A tale of 2 hands:
When joint pain is more than age-related wear-and-tear

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11/10/2023
OHSU/Portland VA

https://sydneyadvancedphysio.com.au/osteoarthritis-and-the-hand/

Objectives

Differentiate hand osteoarthritis from inflammatory arthritis

List the different subsets of inflammatory arthritis that affect the hands

Recognize the salient features of:

Rheumatoid arthritis

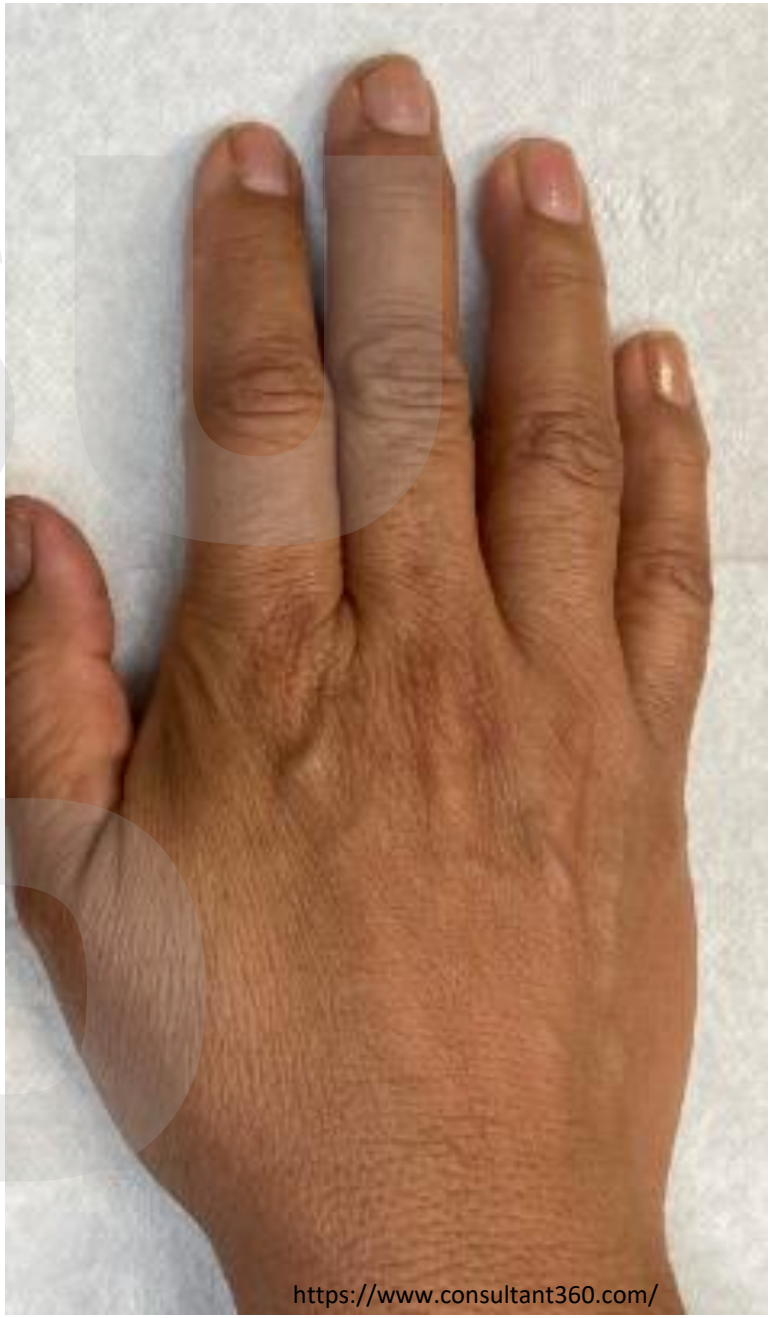
Chronic CPPD arthritis

Psoriatic arthritis

Appreciate approach to diagnosis and treatment of inflammatory arthritis

Case

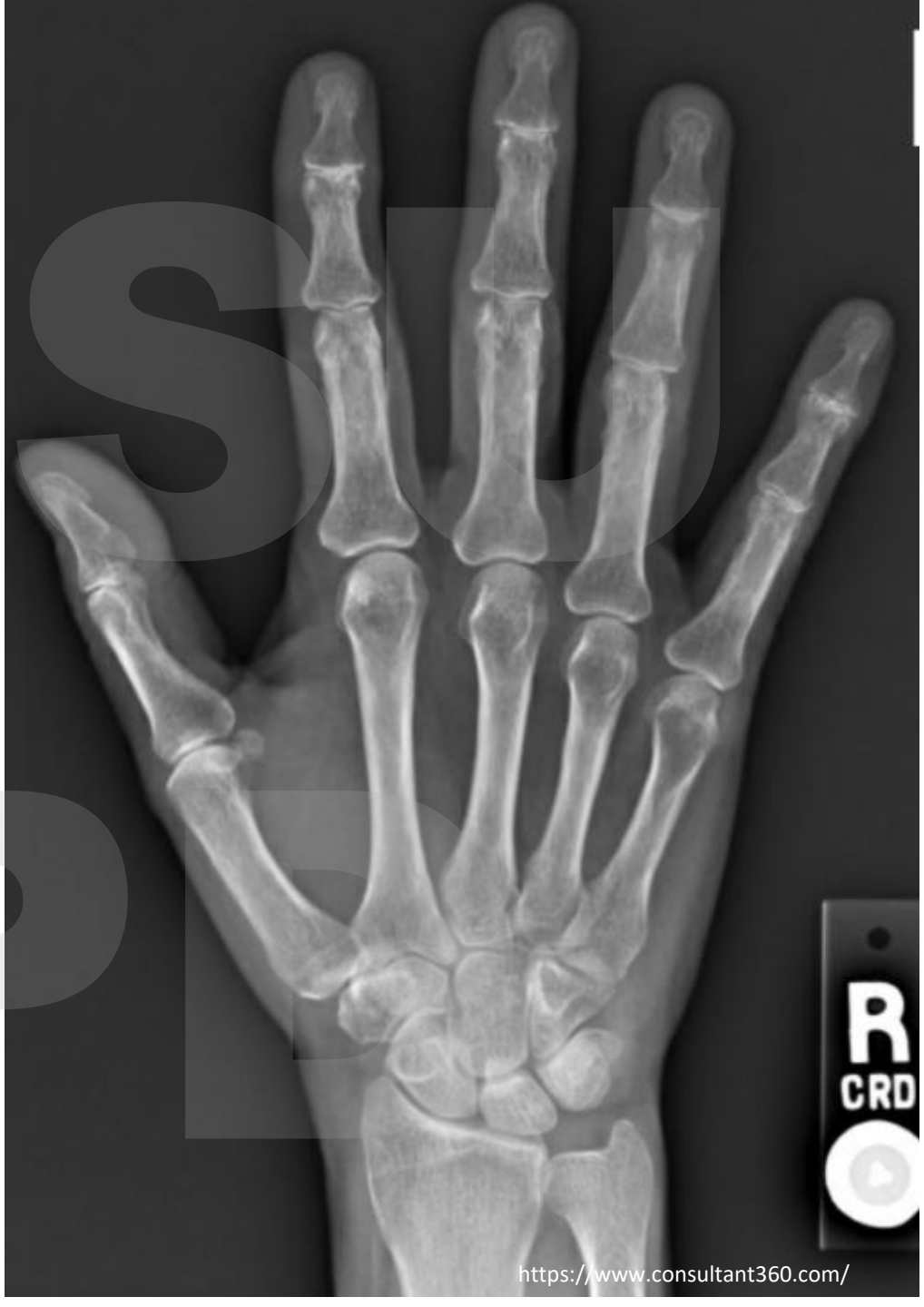
- A 55 year-old woman presents for evaluation of joint pain in her bilateral hands
- Symptoms present for a few years but much worse for last 3 months
- Affecting ADLs
- Associated stiffness
- Virtual visit: Appears to have Heberden's nodes and painful flexion of her fingers
- You order hand x-rays



https://www.consultant360.com/

Case

- X-ray Report: “Joint space narrowing, subchondral cyst, osteophyte formation, and sclerosis at the DIP joints consistent with degenerative joint disease.”
- You diagnose osteoarthritis
- Recommend naproxen 500mg twice daily with food
- See her back in 3 months



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Prevalence of radiographic OA in hands, knees, and hips, from population-based studies

Anatomic site, age, years	Source (ref.)	% with mild, moderate, or severe OA		
		Male	Female	Total
Hands, ≥26	Framingham OA study (6)	25.9	28.2	27.2
Knees[†]				
≥26	Framingham OA study (5)	14.1	13.7	13.8
≥45	Framingham OA study (5)	18.6	19.3	19.2
≥45	Johnston County OA Project (7)	24.3	30.1	27.8
≥60	NHANES III (4)	31.2	42.1	37.4
Hips, ≥45	Johnston County OA Project (10)	25.7	26.9	27.0

Lawrence et al. Arthritis Rheum. 2008 Jan;58(1):26-35.

Prevalence of symptomatic OA in hands, knees, and hips, from population-based studies

Anatomic site, age, years	Source (ref.)	% with symptomatic OA		
		Male	Female	Total
Hands, ≥26	Framingham OA study (6)	3.8	9.2	6.8
Knees				
≥26	Framingham OA study (5)	4.6	4.9	4.9
≥45	Framingham OA study (5)	5.9	7.2	6.7
≥45	Johnston County OA Project (7)	13.5	18.7	16.7
≥60	NHANES III (4)	10.0	13.6	12.1
Hips, ≥45	Johnston County OA Project (10)	8.7	9.3	9.2

25% are symptomatic

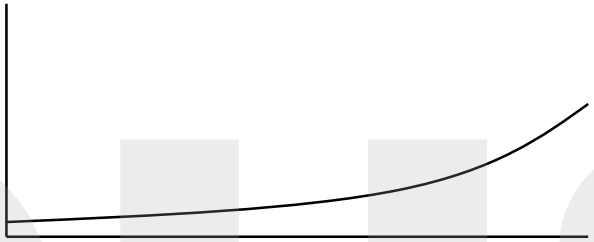
Lawrence et al. Arthritis Rheum. 2008 Jan;58(1):26-35.

Beware of diagnosis symptomatic OA on the basis of radiographs alone

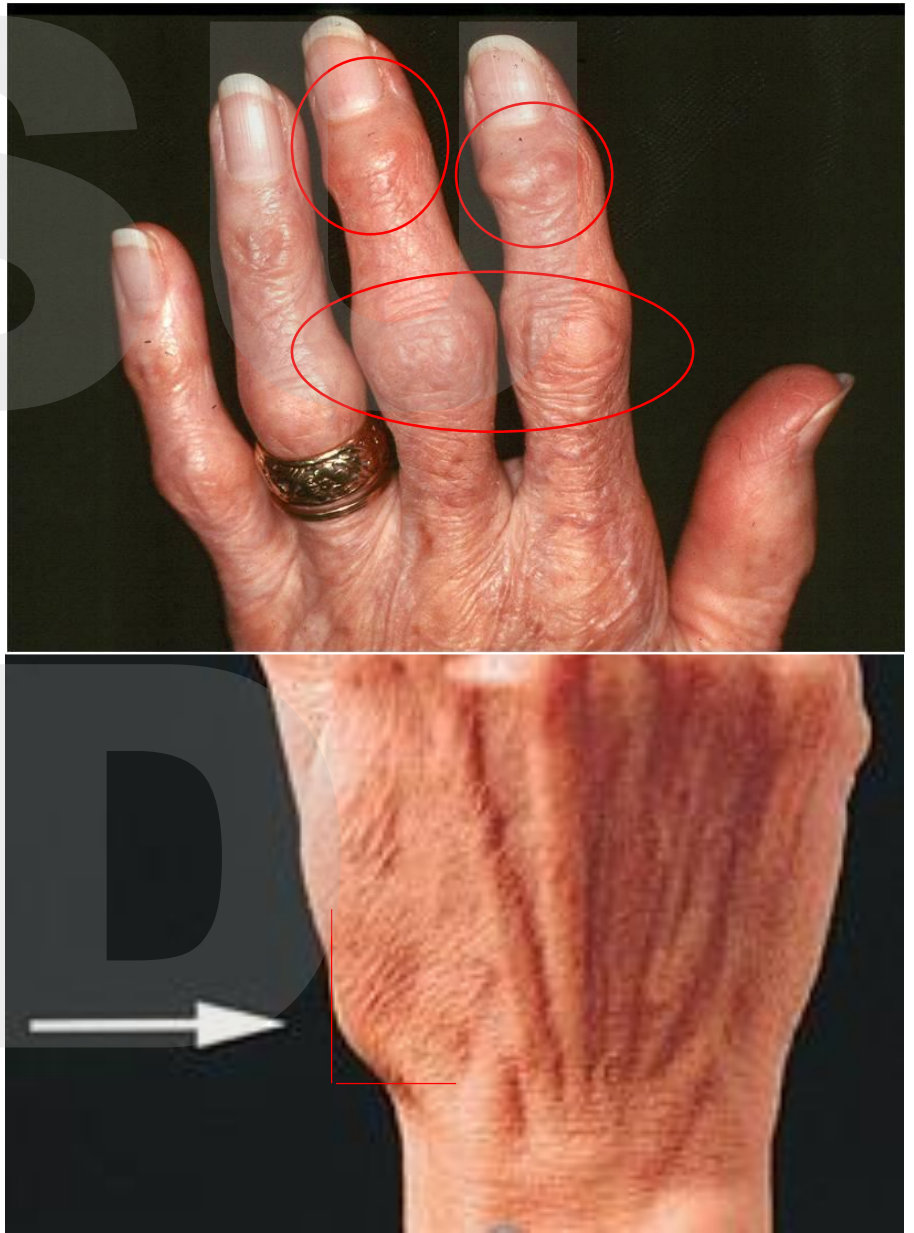
The older the patient, the more likely they are to have radiographic osteoarthritis

Radiographs are there to help support a clinical diagnosis

Osteoarthritis

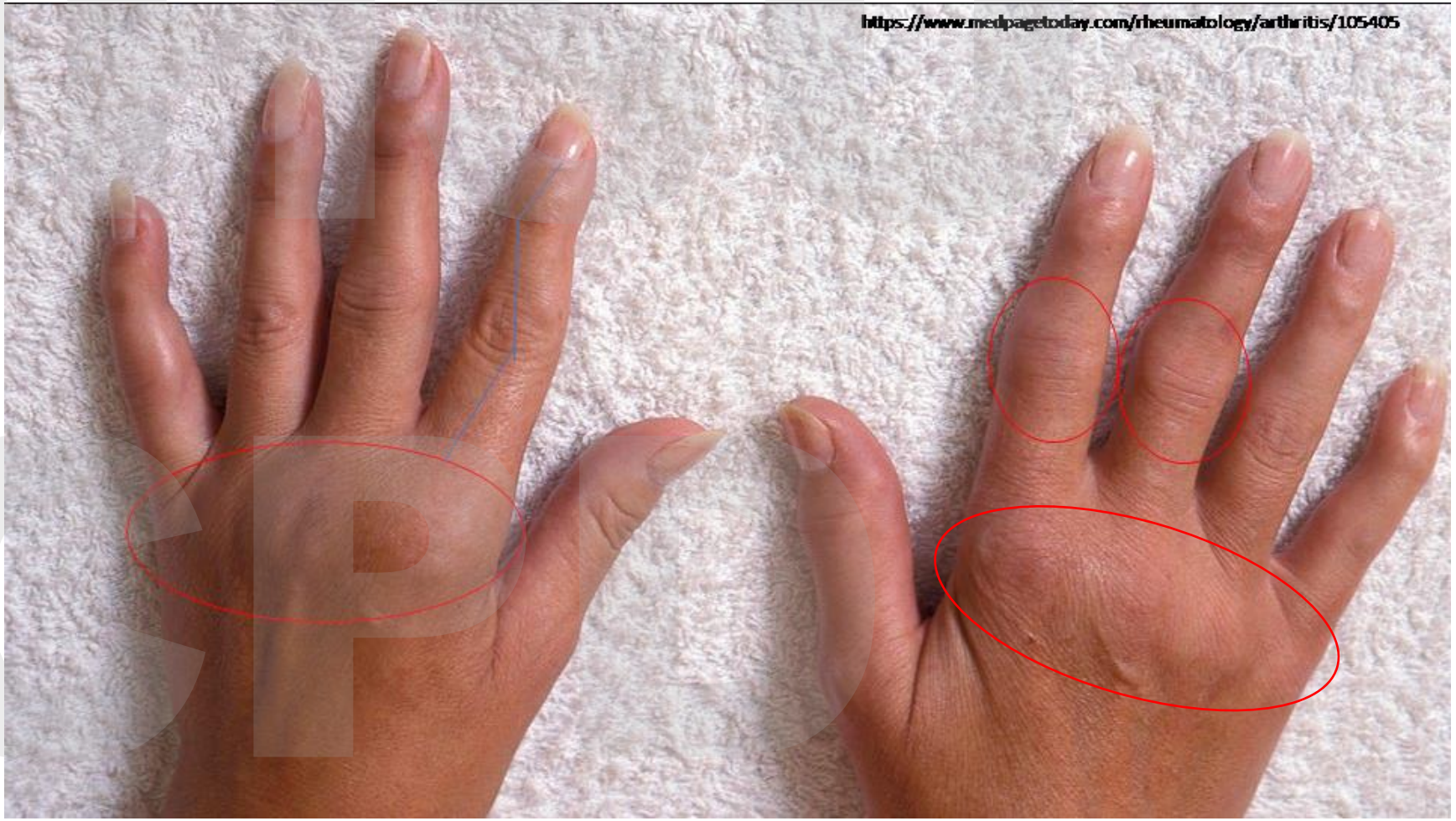


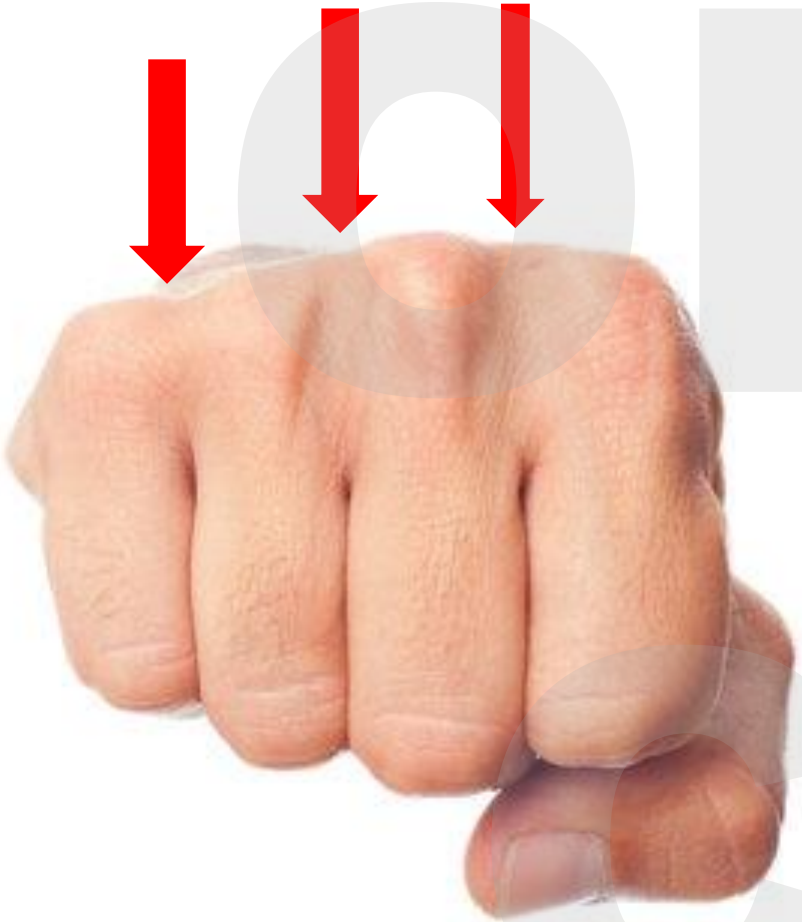
- History
  - Slow steady progression
  - No hot red joints
  - Limited morning stiffness (< 30 min)
  - Mechanical pain: ↑ use, ↓ rest/night
  - No systemic findings
- Physical exam
  - Bony enlargement (DIPs, PIPs)
  - Squaring of the CMC joints, pain with CMC loading (grind test)
  - Crepitus/grating



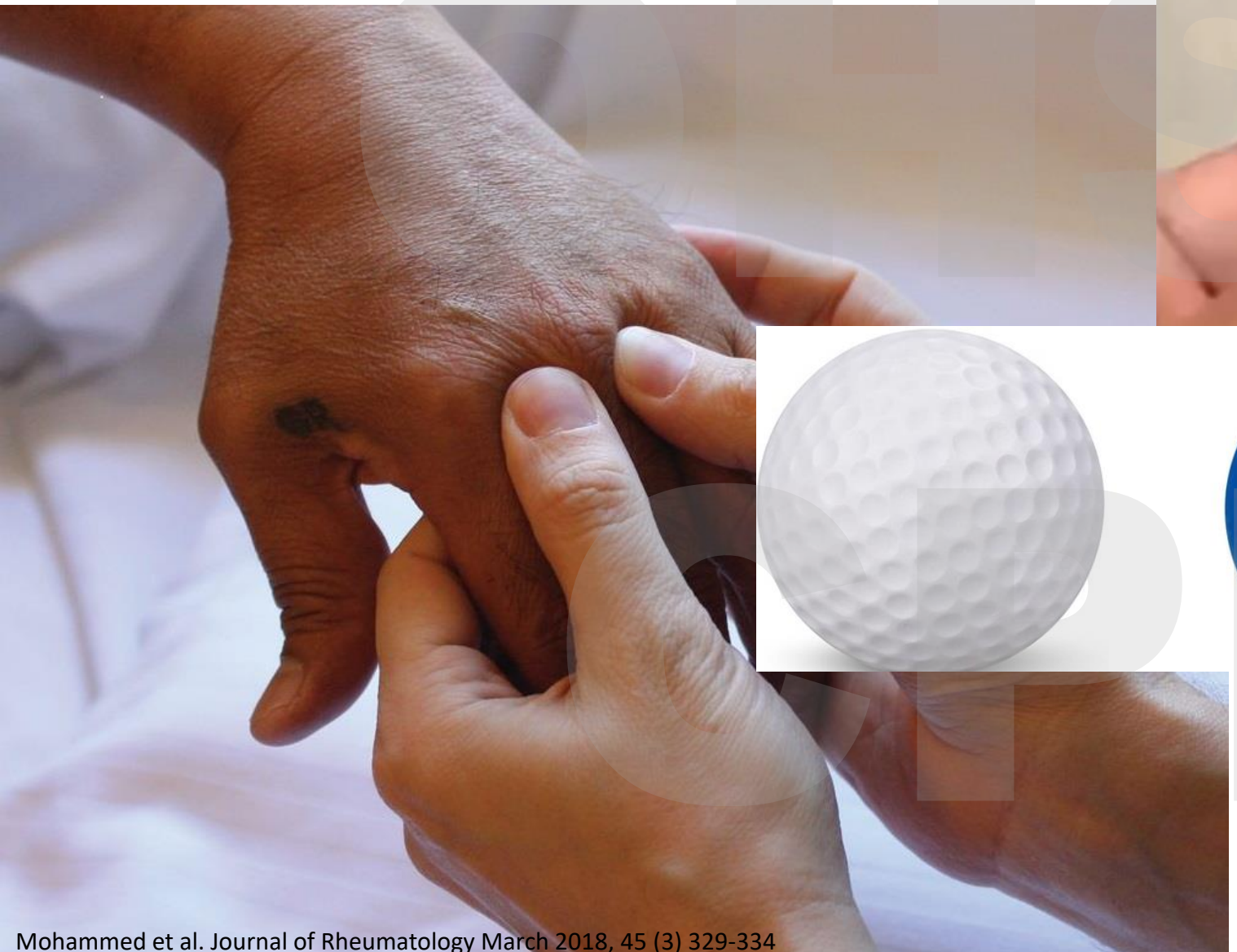
Case: 3 months later

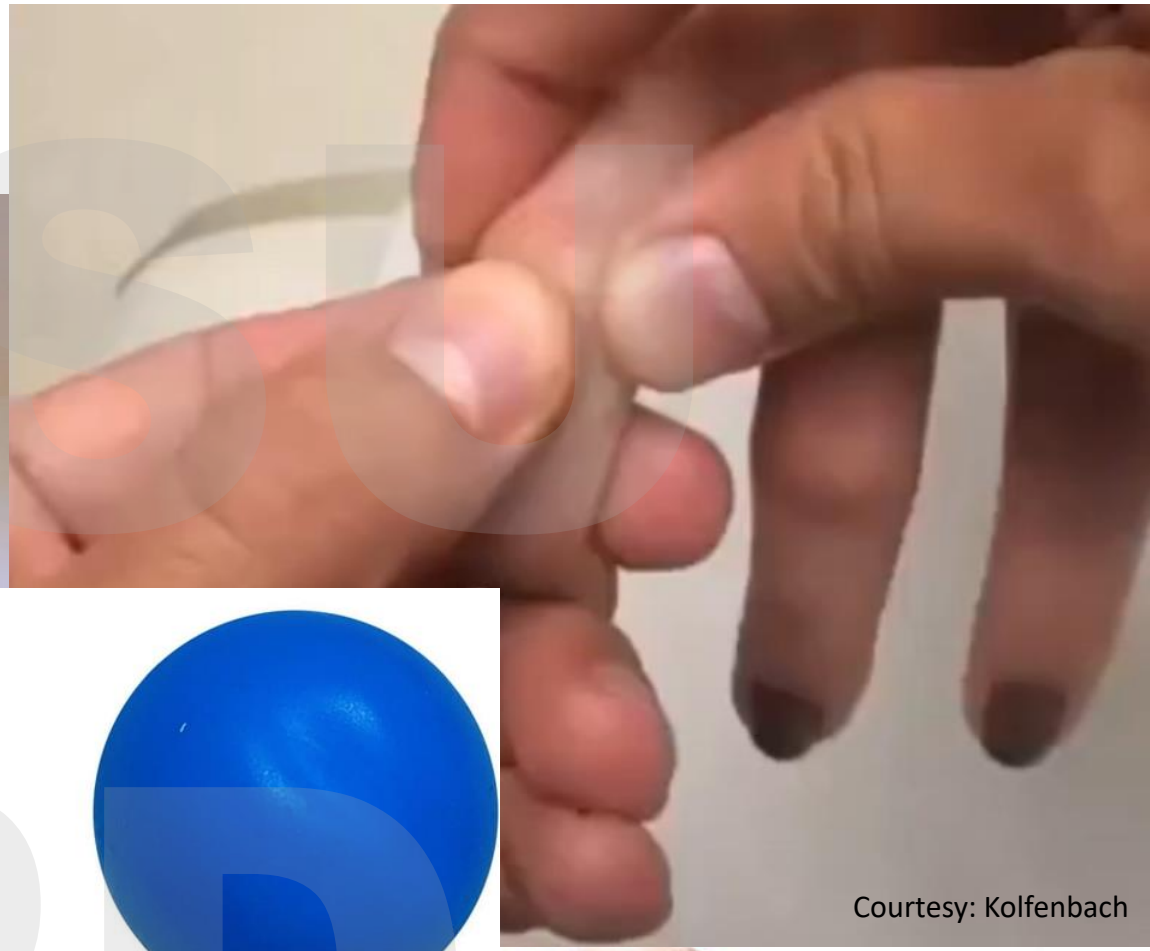
- Not any better
  - Actually worse
  - Pain throughout the day
  - Wax and wane
- AM Stiffness > 1 hour
- Progressive swelling in knuckles and wrists
- Can’t make a fist
- Fatigue





Checking for synovitis



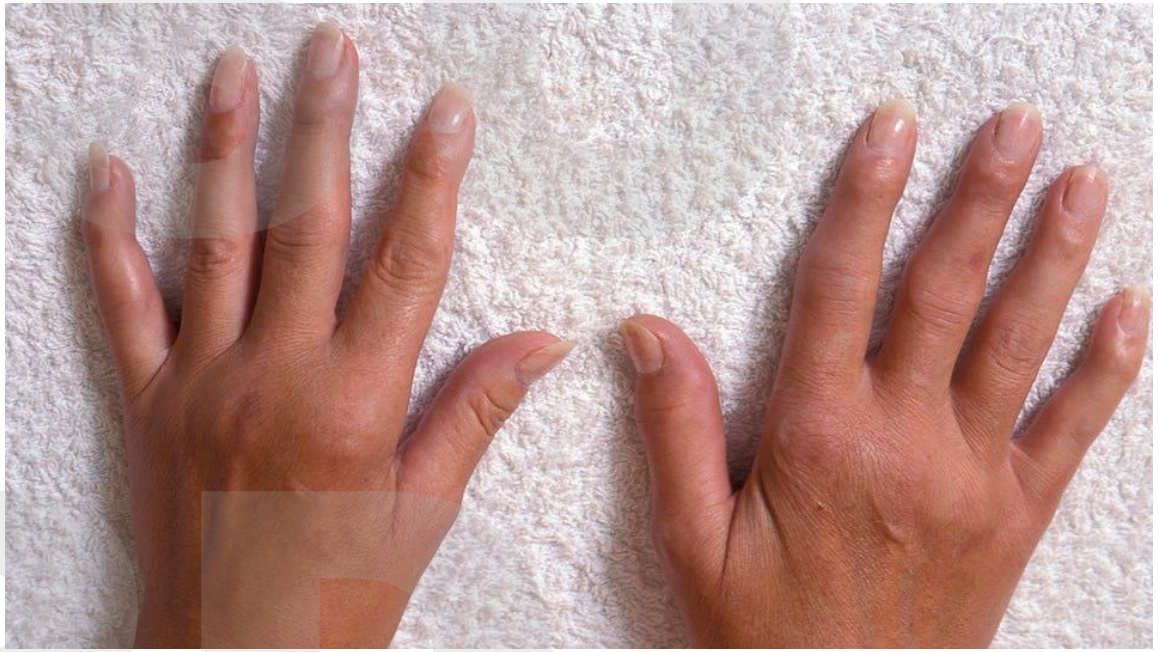


Courtesy: Kolfenbach

Mohammed et al. Journal of Rheumatology March 2018, 45 (3) 329-334

Back to the case

- Symmetrical, bilateral inflammatory polyarthritis
- Metacarpophalangeal joints (MCPs), Proximal Inter-Phalangeal joints (PIPs), and wrists
- Sparing the DIP joints except for Heberden nodes
- Progressive over weeks, months



Differential diagnosis of a chronic inflammatory polyarthritis of the small joints of the hands

- Rheumatoid arthritis
- Psoriatic arthritis
- Calcium Pyrophosphate Disease (CPPD)
- Connective tissue disease
- Chronic viral

Differential Diagnosis of a chronic inflammatory arthritis of the small joints

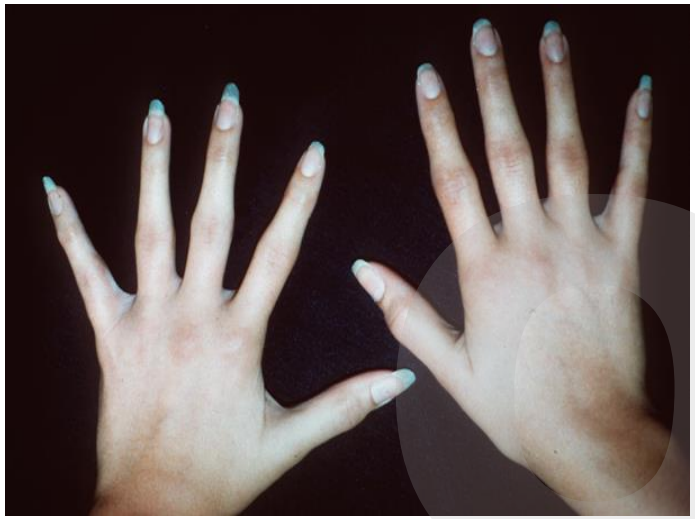
- Rheumatoid arthritis
- Psoriatic arthritis
- Calcium Pyrophosphate Disease (CPPD)
- Connective tissue disease
- Chronic viral
  - Hepatitis C, B, HIV

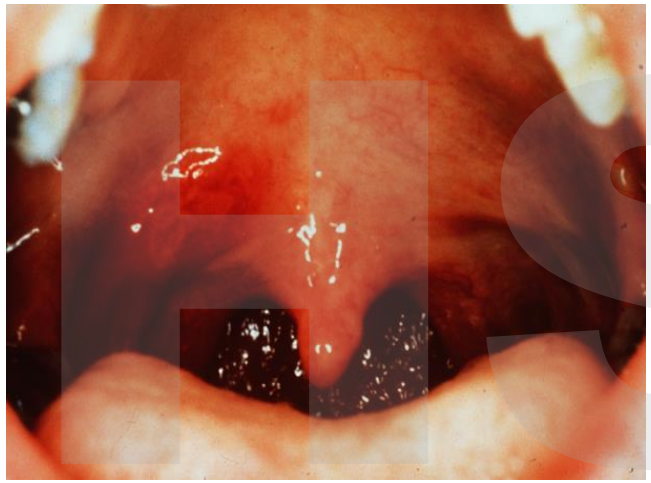
Differential Diagnosis of a chronic inflammatory arthritis of the small joints

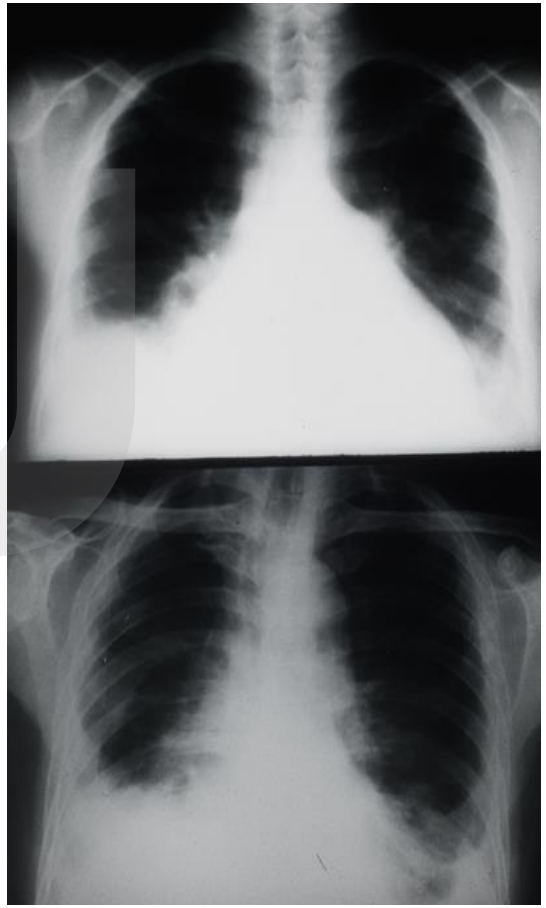
- Rheumatoid arthritis
- Psoriatic arthritis
- Calcium Pyrophosphate Disease (CPPD)
- Connective tissue disease
  - Systemic lupus erythematosus
  - Sjogren syndrome
  - Systemic sclerosis
  - Mixed Connective Tissue Disease
  - Inflammatory Myopathies
- Chronic viral

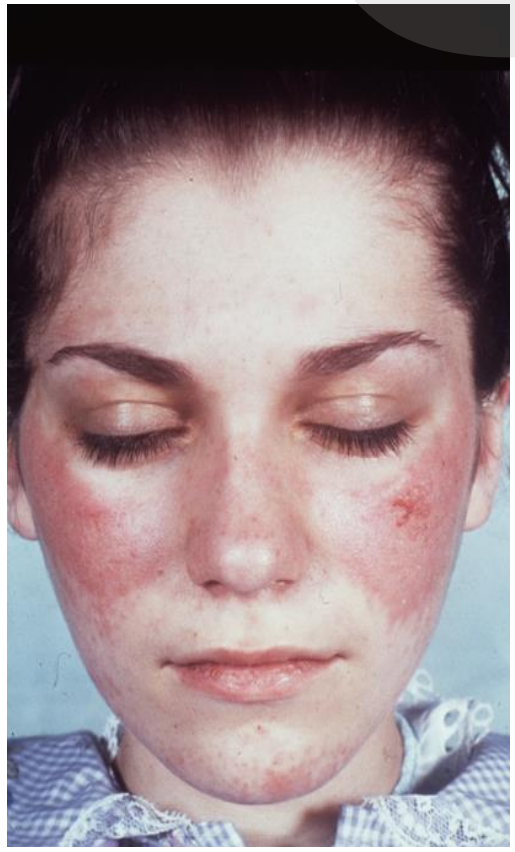
Connective tissue disease: SLE & other

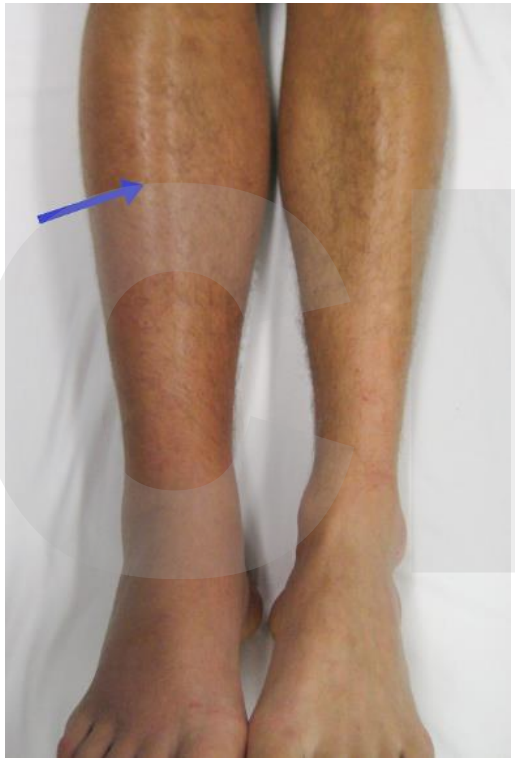
- Typically in young women, but can be any sex, any age
- Inflammatory arthritis + something else
- B symptoms, fatigue
- Rashes, photosensitivity, oral/nasal ulcers, skin tightening
- Sicca symptoms (oral, ocular), Raynaud
- Organ dysfunction
  - Pleuropericarditis, diffuse alveolar hemorrhage, pneumonitis
  - Glomerulonephritis
  - CNS/PNS
- Muscle weakness
- Hematologic: cytopenias, thrombosis

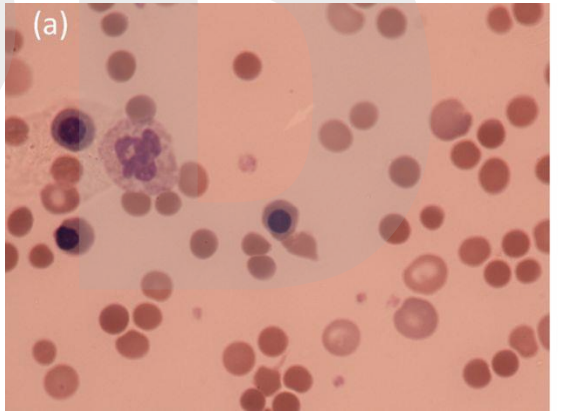


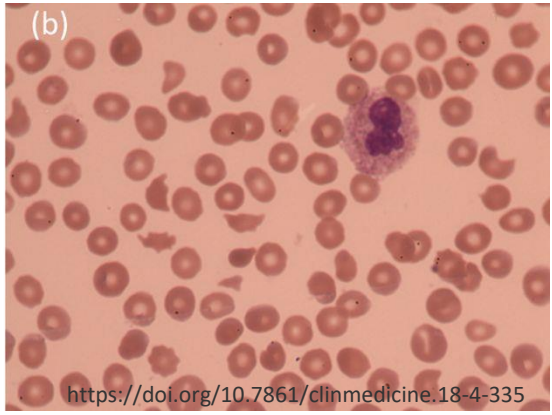






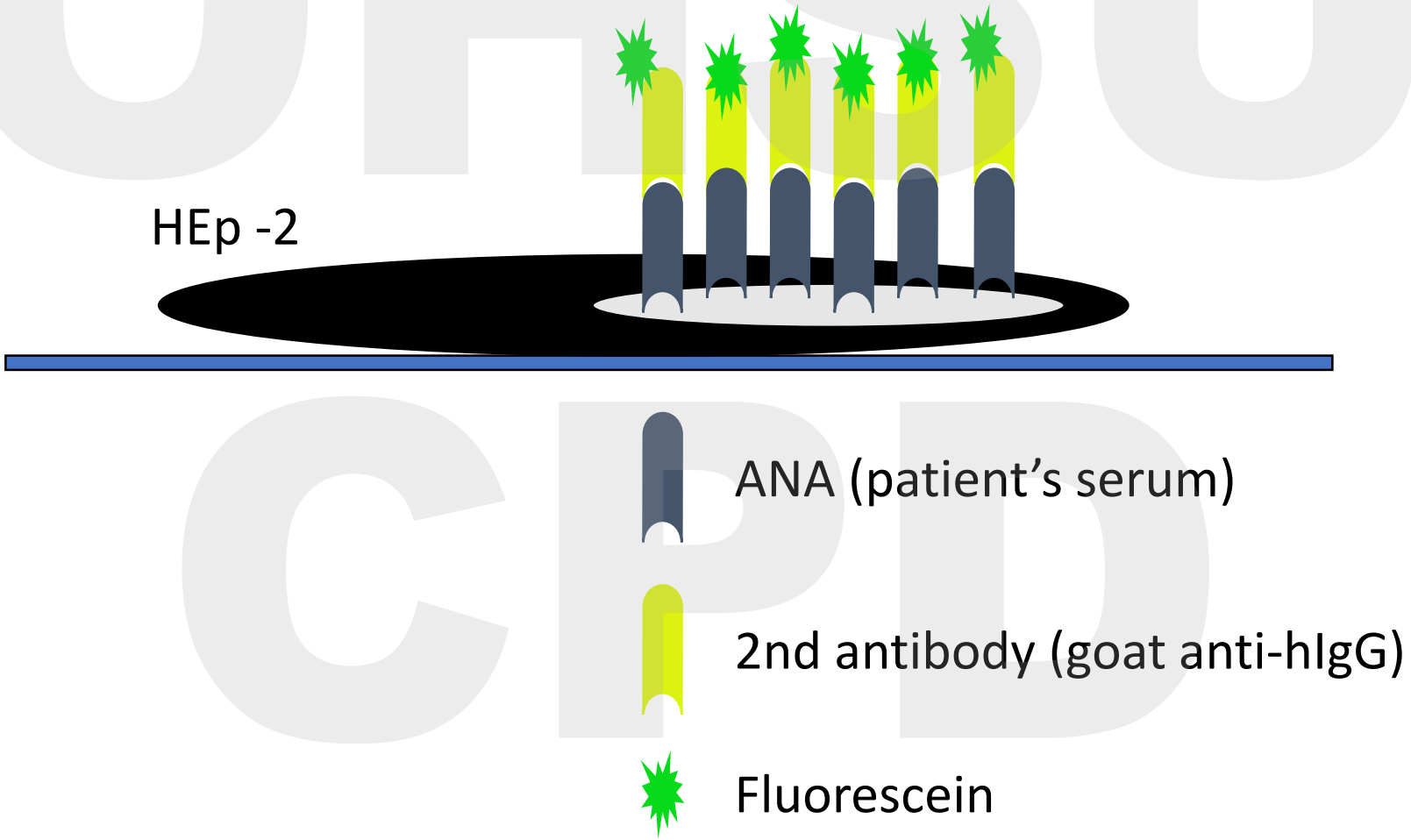




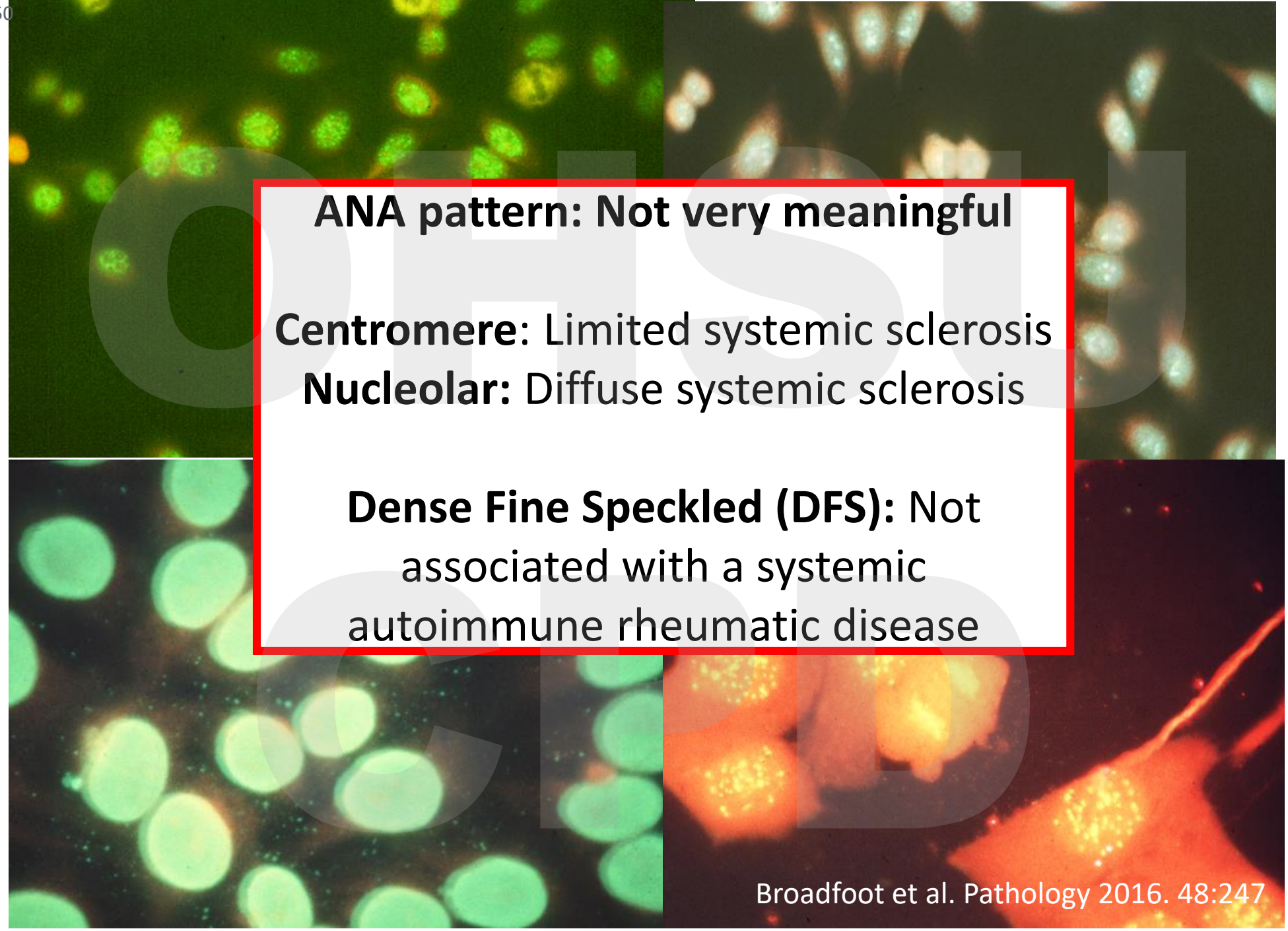


https://doi.org/10.7861/clinmedicine.18-4-335

Antinuclear Antibody- ANA



•. 2016 Apr;48(3):247-50



ANA pattern: Not very meaningful

Centromere: Limited systemic sclerosis
Nucleolar: Diffuse systemic sclerosis

Dense Fine Speckled (DFS): Not associated with a systemic autoimmune rheumatic disease

Broadfoot et al. Pathology 2016. 48:247

+ANA is found in healthy individuals

- What % of normal people have + ANA tests?
  - Young: 2-5%
  - Old: 10-20%
- Does the titer help? Yes
  - 1:40 can be detected in 32% of normal
  - 1:80 can be detected in 12% of normal
  - 1:160 can be detected in 5% of normal

+ANA may be an indication of autoimmunity

- SLE- 95%
- MCTD - 90%
- Sjogren syndrome- 70%
- Systemic sclerosis- 70%
- Dermatomyositis- 50%
- Rheumatoid arthritis- 30%

2011

Choosing Wisely in Rheumatology:

5 Things Internists Need to Know and Practice

N. Lawrence Edwards, MD, MACP, MACR
Professor and Vice Chair
Department of Medicine
University of Florida

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Pearl

Choosing Wisely
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1 Don't test ANA sub-serologies without a positive ANA and a good clinical suspicion of immune-mediated disease.

Yazdani et al. Arth Care &Res 2013

If the ANA is detected, additional antibodies may be ordered ("ENA" panel: Extractable Nuclear Antigen")

- SLE- 95%
  - +anti-dsDNA, +anti-Smith
- Mixed Connective Tissue Disease - 90%
  - +anti-RNP
- Sjogren syndrome- 70%
  - +anti-SSA, +anti-SSB
- Systemic sclerosis- 70%
  - +Anti-Centromere, +Anti-Scl70, +anti-RNAPol3
- Dermatomyositis- 50%
  - Anti-Jo1, myositis panel
- Rheumatoid arthritis- 30%

Other autoimmune and non-autoimmune diseases may be associated with a +ANA

- Autoimmune Thyroid Disease
  - Hashimoto's thyroiditis, Grave's disease
- Autoimmune Liver Disease
  - PBC, autoimmune hepatitis
- Chronic infections
  - viral, endocarditis, TB
- Malignancy
  - lymphoproliferative
- Drug-induced
  - minocycline, hydralazine, procainamide, isoniazid, infliximab

ANA Testing

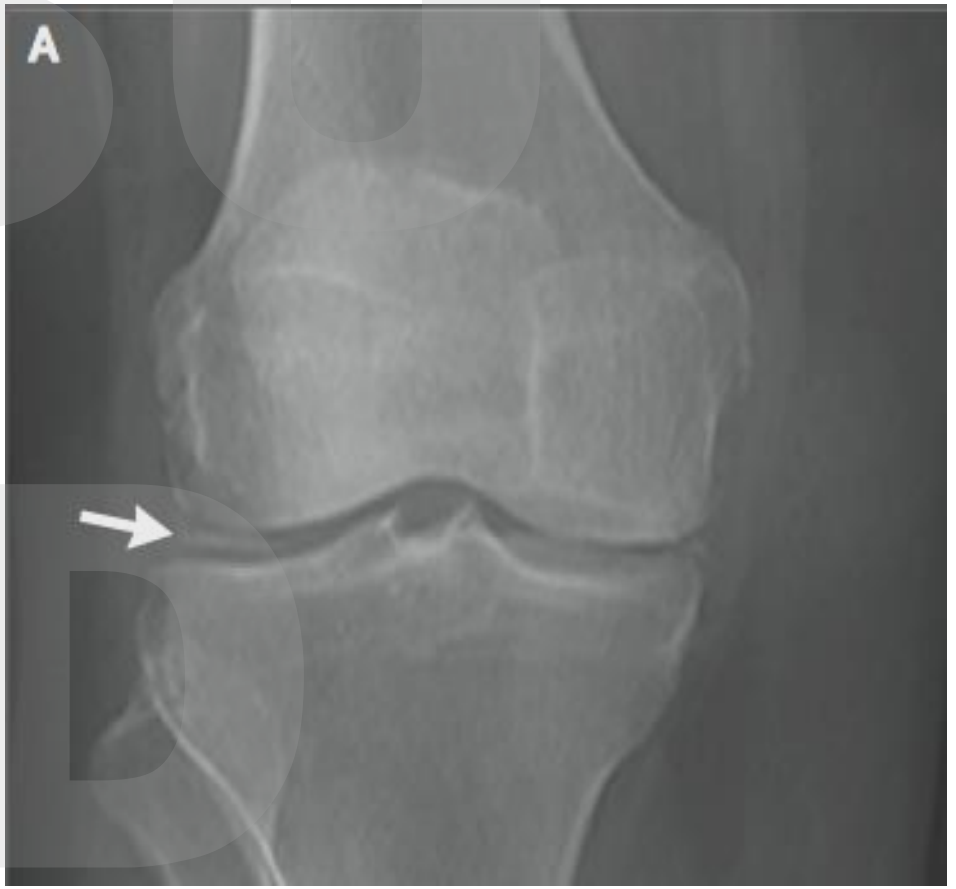
- Indication: clinical syndrome suggesting SLE or other autoimmune disease (not just widespread pain)
- Interpretation
  - Negative ANA pretty much excludes SLE (high sensitivity)
    - Does not exclude Scleroderma, Sjogren syndrome or Dermatomyositis
  - + ANA does NOT diagnose SLE (poor specificity)
  - + ANAs found in health and in non-rheumatic diseases

Differential Diagnosis of a chronic inflammatory arthritis of the small joints

- Rheumatoid arthritis
- Psoriatic arthritis
- Calcium Pyrophosphate Disease (CPPD)
- Connective tissue disease
- Chronic viral

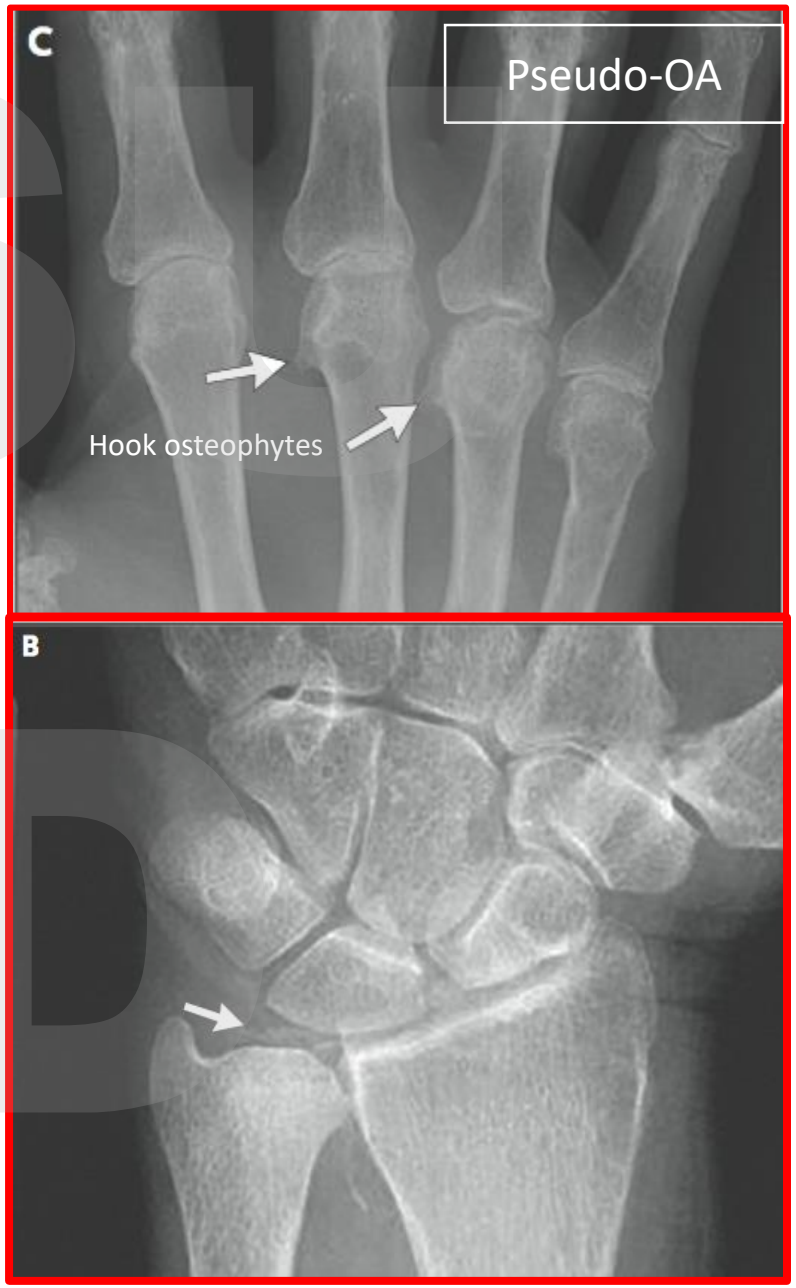
Chronic CPPD Disease: Great mimicker!

- Calcium pyrophosphate Dihydrate Deposition Disease
- Crystalline arthritis
- Most well known for causing “Pseudogout”
- But may mimic RA, OA, neuropathic joint, tumors
- Typical host: > age 50, but increased prevalence with increased age
- Incidental CPPD: “chondrocalcinosis” common
- Or may cause disease



Chronic CPPD Disease: Pseudo-OA, Pseudo-RA

- Chronic pain and mild swelling in the 2nd & 3rd MCPs, and wrists with prolonged stiffness, intermittent exacerbation
- Joint exam may show bony MCP enlargement +/- synovitis
- Serologies: Negative
- Radiographic findings
  - OA changes at the MCPs with subchondral cysts and joint space narrowing
  - Chondrocalcinosis



Pseudo-RA presentation of chronic CPPD

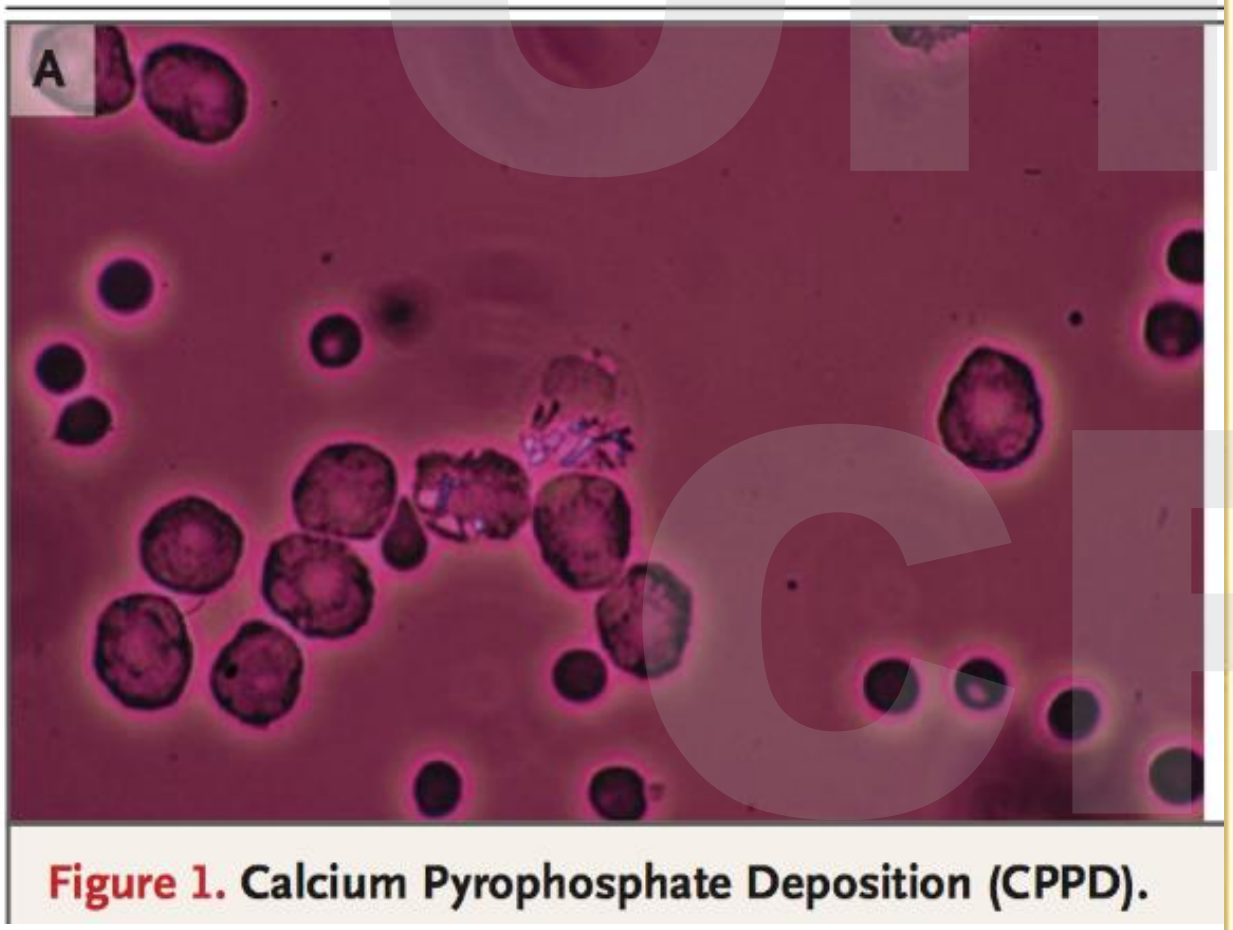
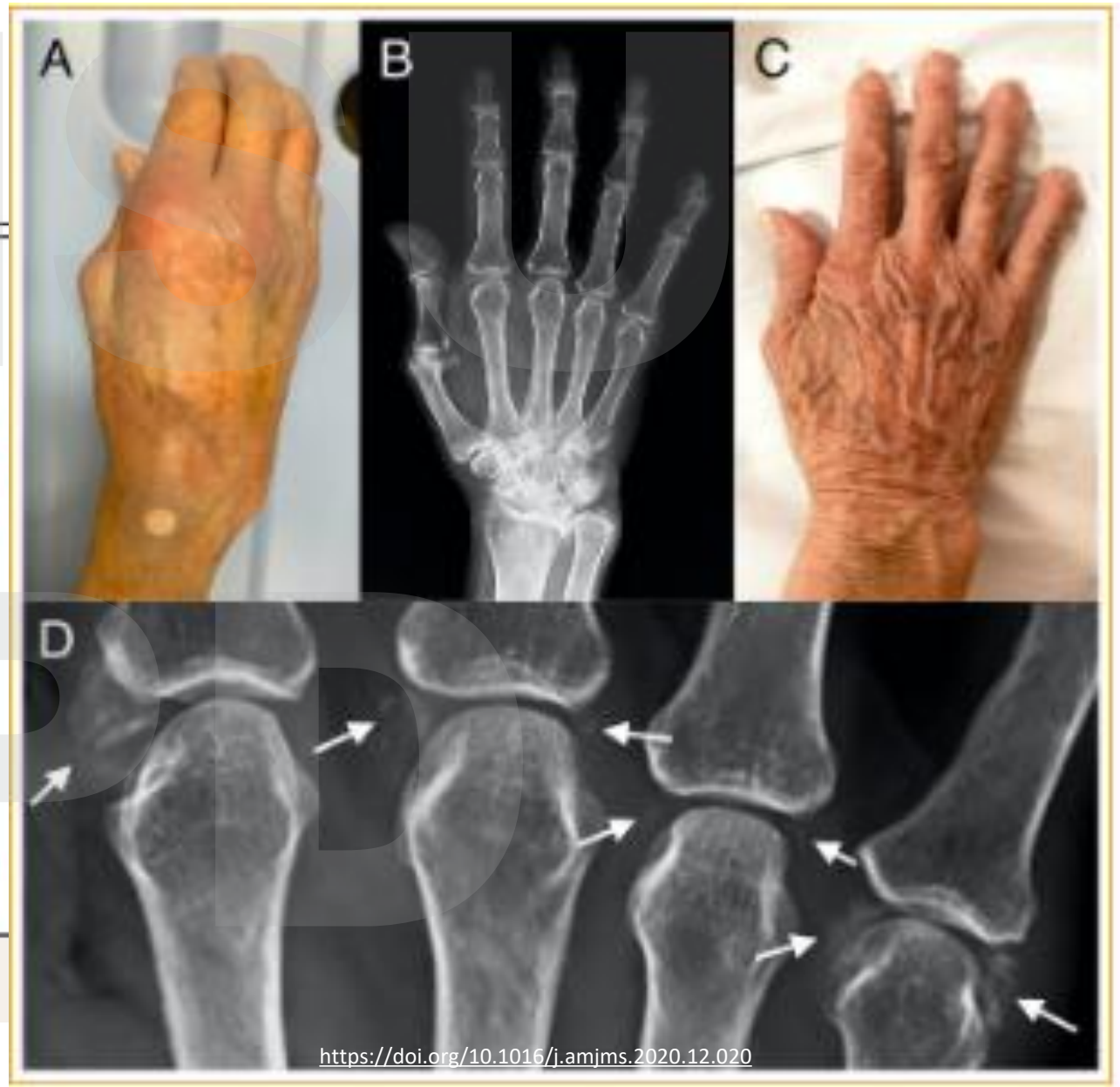


Figure 1. Calcium Pyrophosphate Deposition (CPPD).

NEJM Review



https://doi.org/10.1016/j.amjms.2020.12.020

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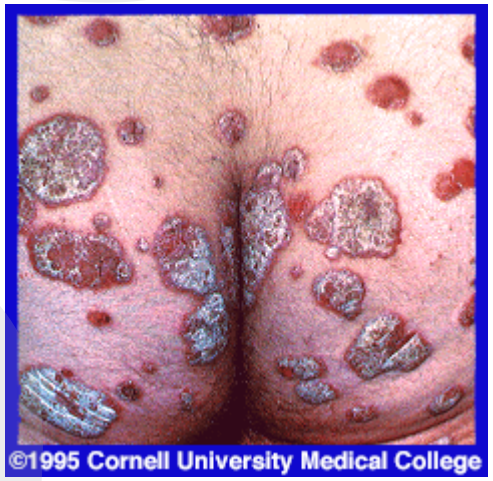
Psoriatic arthritis

- “Inflammatory arthritis associated with psoriasis”
- Psoriasis prevalence 1-3%
  - Up to 30% of patients with psoriasis can get arthritis
- Prevalence psoA 0.3-1%
- Arthritis may begin before psoriasis in 15% of cases



Psoriasis: silvery scaly rash on extensor surfaces,
Pearl: Look at the scalp line, umbilicus, and gluteal cleft, and for nail changes

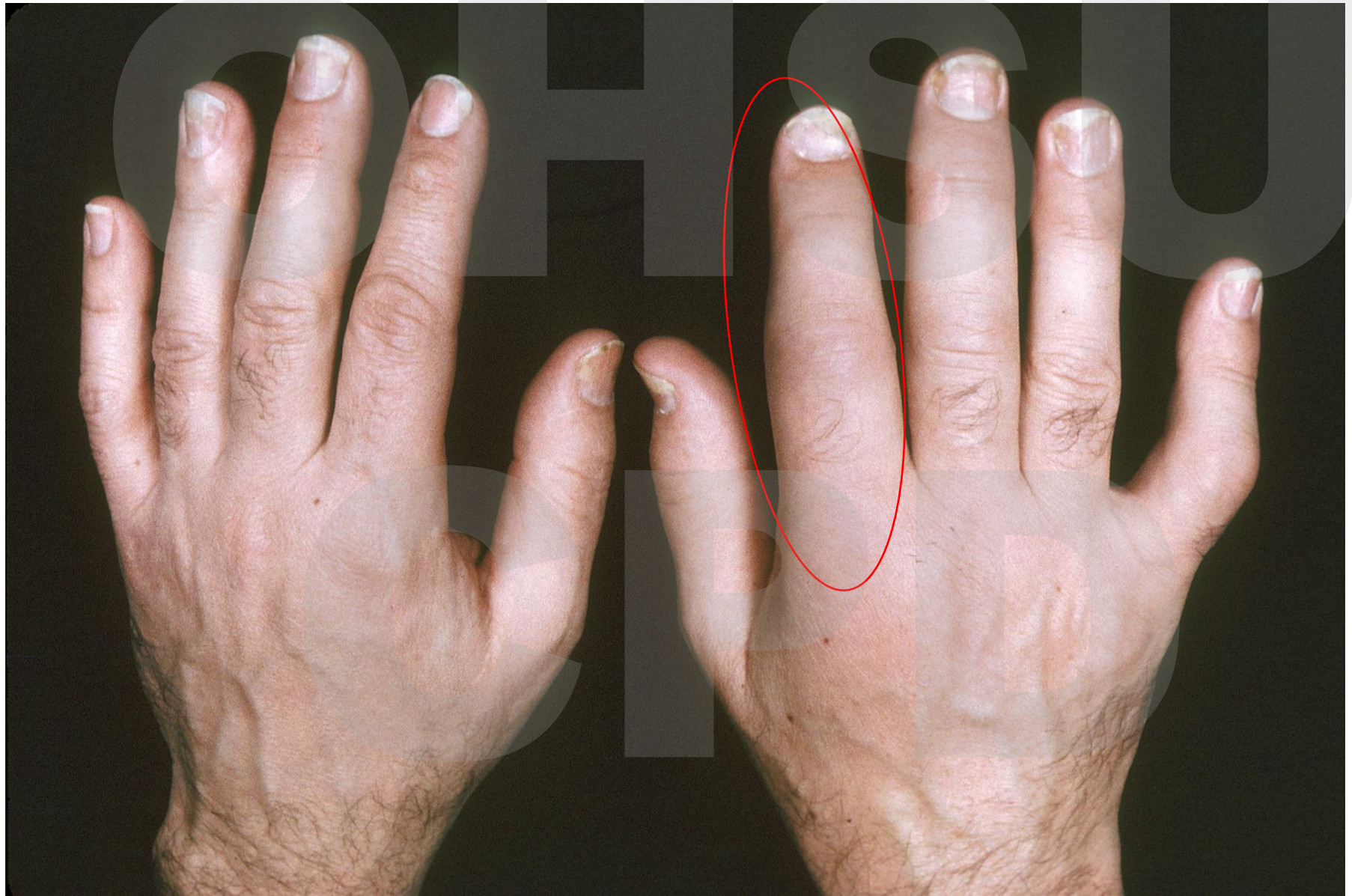
Psoriatic arthritis has 5 classic presentations

- Oligoarthritis (most common)
  - Larger joints
- Polyarthritis
  - Mimics RA
- Spondyloarthritis
  - sacroiliitis
- DIP arthritis
  - Mimics OA
- Arthritis Mutilans
  - Destructive, rare

+

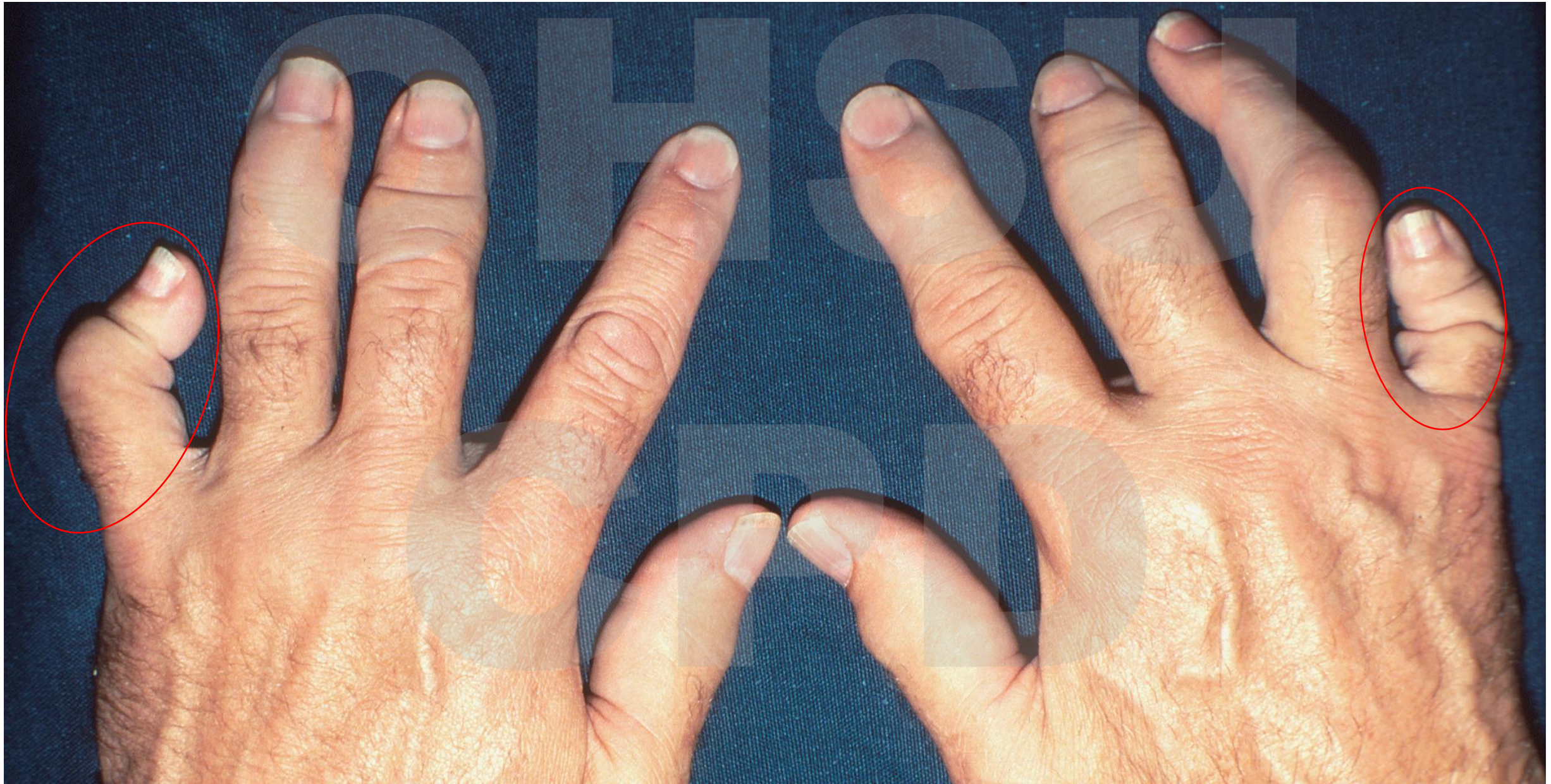
- Personal or family h/o psoriasis
- Dactylitis
- Psoriatic nail disease
- Radiographic evidence of erosions and new bone formation
- Negative RF

Psoriatic arthritis: Ray distribution

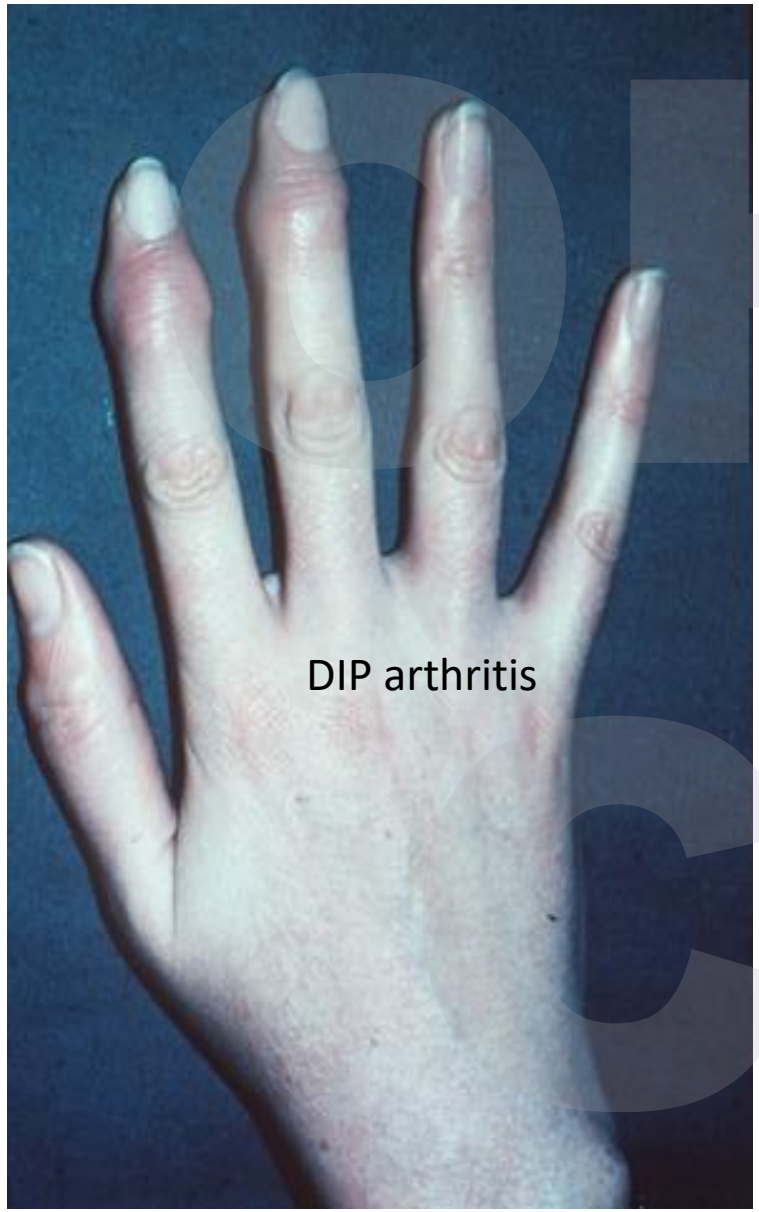


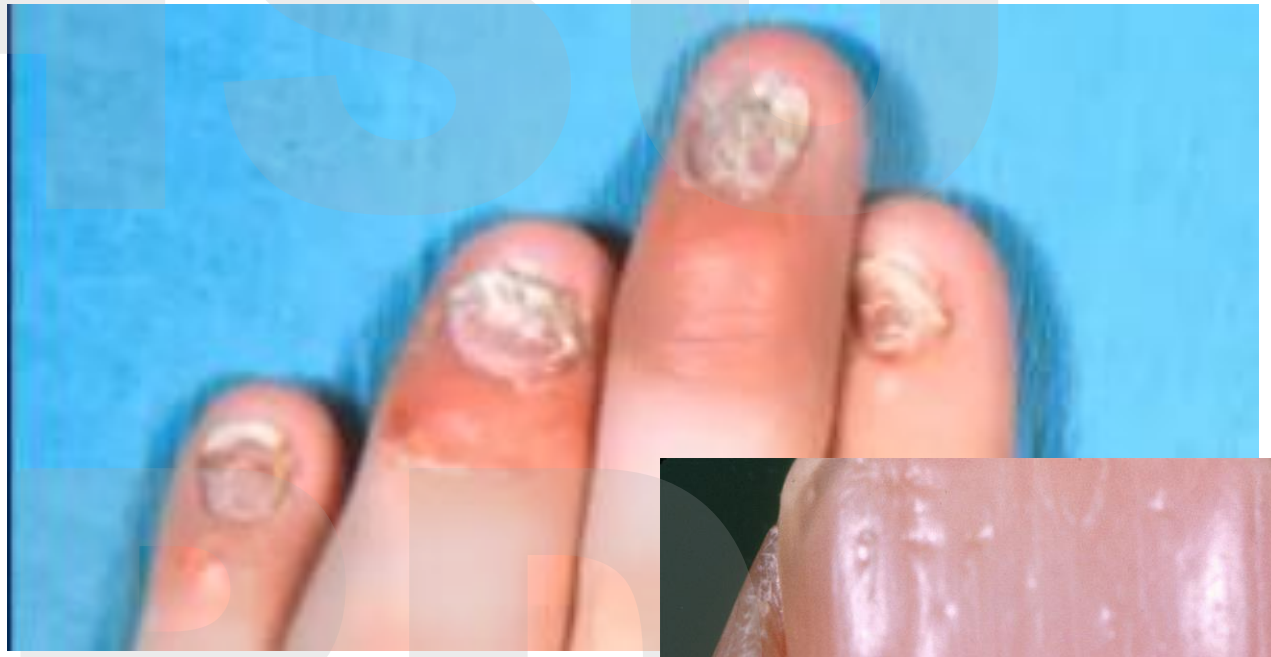
ACR Image Bank

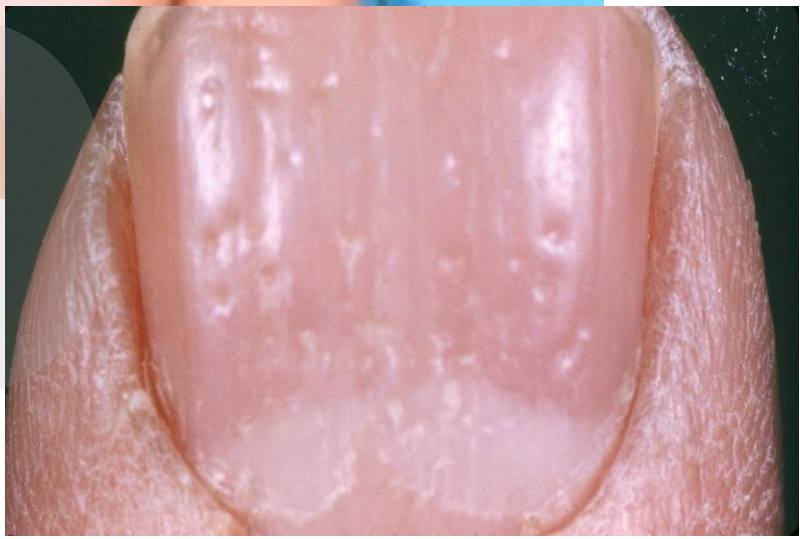
Psoriatic arthritis: Arthritis mutilans



Psoriatic arthritis: DIP disease

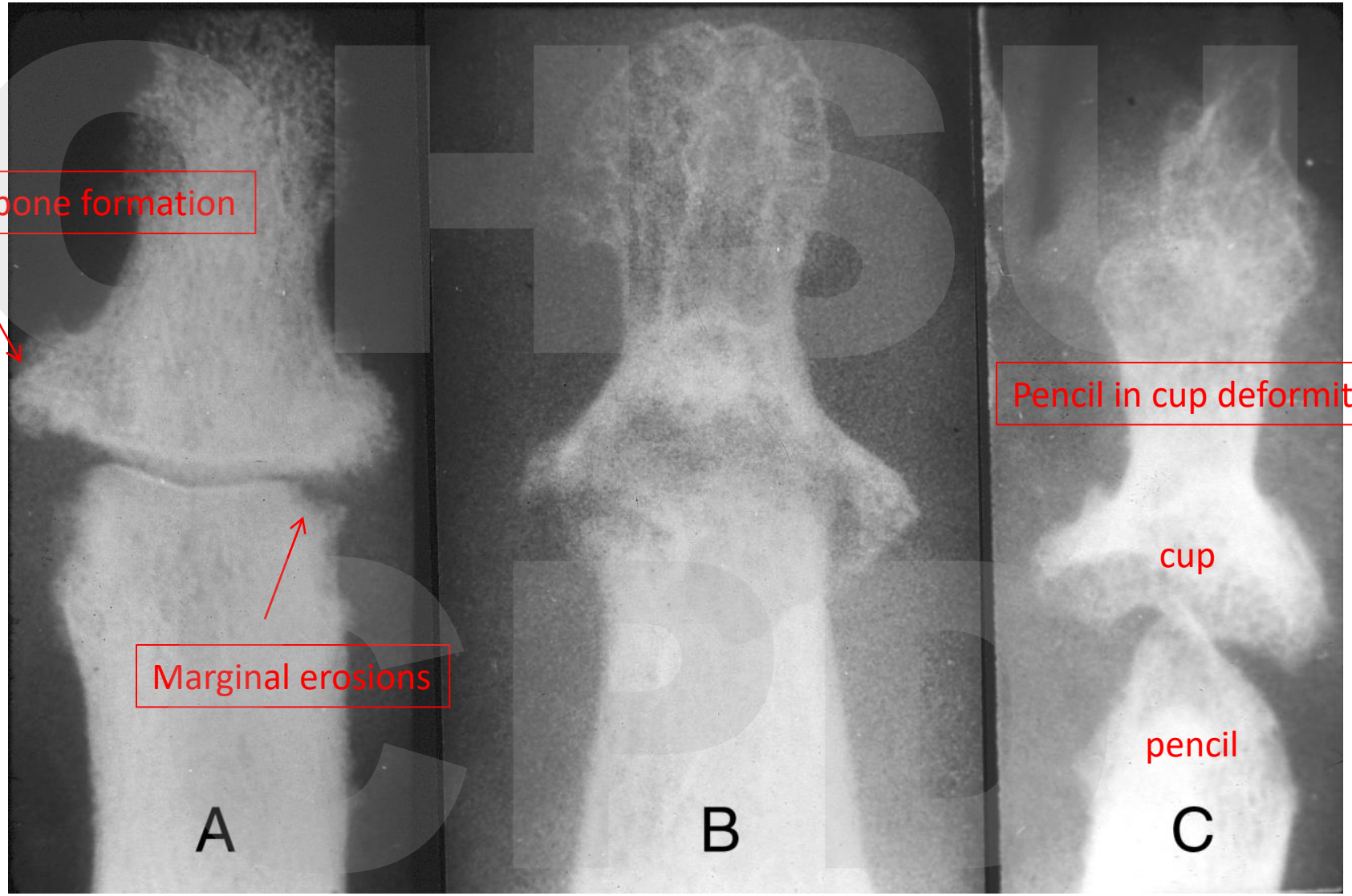






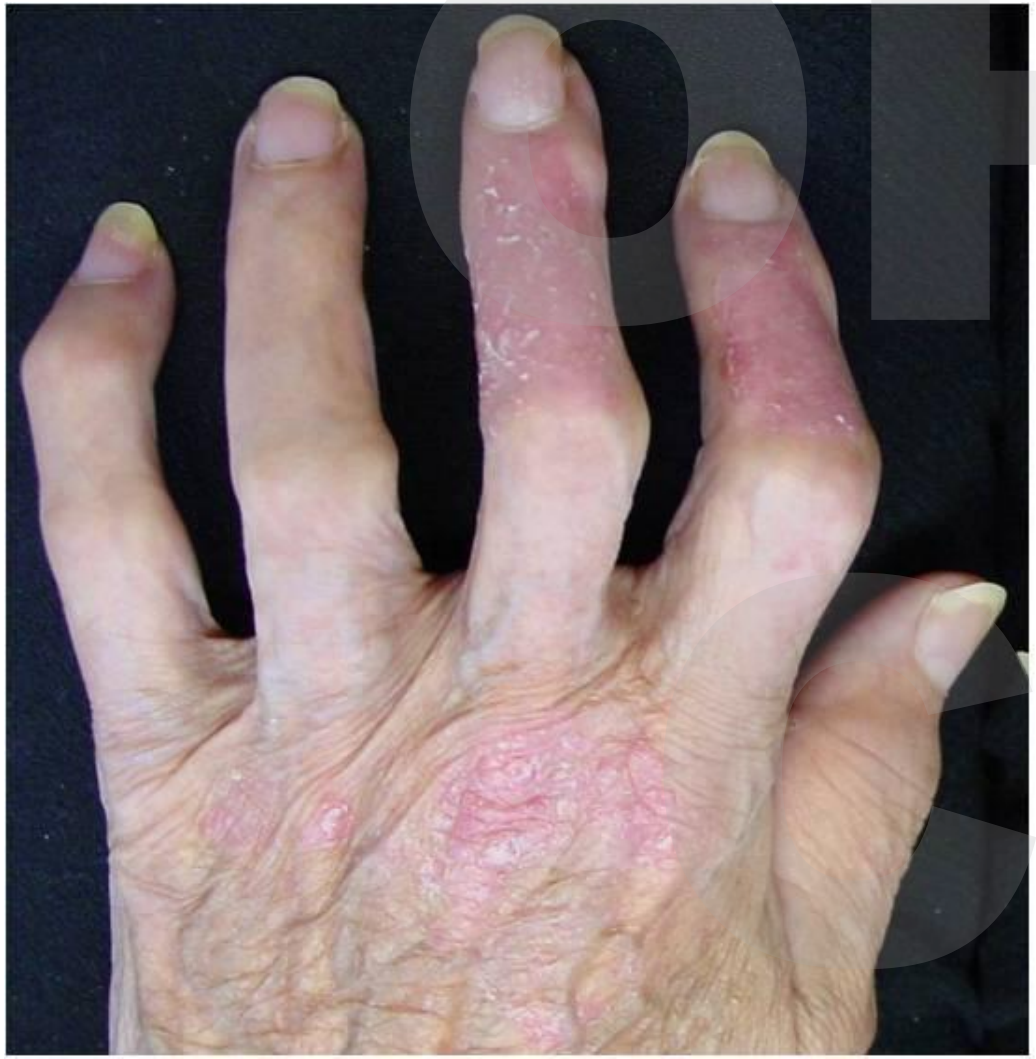
ACR Image Bank

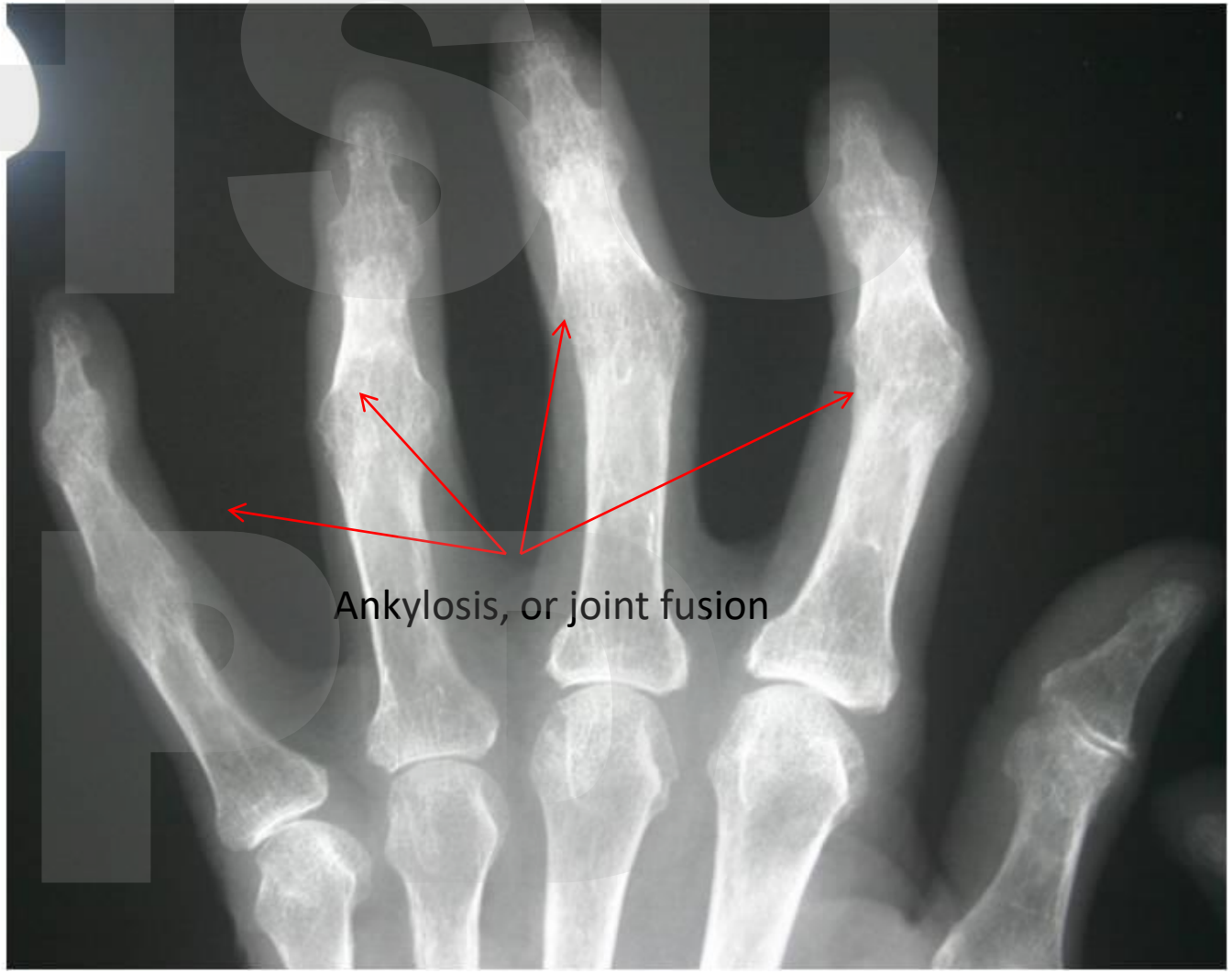
Psoriatic Arthritis: Radiographic appearance



ACR Image Bank

Psoriatic Arthritis: Joint fusion





ACR Image Bank

Psoriatic vs. Rheumatoid Arthritis

	RA	PsA
Female: Male	2-3:1	1:1
Rheumatoid Factor	Yes	No
Joint involvement	Symmetrical, small joints, wrists, MCPs, PIPs, MTPs	Asymmetrical, any joint, oligo-articular onset, ray pattern
Sacroiliitis	No	Yes up to 40%
DIP involvement	No	Yes
Nail Changes	No	Yes
Dactylitis	No	Yes
Erosions	Yes	Yes
New bone formation	No	Yes

Differential Diagnosis of a chronic inflammatory arthritis of the small joints

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- Connective tissue disease
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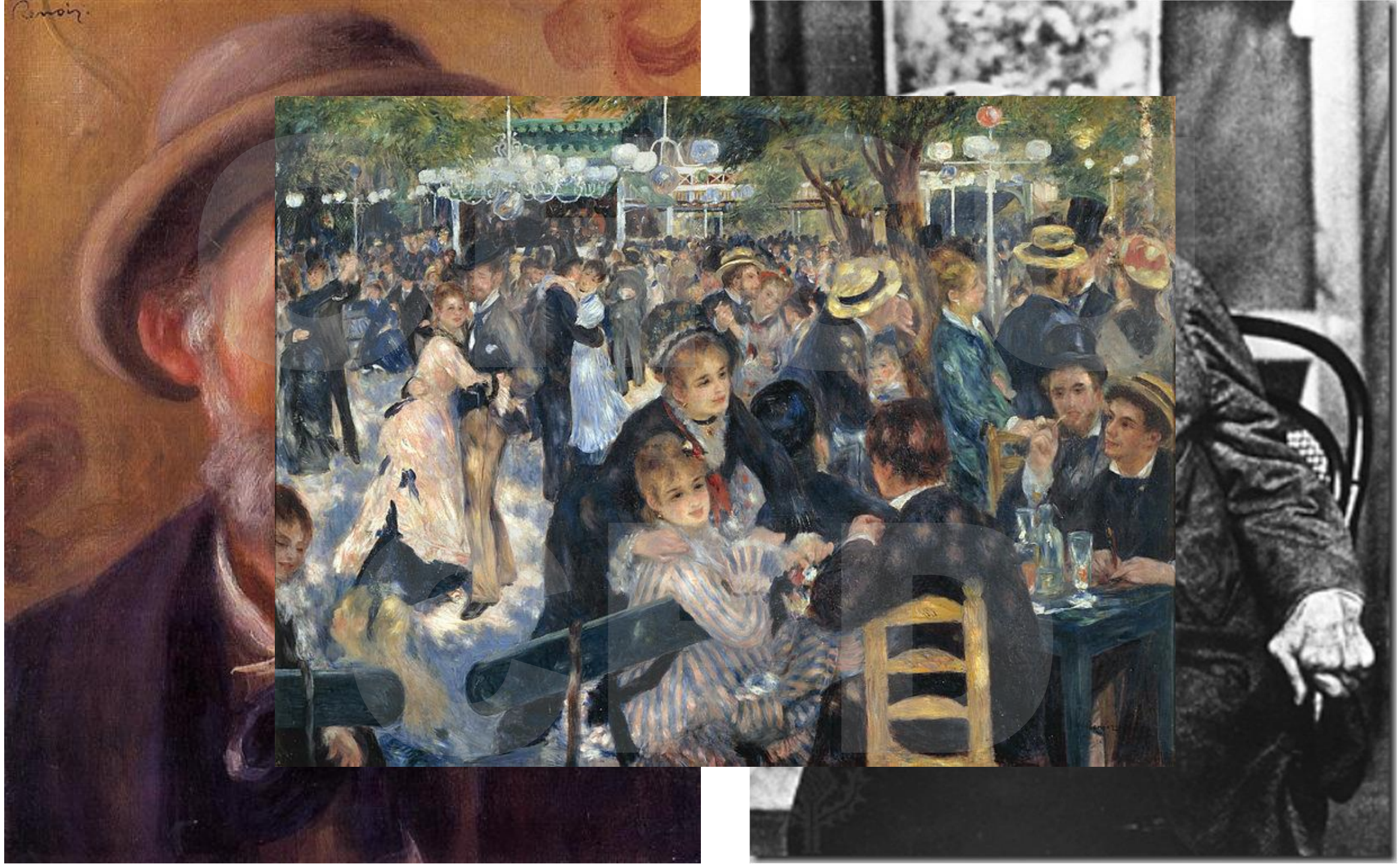
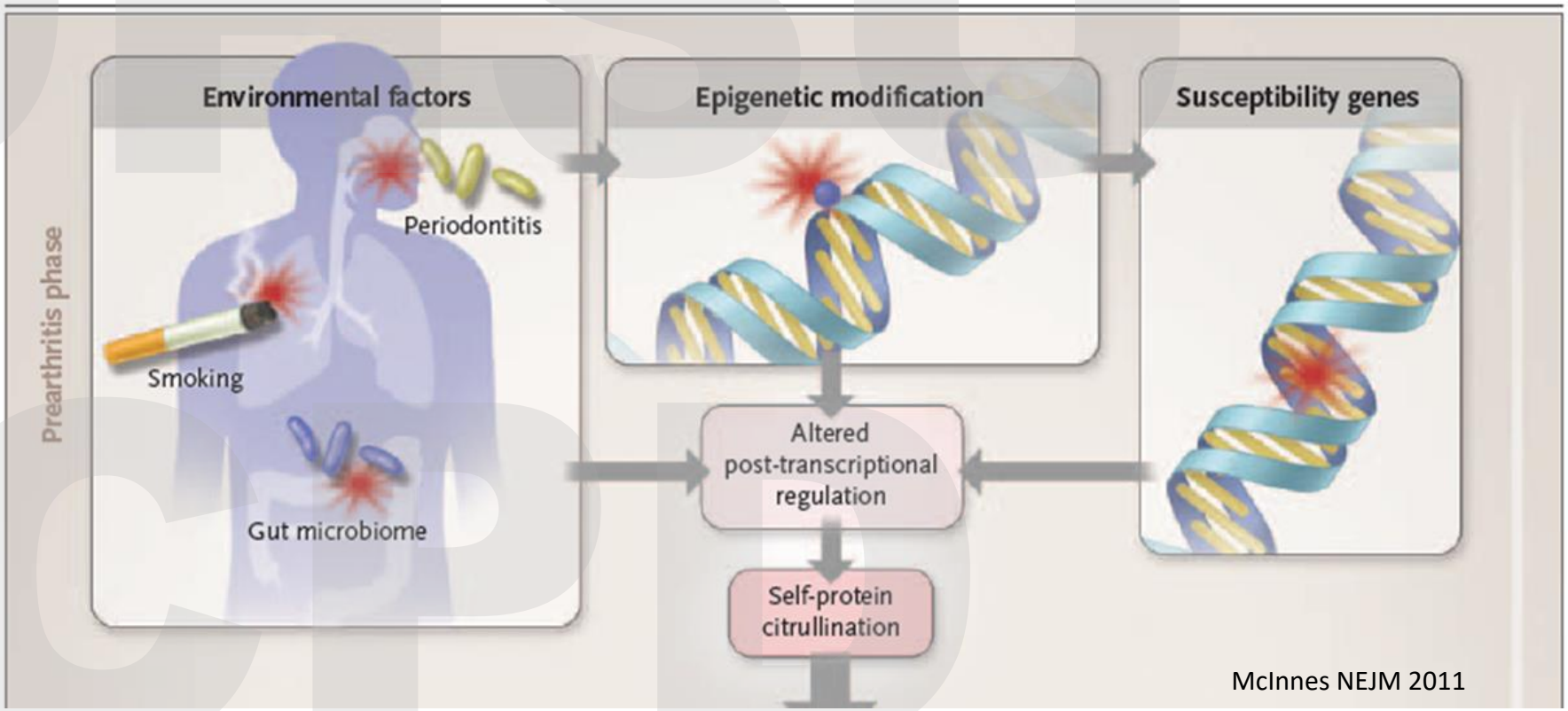


Pierre-Auguste Renoir (1841-1919)

Developed Rheumatoid arthritis ~ 1892
Severe destructive changes by ~ 1903

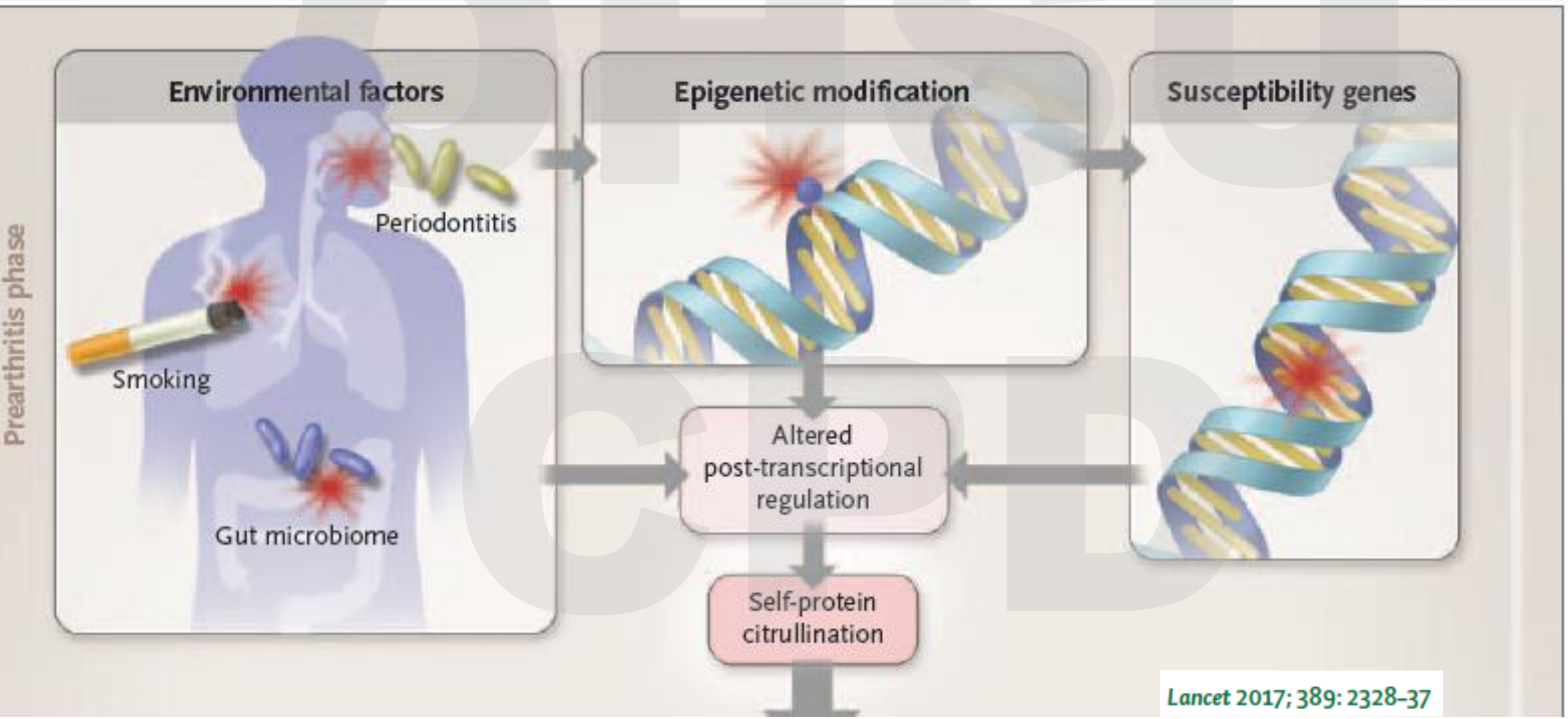
Rheumatoid arthritis

- Gradual onset, progressive daily symptoms
- Joint pain and tenderness
- Morning stiffness > 45 min
- Fatigue
- Joint swelling
- Decreased function

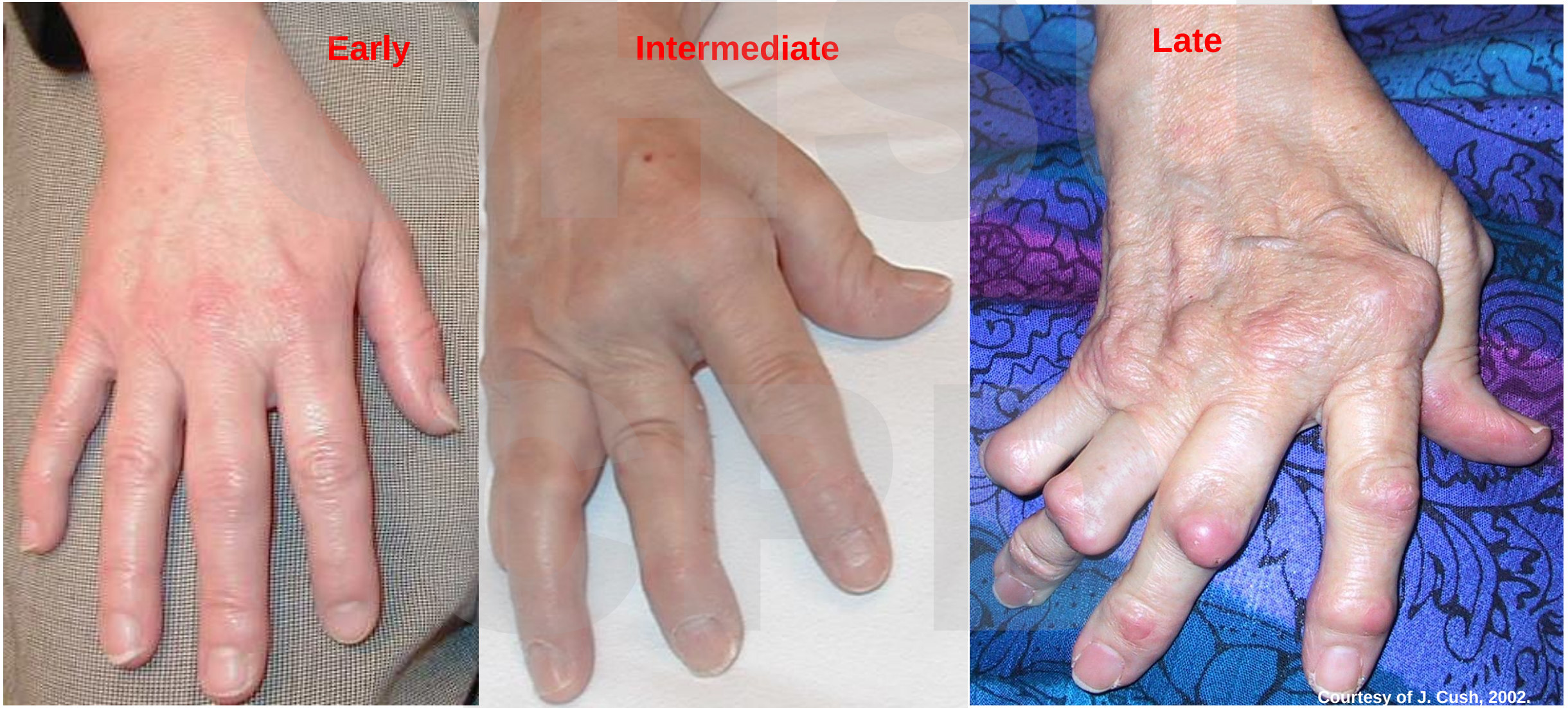


McInnes NEJM 2011

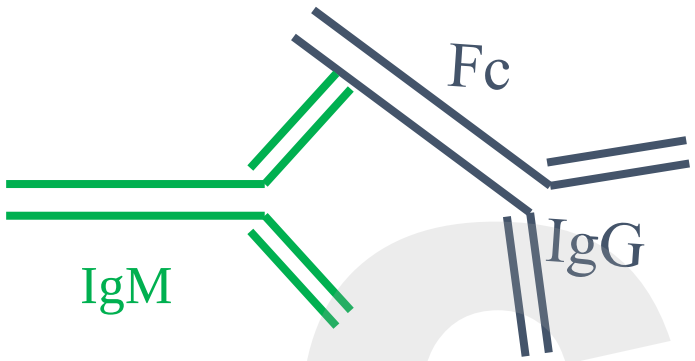
Pathogenesis of Rheumatoid Arthritis



Stages of untreated RA

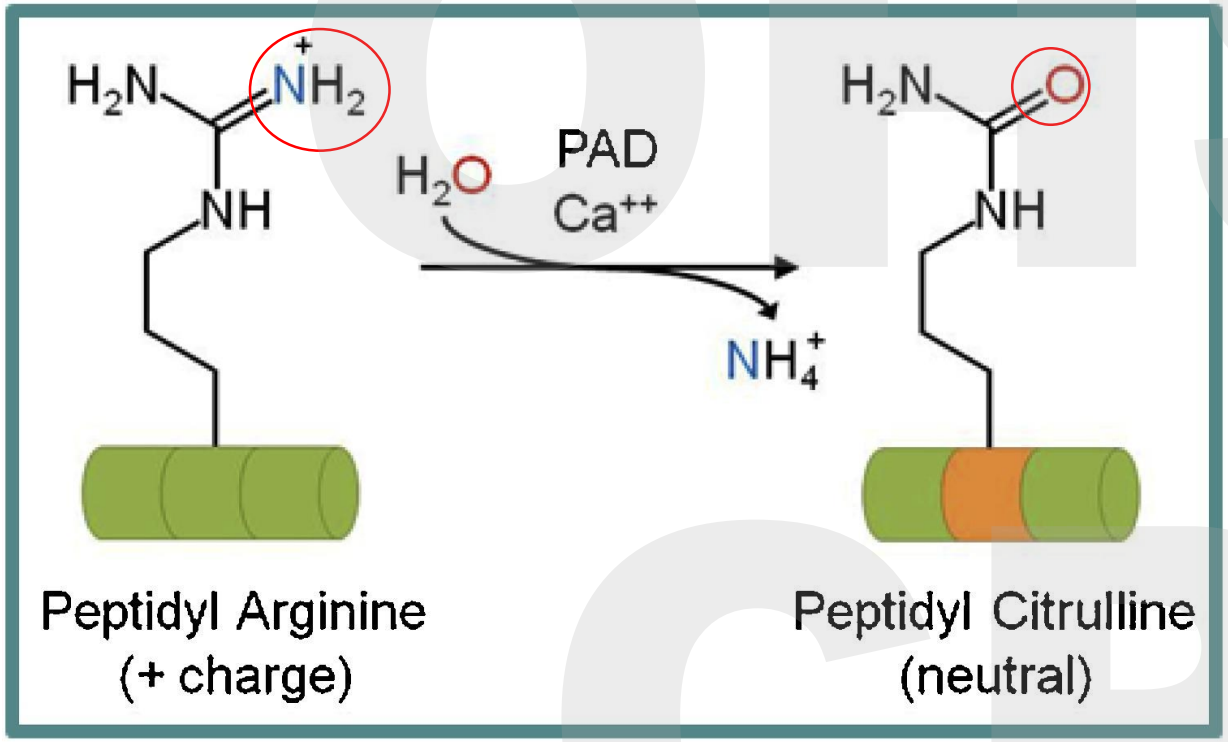


Serologic Testing in RA: Rheumatoid Factor



- Sensitivity 60-80%
- Specificity <70%
- Other causes of +RF
  - Infections
  - Malignancy
  - Other rheumatic diseases
  - Age

Serologic Testing in RA:
Anti-cyclic citrullinated peptide antibody (CCP antibody)



PAD = peptidylarginine deiminase

- Implicated in the pathogenesis of RA
- Sens 70% Spec 95%
- 40% of RF negative patients are ACPA+
- Detected in preclinical state
- Predicts more severe course and erosive disease

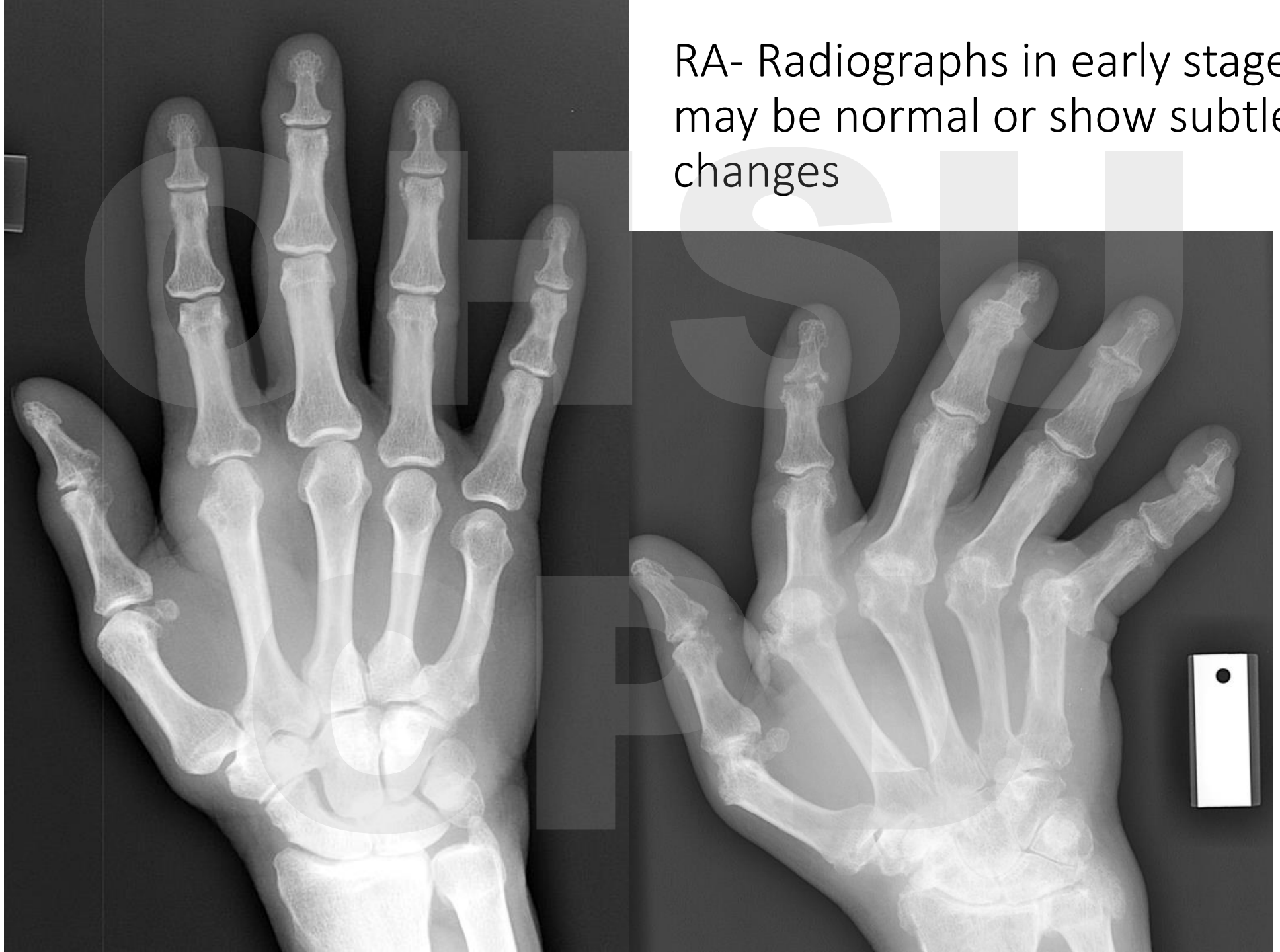
Citrullination:

- Post translational deamination of arginine to citrulline
-Occurs during cell-death and tissue inflammation
-Important consequences for the structure and function of proteins
-New epitopes, immunogenic

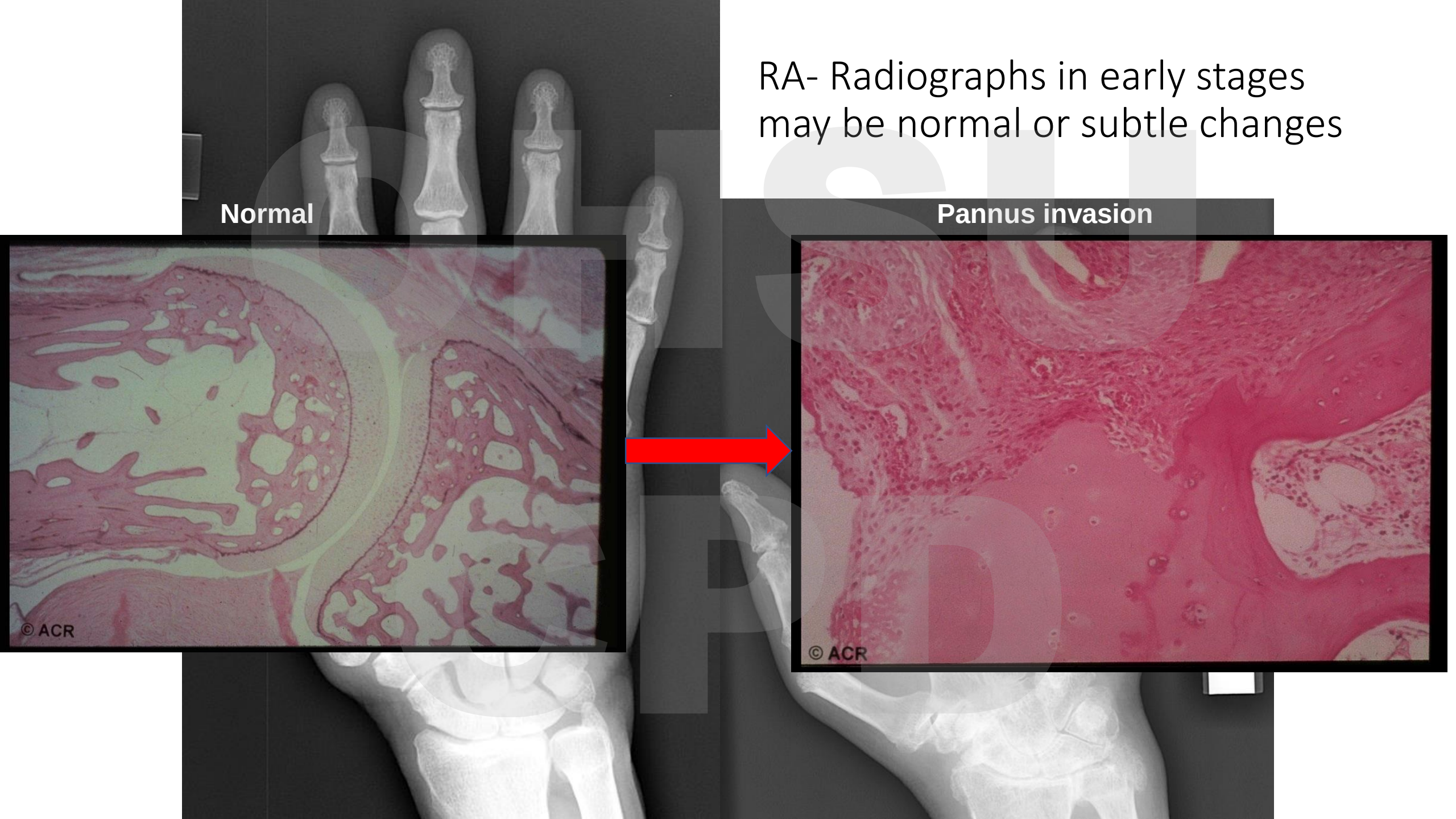
Negative RF and CCP antibody do not rule out RA

- 15% of patients with RA are RF and CCP antibody negative
  - SERONEGATIVE RA
- Exam is key!

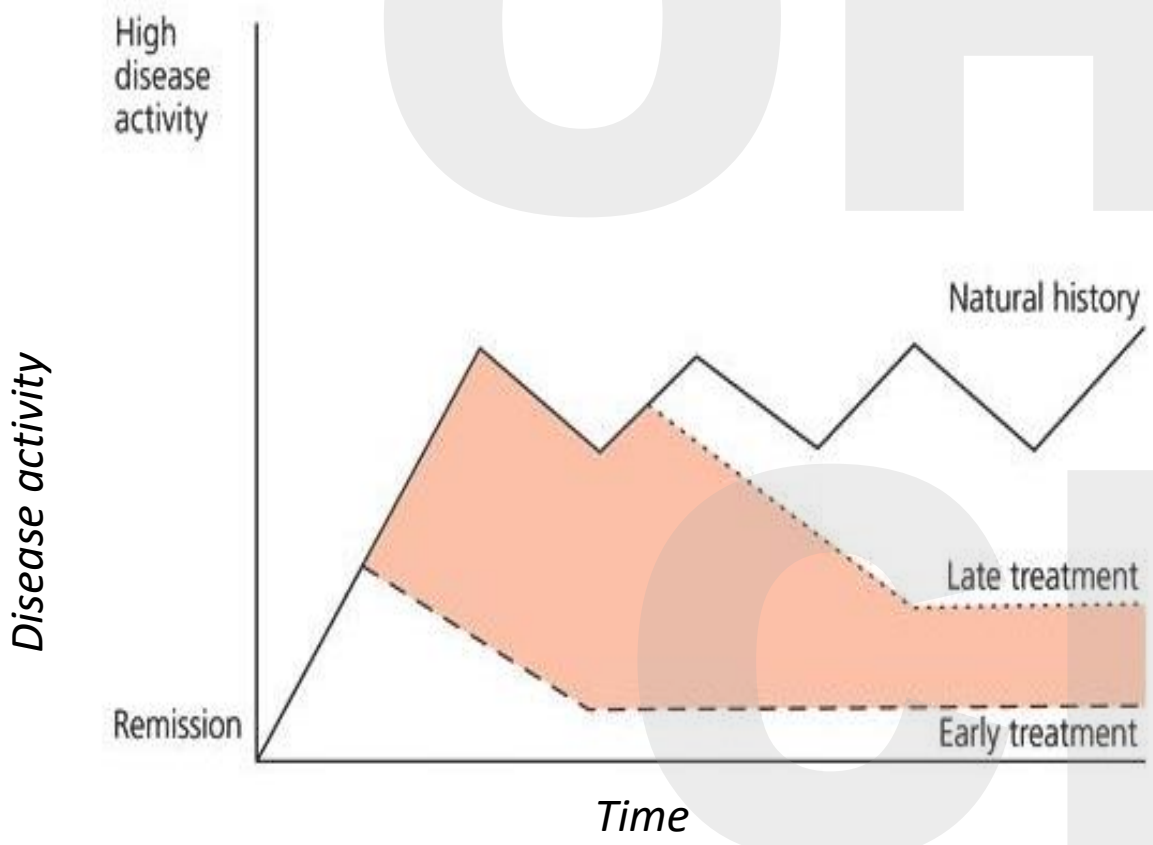
RA- Radiographs in early stages may be normal or show subtle changes



RA- Radiographs in early stages may be normal or subtle changes



Treatment approach

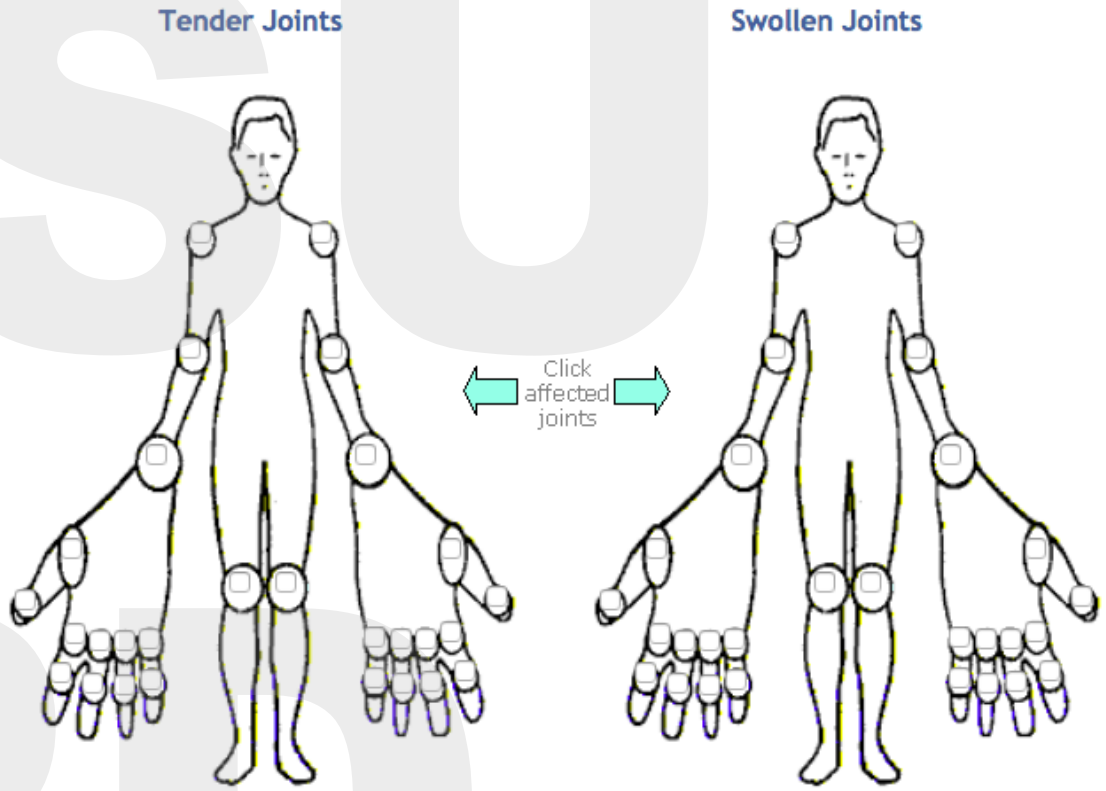


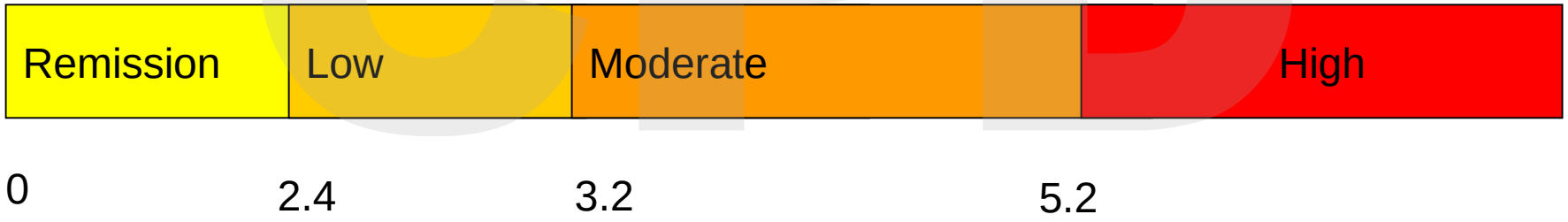
1. Goal is to minimize area under the curve
2. Early diagnosis and treatment:
   - Aim to treat within 3-6 months of symptom onset
   - Early use of DMARDs is associated with more rapid and sustained response

Roberts LJ, et al. Early combination disease modifying antirheumatic drug treatment for rheumatoid arthritis. MJA 2006;184:122–5.

Treatment Strategies

- Diagnose early!
- Start disease modifying therapy immediately
- Avoid prednisone
- Treat-to-target: Aim for low disease activity or remission
  - “Doing well” is not good enough!





Disease-Modifying Anti-Rheumatic Drugs *DMARDS

Oral non-biologics
Methotrexate
Sulfasalazine
Hydroxychloroquine
Leflunomide
Azathioprine

Parenteral Biologics:

TNF inhibitors
Etanercept
Infliximab
Adalimumab
Certolizumab
Golimumab

IL-1 Inhibitor
Anakinra

IL-6 Inhibitor
Tocilizumab
Sarilumab

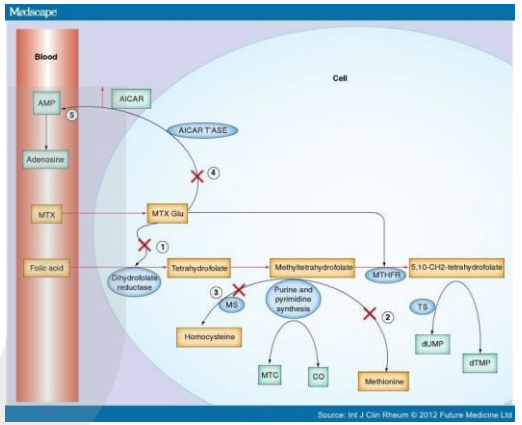
B-cell depletion
Rituximab

T-cell Co-stimulation Blockade
Abatacept

Oral Targeted SYnthetic Drugs:

JAK-inhibition
Tofacitinib
Baricitinib
Updacitinib

Anchor Drug in RA: Methotrexate



Prerequisites

- Normal cbc
- Normal LFTs
- eGFR>50
- Not pregnant or trying to get pregnant
- HCV, HBV negative
- No etoh

Starting dose

- Methotrexate 15 mg ONCE every 7 days
- Folic acid 1 mg daily

Monitoring

- Monitor cbc, LFTs, creatinine q 4-12 weeks
- Escalate dose up to 25 mg qwk
- Use SQ rather than oral
- Vaccinate

How can primary care and rheumatology work together to improve outcomes in RA?

Cardiovascular health

Smoking cessation

Immunizations

Bone Health

Final Words

- Radiographic findings of osteoarthritis are common and may not be the source of musculoskeletal pain
- Ask about inflammatory symptoms: prolonged AM stiffness, rapid/progressive, swelling/redness, limited function
- Look for synovitis on exam
- Ask about extra-articular symptoms
- Test serologies with a differential diagnosis in mind: RF, CCP, ANA
- In general, don’t order ENA sub-serologies if the ANA is negative

QUESTIONS?
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