

Differential Diagnosis of Polyarthrititis/Polyarthralgia

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Disclosures

None.

Polyarthrititis – Outline

1. DDx: includes primary arthritides and systemic disease
 - **History** narrows the field
 - **Physical exam** confirms suspicion
 - Labs and X-rays – can be misleading in the absence of a good history and exam.
2. Common arthritides – a few key points.
3. Summary.

Rheumatology Consult for Joint Pain: Common Chief Complaints

“Doc, my body is full of arthritis.”

“My bones hurt!”

“My joints hurt, but my arthritis test was negative.”

“I have pain all over and tested positive for lupus.”

“I don’t know why I’m here.”

Joints (or not...)

Osteoarthritis
Erosive Osteoarthritis
Rheumatoid arthritis
Gout
CPPD arthropathy
Psoriatic arthritis
Ankylosing spondylitis
Reactive arthritis
Palindromic rheumatism
Undifferentiated polyarthritis
Polymyalgia rheumatica
Fibromyalgia
“Poly-bursitis”
Peripheral neuropathy

Joints PLUS

SLE
Sjögren's syndrome
Systemic sclerosis
Inflammatory myopathy
Adult-onset Still's disease
Sarcoidosis
Relapsing polychondritis
Behçet's disease
Systemic vasculitis
Parvovirus B19 infection
Hepatitis C > B
Acute rheumatic fever
Early Lyme disease
Chikungunya virus
Zika virus

A more basic view of the DDx for polyarticular pain

1. Osteoarthritis
2. Inflammatory arthritis (has its own DDx)
3. Arthralgia (pain without joint abnormality)
4. Bursitis or Tendinitis
5. Myofascial pain / Fibromyalgia

When it is early in the course of symptoms, differentiating among these causes is often difficult for anyone.

Diagnostic Evaluation of Joint Pain

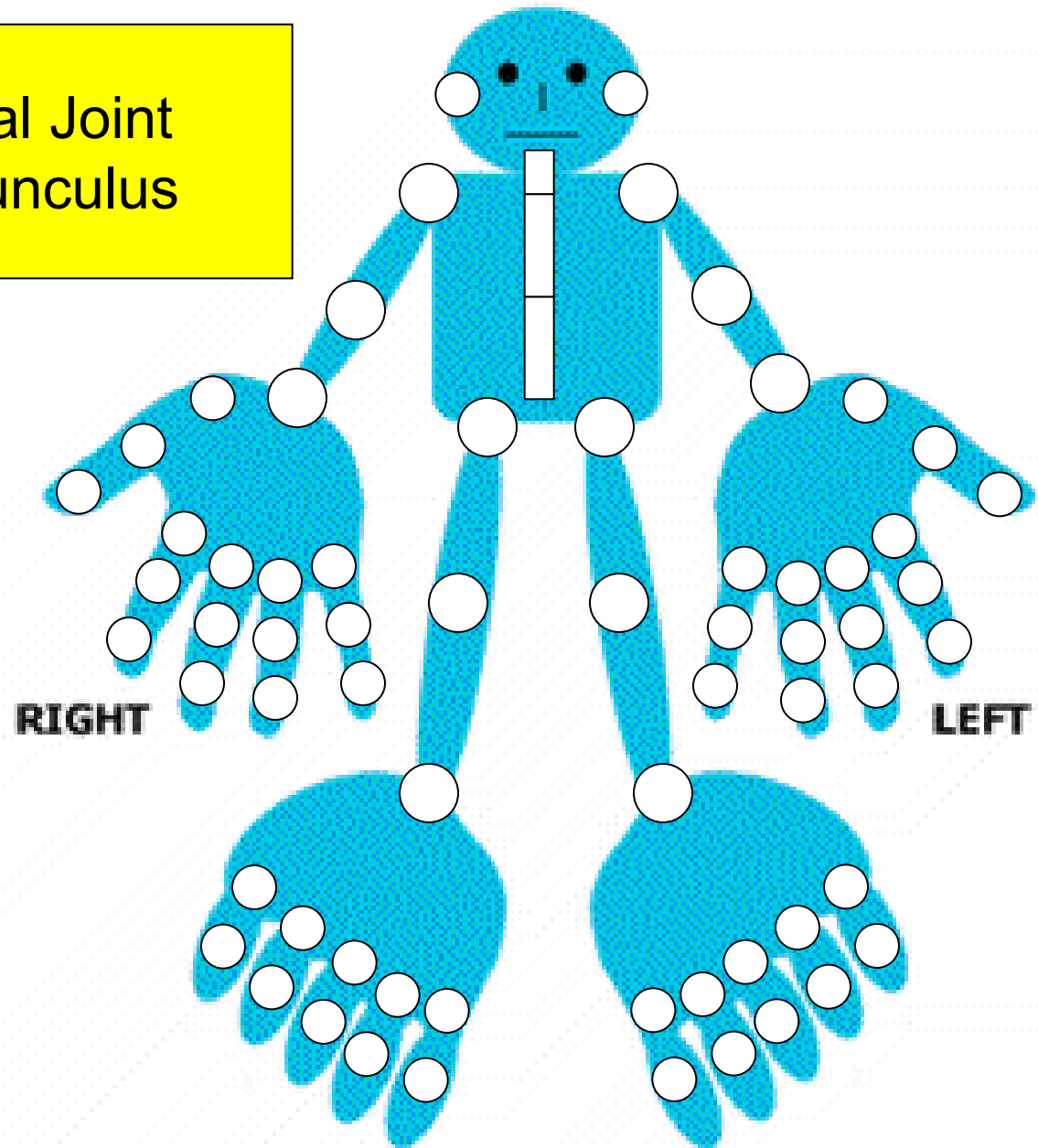
1. A thorough HISTORY and EXAM are critical for differentiating causes of joint pain.

- Is pain localized to joints vs. more diffuse MSK pain?
- Are imaging studies available to provide diagnostic clues?
- Do lab tests support the clinical impression?

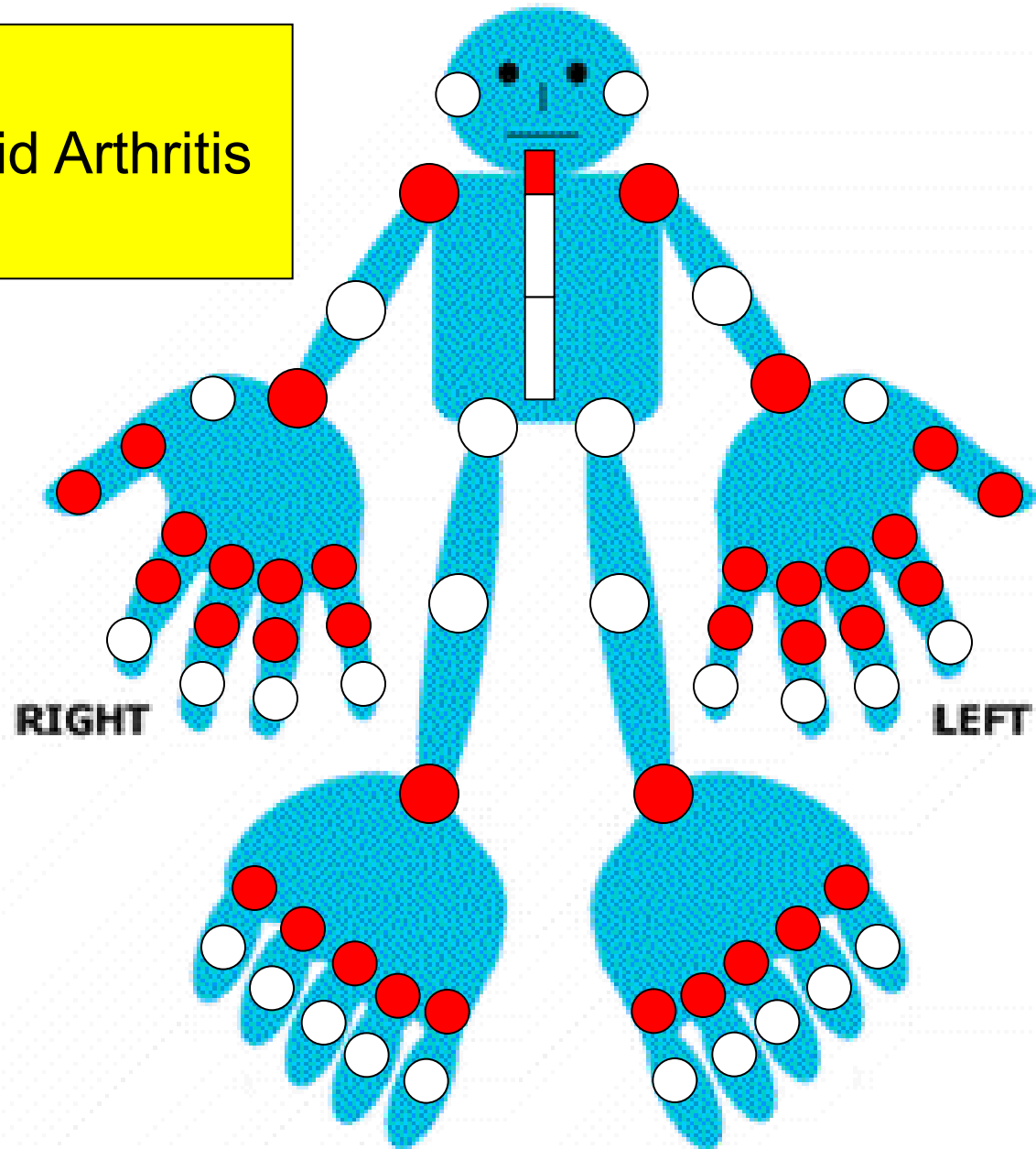
2. Joint pain is like any other clinical problem.

- Like a heart murmur, the significance of joint pain is determined by the company it keeps.
- Interpret a joint exam just like an EKG – pattern recognition may point you to the diagnosis.

Normal Joint Homunculus



Rheumatoid Arthritis



Case 1 – Slam dunk

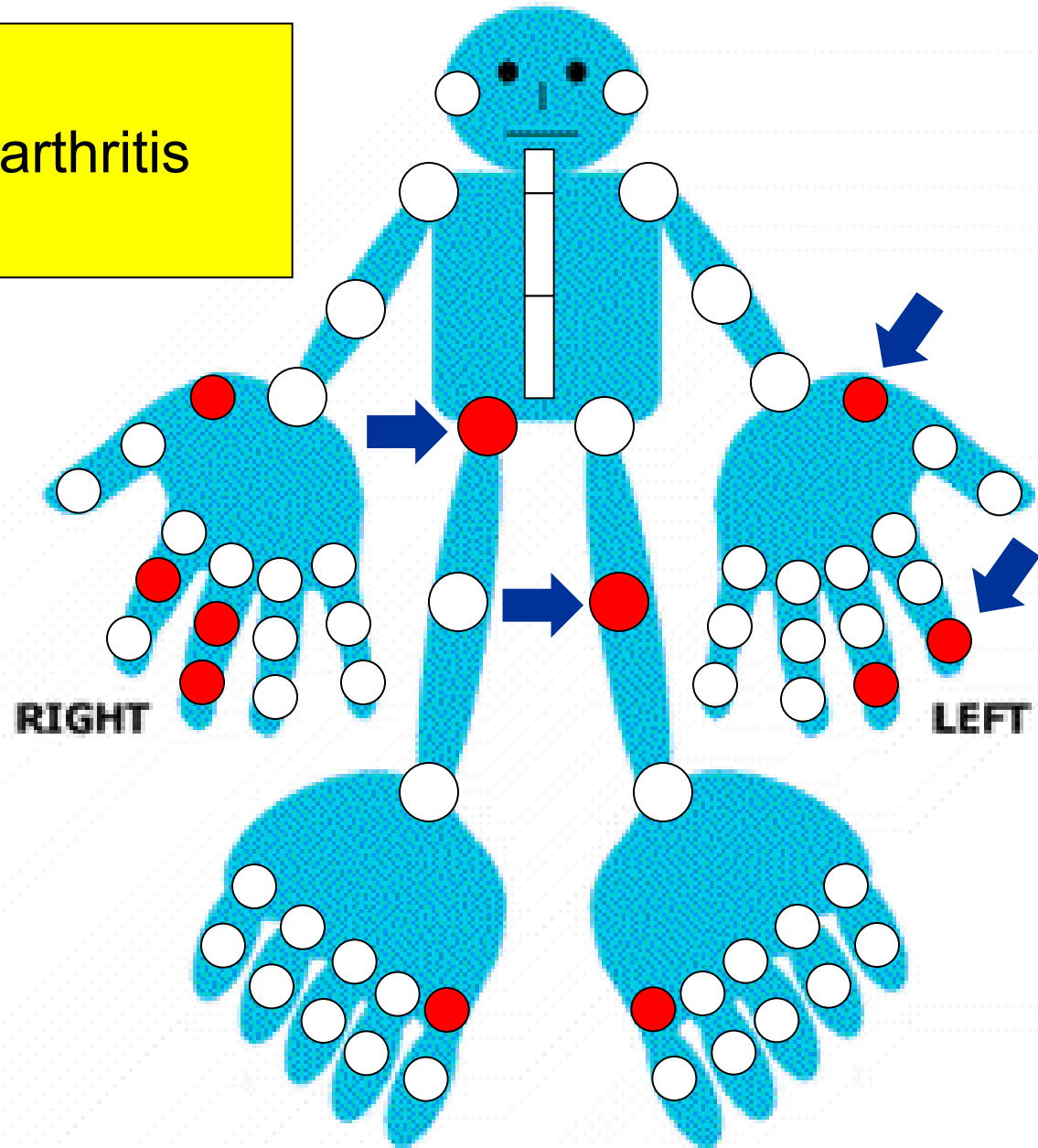
18yF w/ 1 year of joint pain, previously healthy.

- Progressively: **hands (MCPs and PIPs), elbows, shoulders, ankles, feet, jaw.** Knees swollen more recently.
- Pain 8-9/10, with naproxen 5-6/10.
- In college, going to the gym regularly. **+Fatigued.**
- **AM stiffness lasts 4 hours.**
- Can't walk up stairs easily.
- No rashes, no fevers, no weight loss, no alopecia.
- Saw PCP (after a year), ESR 11→25, CRP 11.7 mg/L, RF positive (x2), ANA neg, TSH normal, vit D low (17 ng/mL).
- Tearful in office – **swollen joints = 34, tender joints = 36**

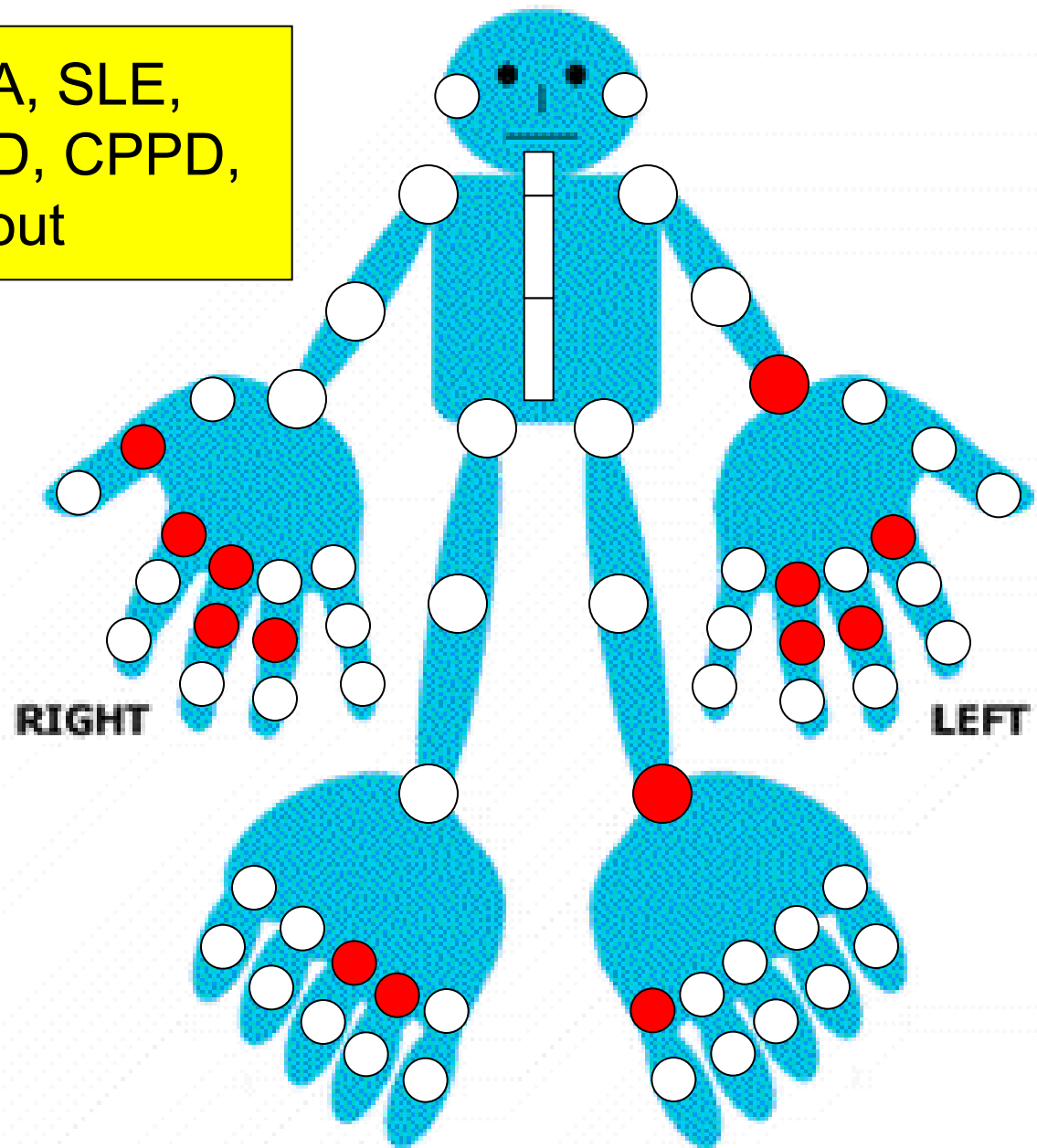
MEDS: naproxen, vitamin D.

LABS: ESR 70, CRP 65 mg/L, **RF 565, CCP 261**, ANA 1:40.

Osteoarthritis



RA, PsA, SLE,
other CTD, CPPD,
Gout



Historical Clues

- Duration - when did it start?
- Location - which joints? (if joints at all...)
- Character - pain, swelling, stiffness?
- Onset - acute or insidious?
- Timing - AM? eve? night? w/rest or activity?
- Treatment - what have you tried?
- Other - symptoms of systemic disease?
- Fam Hx - Gout, OA, RA, psoriasis or PsA.

Duration of Polyarticular Complaints

Acute (days)

→ Typically inflammatory

- Infectious
 - Viral
 - Bacterial (usu. monoarth)
 - Early Lyme disease
- Crystal-induced
 - Often have est. diagnosis of Gout or CPPD
- Reactive arthritis
- *Early chronic cause*

Chronic (wks to yrs)

→ Is it inflammatory or not?

- Rheumatoid
- Psoriatic
- Crystal (think of CPPD > gout)
- Connective tissue dz
- Vasculitis
- Myositis
- Adult Still's disease
- Osteoarthritis
- Fibromyalgia

Inflammatory vs. Non-inflammatory Features of Joint Pain

	Inflammatory	Non-inflammatory
Pain	++ / +++	+ / ++
Stiffness	++ / +++	+ / ++
Swelling	+++	+ / -
Nighttime Pain	++	+ / -
Morning stiffness	> 60 min	< 30 min

Useful questions to ask

Morning Stiffness: How long until you feel the best you are going to feel for the day?

- “Stiffness” has various meanings for patients.

Activity Limitations / Disruptions:

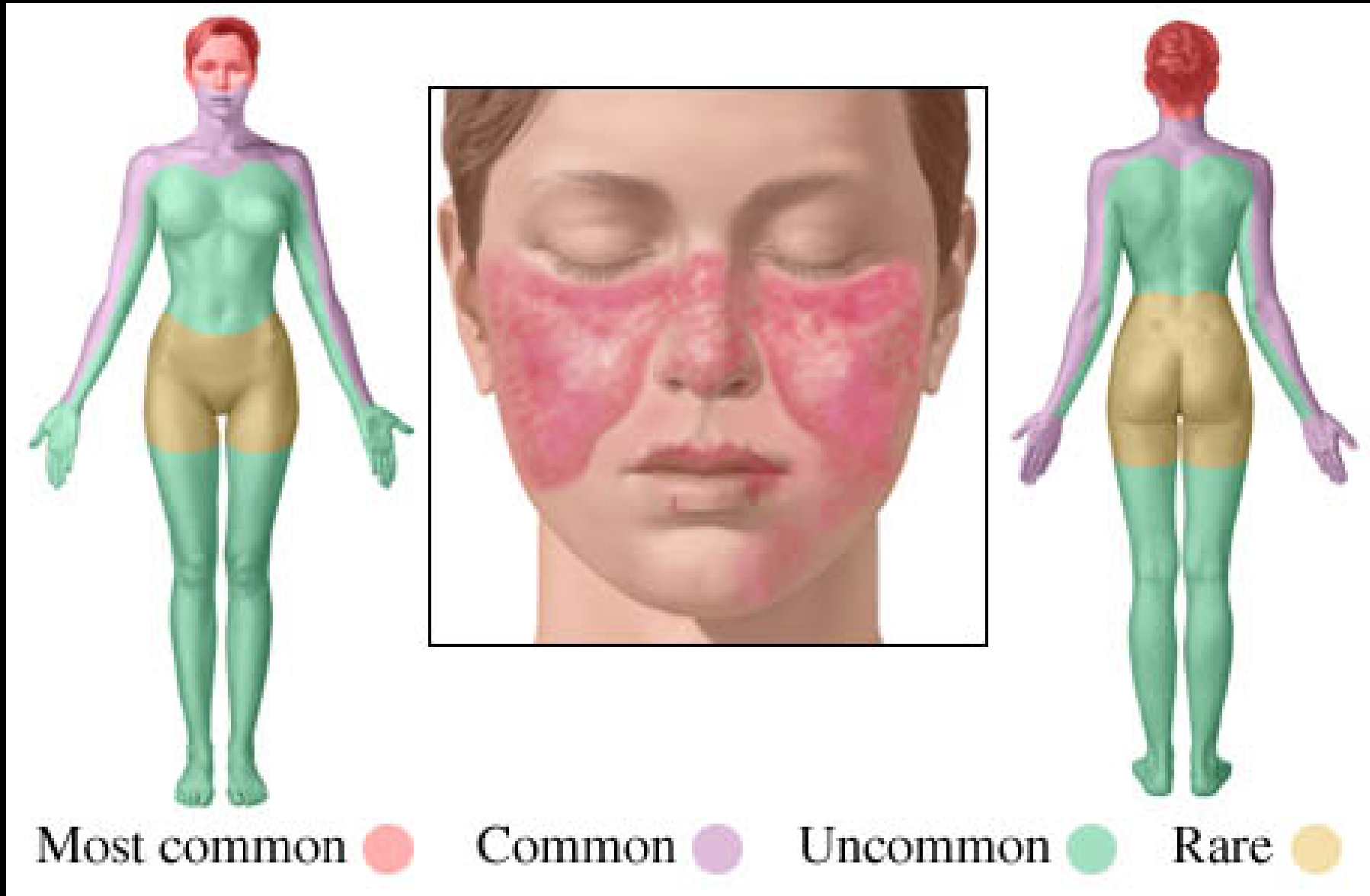
- Do you have difficulty with ADLs? (offer examples)
- Any pleasurable activities you can no longer do?
- How well do you sleep? Does pain wake you?

Physical Exam

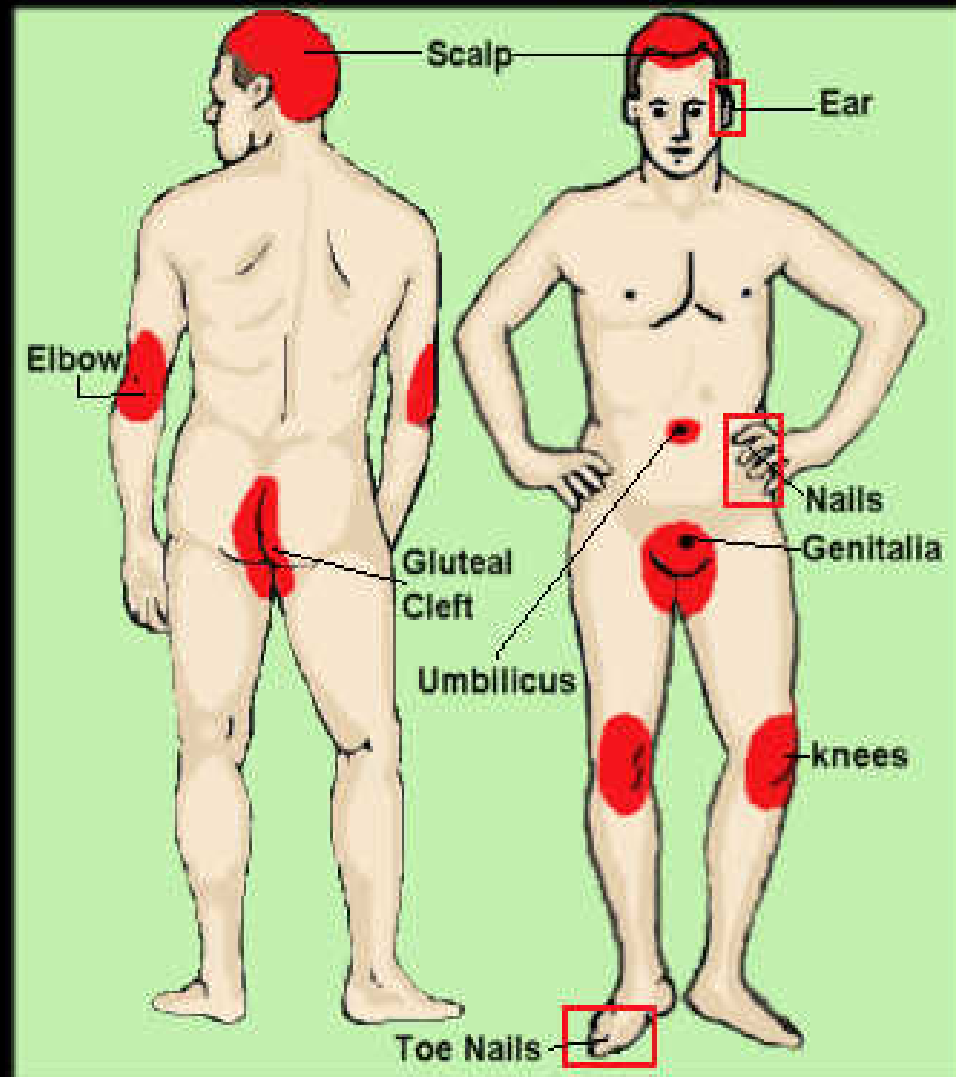
Look for signs of CTD, psoriasis, vasculitis:

- **Skin rash**
 - Sun exposed (SLE, Dermatomyositis, other CTD)
 - Extensor surfaces, umbilicus, gluteal cleft , scalp (Psoriasis)
 - Palpable purpura (Vasculitis)
- **Skin thickening or morphea** (Systemic sclerosis)
- **Hair loss** – thinning, patchy alopecia (SLE)
- **Nails** – pitting/onycholysis (Psoriasis), abnormal nailfold capillaries (CTD)
- **HEENT**
 - dry eye and dry mouth (Sjogren's)
 - oral ulcers/lesions (SLE, Behçet's)
 - ocular inflammation (Spondyloarthritis, RA, Behçet's)
 - abnormal temporal arteries (GCA/PMR)
 - nasal crusts or blood; nose or ear cartilage inflammation (ANCA vasculitis, Relapsing polychondritis)

Photodistribution of SLE Rashes



Distribution of Psoriasis



Palpable purpura



DIP-limited Psoriatic Arthritis



Physical Exam

Joint exam – synovitis (soft tissue swelling +/- effusion) is the hallmark of inflammatory arthritis:

Inspection, Palpation, ROM, Strength, DTRs.

- Erythema, warmth, tender, effusion – EASIER to detect
- Soft tissue swelling (may be subtle) – HARDER to detect
- Neuro exam goes along with MSK exam.
- If only one or a few joints hurt, examine every joint.

		Articular (Joint) Disease			Periarticular/Soft Tissue	
Joint Exam Elements		OA	Inflammatory	Arthralgia	Bursitis or Tendinitis	Myofascial
Inspection	Swelling	varies	yes	no	yes	no
	Erythema	no	varies	no	yes	no
Palpation	Warmth	no	yes	no	yes	no
	Tenderness	along joint line	varies	varies	peri-articular	yes
Movement	ROM	limited	limited	full or limited	full, pain often limits	full
	Pain w/active or passive	both	both	usually both	active > passive	usually both

Some Non-inflammatory / Non-arthritic causes of musculoskeletal pain

Thyroid disease

Fibromyalgia syndrome

Medications (temporally associated with use)

- Cholesterol-lowering agents; SERMs & aromatase inhibitors; anti-thyroid drugs (methimazole, PTU)

Primary sleep disorders

- Obstructive sleep apnea
- Restless legs syndrome

Joint hypermobility / hyperextensibility

- Ehlers-Danlos syndrome

Malignancy

Laboratory Testing

Diagnostically Helpful:

Creatinine and liver enzymes – assess for renal and hepatic dysfunction as signs of systemic illness; baseline for therapy.

CBC – anemia due to chronic inflammation, cytopenias in SLE/CTD, heme malignancy(rare).

Urinalysis – Renal disease is often asymptomatic in SLE and vasculitis.

ESR and CRP – non-specific, often helpful, but often normal in patients with active inflammatory disease. NOTE: a 'high normal' CRP of 7-8 mg/L may be elevated for a given patient.

Laboratory Testing

Not usually helpful diagnostically:

Uric Acid – this is not a diagnostic test for gouty arthritis. Hyperuricemia is a risk factor for gout, so when gout is a possible cause of joint pain it is appropriate to assess the level (i.e., typically NOT in a 30yo woman!).

Lyme serology – only helpful if early Lyme disease is suspected to be the cause of *polyarthralgia*. **Lyme arthritis** is NOT polyarticular – it is a late manifestation of infection with *B. burgdorferi* presenting with inflammatory monoarticular (or oligoarticular) joint disease.

Serological Testing

Serologies support the clinical impression – they are not diagnostic as isolated positive test results.

Anti-CCP Ab (CCP = cyclic citrullinated peptide)

- Highly specific for RA (low titers seen in other dz), a/w extra-articular manifestations and high risk for joint damage.

Rheumatoid factor (RF)

- A reliable marker of RA only in a patient with polyarticular synovitis, otherwise it is non-specific.

Anti-nuclear antibody (ANA)

- Not specific for SLE – positive in other CTDs, RA, autoimmune liver and thyroid disease, healthy individuals.

Additional Testing

HLA-B27 – only helpful if suspecting axial spondyloarthritis, which is not typically polyarticular (usually inflammatory back pain +/- mono- or oligoarticular peripheral arthritis).

Calcium axis evaluation – if CPPD arthropathy confirmed or suspected, assess Ca, Mg, Phos, PTH and 25-OHD. Additional studies to assess for hemochromatosis may also be appropriate if otherwise suspected clinically.

Serum Ferritin – if considering Adult Onset Still's Disease or CPPD arthropathy related to hemochromatosis.

Rules for Polyarthrititis Lab Testing

Salt and Pepper
Peanut Butter and Jelly

Rheumatoid factor and Anti-CCP antibody
ESR and CRP

Case 2 – Not So Crystal Clear

65yM w/ CAD s/p stenting 4 years ago p/w bilateral shoulder pain and stiffness and bilateral knee pain and swelling x3 weeks.

- Feels his symptoms are muscle and joint related.
- Cramping sensation behind both knees.
- Difficulty getting up from low seats (e.g., toilet).
- Nocturnal pain, hard to sleep, AM stiffness lasts hours.
- Advil 400mg 5x/day and Aleve 440mg BID only slight relief.
- Stopped rosuvastatin for 3 days, no improvement in symptoms.
- Avid golfer, no tick bites but worried about Lyme.
- No FH of arthritis or autoimmune disease.

ROS: No rash, headache, eye/vision symptoms, jaw claudication, fever, chills, sweats, unexplained weight loss.

Case 2 (continued)

MEDS: ASA, lisinopril, rosuvastatin, metoprolol, clopidogrel.

EXAM: Looks well, discomfort when moving (shoulders and knees). No ocular inflammation. No lymphadenopathy. Lungs clear. Heart regular, no murmur. No peripheral edema. No rash. No neuro deficits, but strength exam limited by pain. **Unable to abduct right shoulder beyond 90 degrees**, pain on the left with better ROM. **Bilateral knee effusions L > R**, with warmth, tenderness and pain upon flexion. Hip ROM is stiff with only mild discomfort. No abnormalities of hands, wrists, ankles or feet.

LABS: Mild anemia, CMP normal. **ESR 54, CRP 91 mg/L**, ANA negative, **RF negative, anti-CCP negative**, uric acid 5.4 mg/dL, CPK 35, parvovirus negative, Lyme negative.

Case 2 (continued)

IMAGING: None obtained.

PROCEDURE: Bilateral knee arthrocentesis

- 10mL from L knee and 35mL from R knee, yellow fluid with moderate turbidity. Both joints injected with depomedrol.
- **Fluid WBC counts: L knee = 4084, R knee = 2729.**
- Crystal analysis: L knee = no crystals, R knee = +CPPD crystals inside WBCs.

DDx: Polymyalgia rheumatica (no sx of temporal arteritis)

Rheumatoid arthritis, seronegative

Polyarticular CPPD arthropathy (“pseudogout”)

Other inflammatory arthritis

Rx: Prednisone 15mg daily (cures all ills ... at least initially!)

Radiographs (usually normal at first)

RA = soft tissue swelling, **periarticular osteopenia**, joint space narrowing, **marginal erosions**.

OA = **osteophytes**, narrowing, central erosion, **subchondral sclerosis** and **subchondral cysts**.

Gout = calcified tophi, **overhanging edges** (“rat bite” erosions).

CPPD = chondrocalcinosis (wrist, knee, hips/pelvis).

PsA = **periostitis**, erosion, narrowing, fusion, **pencil-in-cup deformity**.

SLE = **non-erosive**, reducible ulnar deviation.

SSc = calcinosis (in soft tissue), distal tuft resorption.

Osteoarthritis

Epidemiology

- Rare <35yo, incidence and prevalence increase with age (>80% of population >55yo in some form).
- Numerous risk factors, both environmental and genetic.

Diagnostic considerations

- Joints most affected: hand IP joints, feet, knees, hips, spine.
- Distinguishing between Inflammatory vs. Non-inflammatory OA may affect therapy.
- May be associated with CPPD crystal deposition (with evident chondrocalcinosis on radiographs).
- Typical radiographic changes develop over years.

Osteoarthritis (and osteopenia)



Erosive osteoarthritis



CPPD Arthropathy



Rheumatoid Arthritis

Epidemiology

- 1% of Caucasian population, up to 5% of women >65yo.
- Women affected 2-3x > Men.
- Occurs at any age, peak incidence 50-75yo.
- Genetics and smoking identified as risk factors.

Diagnostic considerations

- Constitutional symptoms: fatigue, weight loss, occ. fever.
- Numerous extra-articular organs can be involved (40% of pts over lifetime): skin, bone, muscle, eye, heart, lung, CNS, PNS.
- Recent guidelines devised to promote EARLY diagnosis.
- Radiographs normal in early disease, and we like to keep them that way!
- RA and fibromyalgia are often co-morbid, sometimes leading to diagnostic confusion or a delay in the diagnosis of seronegative RA.

Normal
hand



Rheumatoid
arthritis

Bone
erosion

Bone
displacement



Rheumatoid arthritis (early)



Case 3 – A Cautionary Tale

68yoM with alcohol use disorder (sober 2 years), h/o Lyme arthritis (knee), polyarticular synovitis with effusions and bursitis.

Labs:

ESR 54 mm/hr
CRP 68.9 mg/L
HCT 34.5 %
Plts 633,000
RF 537
Anti-CCP 237



This is NOT
Lyme arthritis!!!



2/2010



9/2014



2/2010



9/2014



Psoriatic Arthritis

Epidemiology

- Male:Female equally affected
- Age of onset 30s and 40s
- Psoriasis - up to 30% have arthritis
 - 20-40% involves spine or SI joints
 - Arthritis may precede skin disease

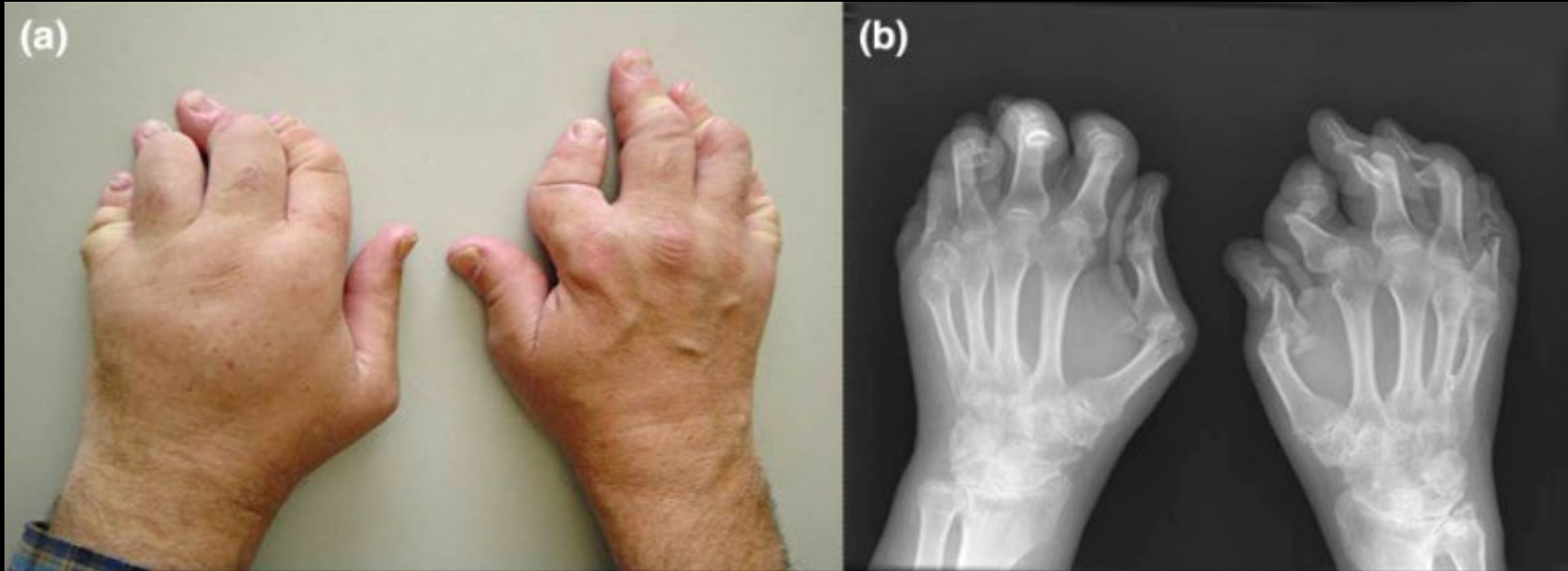


Extra-articular Features

- Psoriatic skin lesions - typically thick scale on erythematous base, but some variability
- Fingernails: pitting, onycholysis, transverse depressions
- Eye inflammation (30%) - conjunctivitis, iritis
- Dactylitis, tendinitis

5 subtypes: Spondyloarthritis, Mono/oligoarthritis, Polyarthritis, DIP-limited arthritis, Arthritis mutilans.

Psoriatic Arthritis, Mutilans type



Dactylitis
“sausage digits”



Psoriatic arthritis AND Osteoarthritis



SLE Arthropathy

- Joint pain and fatigue are the most common presenting symptoms of SLE.
- Up to 95% of SLE patients have arthritis.
- Symmetrical, polyarticular usu. involves knees, wrists, PIP joints.
- Non-erosive, migratory, may resolve in a given joint in <24h.
- Lax joint capsules, tendons, ligaments = reducible deformity.
- Often pain >> physical findings.

Lupus arthropathy





Diffuse osteopenia. Joint space loss in wrists. Ulnar deviation. Thumb IP joints subluxed. NO joint erosions.

Case

75yF with recent onset of headache, proximal MSK aching (neck/shoulders > hips), decline in vision and elevated inflammatory markers.

2mo proximal pains ("all her bones hurt"), assoc with:

- temporal headaches and scalp tenderness.
- decline in vision starting after 3 weeks of symptoms.
- appetite off, has lost ~15-20 lbs.
- Feels "numbness" along the left side of her face and jaw, as well as a feeling of swelling in this area and over the forehead.
- Notes from recent EW visit, "She describes her jaw pain as "an electric shock" which is worse with chewing."
- ESR 91 and CRP 126 mg/L. ANA, RF, anti-CCP negative.

ANY THOUGHTS ON A DIAGNOSIS?

Case (cont'd)

Started on prednisone 80mg daily (worrisome story).

- Temporal artery biopsy (performed 3 days later).
- Ophthalmology evaluation.

RESULTS:

- TA biopsy = negative for arteritis.
- Eye exam = cataracts.
- Feels much better on prednisone.
- Tapered dose to 20mg/day since TA biopsy negative.

Case (cont'd)

1 month later:

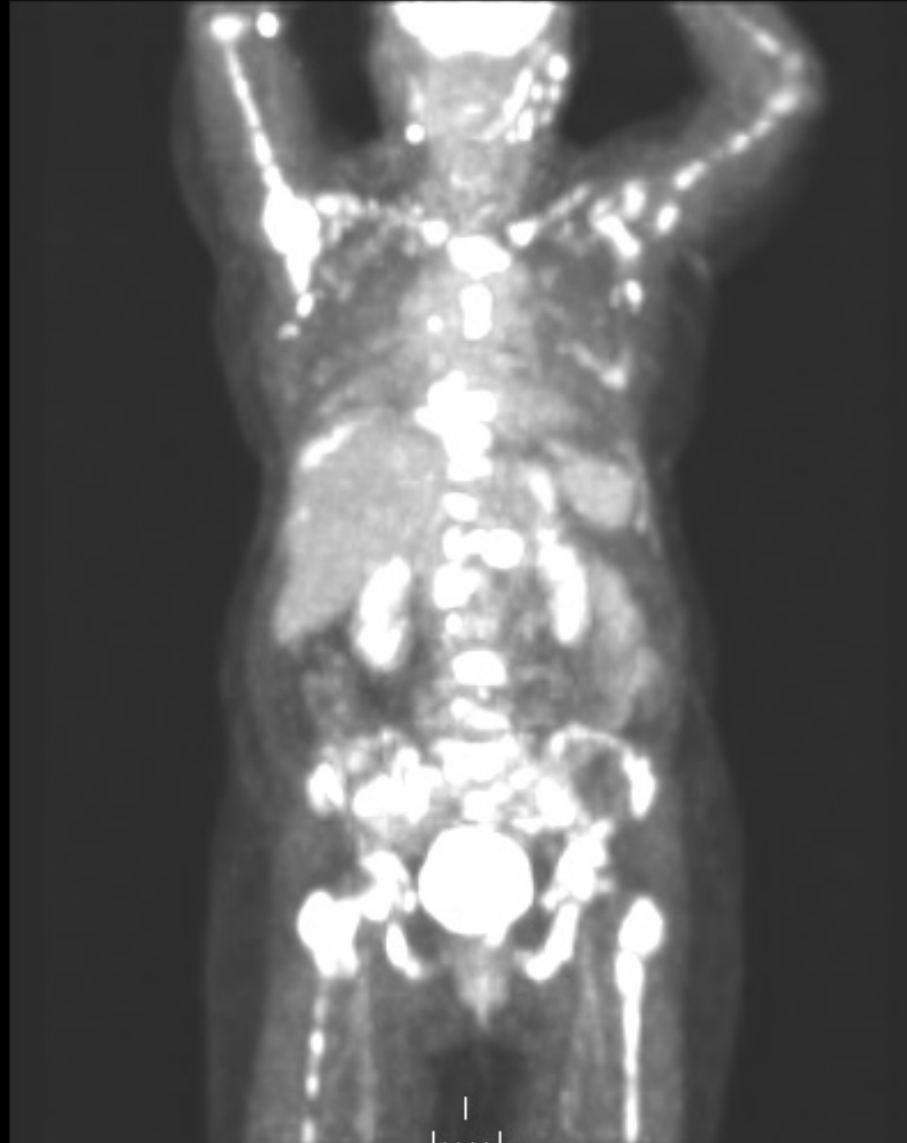
- Proximal aching has recurred on 20mg/day, just as severe.
- Vision stable, some headaches, not as bad.
- She reports increasing her prednisone to 80mg/day (on her own) to control symptoms, now at 40mg/day, a little better.
- ESR 83 and CRP 125 mg/L.

NOW WHAT?!?

- Advised to continue prednisone 40mg/day → ? Biopsy neg GCA
- Time to think...

Presents to EW the following week with temp 103, left sided neck swelling and pain. CT with 1.3cm hypodensity in the left neck with surrounding inflammation. ? Abscess, ? Lymph node.

Lymphoma,
not PMR/GCA



Key Points

1. History and physical examination are critical to identifying the etiology of joint complaints.
2. Distinguish inflammatory from non-inflammatory joint pain.
3. Non-articular symptoms suggest systemic inflammatory disease.
4. Inflammatory joint disease can cause rapid damage, so early diagnosis and treatment are critical.

Next Best Steps

- Focus on dissecting the history of patients with joint complaints to improve diagnostic acumen.
- Pursue rational testing (lab studies and imaging) in the evaluation of joint pain rather than a screening or “shotgun” approach.