Differential Diagnosis of Polyarthritis/Polyarthralgia

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Disclosures

None.

Polyarthritis – Outline

1. DDx: the broad array of choices
   - History narrows the field
   - Physical exam confirms suspicion.
   - Labs and x-rays = icing on the cake (and don't get tripped up!)
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 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 (incl. erosive)
Rheumatoid arthritis
Gout
CPPD arthropathy
Psoriatic arthritis
Ankylosing spondylitis
Reactive arthritis
Palindromic rheumatism
Undiff. 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

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. Embrace the challenge!

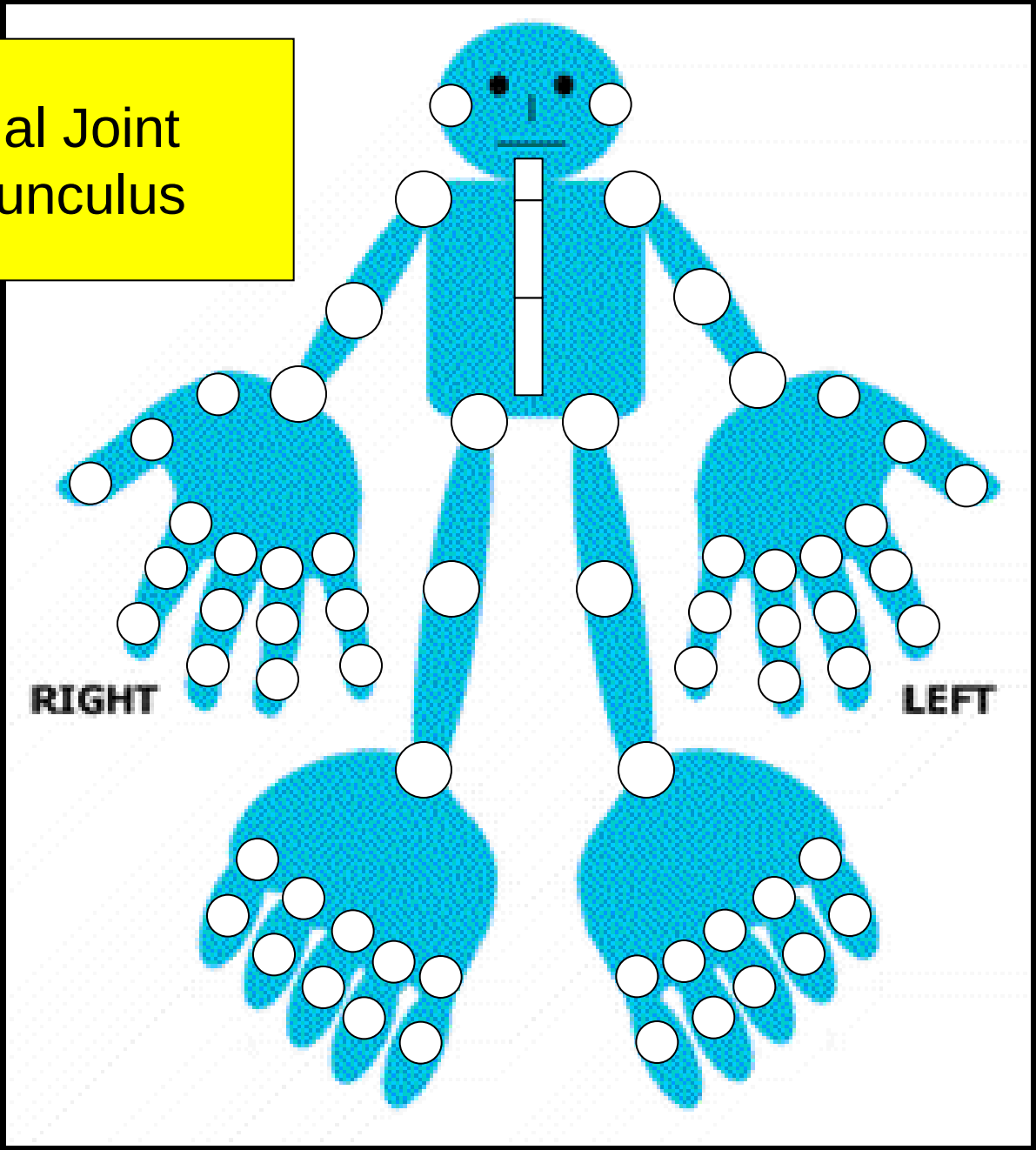
Diagnostic Evaluation of Joint Pain

1. A thorough HISTORY and EXAM are critical for differentiating causes of joint pain.
   - Is the pain really localized to joints, or is it more diffuse?
   - Laboratory studies and radiographs merely provide supportive diagnostic and prognostic information.

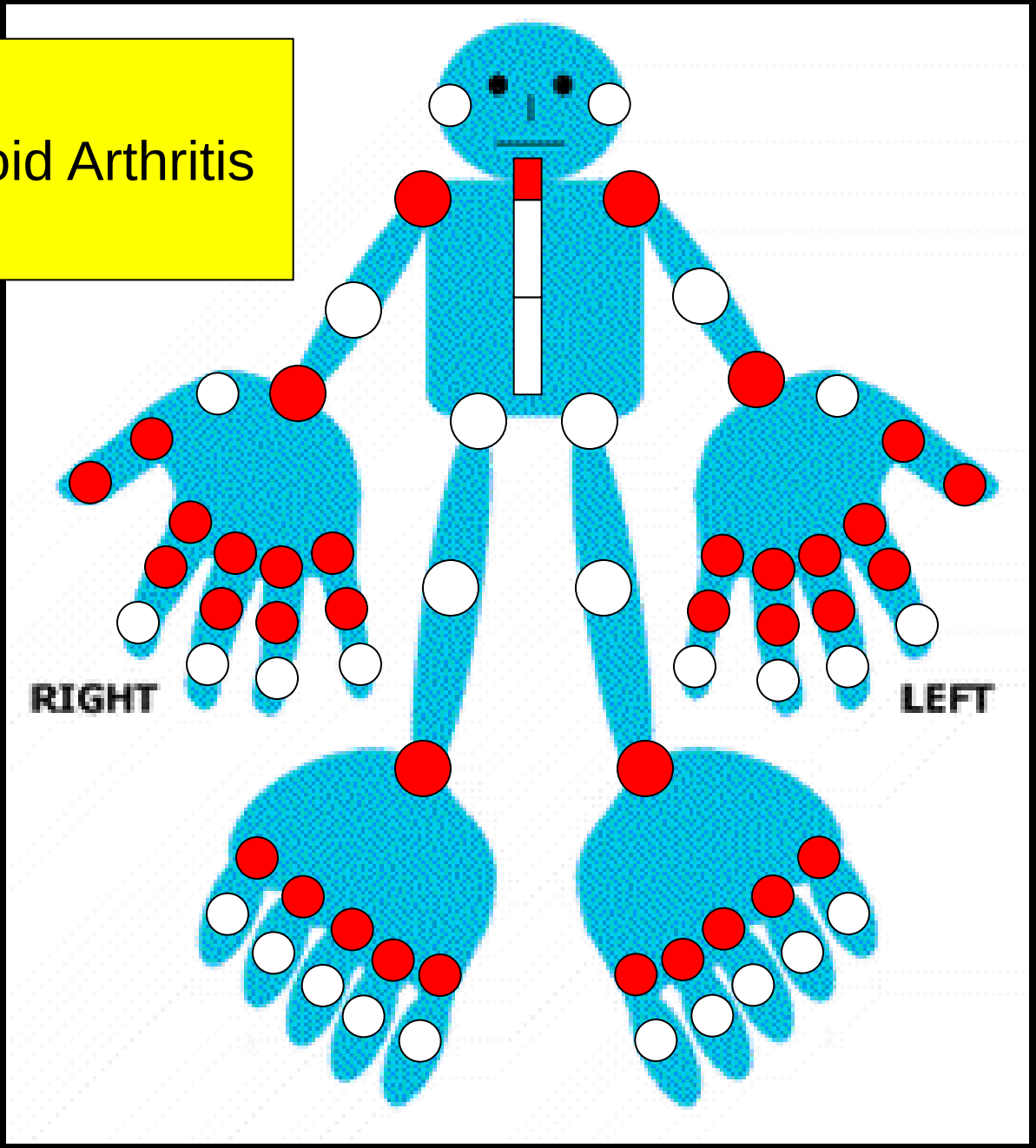
2. Joint pain is like a heart murmur.
   - Significance is determined by the company it keeps.

3. Read a joint exam like an EKG.
   - Pattern recognition may point you to the diagnosis.

Normal Joint Homunculus



Rheumatoid Arthritis



Case

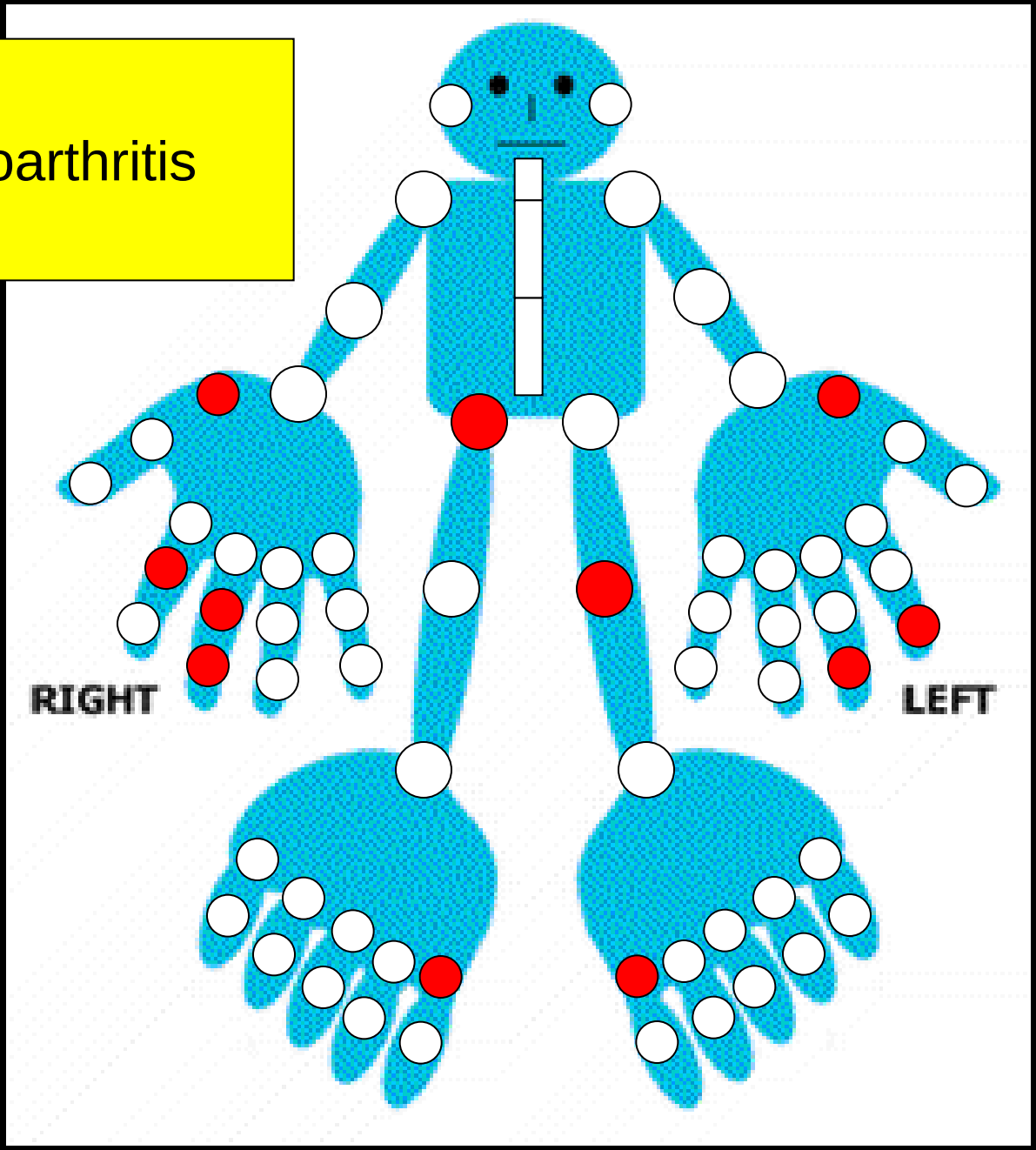
18yF w/ 1 year of joint pain, previously healthy.

- 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 (while on vacation).
- Mother notes gait is affected. 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.

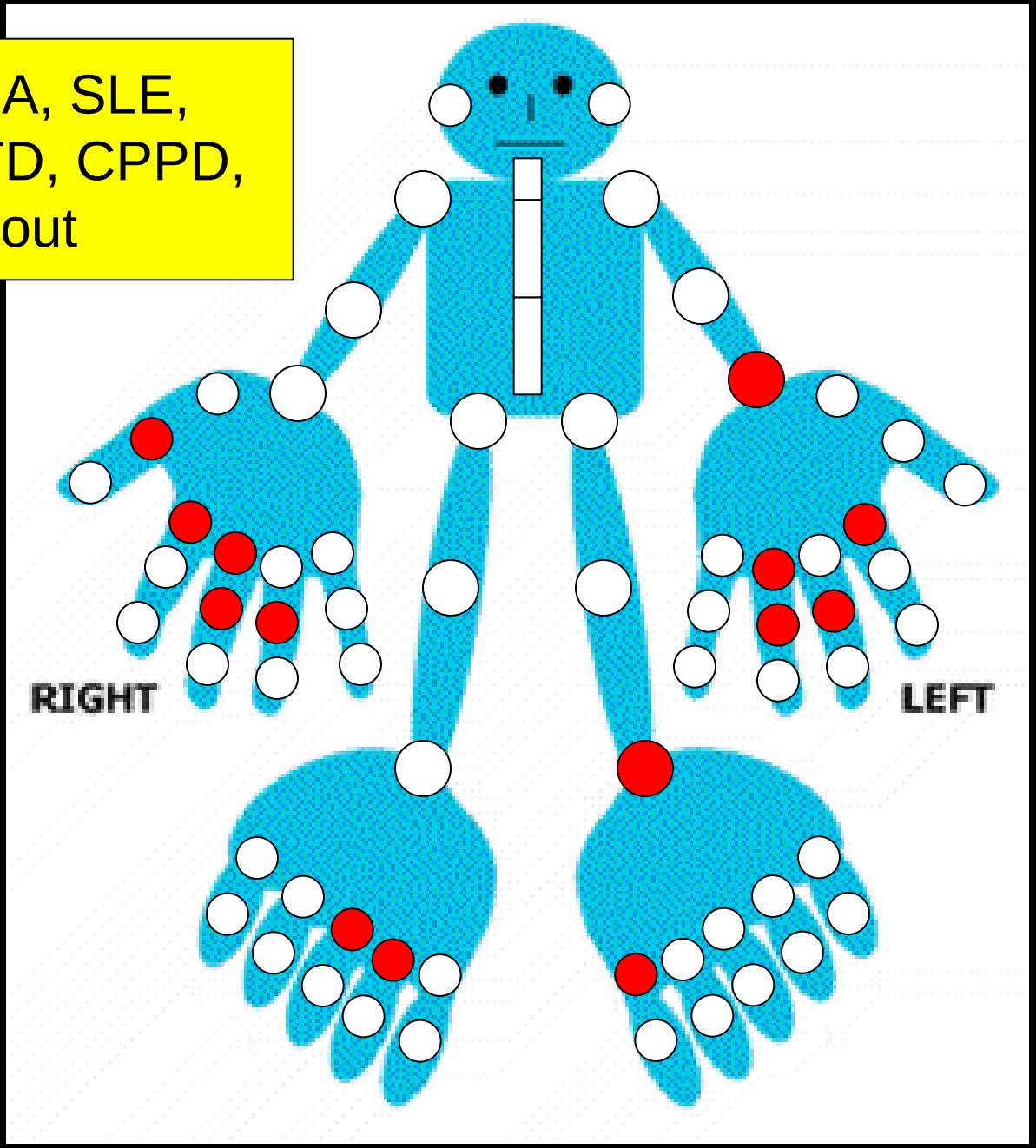
<u>MEDS</u>: naproxen, vitamin D.

<u>LABS</u>: 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? with rest or activity?

Treatment - what have you tried?

Other - symptoms of connective tissue disease?

Family History - Gout, OA, RA, psoriasis or PsA especially.

Duration of Polyarticular Complaints

Acute (days)

→ Typically inflammatory

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

Chronic (wks to yrs)

→ Is it inflammatory or not?

- Rheumatoid
- Psoriatic
- Crystal
- Connective tissue dz
- Vasculitis
- Myositis
- Adult Still's disease
- Osteoarthritis
- Fibromyalgia

Inflammatory vs. Non-inflammatory Features

	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:

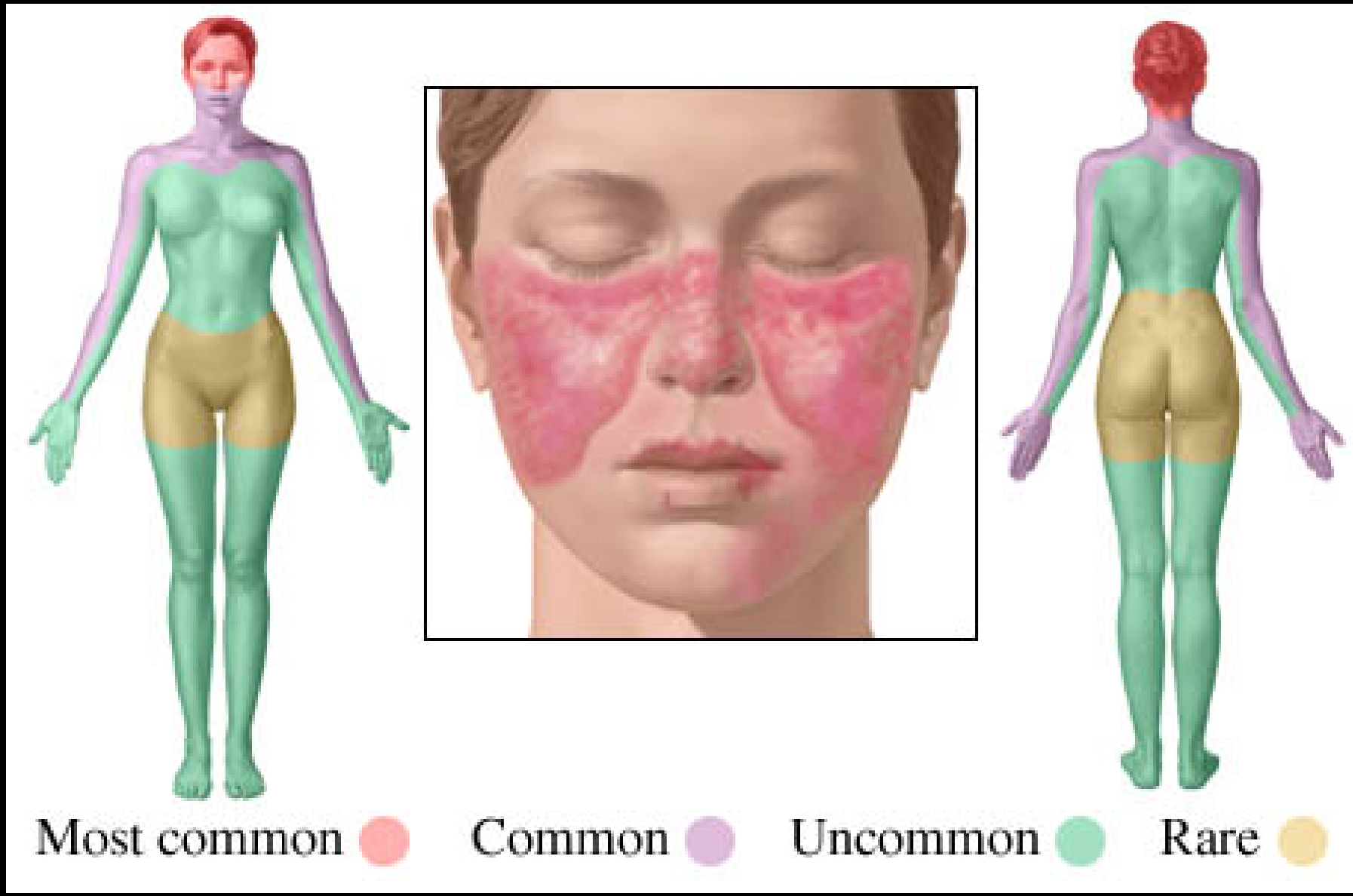
- Do you have difficulty with ADLs? (offer examples)
- What would you like to be doing that you can no longer do?
- How well do you sleep? Does pain wake you from sleep?

Physical Exam

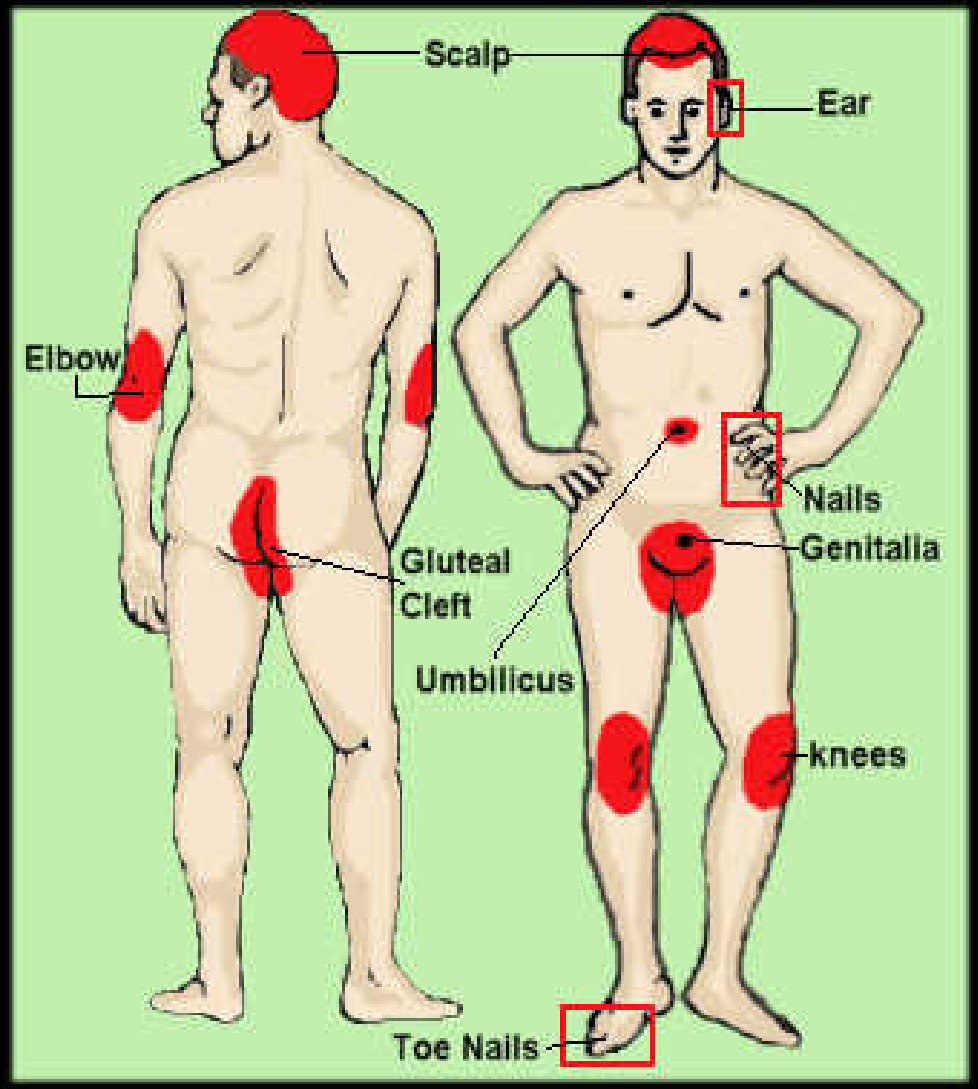
Look for signs of CTD, psoriasis, vasculitis:

- **Skin rash**
  - Sun exposed (SLE, Dermatomyositis, other CTD)
  - Extensor surfaces, umbilicus, gluteal cleft (Psoriasis)
  - Palpable purpura (Vasculitis)
- **Skin thickening or morphea** (Systemic sclerosis)
- **Hair loss** – thinning, patchy alopecia. (SLE)
- **Nails** – pitting, onycholysis, abnormal nailfold capillaries.
- **HEENT**
  - ocular inflammation, dry eye
  - oral ulcers/lesions, dry mouth (esp. salivary pooling)
  - abnormal temporal arteries
  - nasal crusts or blood; nose or ear cartilage inflammation

Photodistribution of SLE Rashes

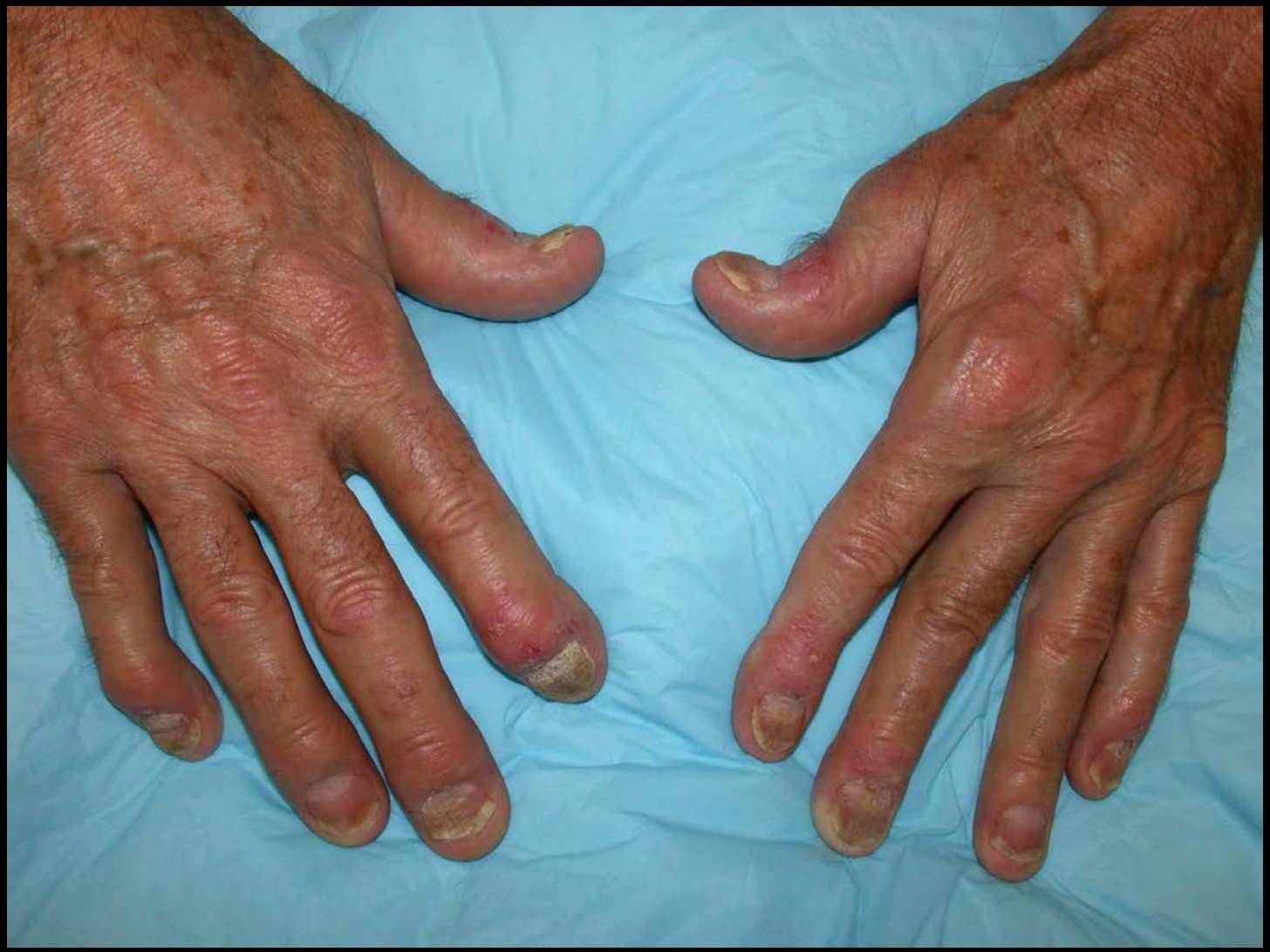


Distribution of Psoriasis



http://www.moondragon.org/health/disorders/psoriasis.html

DIP-limited Psoriatic Arthiritis



Physical Exam

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

- **Inspection, Palpation, ROM, Strength, DTRs.**
  - Erythema, warmth, tenderness, 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)
- 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 – if I was only allowed one test, this would be it. 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., 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 spondyloarthritis, which is not typically polyarticular (usually presents as 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.

Case

50yF w/ unremarkable medical history.

10/2013: Awakens w/ acute L shoulder pain, worsening → nausea and SOB. RN daughter → EW.

- ? MI → work up negative
- Shoulder x-ray = normal; C-spine x-ray = degen. disc disease
- Cervical radiculopathy suspected, Rx prednisone, taper down from 60mg daily → improved in ~3-5 days.

11/2013: Recurrent intense L shoulder pain → nv. Root injection, then pain in R shoulder. Symptoms alternate, L then R, then L, etc. MCP joints start hurting (trouble holding a pen), right groin, right wrist, left wrist. She noted swelling of MCP joints.

- Can have completely pain free days, estimates joint pain on 3-4 days per week. No AM stiffness.

→ Yesterday pain free. No swollen or tender joints on exam.

Case (continued)

Complete ROS: Negative. (nothing suggests CTD or vasculitis)

MEDS: Ibuprofen prn.

FH: Grandmother had arthritis in her feet.

HAND X-RAYS: Mild DJD of DIP and triscaphe joints in the wrist.

LABS (1/21/2014, asymptomatic):

- Renal and hepatic indices normal. TSH normal.
- CBC unremarkable.
- ESR 12
- CRP 2.2 mg/L
- ANA 1:160, with strongly +anti-Ro (denies dry eye/mouth)
- RF negative.
- Anti-CCP 258 (very high positive)

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

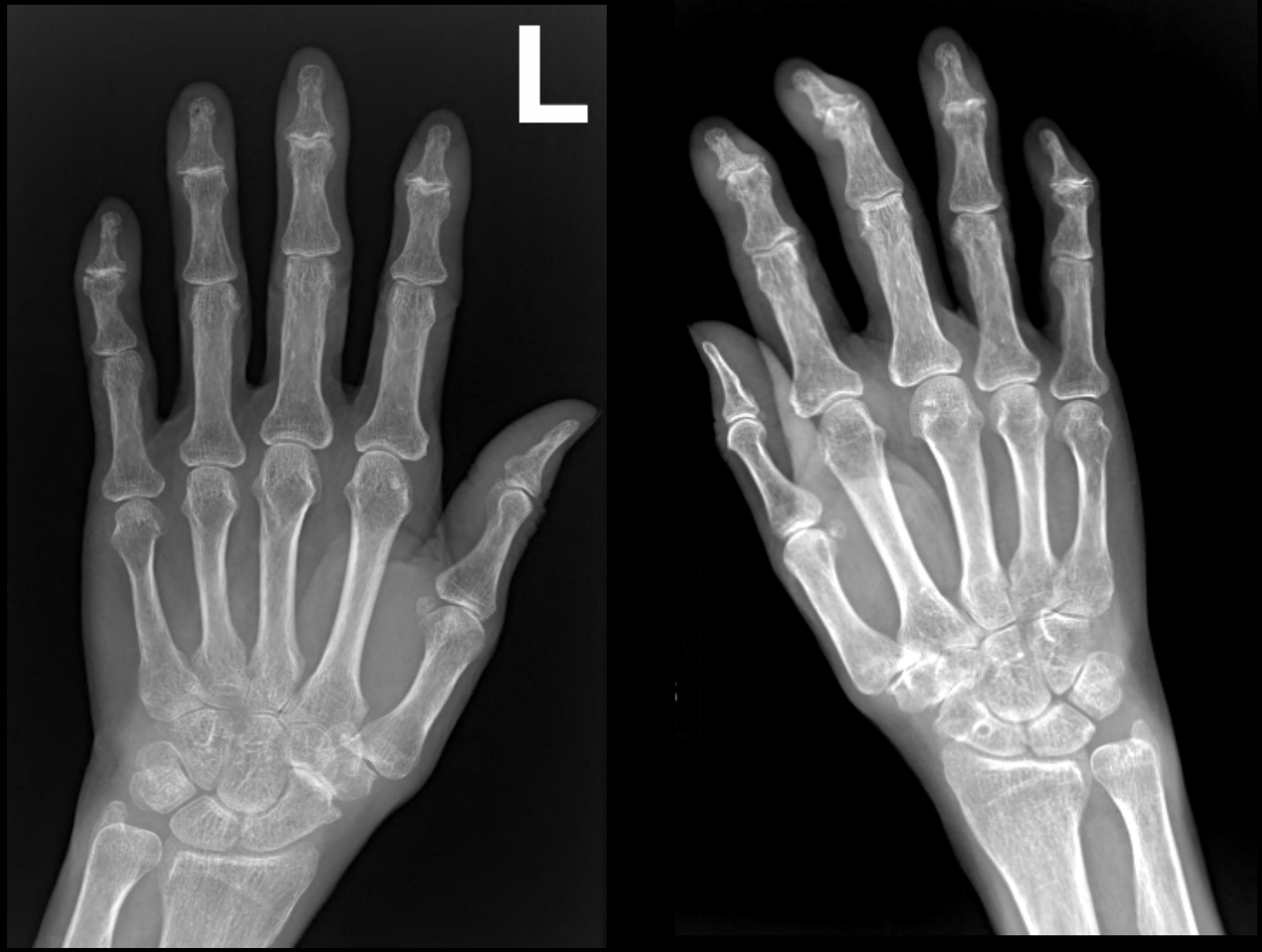
Epidemiology

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

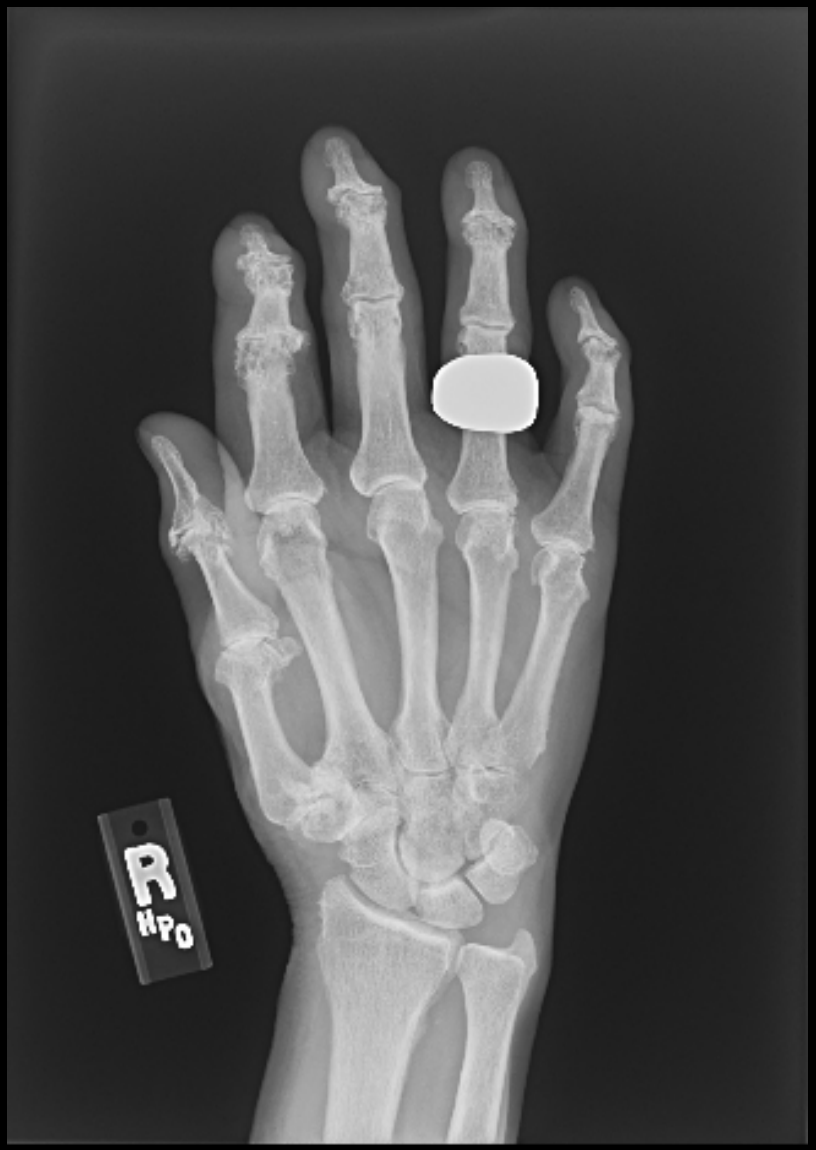
Diagnostic considerations

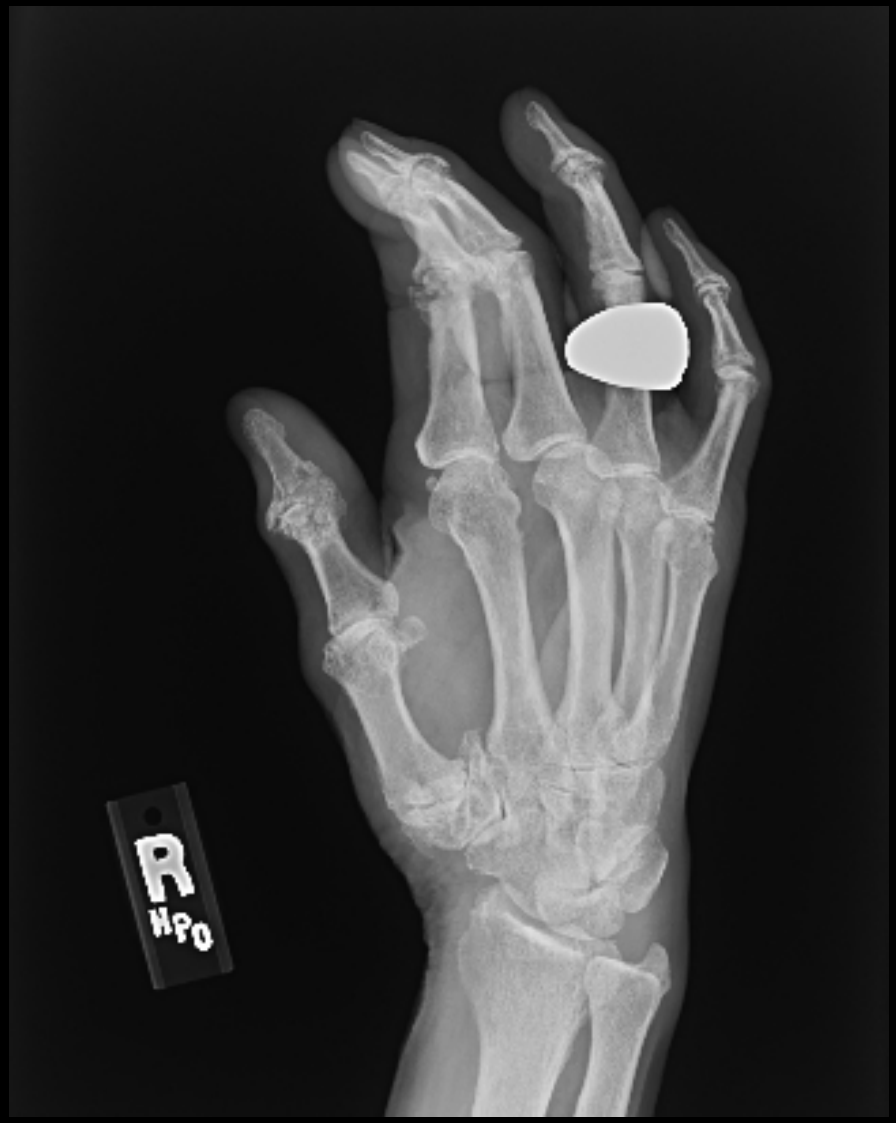
- Joints most affected: hands, feet, knees, hips, spine.
- Distinguishing between Inflammatory vs. Non-inflammatory OA may affect therapy.
- May be associated with CPPD crystal deposition (with evident chondrocalcinosis on radiographs).
- Typical radiographic changes develop over years.

Osteoarthritis (and osteopenia)

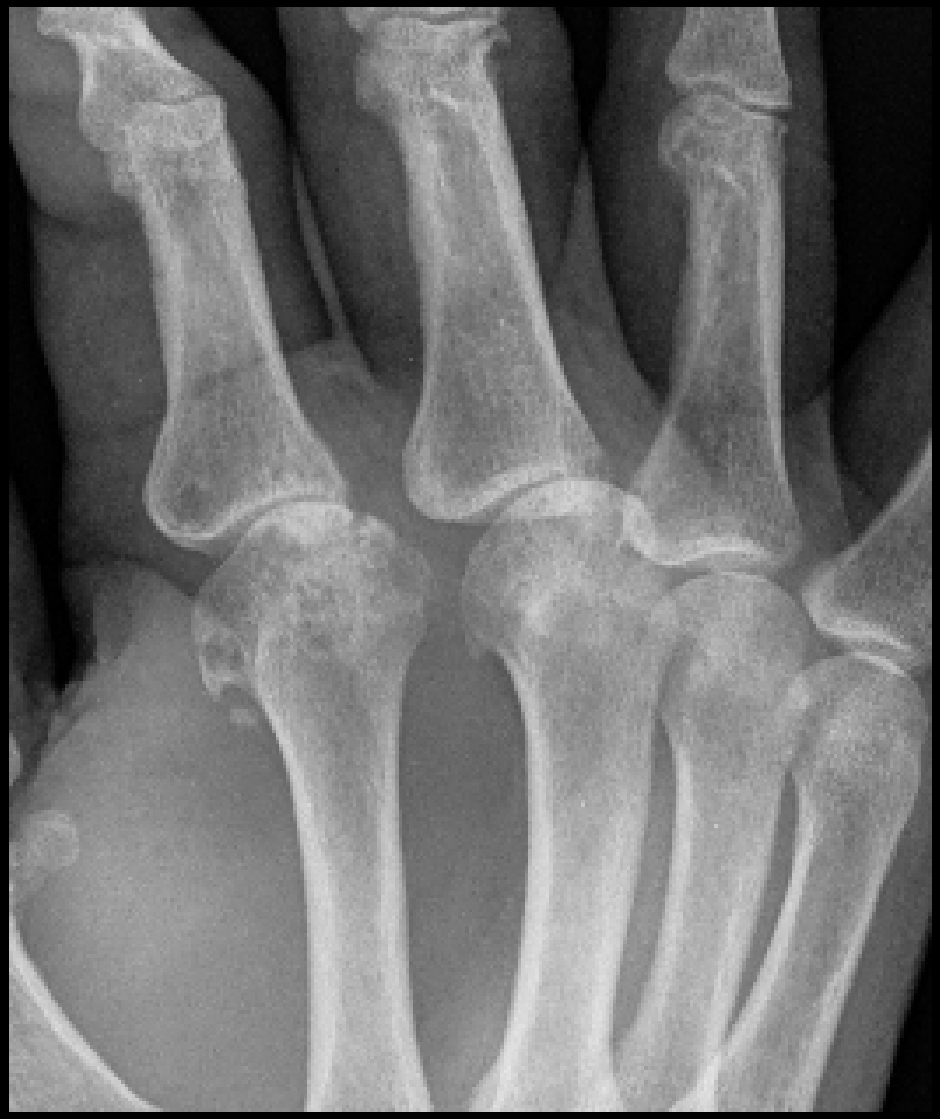


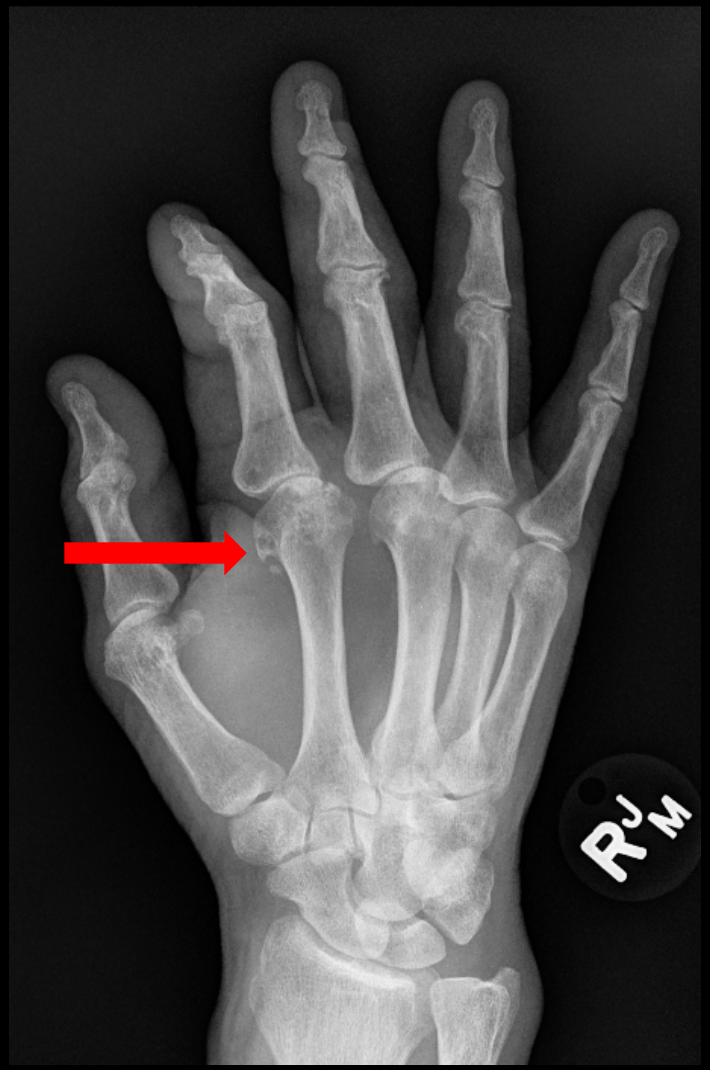
Erosive osteoarthritis





CPPD Arthropathy





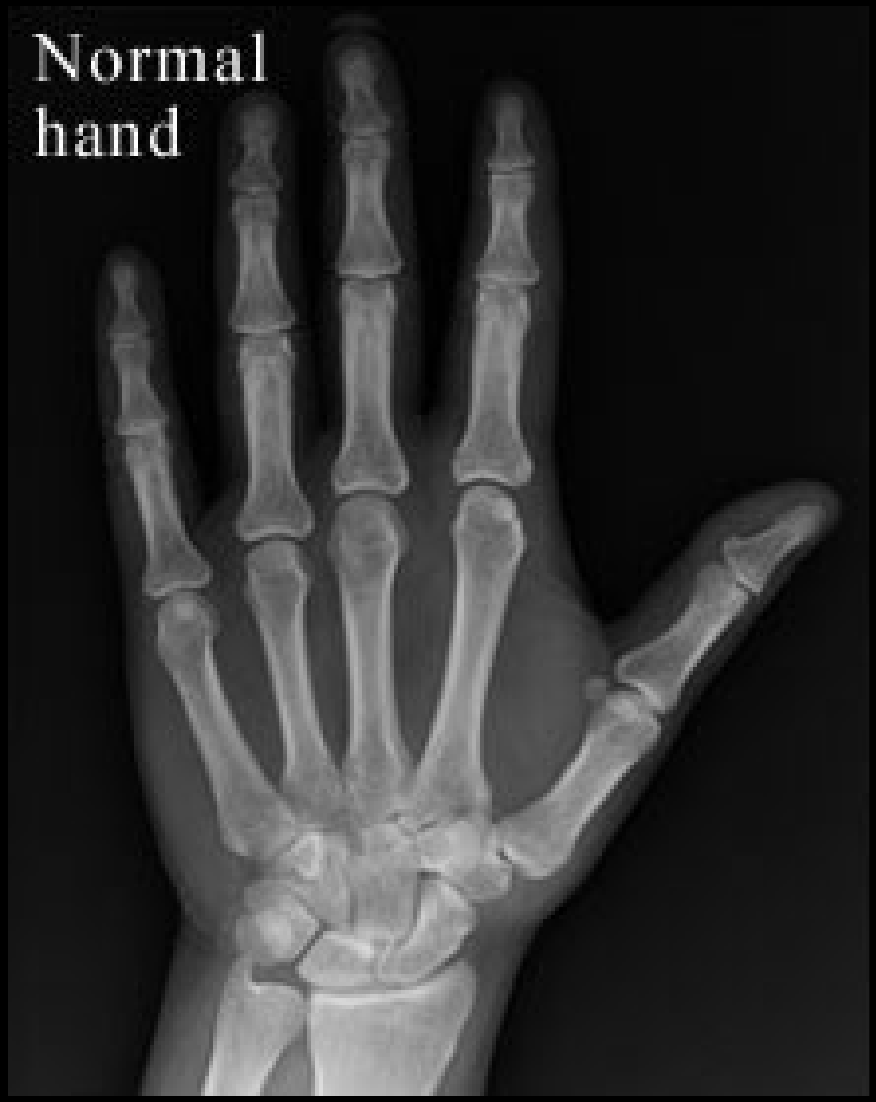
Rheumatoid Arthritis

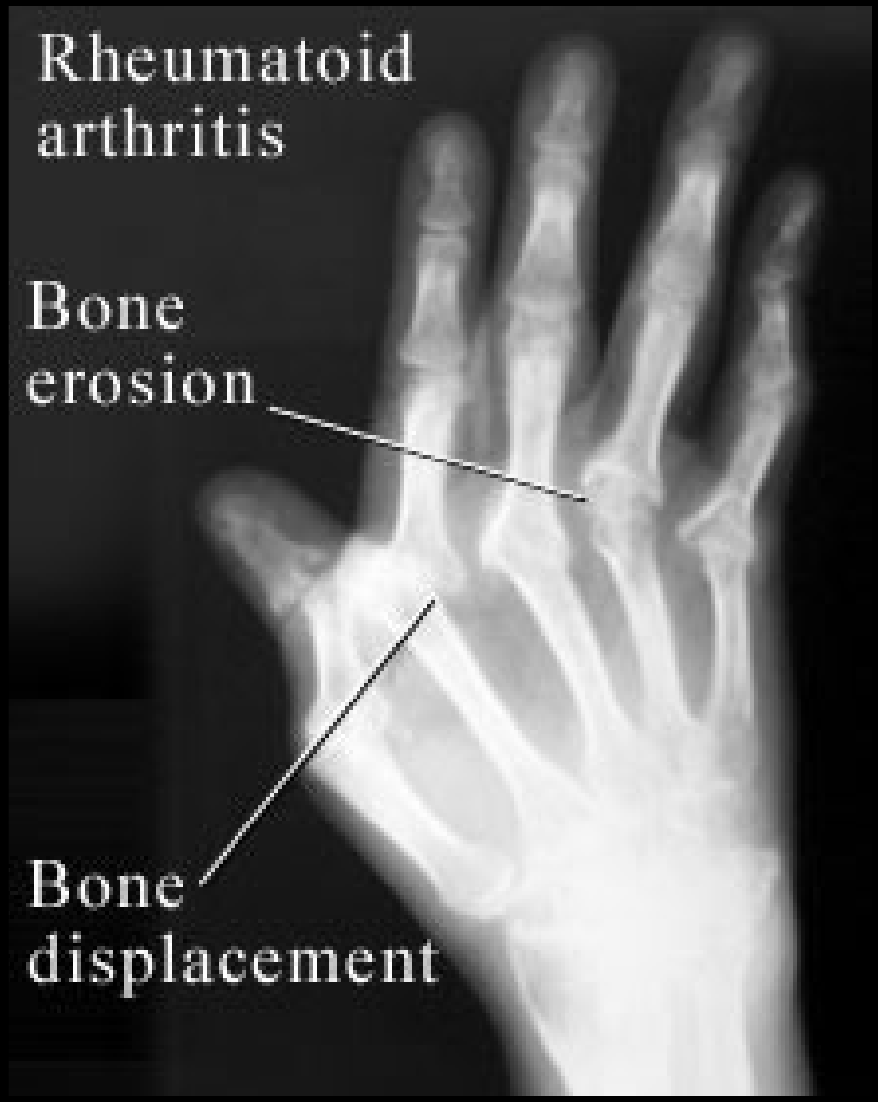
Epidemiology

- 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.

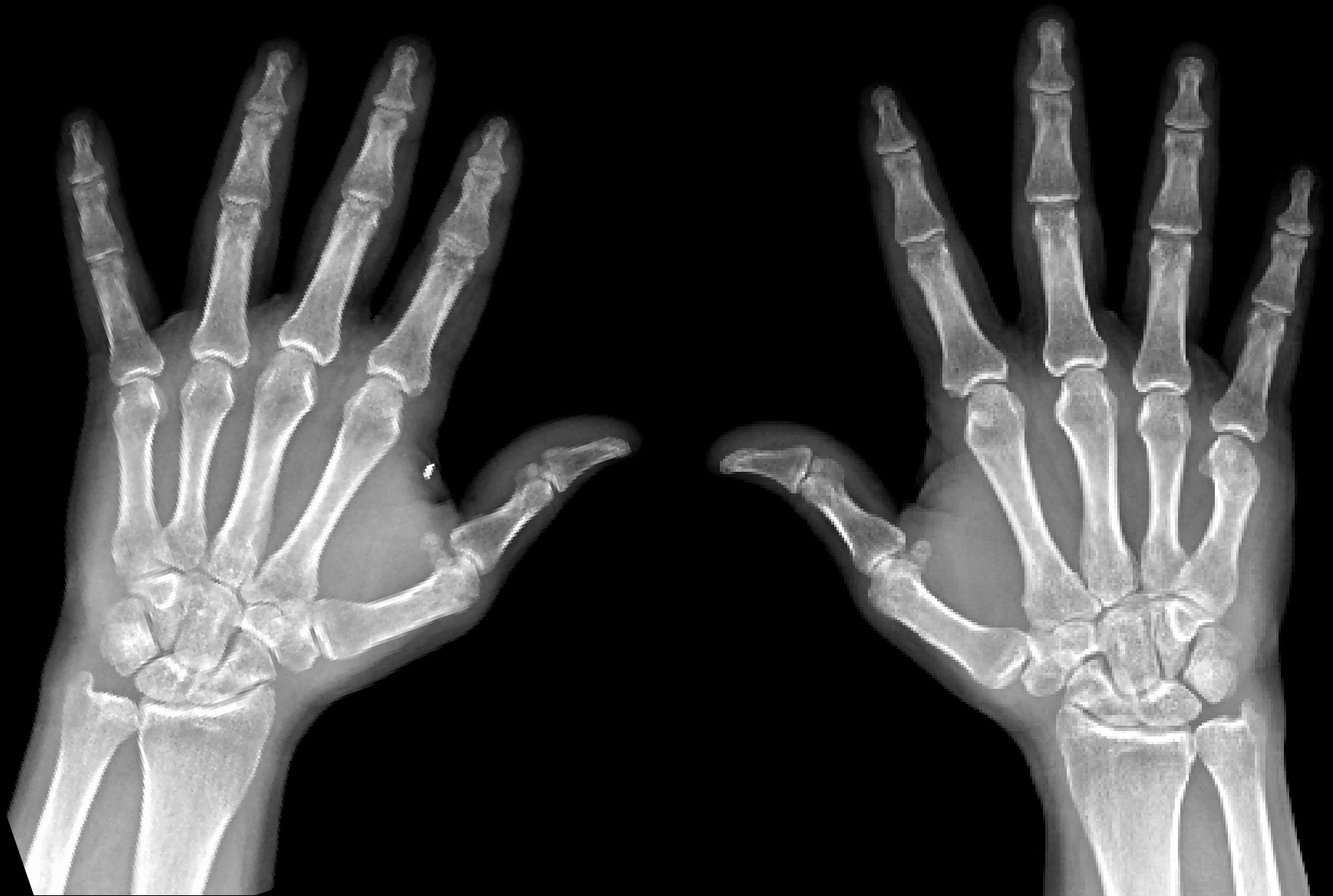
Diagnostic considerations

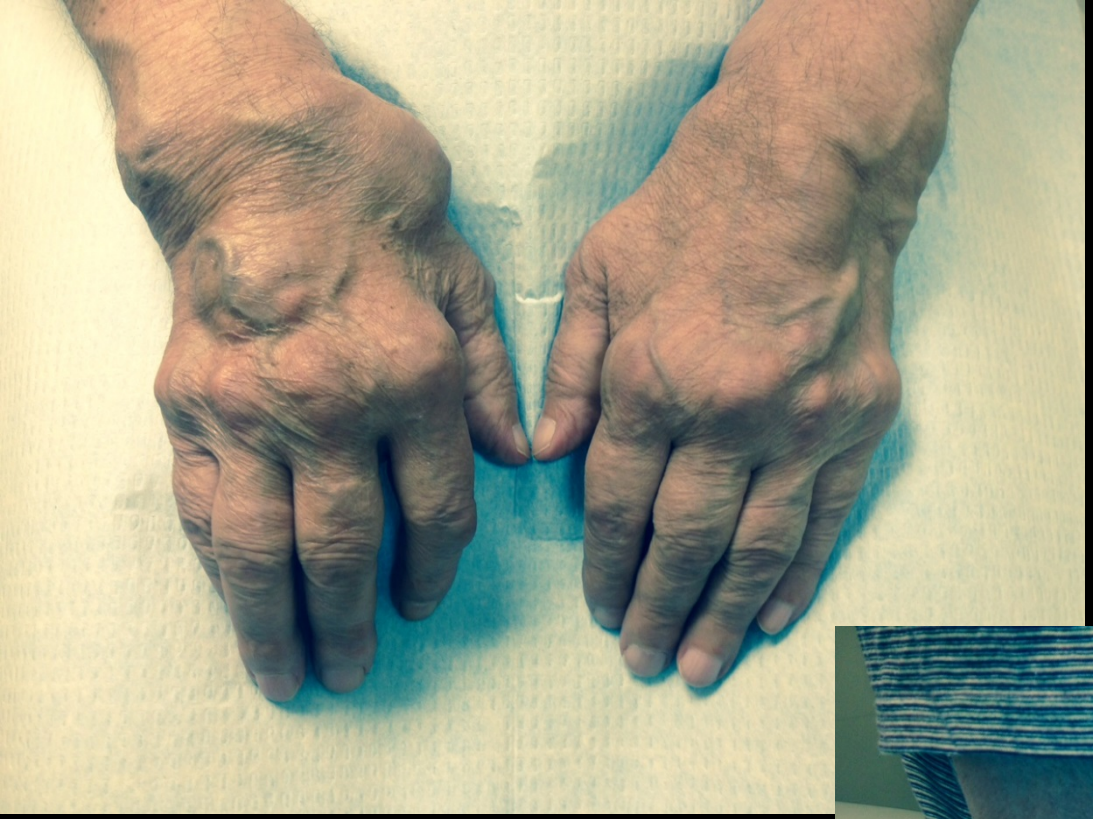
- Constitutional symptoms: fatigue, weight loss, occ. fever.
- Numerous extra-articular organs can be involved (40% of pts over lifetime): skin, bone, muscle, eye, heart, lung, CNS, PNS.
- Radiographs normal in early disease, and we like to keep them that way!
- RA and fibromyalgia are often co-morbid,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


Normal
hand


Rheumatoid
arthritis
Bone
erosion
Bone
displacement

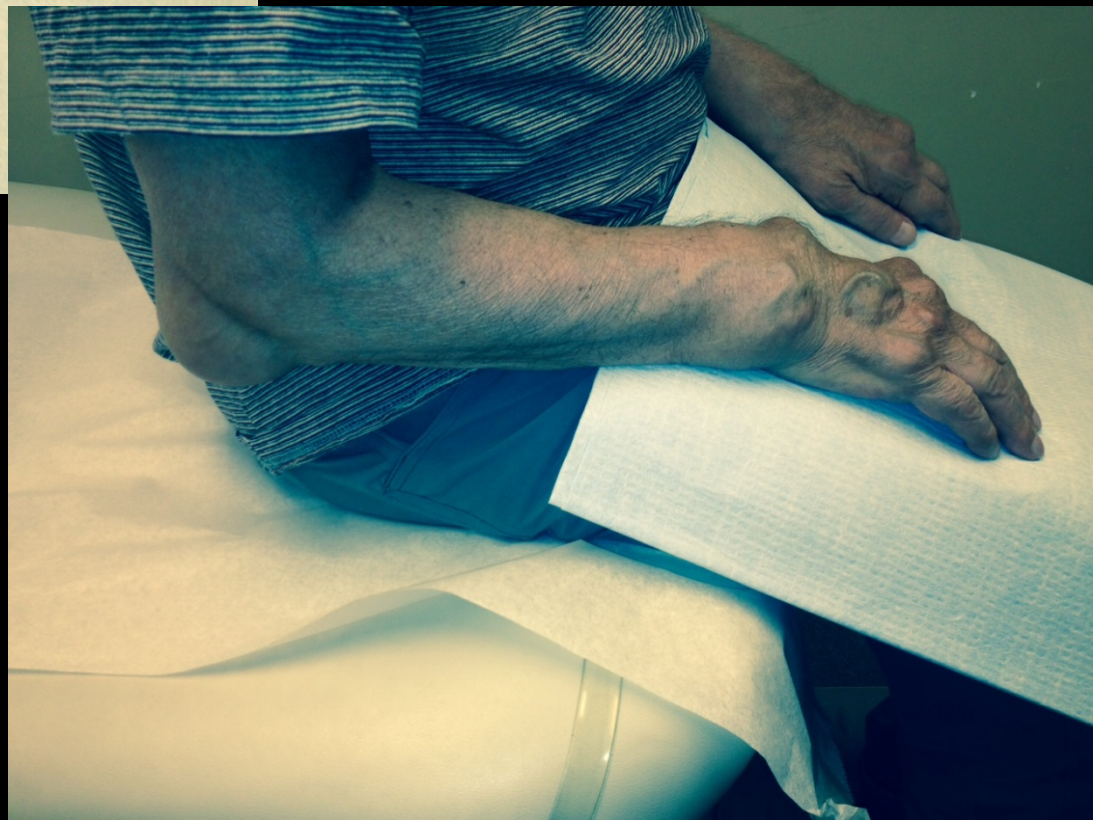
Rheumatoid arthritis (early)





68yo M

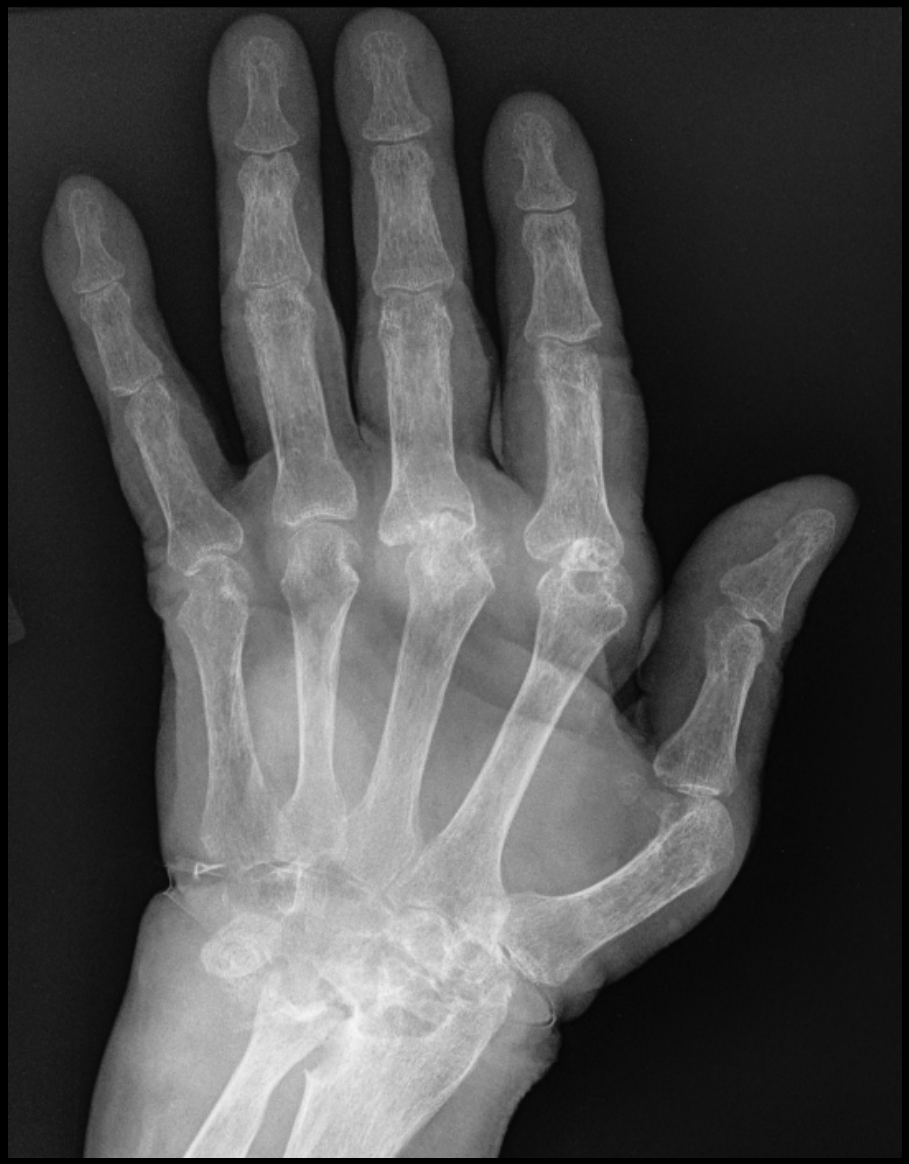
- Lyme arthritis (knee)
- Polyarticular synovitis with effusions
- Alcoholism (last drink 2 years ago)

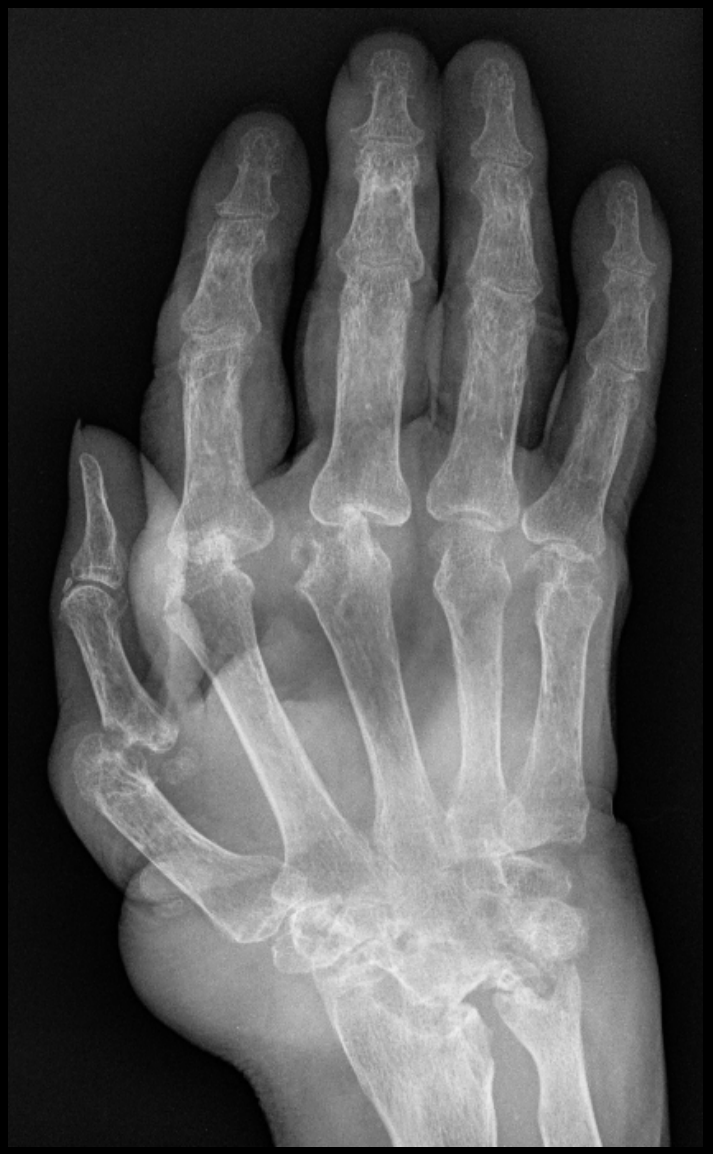


Labs:

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

Rheumatoid arthritis (late, severe)

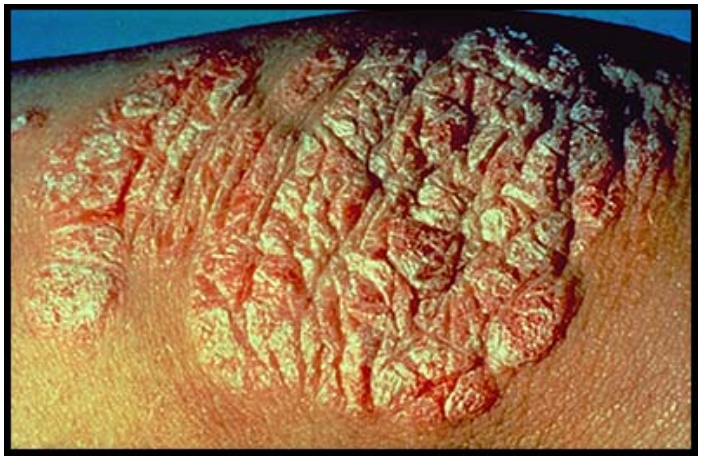




Psoriatic Arthritis

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

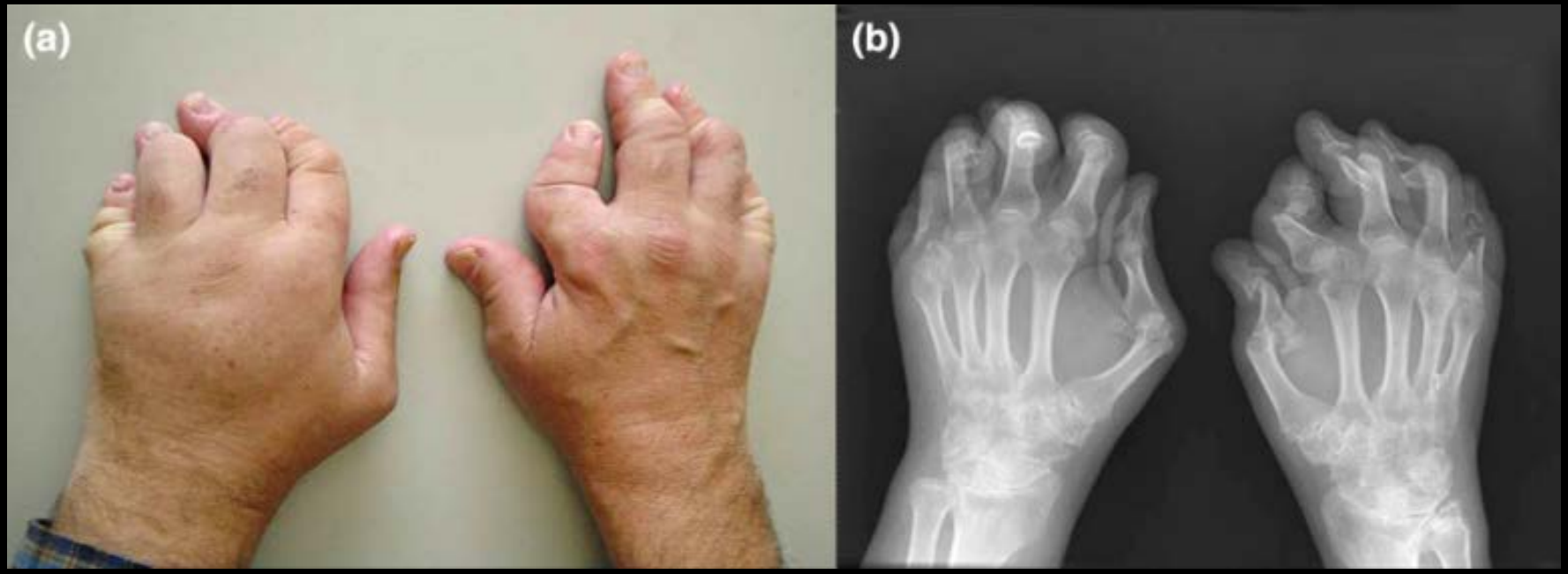


Extra-articular Features

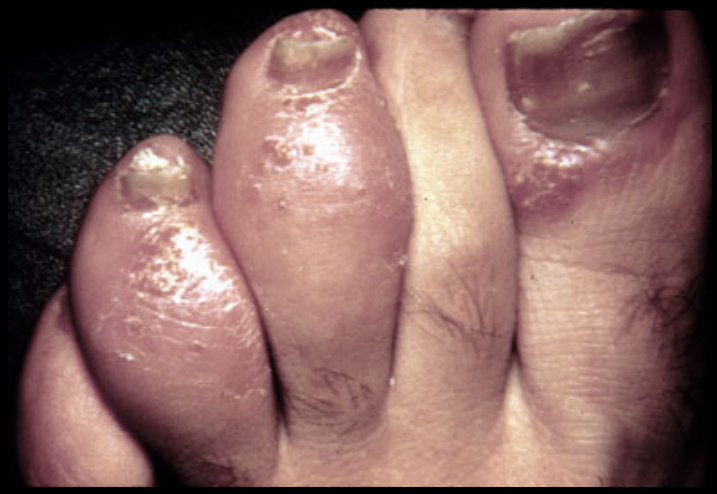
- Psoriatic skin lesions - typically thick scale on erythematous base, but some variability
- Fingernails: pitting, onycholysis, transverse depressions
- Eye inflammation (30%) - conjunctivitis, iritis
- Dactylitis, tendinitis

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

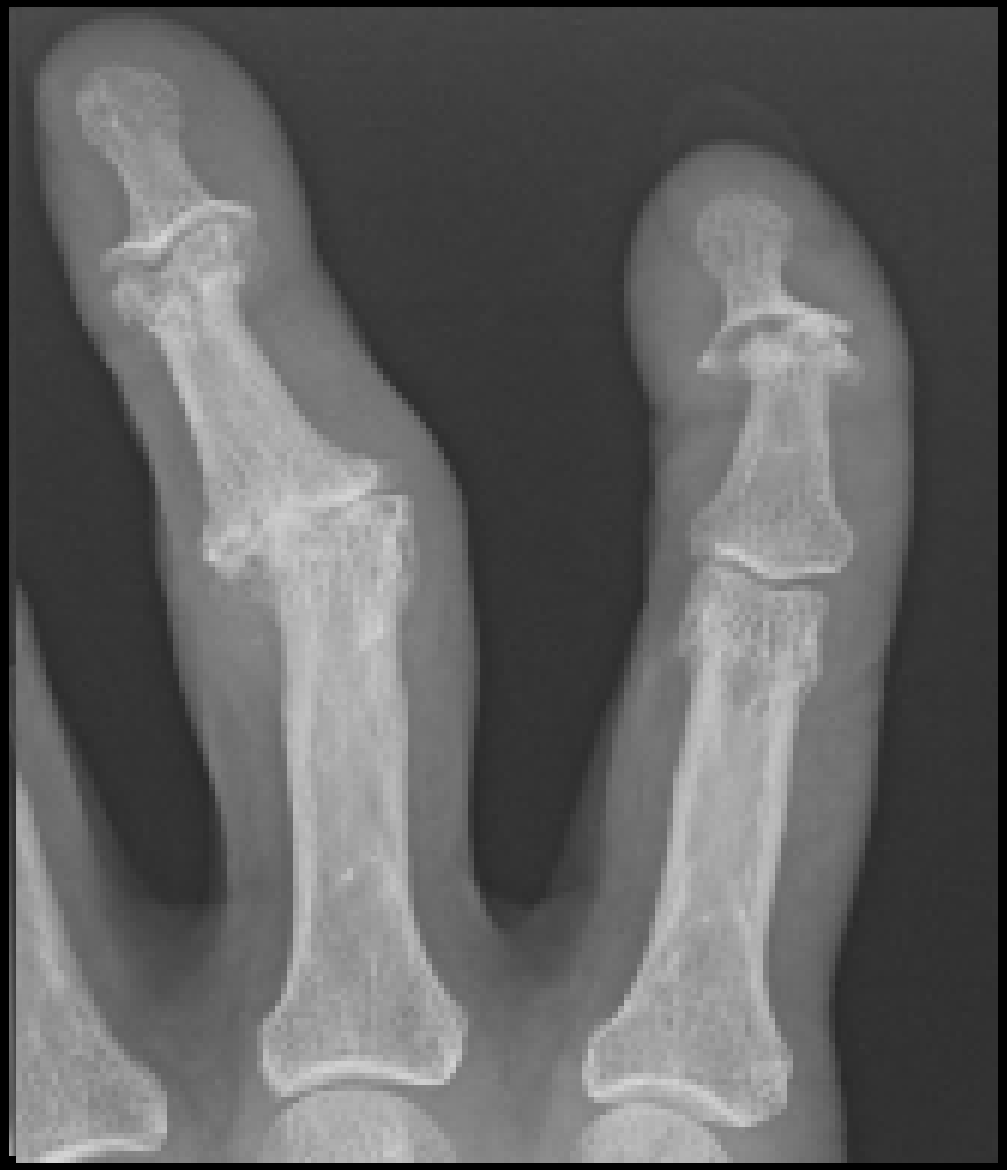
Psoriatic Arthiritis, Mutilans type

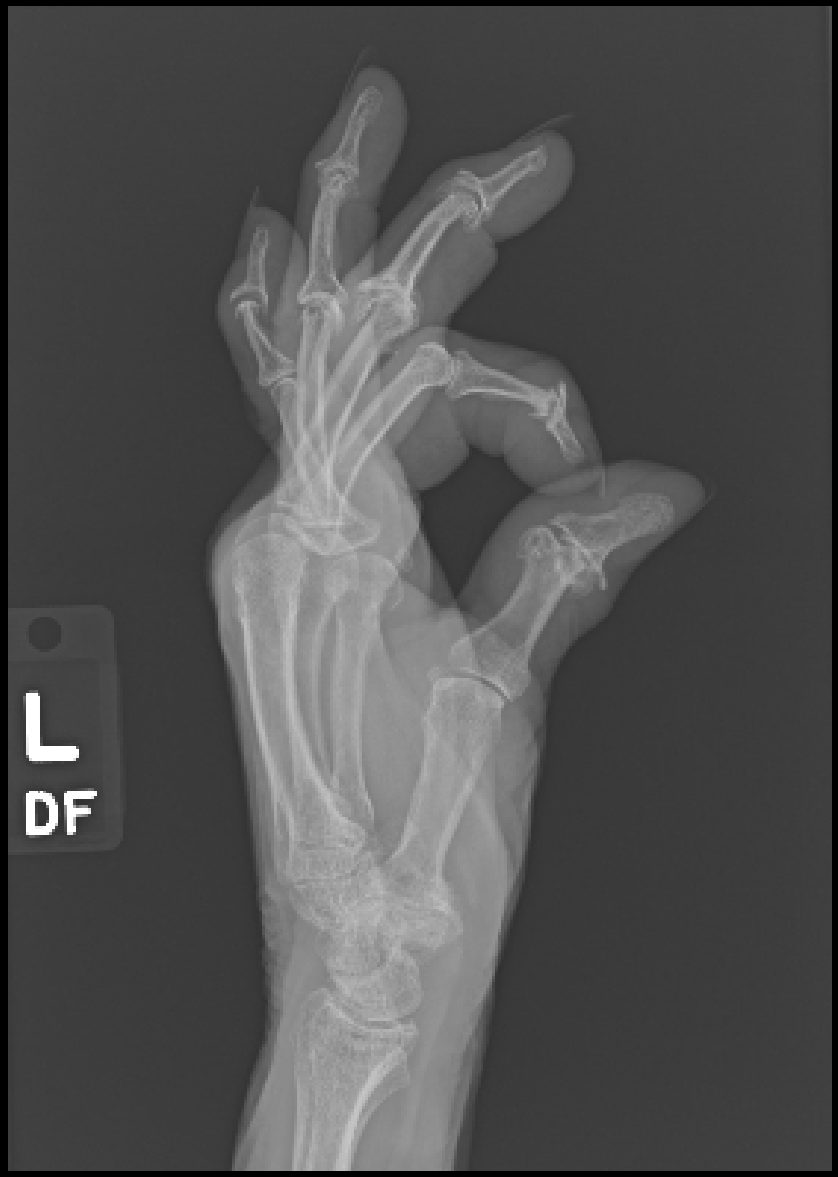


Dactylitis
“sausage digits”



Psoriatic arthritis AND Osteoarthritis

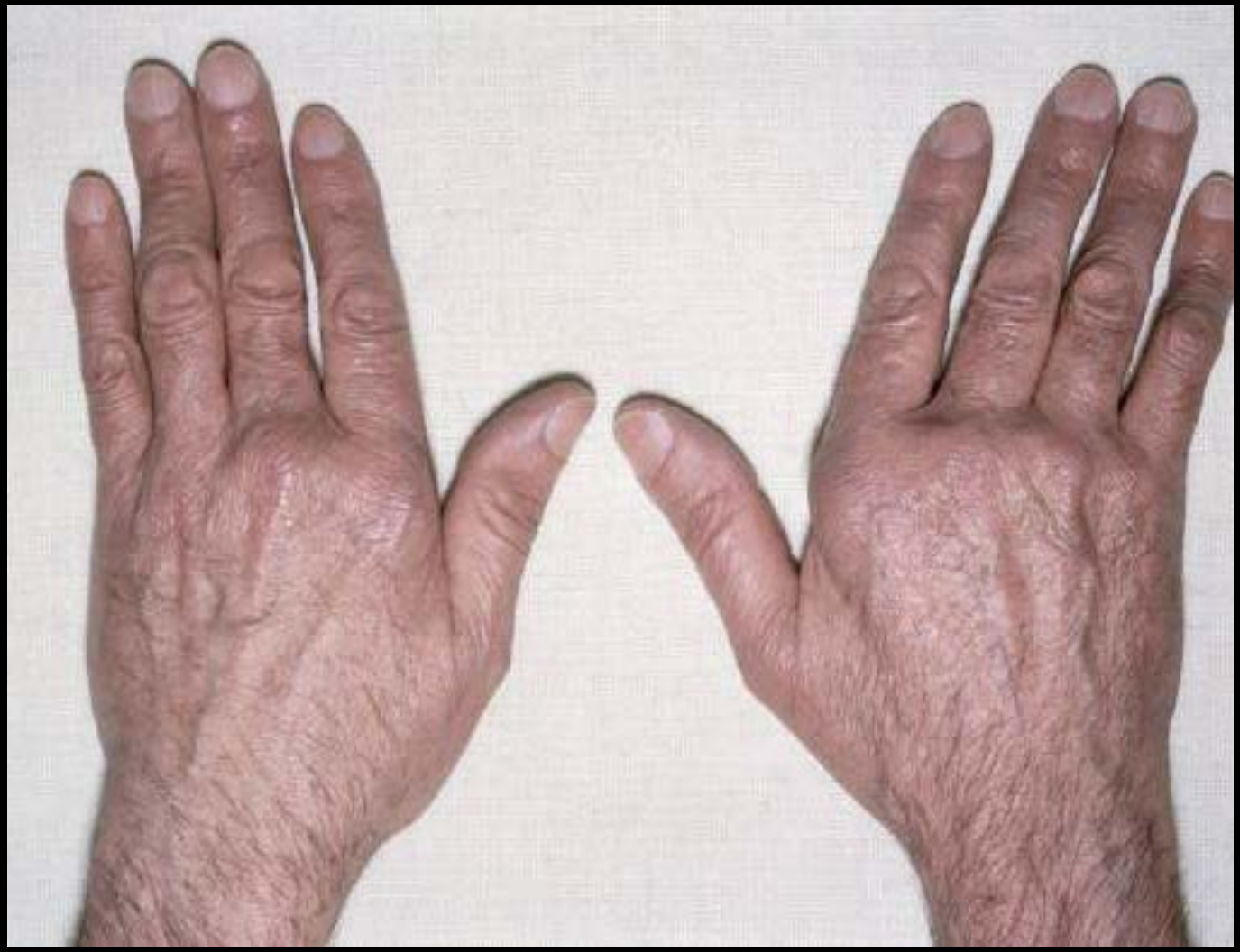


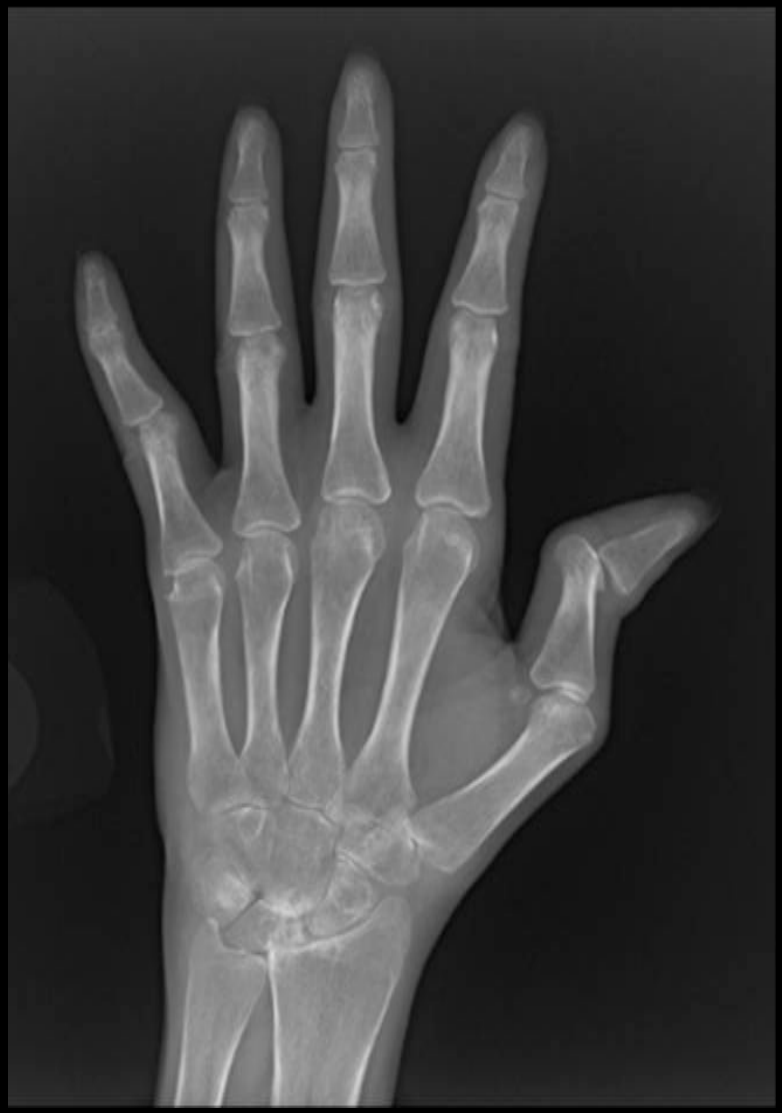


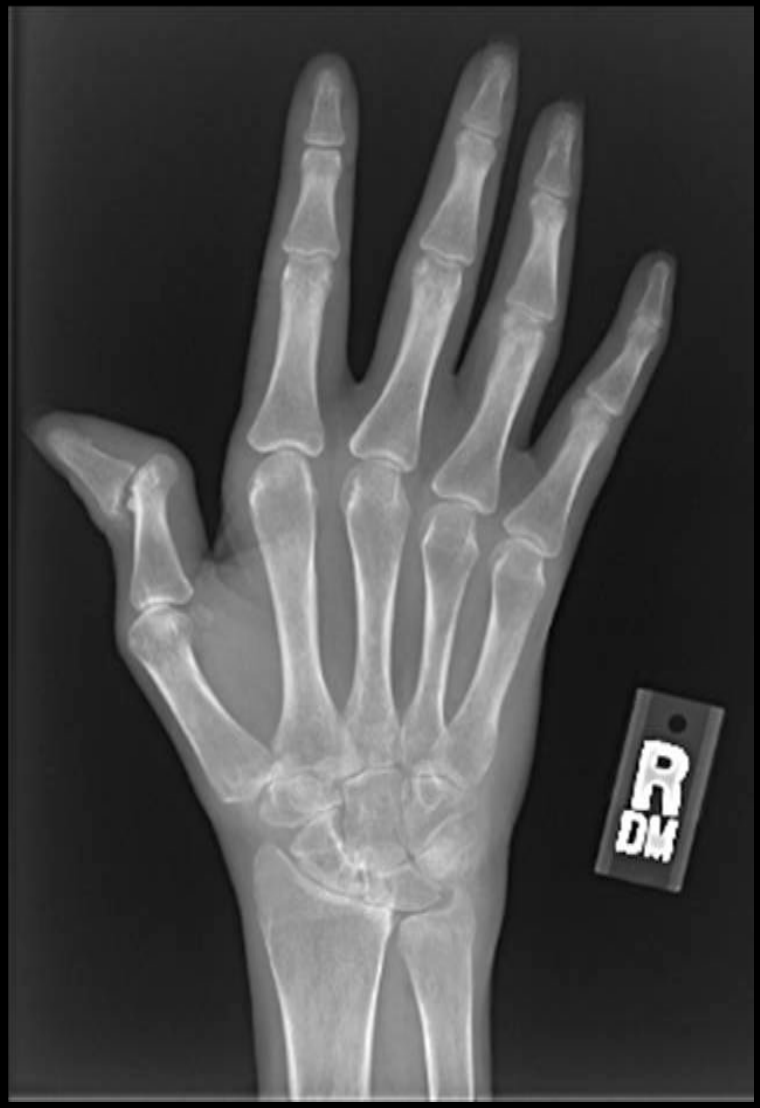
SLE Arthropathy

- 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:

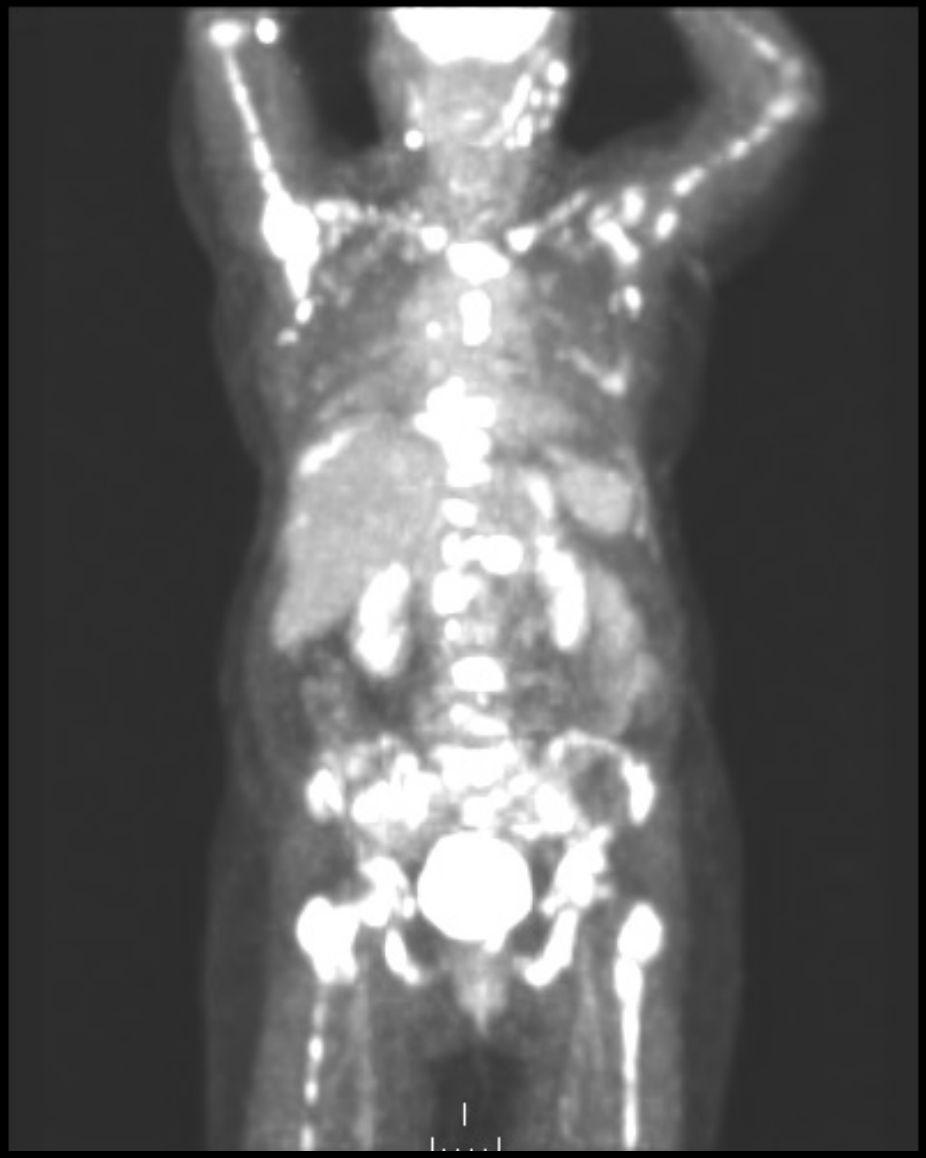
- Proximal aching has recurred on 20mg/day, just as severe.
- Vision stable, some headaches, not as bad.
- She reports increasing her prednisone to 80mg/day (on her own) to control symptoms, now at 40mg/day, a little better.
- ESR 83 and CRP 125 mg/L.

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



Summary

1. The DDx for polyarthritis is large, though a patient's history and demographics quickly narrow the field.
2. Identifying the pattern of joints involved and identifying active synovitis (or not) very often yields the correct diagnosis.
3. Recognizing non-articular signs and symptoms are critical for identifying patients with complex systemic inflammatory disease.

Summary

4. Laboratory tests merely support or confirm the clinical impression – they are not useful as diagnostic screening tools.
5. Radiographs are very often normal in the early stages of joint disease.

Thank you for your attention!