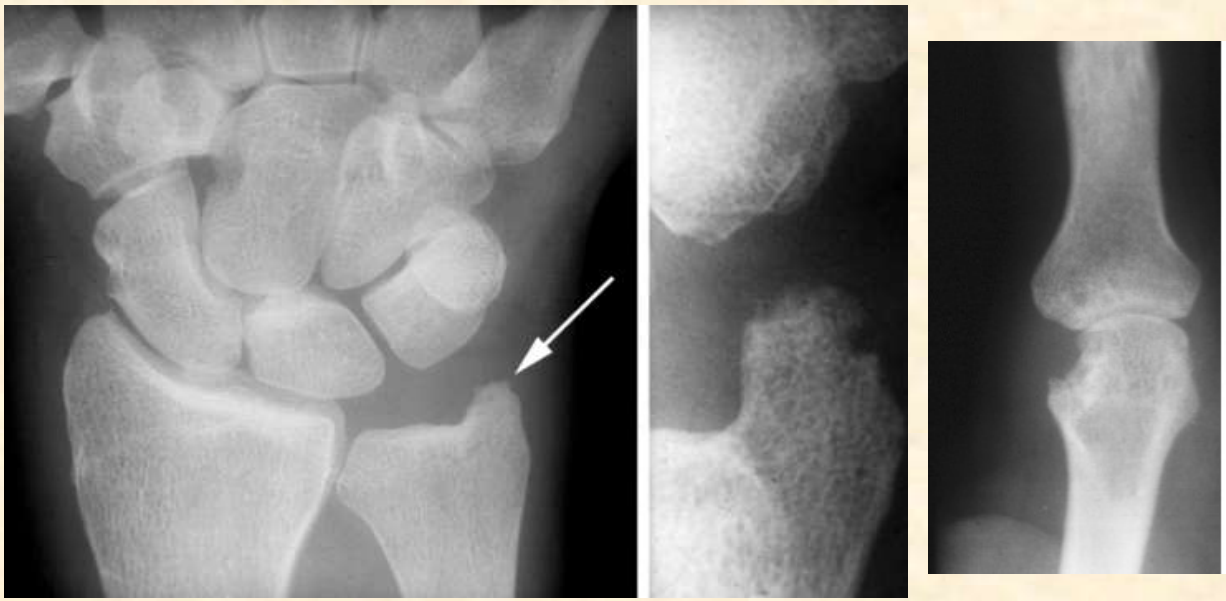


Image credit: American College of Rheumatology Image Bank, Copyright 2023

Work Up- Labs

- Rheumatoid factor
- Anti-CCP antibodies
- Sedimentation rate
- C-reactive protein
- ANA?

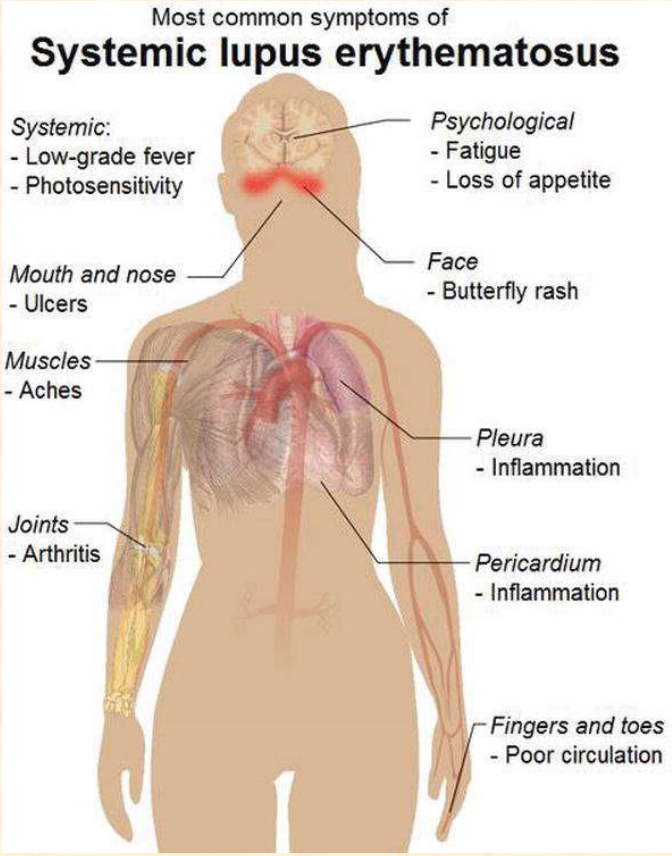
Labs should confirm your clinical diagnosis

Watch for systemic inflammation clues!

- Rashes like “easy sunburns” after just a few minutes of sun exposure, especially on face
- Mouth and nasal ulcerations
- Chest pain with breathing or positional changes
- Unexplained fatigue

ANA is positive in 99% of SLE patients, but up to 10% normal patients

Lupus Work Up



Zaman, G. S. (2017). Introduction and Physiology of Lupus. InTech. doi: 10.5772/intechopen.68635

Box: Basic Investigations for SLE

Complete blood count

Direct Coombs test (indicated if patient presents with hemolytic anemia and reticulocytosis)

Comprehensive metabolic panel

Erythrocyte sedimentation rate

C-reactive protein

Urinalysis

Serologic tests (ANA and, if positive, anti-dsDNA, anti-SSA/SSB, anti-Smith/RNP antiphospholipid antibodies); negative ANA result is inconsistent with diagnosis of SLE

Complement C3 and C4

Creatine phosphokinase (indicated in patients presenting with muscle weakness)

ANA = antinuclear antibody; dsDNA = double-stranded DNA; SLE = systemic lupus erythematosus.

Ann Intern Med. 2020 Jun 2;172(11):ITC81-ITC96

Comparison

	Spondyloarthritis	Rheumatoid Arthritis	SLE
Population	M>F 2:1	F>M 3:1	F>M 8:1
Symptoms	Inflammatory low back pain, enthesitis, large and small joint inflammatory arthritis	Small joint symmetric arthritis (hands and feet) that may have erosive changes	Malar rash, mucosal ulcerations, small joint predominant pains, fatigue, fevers
Comorbidities	Psoriasis Inflammatory Bowel Disease (Crohn's disease, ulcerative colitis) Uveitis	Scleritis ILD Vasculitis	Serositis Nephritis Cytopenias Raynaud's
Exam	Limited forward flexion (Schober test)	Small joint synovitis, ulnar deviation, rheumatoid nodules	Small joint predominance, non erosive disease
Labs	HLA B27 positive in 90% of AS patient cases	Rheumatoid Factor (RF) Anti-CCP (ACPA)	Cytopenias, renal disease, ANA positive

Muscle Pain

Case 3

- A 43 year old woman with a history of obesity, well managed HTN with medications, and prediabetes comes to your clinic to establish care. She has complaints that she has severe muscle pains for years, as well as terrible fatigue. She said that she hurts everywhere, and has a hard time localizing the worst pain for you. She said that she feels weak and doesn't do much physical acti… …ain. She describes a sedentary lifestyle beca…
- On exam her vitals are T 98.2, BP 12… exam is remarkable for exquisite ten… joint swelling is present. Strength ex…
- What diagnoses would you consider?

No inflammatory features with this disease

Fibromyalgia

- Very common, 2-3% population world wide
- Pain out of proportion to the stimulus (hypersensitivity), poorly localized
- Unrefreshing sleep with terrible fatigue
- Limited energy
- Cognitive dysfunction
- Psychiatric disorders
- Often complaints of being weak, but on strength exam they have full strength

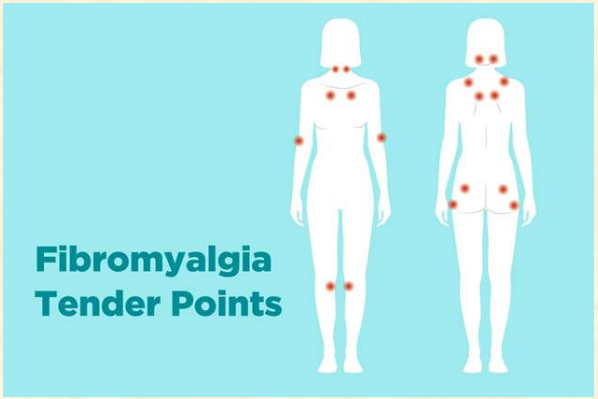
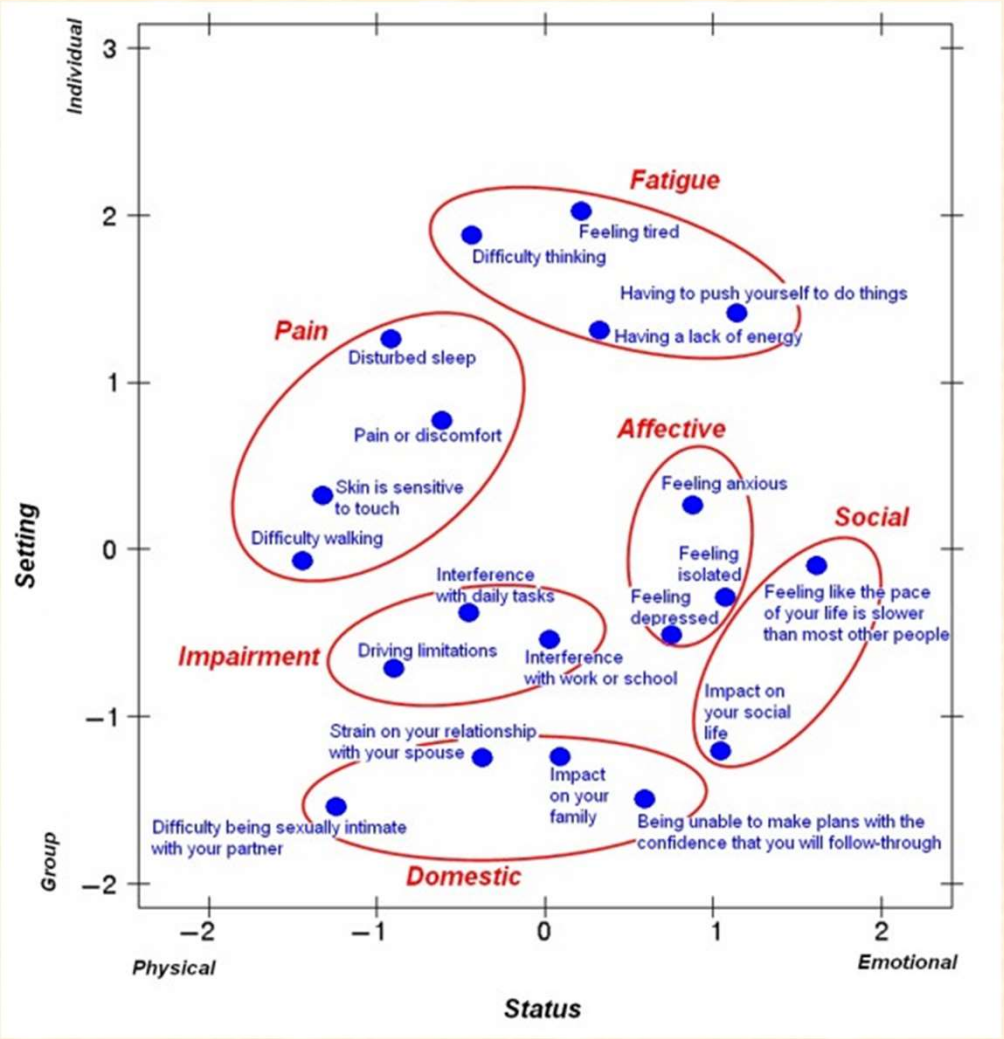
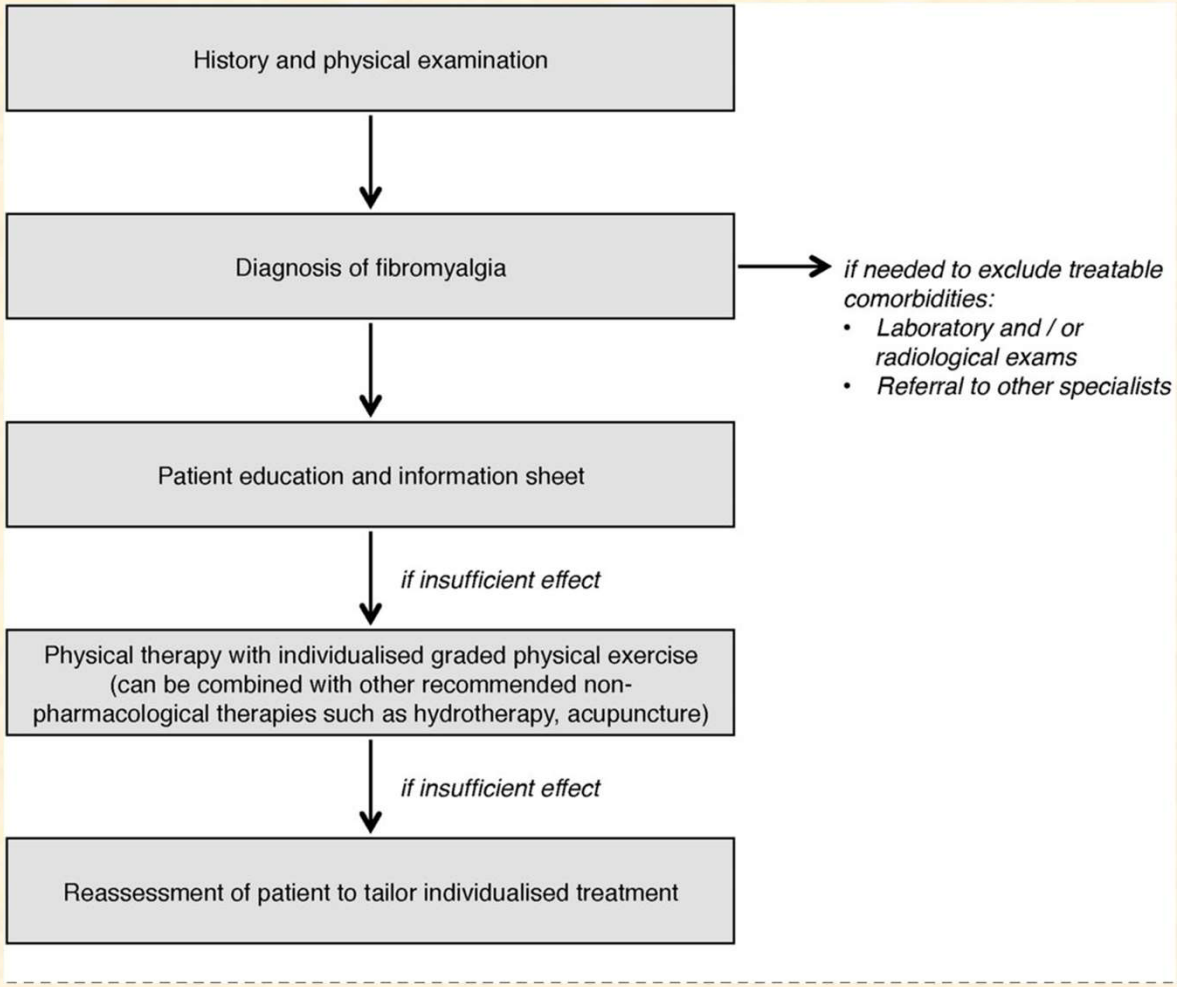


Image credit: Creakyjoints.org

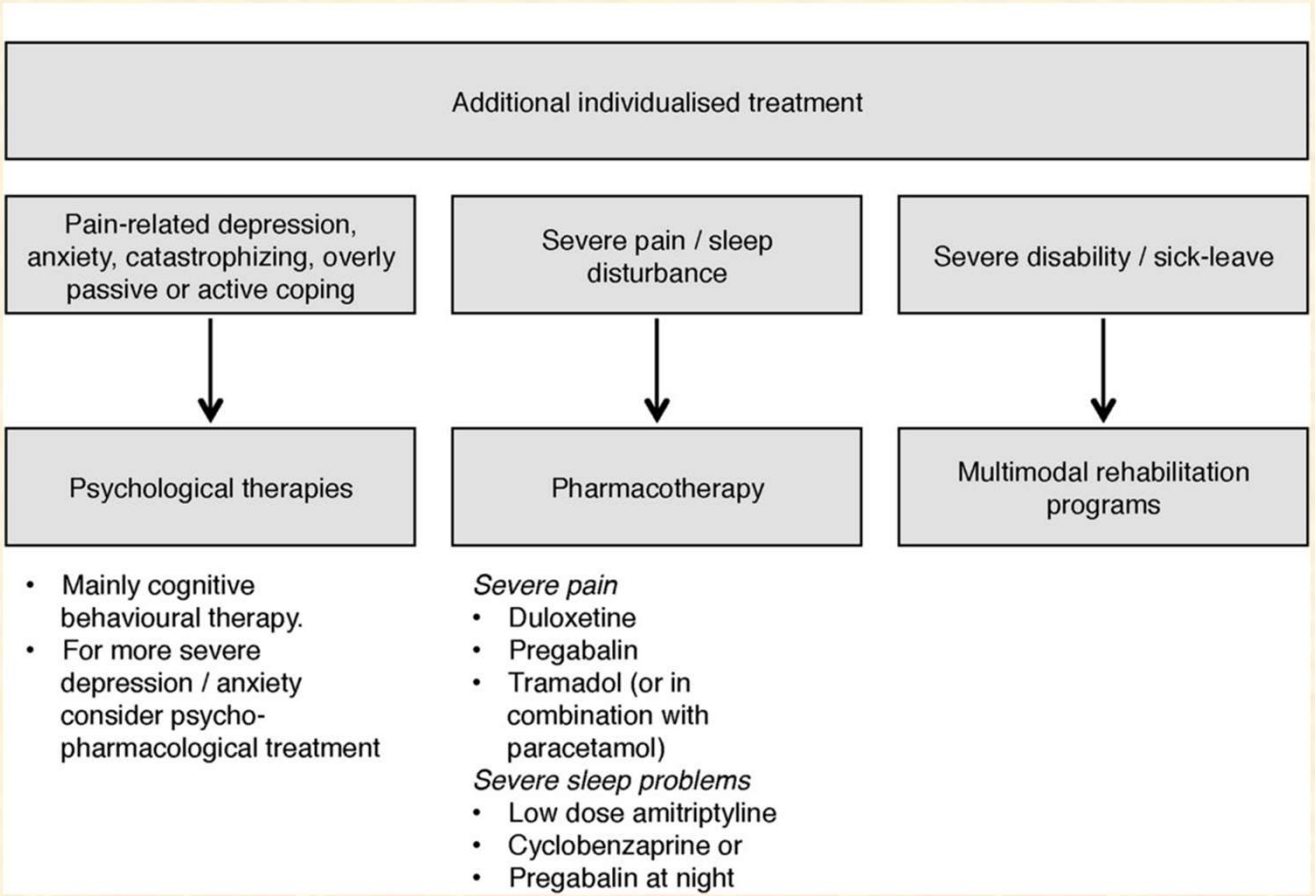
Dimensions of Fibromyalgia



BMC Musculoskelet Disord 2010;11:134.



Annals of the Rheumatic Diseases 2017;**76:**318-328

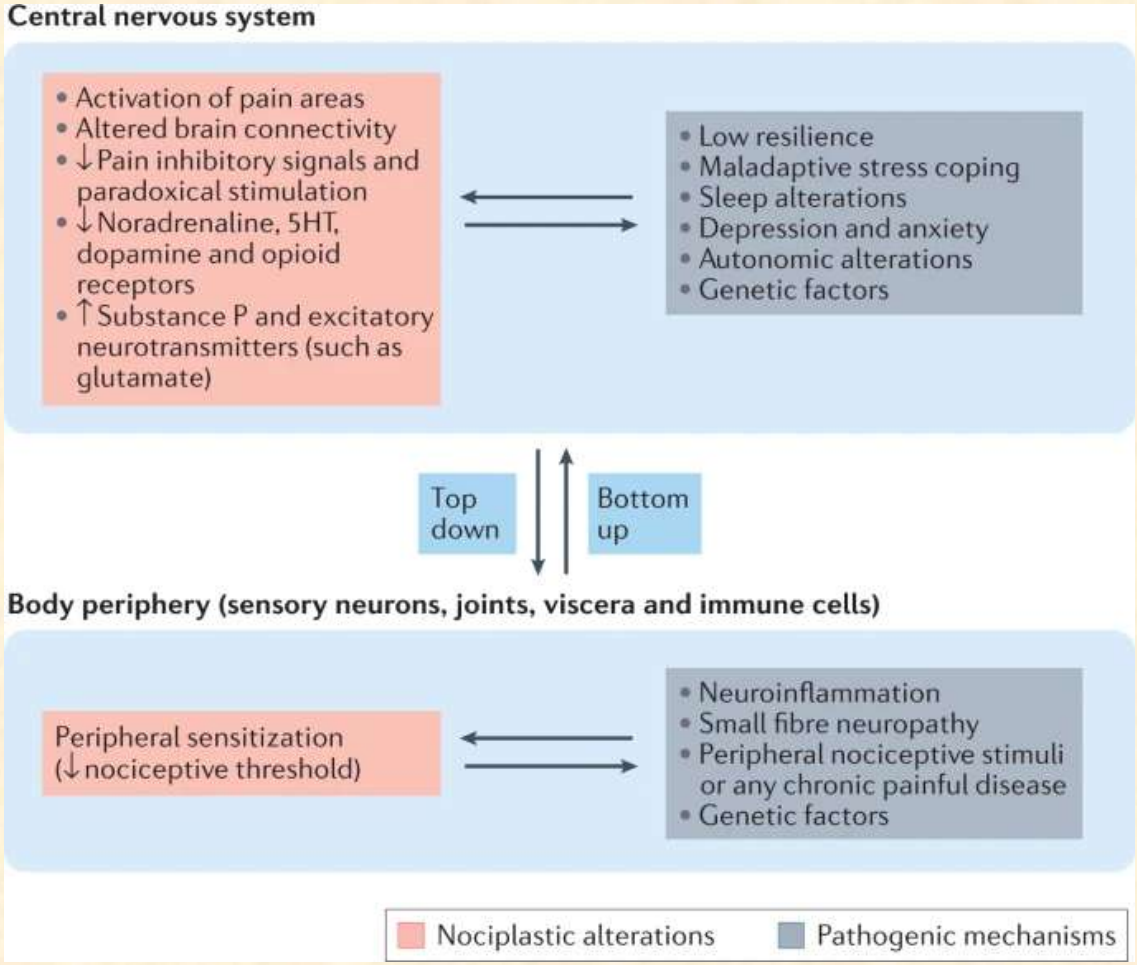


Annals of the Rheumatic Diseases 2017;**76:**318-328

Patient Education

- The symptoms are not caused by an organic disease (such as abnormality of muscles or joints) but are instead based on a functional disorder.
- The legitimacy of the ailment should be acknowledged.
- The symptoms are persistent in nearly all patients.
- Total relief of symptoms is seldom achieved.
- The symptoms do not lead to disablement and do not shorten life expectancy.
- Most patients learn to adapt to the symptoms over time.
- The goals of treatment are improvement in quality of life, maintenance of function (functional ability in everyday situations), and reduction of symptoms.
- The ability of the patient to modulate symptoms via self-management strategies should be emphasized

Evid Based Complement Alternat Med. 2013;2013:528952. doi: 10.1155/2013/528952.

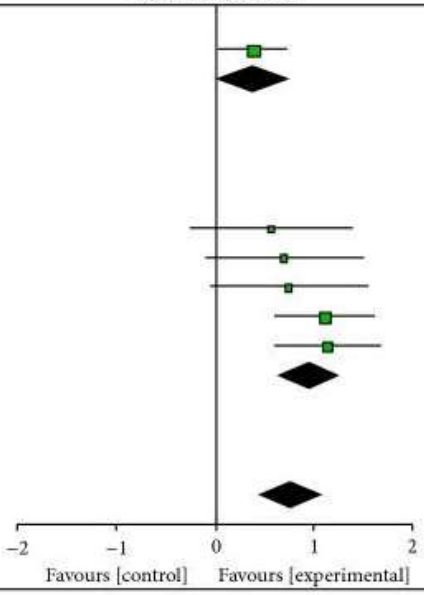


Nat Rev Rheumatol 16, 645–660 (2020).

Exercise

(b) Effect of exercise on FMS severity. SD: standard deviation; IV: inverse variance; CI: confidence interval

Study or subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. mean difference IV, random, 95% CI
3.1.1 Physical component of HRQOL. Analysis by intention-to-treat								
Larsson et al. 2015. Muscle strengthening	34.5	9.1	56	31.2	7.9	67	28.0%	0.39 [0.03, 0.75]
Subtotal (95% CI)			*56*			*67*	*28.0%*	*0.39 [0.03, 0.75]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 2.12$ ($p = 0.03$)								
3.1.2 Physical component of HRQOL. Analysis per protocol								
García-Martínez et al. 2010. Combined exercise	36.4	12.9	12	30	8	12	10.7%	0.58 [−0.24, 1.40]
Bircan et al. 2008. Aerobic exercise	38.92	6.11	13	34.49	6.02	13	11.1%	0.71 [−0.09, 1.50]
Bircan et al. 2008. Muscle strengthening	45.44	7.71	13	38.66	9.78	13	11.1%	0.75 [−0.05, 1.55]
Gavi et al. 2014. Muscle strengthening	35.65	7.8	35	27.01	7.61	35	20.3%	1.11 [0.60, 1.61]
Gavi et al. 2014. Flexibility	34.15	9.2	31	24.37	7.58	31	18.8%	1.15 [0.61, 1.69]
Subtotal (95% CI)			*104*			*104*	*72.0%*	*0.95 [0.66, 1.24]*
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.29$, df = 4 ($p = 0.68$); $I^2 = 0\%$								
Test for overall effect: $Z = 6.46$ ($p < 0.00001$)								
Total (95% CI)			*160*			*171*	*100.0%*	*0.77 [0.47, 1.08]*
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 8.09$, df = 5 ($p = 0.15$); $I^2 = 38\%$								
Test for overall effect: $Z = 4.94$ ($p < 0.00001$)								
Test for subgroup differences: $\chi^2 = 5.80$, df = 1 ($p = 0.02$), $I^2 = 82.8\%$								



Biomed Res Int. 2017;2017:2356346.

Physical Non-Drug Treatments

- Massage administered by trained PT
  - Manual lymph drainage
  - Connective tissue massage
  - Myofascial release
- Acupuncture
  - Meta-analysis 6 well-designed studies (N=323) showed no significant pain improvement
  - May reduce insomnia

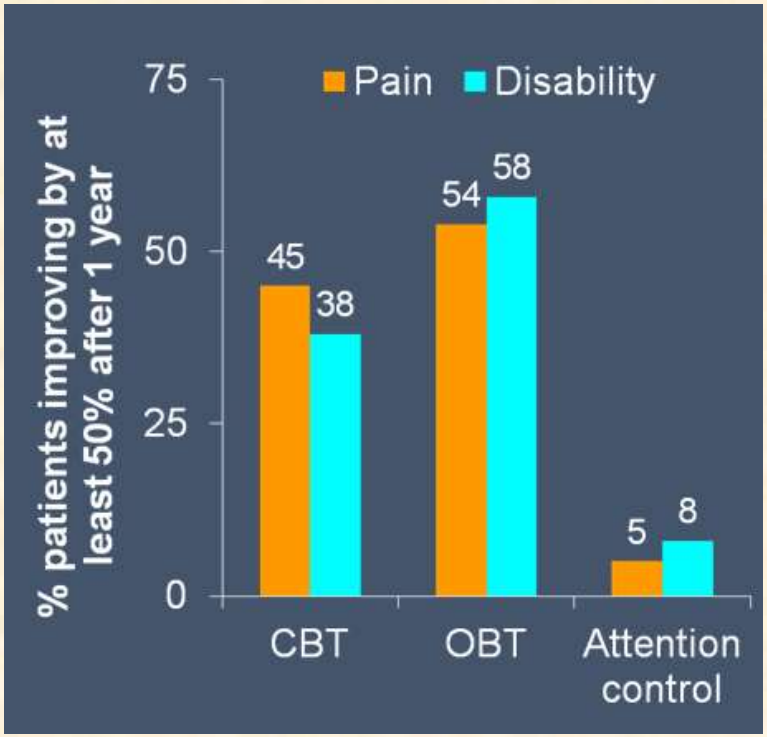
Open Rheumatol J 2009;3:25–9.
Complement Ther Clin Pract. 2021;45:101477

Effective Psychological Skills

	Cognitive-behavioral	Operant-behavioral
Definition	Replace maladaptive thoughts and behaviors with positive coping strategies and adaptive behaviors	Reduce undesirable pain reinforcement
Example	Pain flares after shopping. BEFORE: "This pain will never get better. I'm doomed to spend the day in bed!" AFTER: "I need to pace my activities better and add in some extra flare management techniques when my pain increases."	• Stop expressing pain, grimacing, moaning • Increase activity • Take medications on time-contingent basis rather than in response to pain • Teach significant others to avoid being overly solicitous

Other Non-Drug Treatments

- Psychological therapies
  - Relaxation
  - Stress management
  - CBT
  - OBT
- Lifestyle modifications
  - Weight management
  - Sleep hygiene
  - Smoking cessation



Arthritis Rheum 2007;57:830-6.

Medication Recommendations

1st tier	2nd tier	3rd tier
• SNRIs – *Duloxetine 60 mg QD or BID – *Milnacipran 50-100 mg BID • *Pregabalin 450 mg daily divided	• TCA – Amitriptyline 25 mg QHS • Gabapentin 400-800 mg TID • Tramadol 37.5 mg + APAP 325 mg QID • Muscle Relaxants - Cyclobenzaprine 10-40 mg in divided doses - Tizanidine up to 12 mg in divided doses	• SSRIs – Fluoxetine 10-60 mg daily – Paroxetine 20-40 mg daily

*FDA approved for fibromyalgia

Fibromyalgia. A Practical Clinical Guide. New York, NY: Springer, 2011
Arthritis Rheum. 2004 Feb 15;51(1):9-13
Pain Physician. 2002 Oct;5(4):422-32

Comparison

	Fibromyalgia
Population	2:1 F:M, any age but onset typically 20-55
Symptoms	Diffuse poorly localized muscle pain and fatigue
Comorbidities	Obesity, depression/anxiety, sleep disorders
Exam	Tenderness to light touch throughout
Labs	Should be normal

Case 2

- A 78 year old male with a history of COPD and eczema comes in to clinic for evaluation. He describes terrible pain and weakness. He said that it came on in the last month. He tried to stand up to greet you as you walked in the room, but he had to sit back down. His son, who is a physician assistant, said that he [illegible] polymyositis recently and he thinks this is [illegible]
- On exam, his vitals show T[illegible] MI 24. He has mild scattered wheez[illegible] shows no swollen joints. On strengt[illegible] his deltoids, and hip flexion is [illegible]
- You share with him your diagn[illegible]

Pain causing weakness is the key feature of this condition

Polymyalgia Rheumatica

- Age of onset exclusively over age 50
- Incidence increases each decade over age 50
- Proximally and bilaterally distributed aching and morning stiffness persisting for at least two weeks
- Pain causing weakness
- No muscle inflammation, CK is normal
- Often inflammatory markers are elevated, Erythrocyte sedimentation rate (ESR) (Westergren) ≥40 mm/h.
- Rapid resolution of symptoms with low-dose glucocorticoids

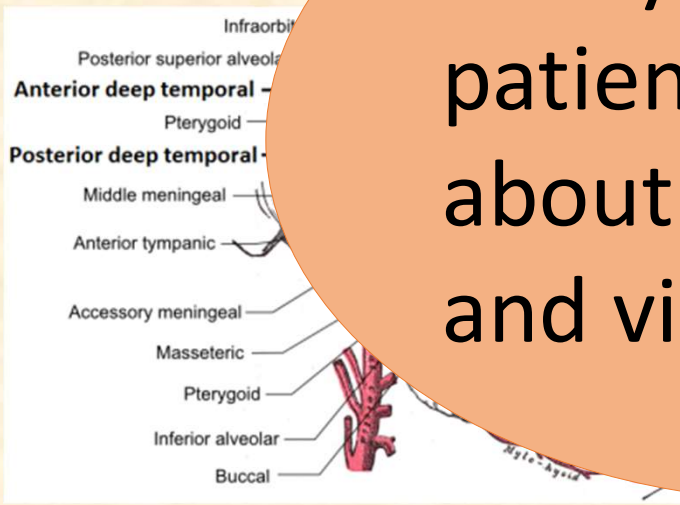
PMR

- Age over 50, peak age 70-80
- F:M 2-3:1
- Caucasian
  - Uncommon in Asian, African-American, and Latino populations
  - Although- all racial and ethnic groups may be affected
- Common
  - PMR incidence per 100,000 residents aged 50 years or more was 112.6 (137.7 in women and 83.2 in men)
  - The overall annual incidence of PMR was 63.9 (95% confidence interval [CI] 57.4, 70.4) per 100,000 population aged ≥50 years

J Rheumatol. 1997 Sep;24(9):1739-43
Arthritis Care Res (Hoboken). 2016 Oct 21.

PMR and Giant Cell Arteritis

- Approximately 10 % of patients will develop GCA, may be a spectrum of disease and should screen for symptoms of G
- => New headaches, scalp tend
claudication, vision loss



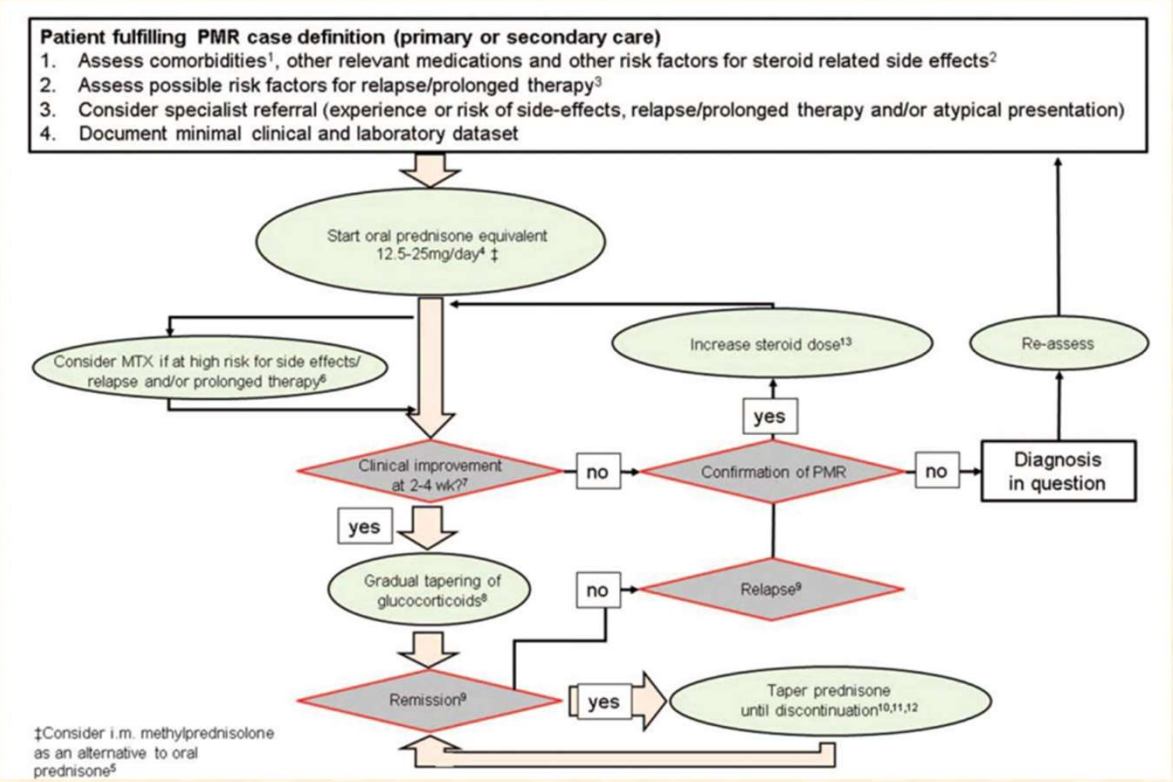
Always ask patients with PMR about headache and vision changes

PMR treatment: EULAR/ACR Recommendations

- Start minimum effective dose prednisone in the range of 12.5 to 25 mg daily
- Taper to 10 mg within 4-8 weeks
- Further taper by 1 mg/ month as tolerated
- Consider MTX in refractory cases
- Consider early MTX in patients with high risk for relapse (women, high initial ESR, peripheral arthritis) or comorbidities

Dejaco et al, Annals Rheum Dis, 2015

Treatment Algorithm



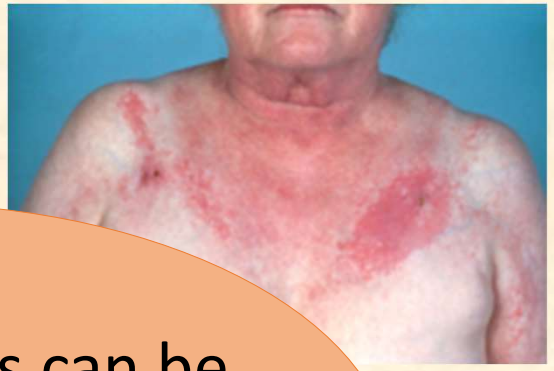
Dejaco et al, Annals Rheum Dis, 2015

Comparison

	Fibromyalgia	Polymyalgia Rheumatica
Population	2:1 F:M, any age but onset typically 20-55	2-3:1 F:M, age over 50 (70-80)
Symptoms	Diffuse poorly localized muscle pain and fatigue	Pain causing weakness in shoulder and hip girdle
Comorbidities	Obesity, depression/anxiety, sleep disorders	*Watch for Giant Cell Arteritis
Exam	Tenderness to light touch throughout	Weakness in proximal muscle groups due to pain
Labs	Should be normal	ESR

Case 3

- A 58 year old female comes in for new patient evaluation. She has complaints of muscle pains and a bad sunburn on the chest, back, and face, as well as overall weakness. She hasn't gone to a doctor in years and she claims that she is without any health problems other than her smoking history.
- On exam, VS: T98.5, HR 85, BP 128/75, R 10, BM
- She has erythema around the eyelids
anterior chest wall. Hands have s
with skin thickening on the dors
strength in her deltoids, thoug
flexion and extension. Hip flex
Ankle plantar and dorsiflexion

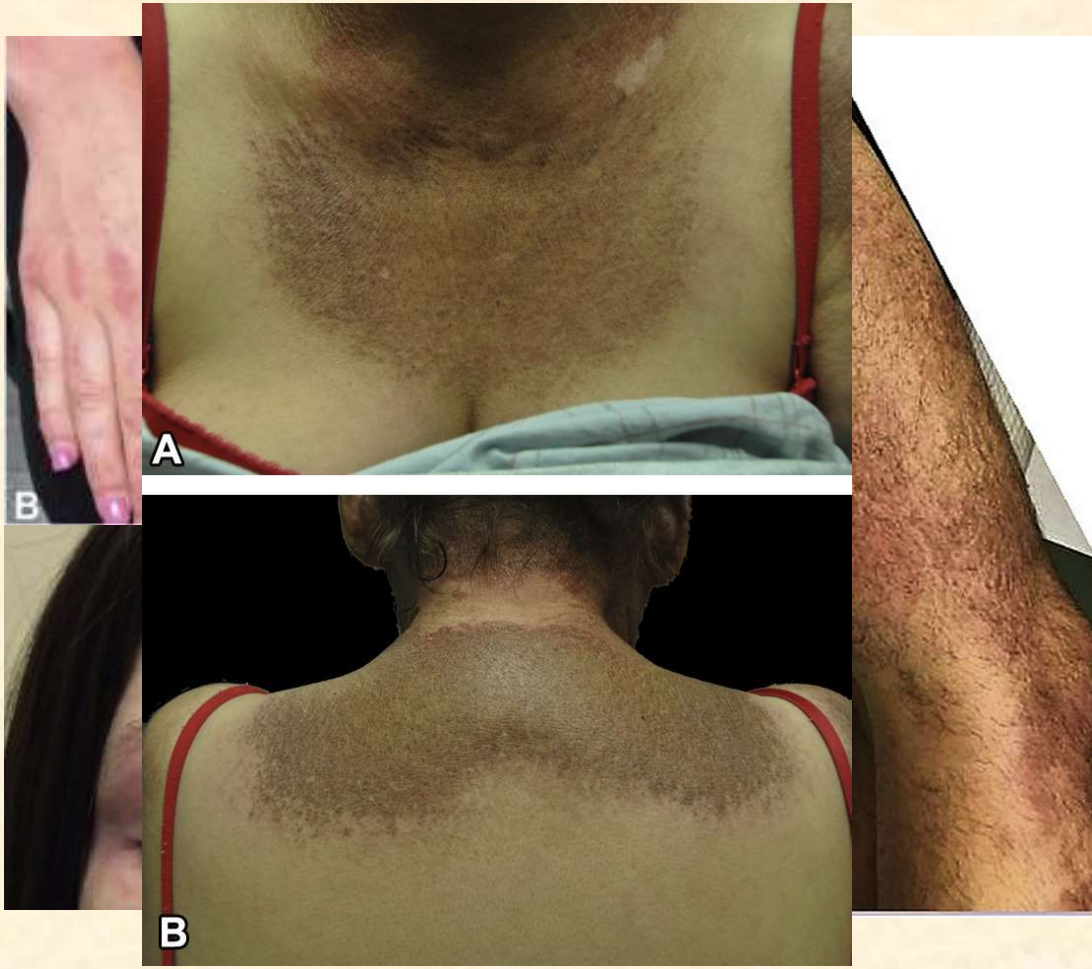


College of
umatology

Dermatomyositis can be painful, while polymyositis is painless weakness

Dermatomyositis

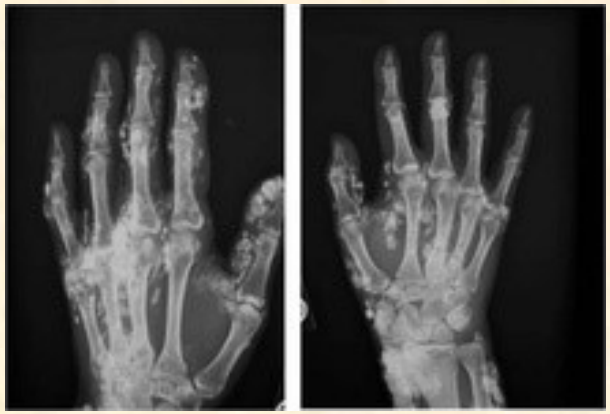
- Skin involvement:
  - Gottron's papules
  - Heliotrope rash
  - Holster sign
  - Shawl sign
- Muscle involvement: limb girdle proximal weakness present in about 80%, about 20% will have muscle pain. Ask about dysphagia.

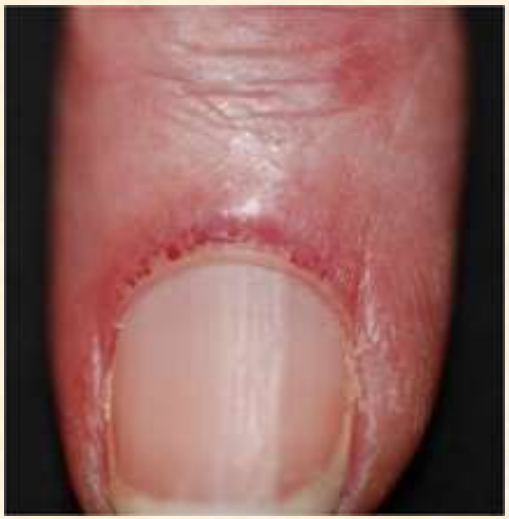


J Am Acad Dermatol. 2020 Feb;82(2):267-281

Other exam findings

- Inflamed or swollen areas around fingernails
- Calcinosis





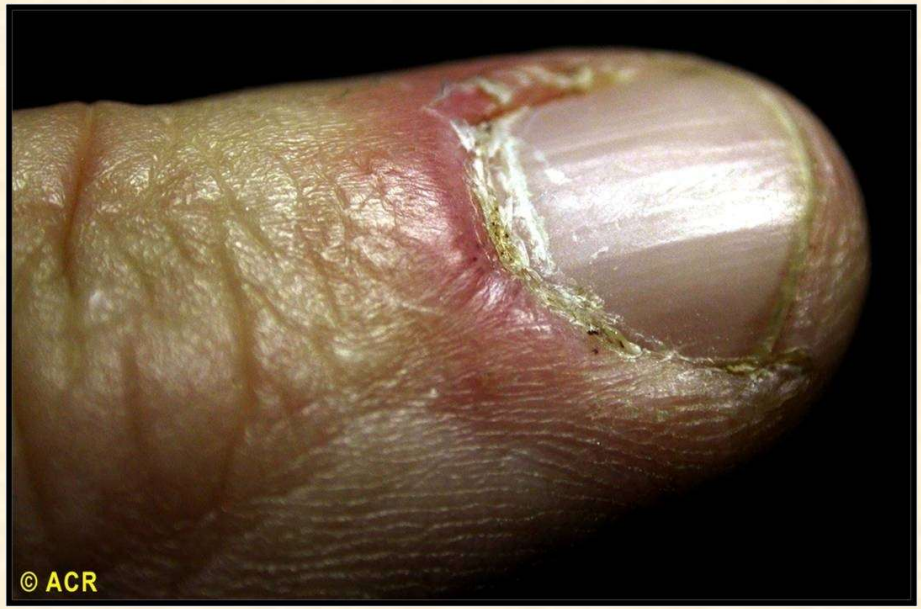


Image Credit: American College of Rheumatology

Dermatomyositis

- Prevalence estimated at 1 to 6 per 100,000 adults in the United States
- 2:1 Female: Male ratio
- All races, especially African American
- Bimodal age distribution:
  - Pediatric 4-14
  - Age 40-60
- Lab work up: CK, aldolase, AST, ALT
- Consider malignancy work up
- Refer to rheumatology

Muscle Nerve. 2012 May;45(5):676-83
Front Immunol. 2017 Aug 21;8:992
J Am Acad Dermatol. 2020 Feb;82(2):267-281

Comparison

	Fibromyalgia	Polymyalgia Rheumatica	Dermatomyositis
Population	2:1 F:M, any age but onset typically 20-55	2-3:1 F:M, age over 50 (70-80)	2:1 F:M, age 40-60
Symptoms	Diffuse poorly localized muscle pain and fatigue	Pain causing weakness in shoulder and hip girdle	Rashes, weakness, muscle pains, dysphagia
Comorbidities	Obesity, depression/anxiety, sleep disorders	*Watch for Giant Cell Arteritis	Consider malignancy work up
Exam	Tenderness to light touch throughout	Weakness in proximal muscle groups due to pain	Proximal true muscle weakness and possibly pain
Labs	Should be normal	ESR	CK, aldolase, AST, ALT

Key Points

- Recognize inflammatory low back pain features
- Watch for enthesitis, dactylitis, spondylitis and sacroiliitis features that would prompt a work up for a more systemic disease
- Recognize patterns- often by the time you see the patient with inflammatory arthritis they may have had prior episodes that were missed
- Clinical features of inflammatory joint pain- warmth, swelling, limited range of motion, no preceding injury or out of proportion to prior injury

Key Points (continued)

- When a patient has muscle pain, evaluating true weakness from pain causing weakness is key
- Identify muscle pain patterns (diffuse versus limb-girdle)
- Watch for GCA in PMR!
- Recognize rashes and ILD as features of dermatomyositis

Questions?