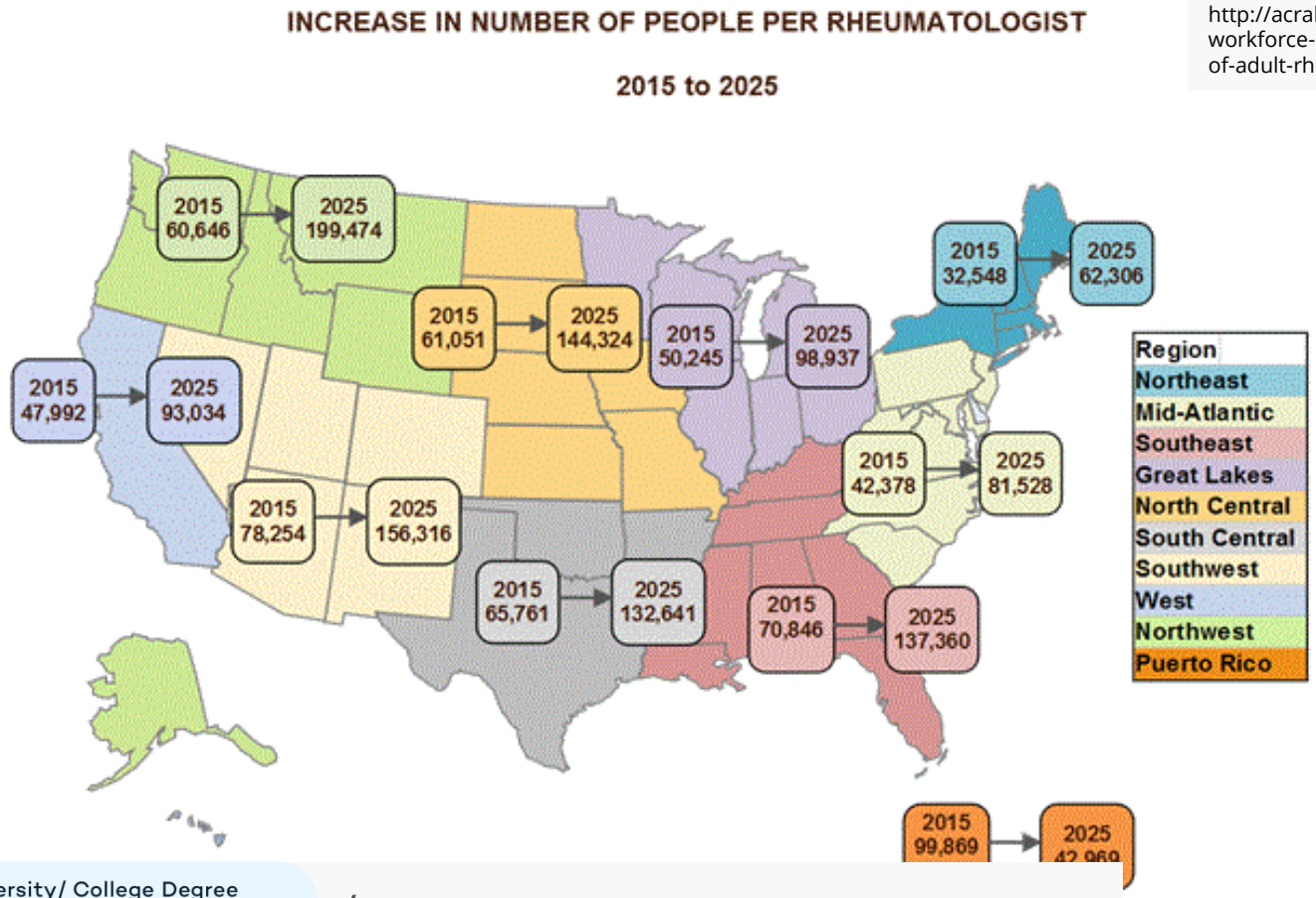
Virginia Mason™

Inflammatory Arthritis

Erin M. Bauer MD
Rheumatology
May 2023

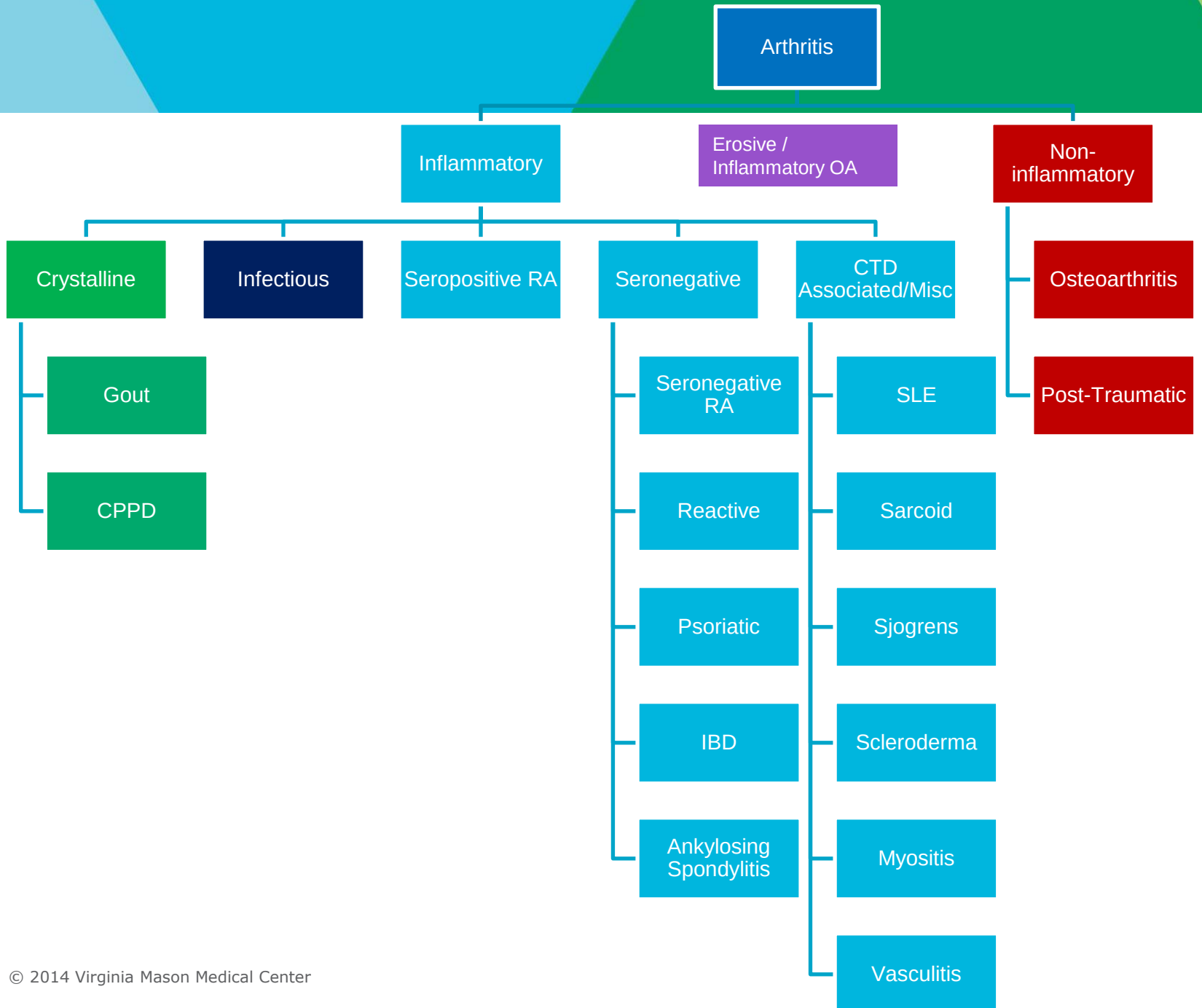
Figure 1. Adult Rheumatologists per Population, 2015 compared to 2025



Lawrence-Wolff K, Hildebrand B, Monrad S, Ditmyer M, Fitzgerald J, Erickson A, Bass AR, Battafarano D. 2015 ACR/ARHP Workforce Study in the United States: A Maldistribution of Adult Rheumatologists [abstract]. *Arthritis Rheumatol.* 2016; 68 (suppl 10). http://acrabstracts.org/abstract/2015-acrarhp-workforce-study-in-the-united-states-a-maldistribution-of-adult-rheumatologists/. Accessed January 17, 2017.

Agenda

- Inflammatory Arthritis
- Laboratory work up
- Radiographic work up
  - RA
  - PsA
  - SpA



Inflammatory vs. Non-inflammatory joint pain

Evaluation of joint pain
- History
- Physical Exam
- Serologic work up
- Radiographic work up

Crystalline Arthropathies

Inflammatory vs. Non-inflammatory joint pain

Feature	Inflammatory Joint Pain	Noninflammatory Joint Pain	Soft Tissue Injury Tendon/Bursa, etc.
Symptoms			
Morning stiffness	Usually > 30 min	Local usually < 30 min	Localized and brief
Constitutional symptoms	Present (fever, malaise)	None	None
Time of major discomfort	After prolonged inactivity	After prolonged use	During and after use
Locking/instability	Unlikely in acute joint disease	Suggests internal joint derangement	Unusual unless tendon damage/tear present
Signs			
Swelling	Common	Can be bone	Unusual
Tenderness	Diffuse over joint space	Mild over joint line	Localized periarticular
Inflammation	Common	Unusual	Over tendon/bursa
Instability	Uncommon	Occasional	Uncommon
Multisystem disease	More common	No	Unusual

*Adapted from 1996 ACR guidelines for evaluation of adults with acute musculoskeletal symptoms.
From Schmerling R, Fuchs H: Guidelines for the initial evaluation of the adult patient with acute musculoskeletal symptoms, *Arthritis Rheum* 39:1–8, 1996.

HPI:

- Age, occupation, and social, drug, travel and sexual history
- Time of day when pain is the worst
- Aggravating and relieving factors
- Swelling/redness/warmth?
- Presence of systemic symptoms
  - Ocular, oral, respiratory, gastrointestinal or skin symptoms
- Recent infection or trauma?

Case 1

24 yo F with asthma presenting to primary care clinic with 2 months of “joint pain”

Factors for Assessment	Answer eliciting questionnaire
P- Palliative factors	‘What makes it better?’
Provocative factors	‘What makes it worse?’
Q- Quality	‘What exactly is it like?’
R- Radiation	‘Does it spread anywhere?’
S- Severity	‘How severe is it?’ ‘How much does it affect your life?’
T- Temporal factors	‘Is it there all the time or does it come and go?’

Case 1

24 yo F with asthma presenting to primary care clinic with 2 months of “joint pain”.

P: “Taking NSAIDs first thing in the AM. I feel decent by lunch time”

Q: “Deep stiffness, achy”. “My hands, wrists and toes feel hot and full”

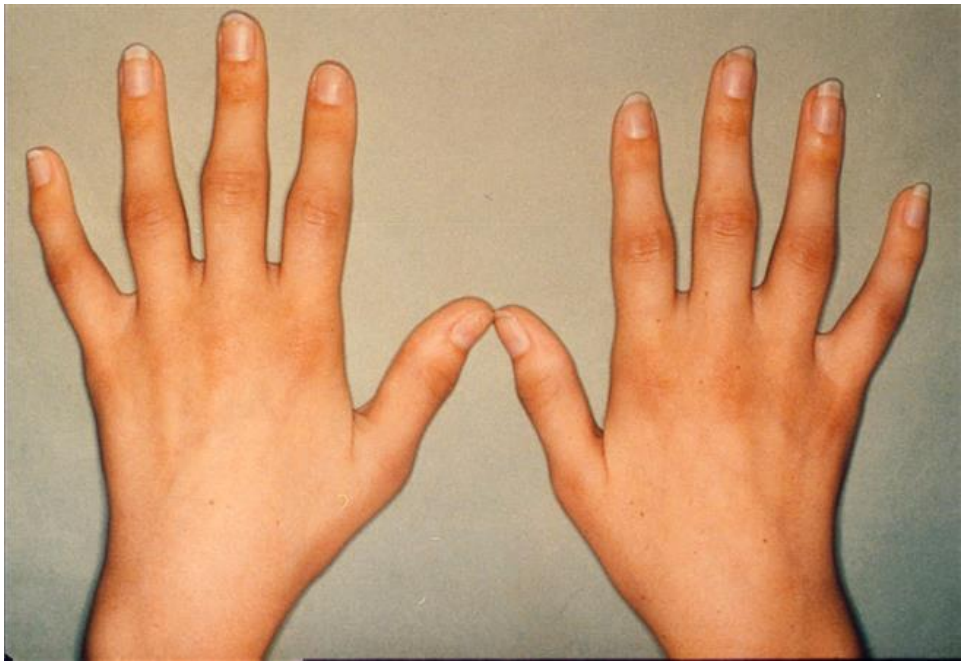
R: “Really feels deep in the joints, not spreading”

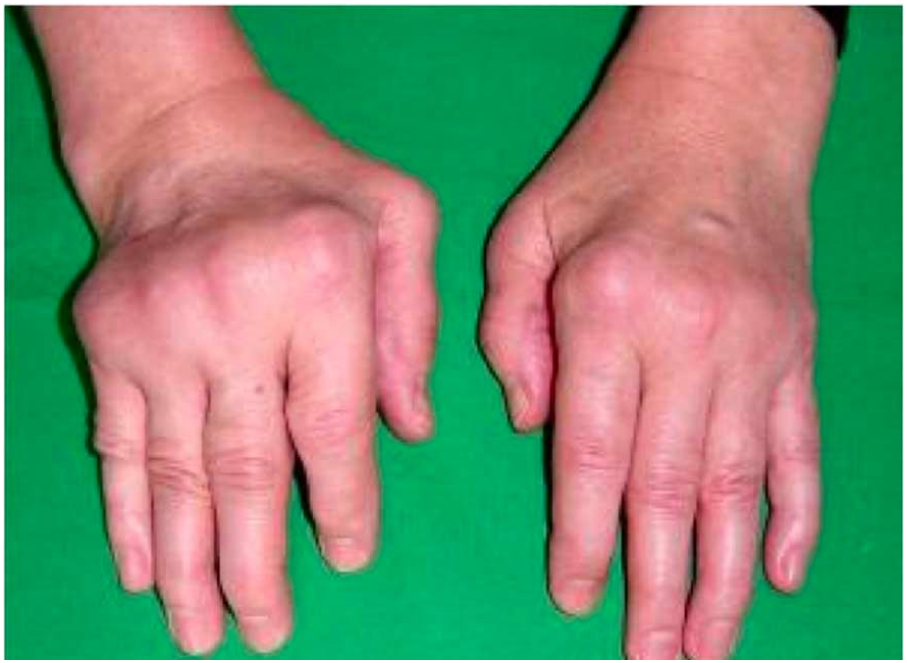
S: “Keeping me from being able to button my shirts in the morning, hard to hold a cup”

T: “Wakes me up around 3 AM, I feel better after a hot shower and stretching/2-3 hours”

Relatively sudden onset
No recent illnesses or exposures
No history of psoriasis, uveitis, inflammatory bowel disease
No family history of autoimmune disease

Case 1





On exam: fullness of the MCPs and PIPs. Tender over the radiocarpal joints and MTP 5 bilaterally

Case 1

Labs?

A. Rheumatoid Factor and CCP
B. Erythrocyte Sedimentation Rate (ESR)
C. Anti Nuclear Antibody (ANA)
D. HLA B27

Case 1

Labs?

A. Rheumatoid Factor and CCP

B. Erythrocyte Sedimentation Rate (ESR)

C. Anti Nuclear Antibody (ANA)

D. HLA B27

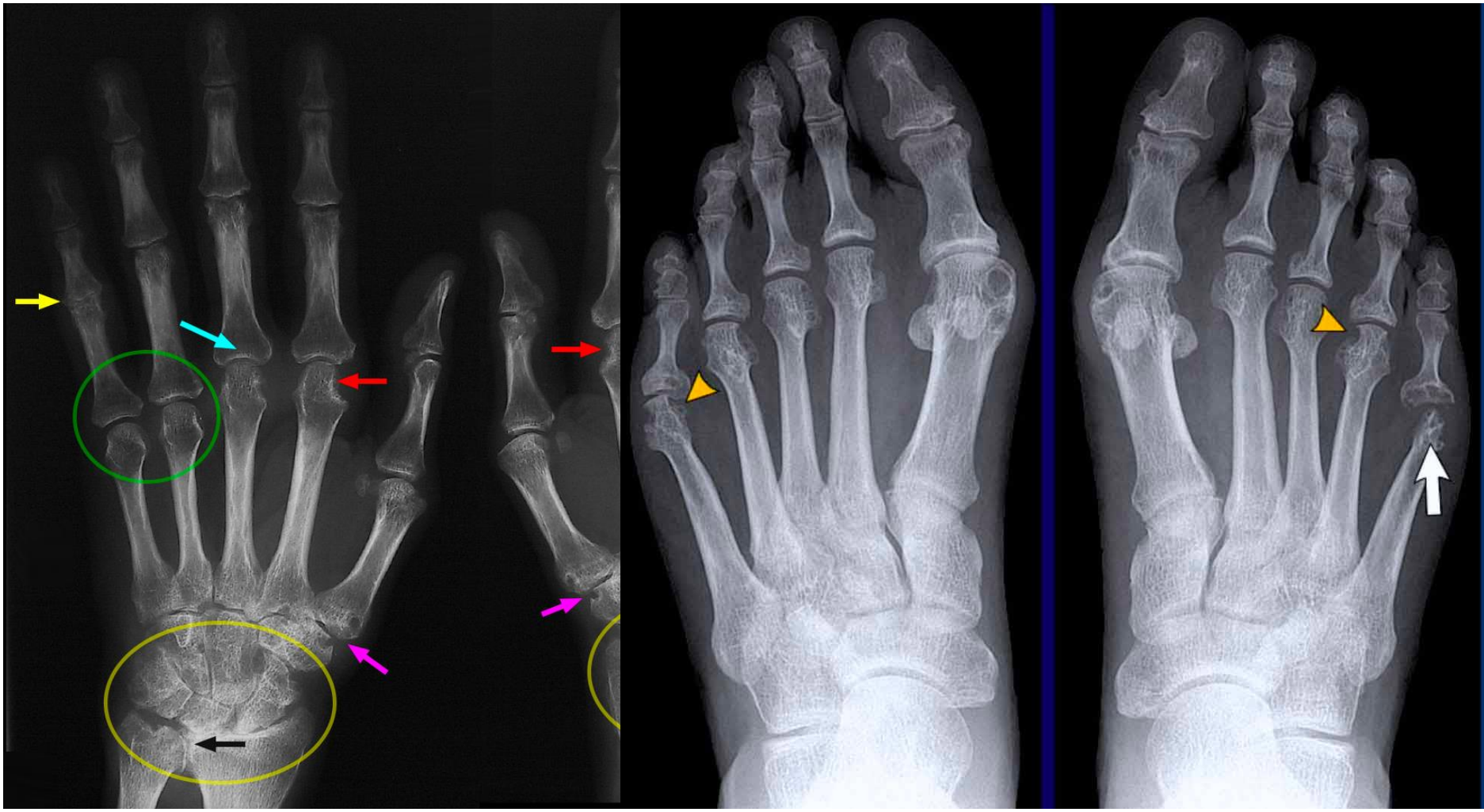
Case 1

Labs?

- RF 205 (<19), CCP 250 (<5)
- ESR: 25 (<20), CRP: 12 (<0.5)
- ANA 1:80 in homogenous pattern
- HLA B27: negative

Case 1

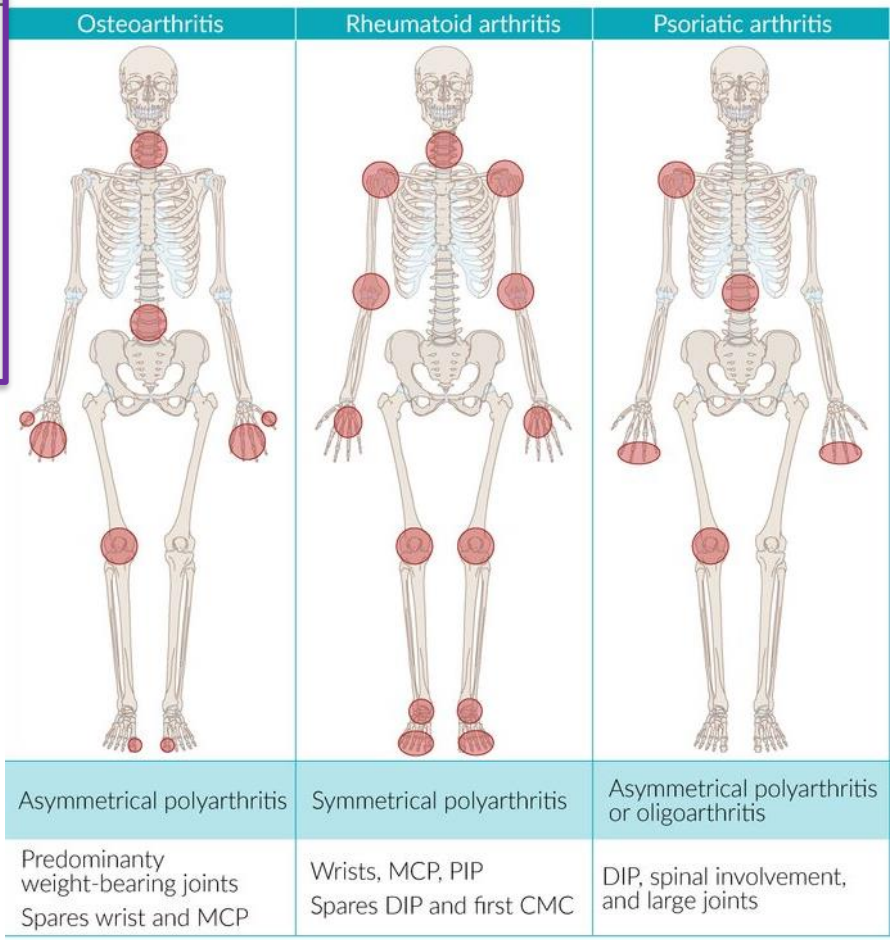
Imaging:



Classification Criteria (ACR/EULAR 2010)

Criteria	Score
Joint distribution	
1 large joint	0
2-10 large joints	1
1-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
Serology	
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
Symptom duration	
<6 weeks	0
≥6 weeks	1
Acute phase reactants	
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1

A score of six or more equates to definite RA. This requires that the patient has at least one joint with definite synovitis and that the synovitis is not better explained by another disease. The score may be retrospective or prospective. ACPA, anti-citrullinated peptide antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor.



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The major nonrheumatic diseases associated with rheumatoid factor (RF)-positivity

Condition	Frequency of RF, percent
Aging (>age 60)	5 to 25
Infection	
Bacterial endocarditis*	25 to 50
Hepatitis B or hepatitis C*	20 to 75
Tuberculosis	8
Syphilis*	Up to 13
Parasitic diseases	20 to 90
Leprosy*	5 to 58
Other viral infection*	15 to 65
Pulmonary disease	
Sarcoidosis*	3 to 33
Interstitial pulmonary fibrosis	10 to 50
Silicosis	30 to 50
Asbestosis	30
Miscellaneous diseases	
Primary biliary cholangitis*	45 to 70
Malignancy*	5 to 25
After multiple immunizations	10 to 15

* Refers to disorders that may cause symptoms suggestive of rheumatoid arthritis. The best-documented examples of viral infection (in addition to hepatitis B and C) are rubella, mumps, influenza, and HIV. Chagas' disease, Leishmaniasis, onchocerciasis, and schistosomiasis are major parasitic diseases. B cell neoplasms are the most common malignancies.

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Although ACPA testing is more specific than RF for RA, positive results can occur in other diseases:

- Primary Sjogren's Syndrome, Psoriatic Arthritis
- Tuberculosis
- Chronic lung disease (alpha-1 antitrypsin deficiency, chronic obstructive pulmonary disease

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Viral Pathogen	Characteristic Clinical Features
Chikungunya	History of travel to endemic area + history of acute febrile illness with severe polyarthritis and or tenosynovitis
Rubella	Intensely erythematous maculopapular rash that migrates from head to toes/fingers
Parvovirus	Migratory, often additive, arthralgia and arthritis with flu-like illness and variable presence of transient erythematous rash on face or extremities
Hepatitis B	HBV transmission risk factors with polyarthritis and variable presence of pruritis, urticaria
Hepatitis C	HCV transmission risk factors with tenosynovitis, arthralgia, variable presence of purpura (usually affecting lower extremities)
HIV	HIV risk factors associated with features of psoriasis or reactive arthritis

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Erythrocyte sedimentation rate (ESR)
The rate (expressed in mm/hour) at which erythrocytes suspended in plasma fall when placed in a vertical tube
Indirect measure of acute phase response- fibrinogen

Influenced by:
immunoglobulins
changes in erythrocyte size, shape, and number
age, sex, adipose tissue

Increased ESR:
- Systemic and localized inflammatory and infectious diseases
- Malignant neoplasms
- Tissue injury/ischemia
- Trauma

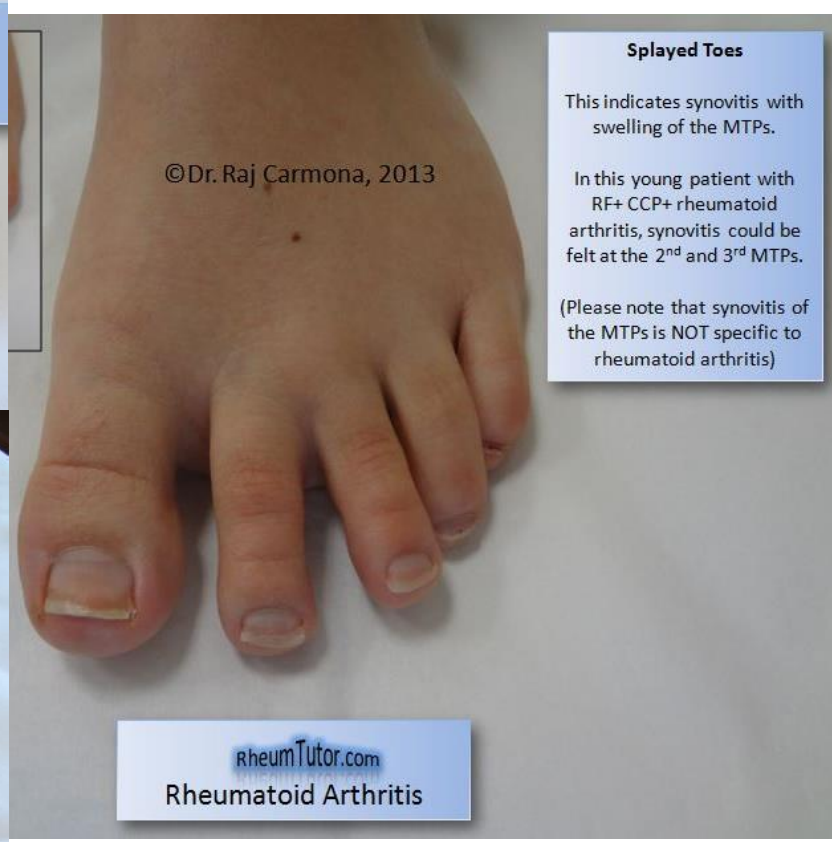
C-reactive protein
Influenced by age, sex, and ethnicity

Markedly elevated levels of CRP are strongly associated with infection

CRP both rises and falls more rapidly than the ESR


Volar subluxation of MCPs
Metacarpal heads appear prominent because proximal phalanges have subluxed under them.
Swan Neck Deformity
Extension of PIP, flexion of DIP (4th finger)
Z-deformity of Thumb
Flexion of MCP, extension of IP
©Dr. Raj Carmona, 2013


Dorsal subluxation of Ulnar head (due to interruption of radioulnar ligament).
Radial deviation of hand at the wrist
Ulnar deviation of fingers at MCPs
©Dr. Raj Carmona, 2013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Splayed Toes
This indicates synovitis with swelling of the MTPs.
In this young patient with RF+ CCP+ rheumatoid arthritis, synovitis could be felt at the 2nd and 3rd MTPs.
(Please note that synovitis of the MTPs is NOT specific to rheumatoid arthritis)
RheumTutor.com
Rheumatoid Arthritis

Case 2

55 yo M with BMI >35, hypertension, hyperlipidemia presenting with 2 years of "joint pain".

P: "Taking NSAIDs first thing in the AM which helps, feeling a little better by lunch"

Q: "Deep stiffness, achy". "Swelling in the right knee, left heel and both elbows"

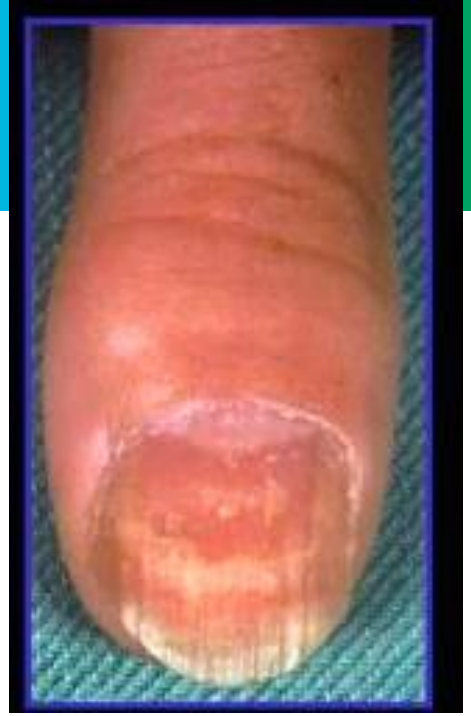
R: "The pain seems to spread from my joints up the tendons"

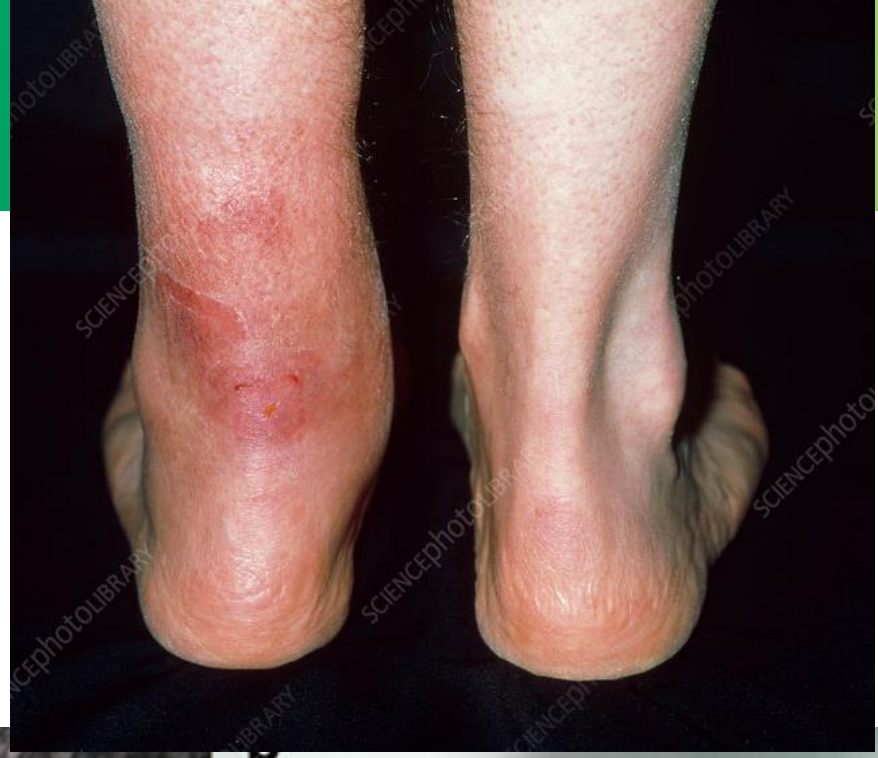
S: "Been tolerable for a couple years but getting worse last few months

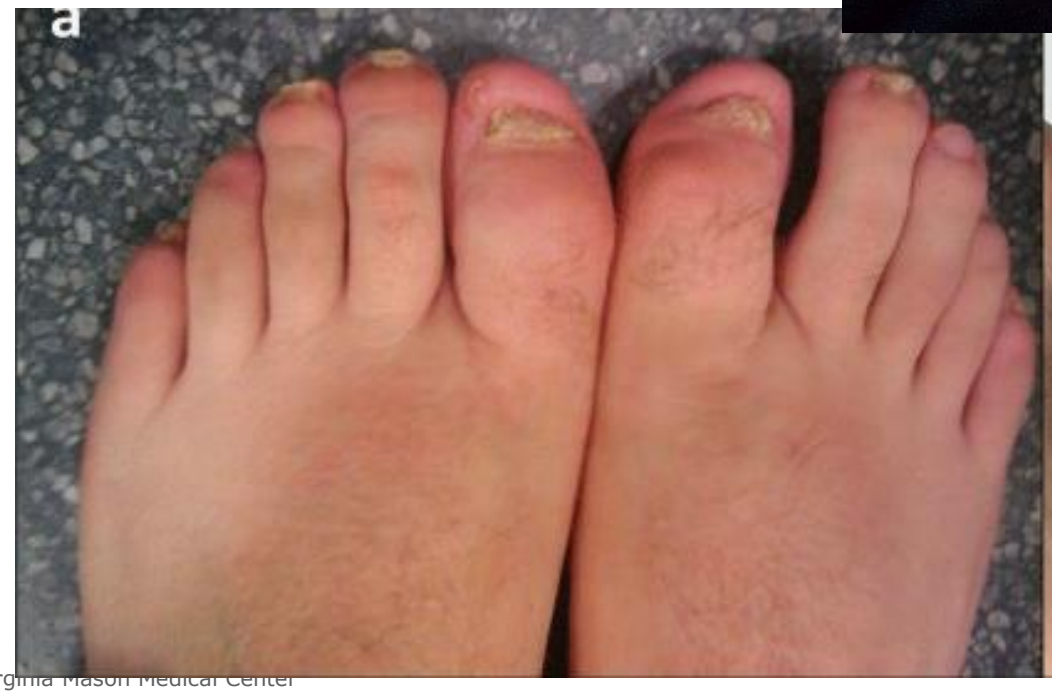
T: "Wakes me up around 5 AM, I feel better after a hot shower and stretching/2-3 hours"

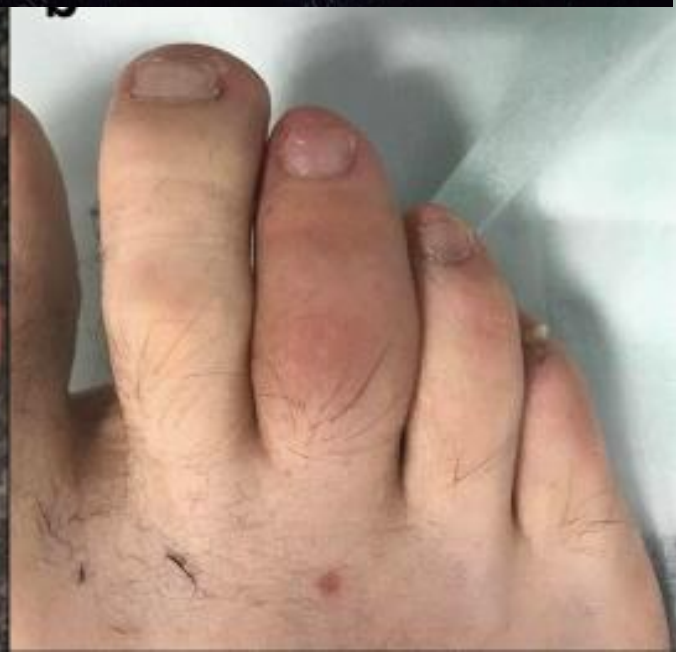
No recent illnesses or exposures
No rashes
Mother with psoriasis, brother with ulcerative colitis

Case 2









Case 2

Labs?

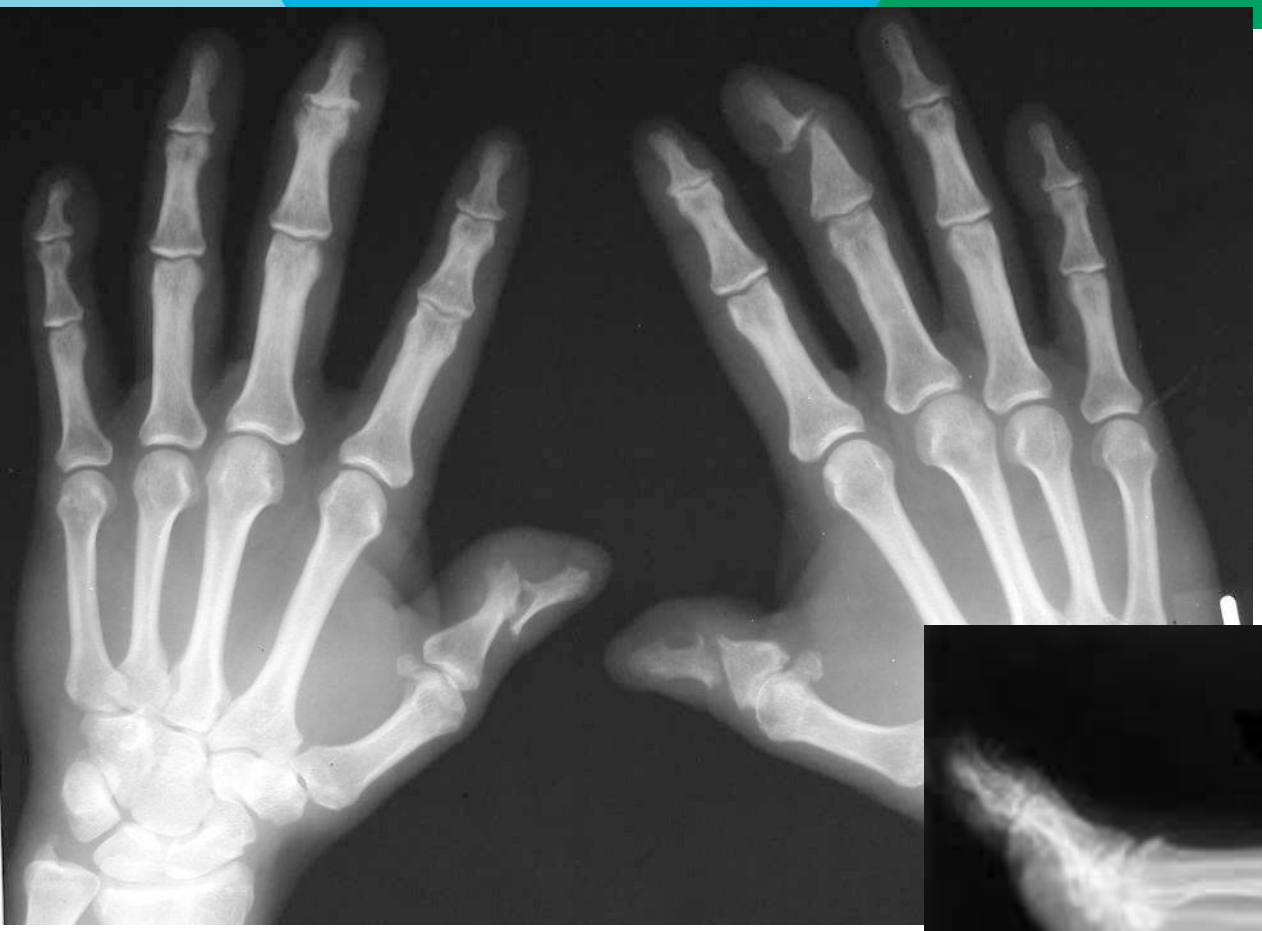
A. Rheumatoid Factor and CCP
B. Erythrocyte Sedimentation Rate (ESR)
C. Anti Nuclear Antibody (ANA)
D. HLA B27

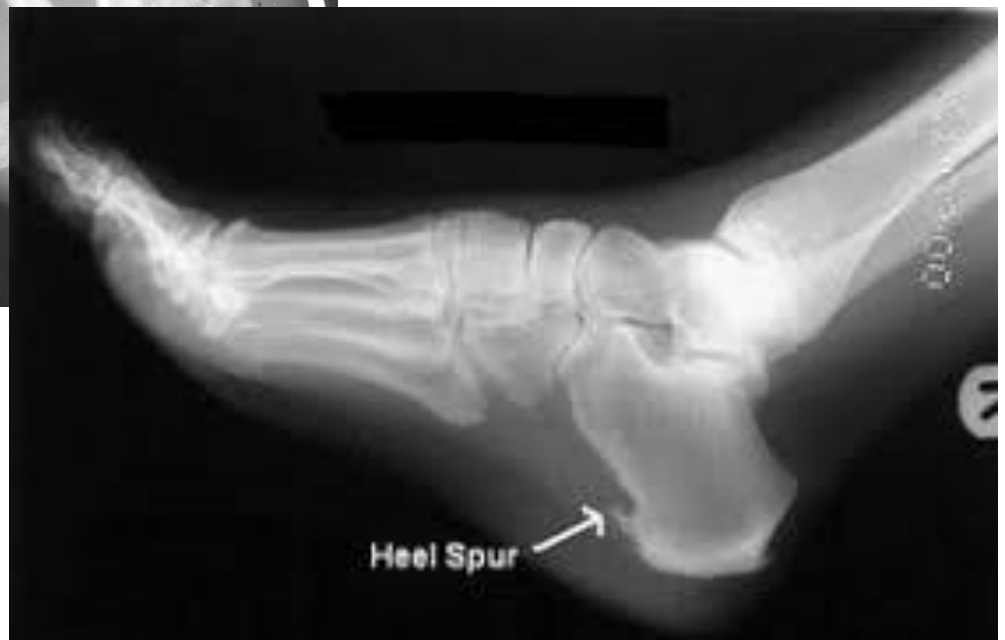
Case 2

Labs?

A. RF/CCP negative
B. ESR/CRP normal
C. ANA 1:80 homogenous
D. HLA B27: negative

Case 2 Imaging





Classification Criteria

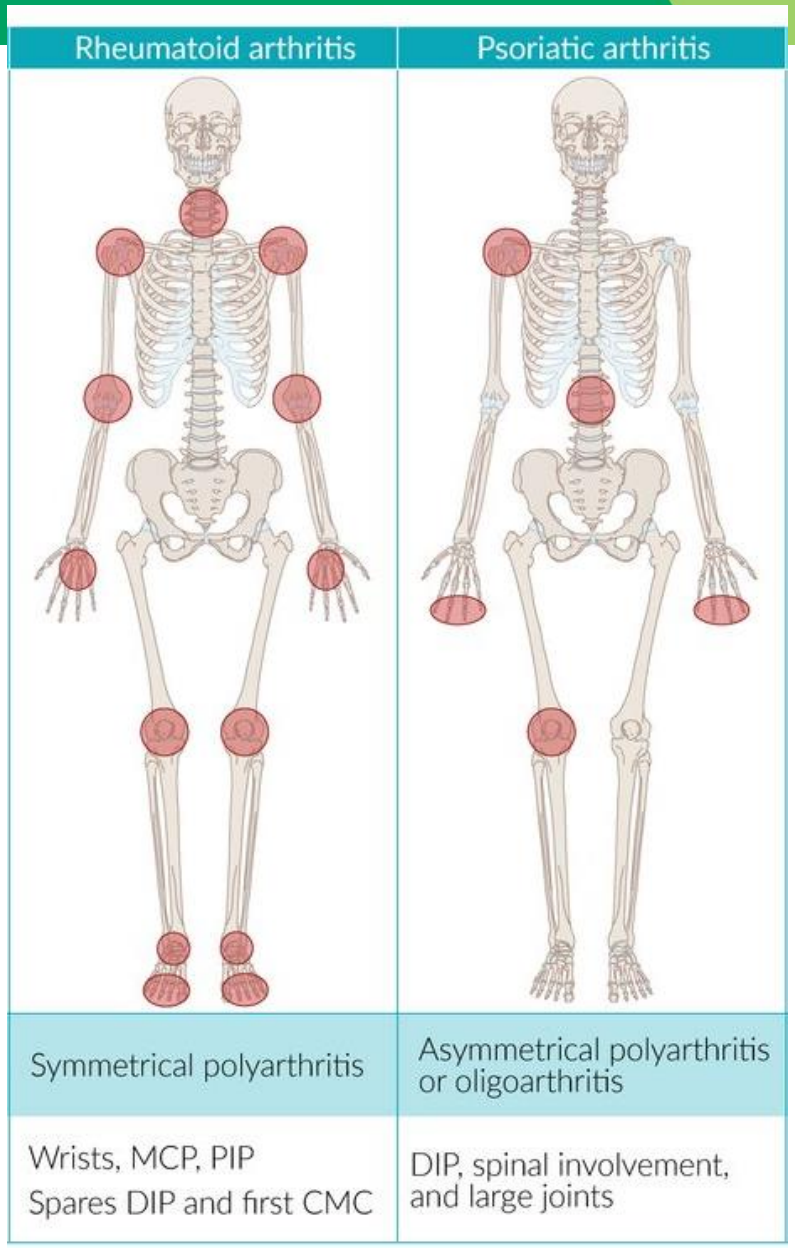
Table. The CASPAR classification criteria for PsA

To be classified as having PsA, a patient must have inflammatory articular disease (joint, spine, entheseal) with ≥ 3 of the following 5 points:

Criterion	Description
1. Evidence of psoriasis (one of a, b, c):	
(a) Current psoriasis[a]	Psoriatic skin or scalp disease currently present, as judged by a rheumatologist or a dermatologist
(b) Personal history of psoriasis	A history of psoriasis obtained from patient or family physician, dermatologist, rheumatologist, or other qualified health care professional
(c) Family history of psoriasis	A history of psoriasis in a first- or second-degree relative by patient report
2. Psoriatic nail dystrophy	Typical psoriatic nail dystrophy, including onycholysis, pitting, and hyperkeratosis observed on current physical examination
3. Negative test result for RF	By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range
4. Dactylitis (one of a, b):	
(a) Current	Swelling of an entire digit
(b) History	A history of dactylitis recorded by a rheumatologist
5. Radiological evidence of juxta-articular new bone formation	Ill-defined ossification near joint margins (excluding osteophyte formation) on plain x-ray films of hand or foot

CASPAR, CIASsification criteria for Psoriatic ARthritis; PsA, psoriatic arthritis; RF, rheumatoid factor; ELISA, enzyme-linked immunosorbent assay.

[a] Current psoriasis scores 2; all other items score 1.



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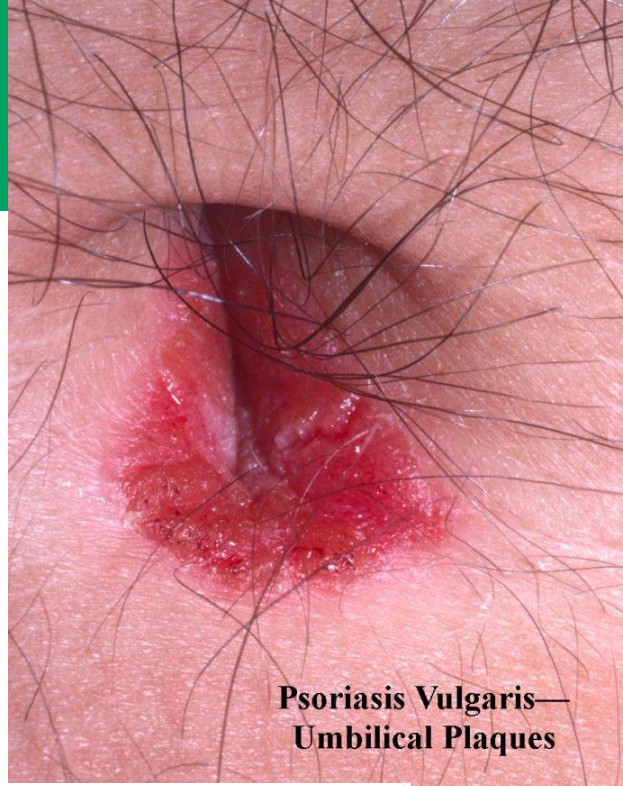

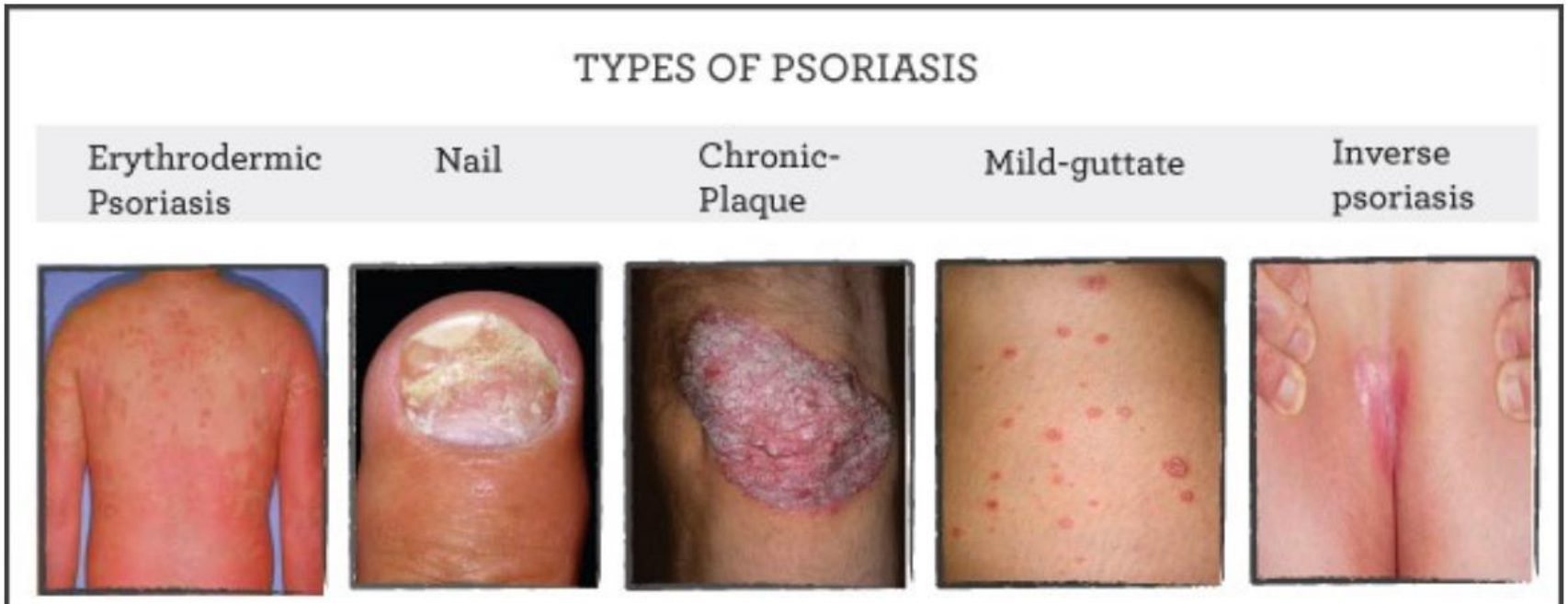

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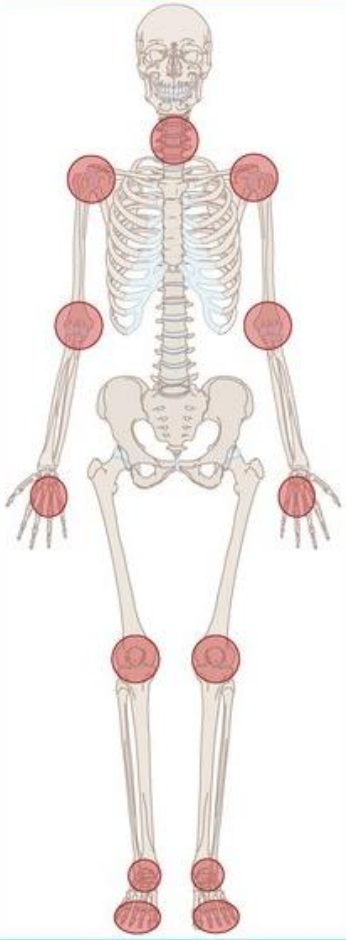
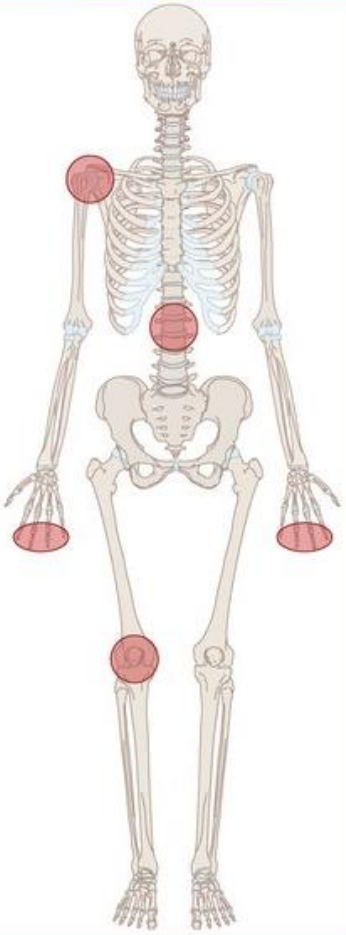
Rheumatoid arthritis	Psoriatic arthritis
	
Symmetrical polyarthritis	Asymmetrical polyarthritis or oligoarthritis
Wrists, MCP, PIP Spares DIP and first CMC	DIP, spinal involvement, and large joints

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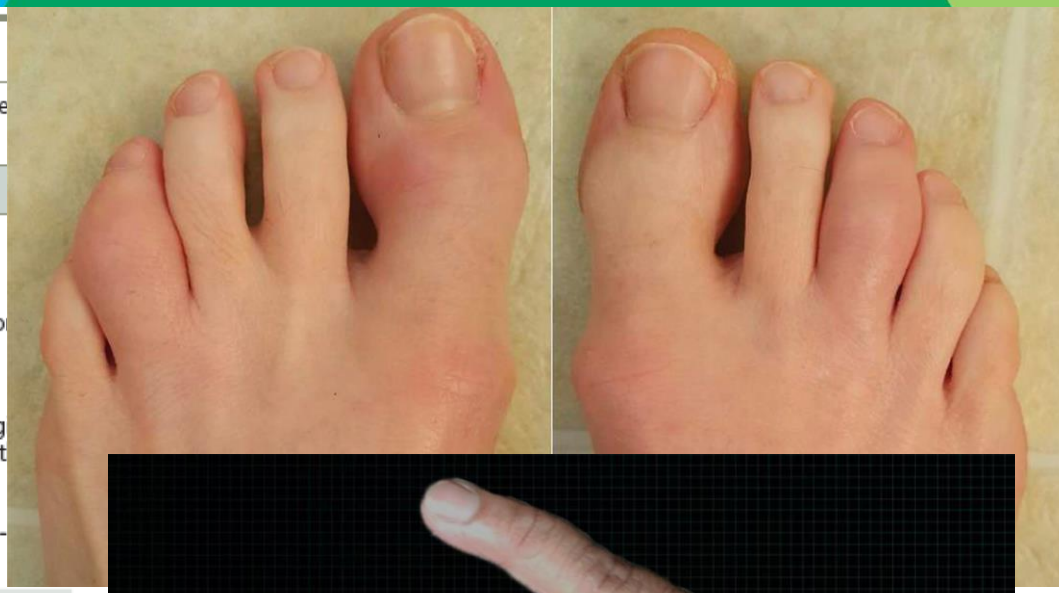
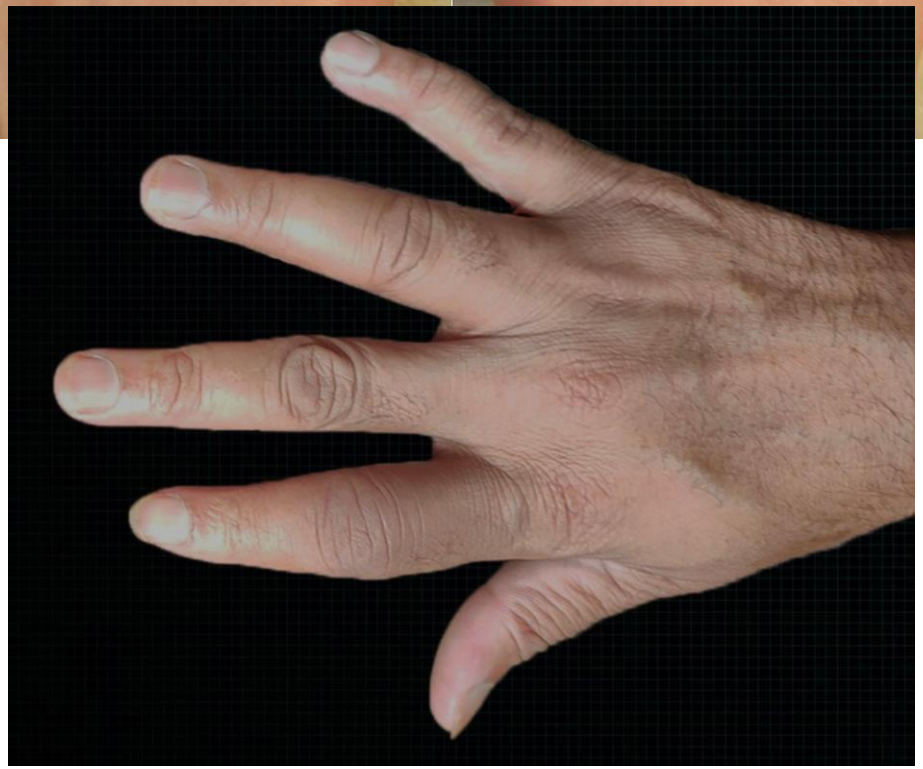




Case 3

69 yo F with hypertension presenting with 6 months of "joint pain".

P: "Taking NSAIDs first thing in the AM and PM, worse by the end of the day

Q: Constant dull, burning pain in the PIPs and DIPs, some "wrist" pain

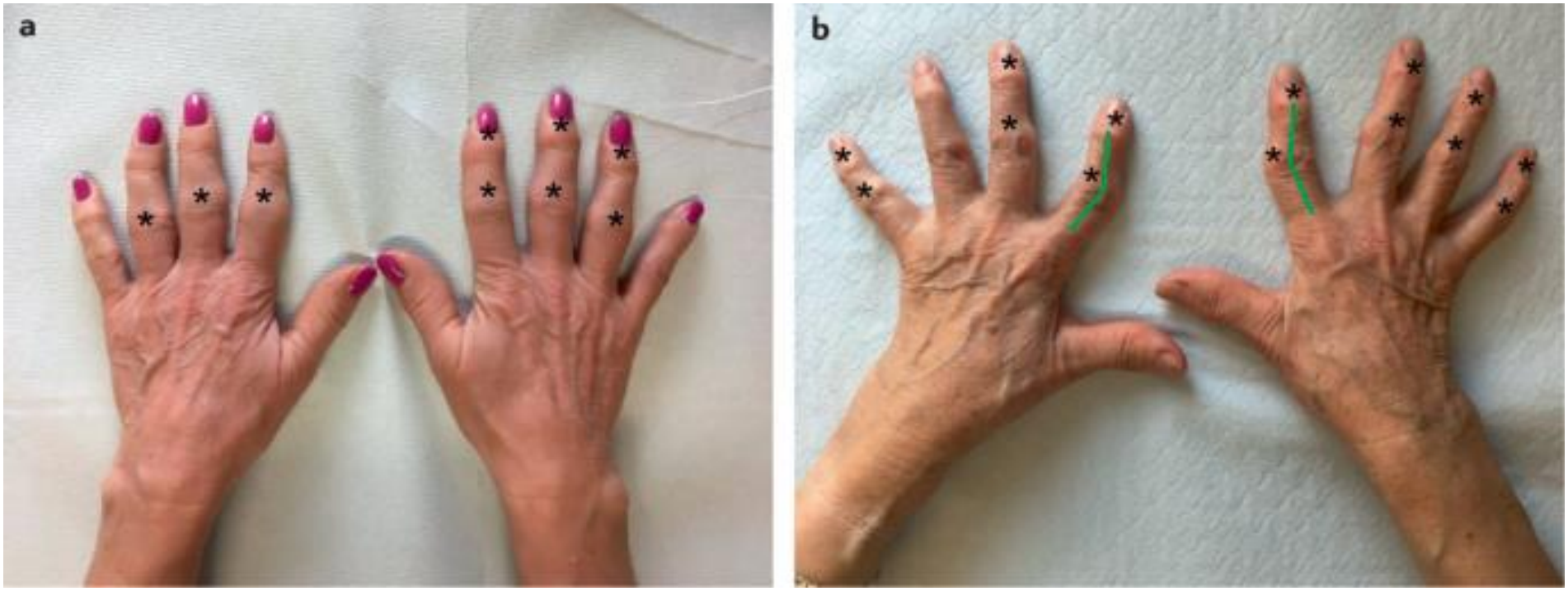
R: "pain stays in the hands"

S: "Been tolerable for a couple years but getting worse last few months

T: "I wake up feeling stiff all over but never gets better, worse with gardening

No recent illnesses or exposures
No rashes
No family history of autoimmune disease, mother with hand OA

Case 3



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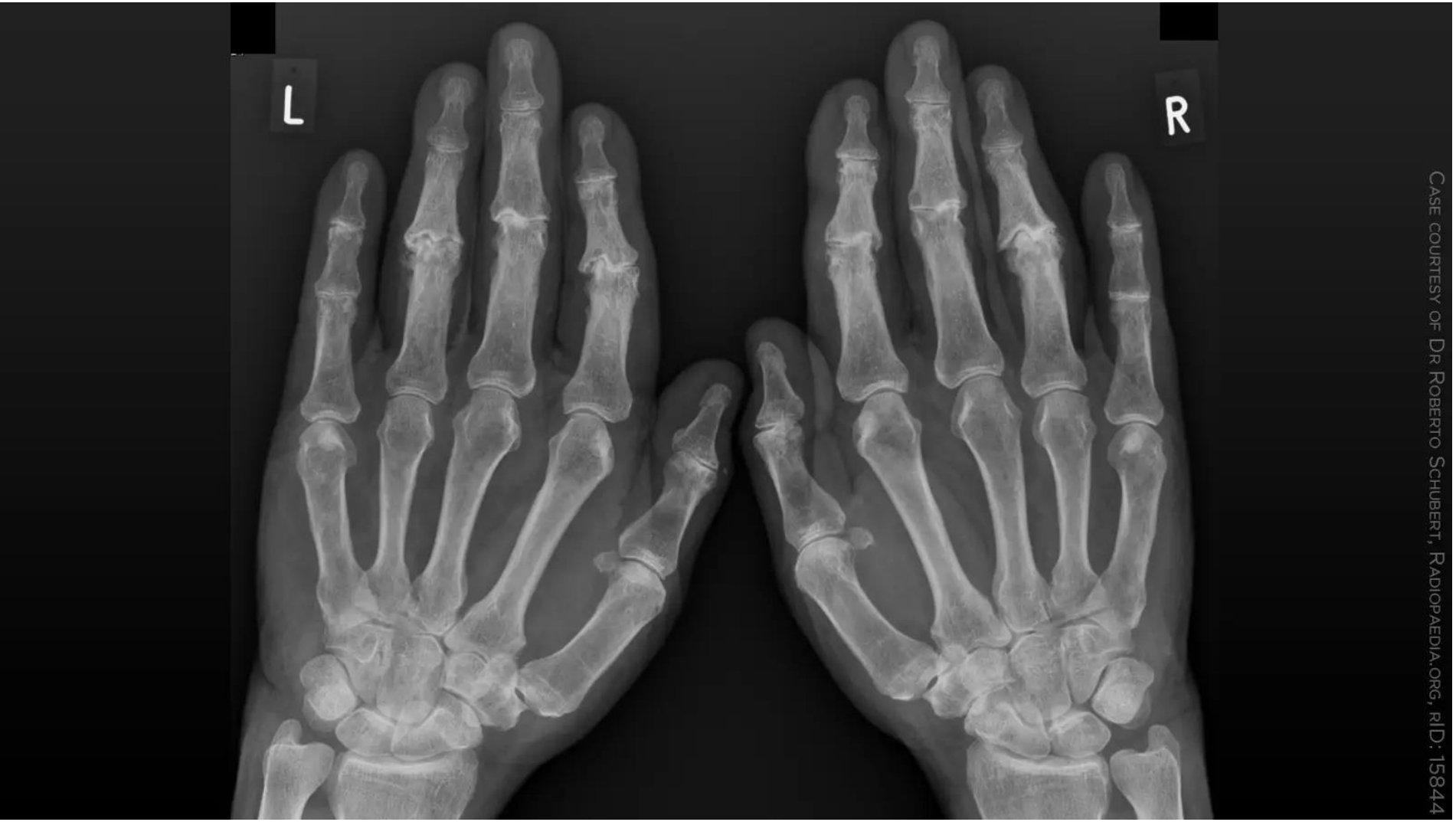
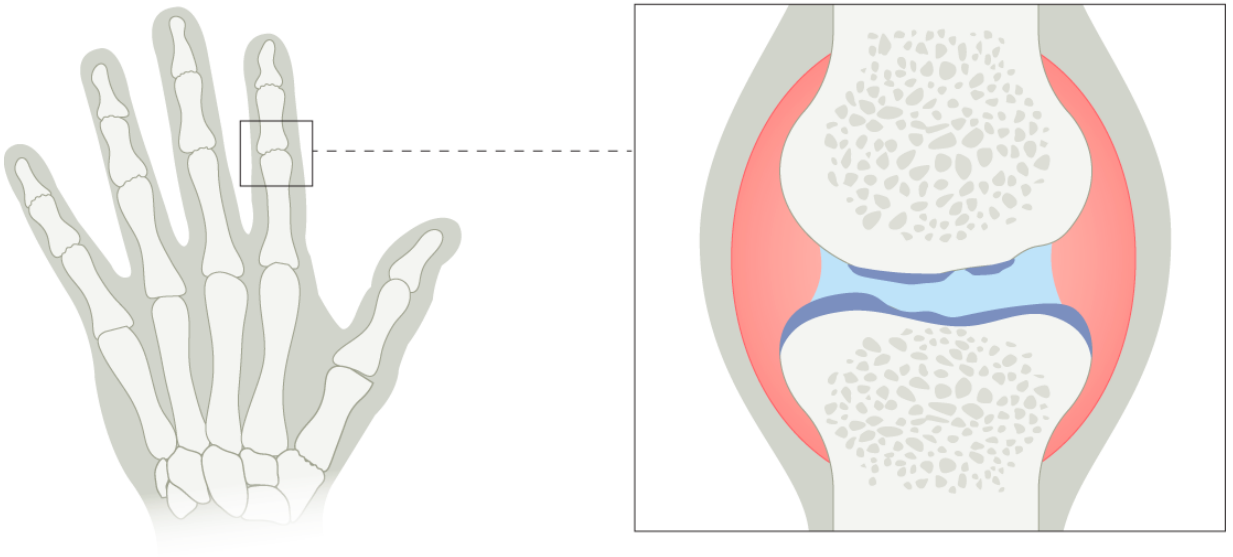
Radiology



Erosive Osteoarthritis



Risk factors

- Female sex
- Obesity
- Hypertension
- Dyslipidaemia

Ultrasonography features

- Joint effusion
- Synovial hypertrophy
- Capsule distention
- Power Doppler positivity
- Cysts

Biomarkers

- ESR
- sIL-2
- CRP
- CTX I
- Col2-3/4C
- MPO
- Visfatin
- CLU
- C2C
- CS846
- HA
- Coll2-1NO_2

Radiological features

- Central collapse
- Joint-space narrowing
- Gull-wing erosions
- Sawtooth erosions
- Ankylosis
- Osteophytes
- Malalignment

Symptoms and signs

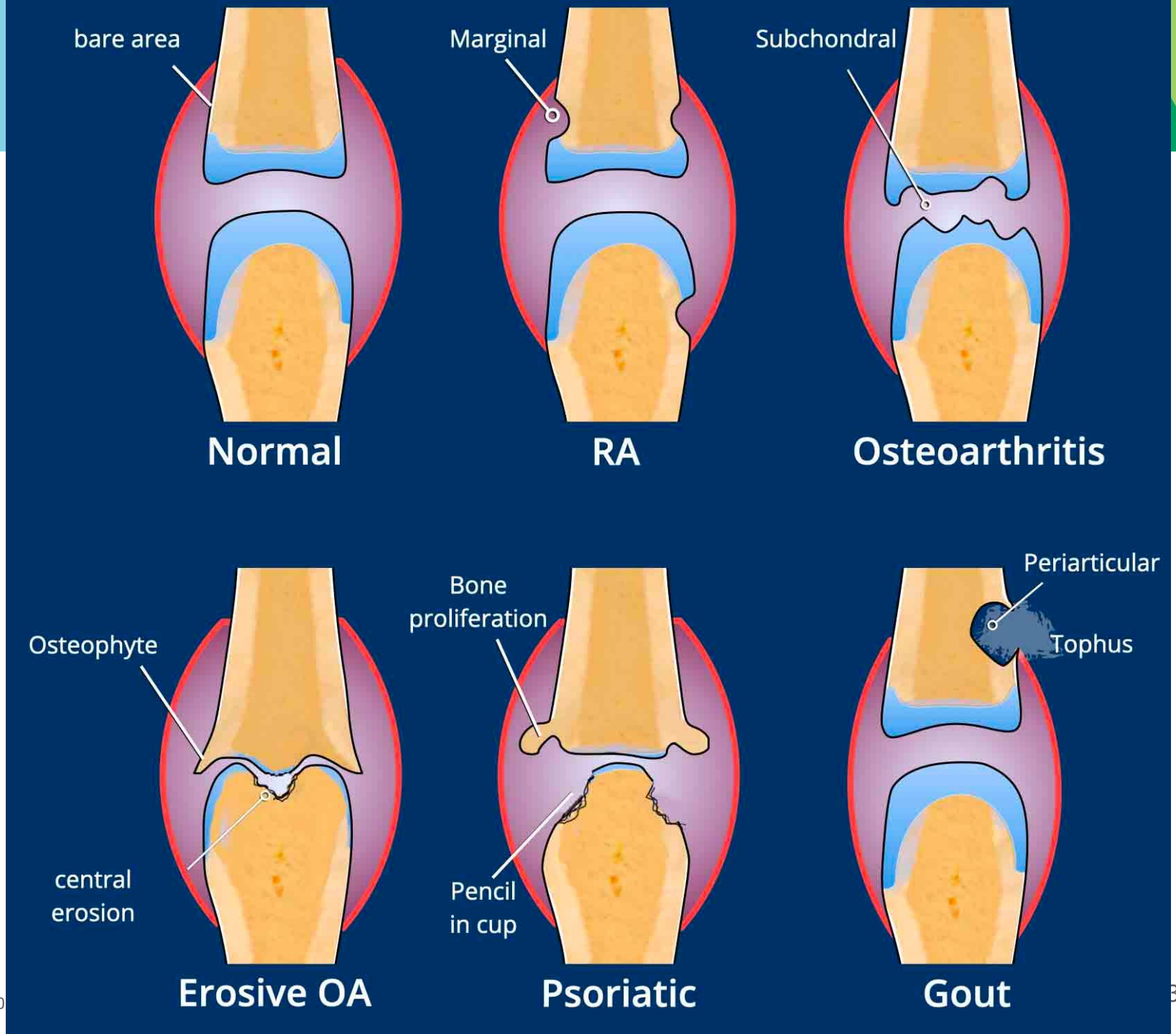
- Pain
- Swelling
- Calor
- Dysaesthesia
- Nodes in DIP and PIP joints
- Redness
- Tenderness
- Subluxation
- Instability
- Ankylosis

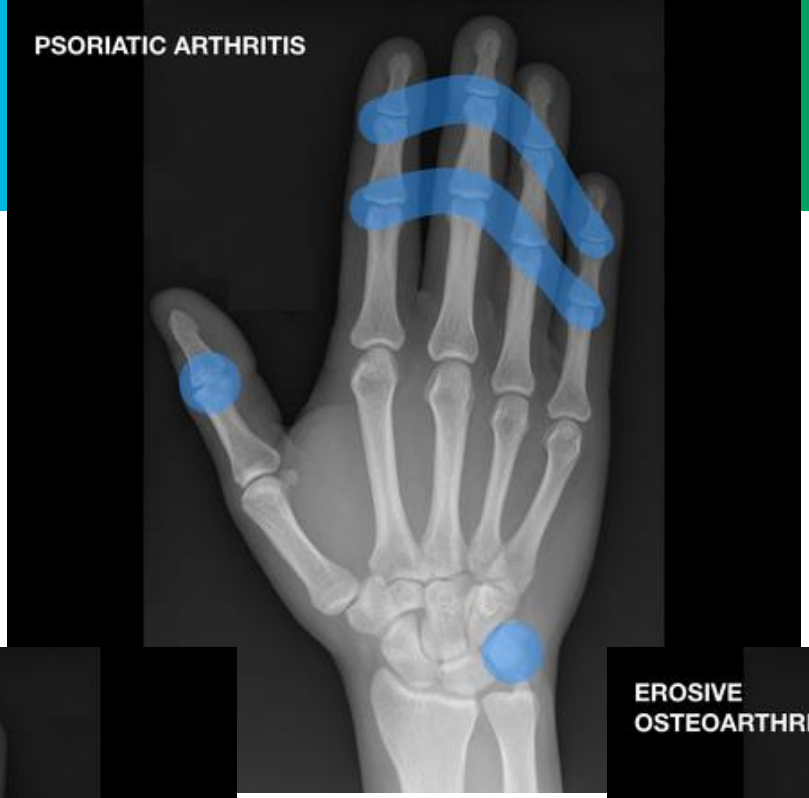
MRI features

- Osteophytes
- Malalignment
- Erosion
- Flexor tenosynovitis
- Joint-space narrowing
- Bone-marrow lesions
- Synovitis

Genetic predisposition

- Genotypes *SERPINA1-PI*MS* and *IL1B 5810 AA*
- HLA alleles *A23*, *A26*, *A29*, *B38*, *B44*, *DRB1*01* and *DRB1*07*


bare area
Normal
Marginal
RA
Subchondral
Osteoarthritis
Osteophyte
central erosion
Erosive OA
Bone proliferation
Pencil in cup
Psoriatic
Periarticular
Tophus
Gout


PSORIATIC ARTHRITIS


RHEUMATOID ARTHRITIS
Craig Hacking
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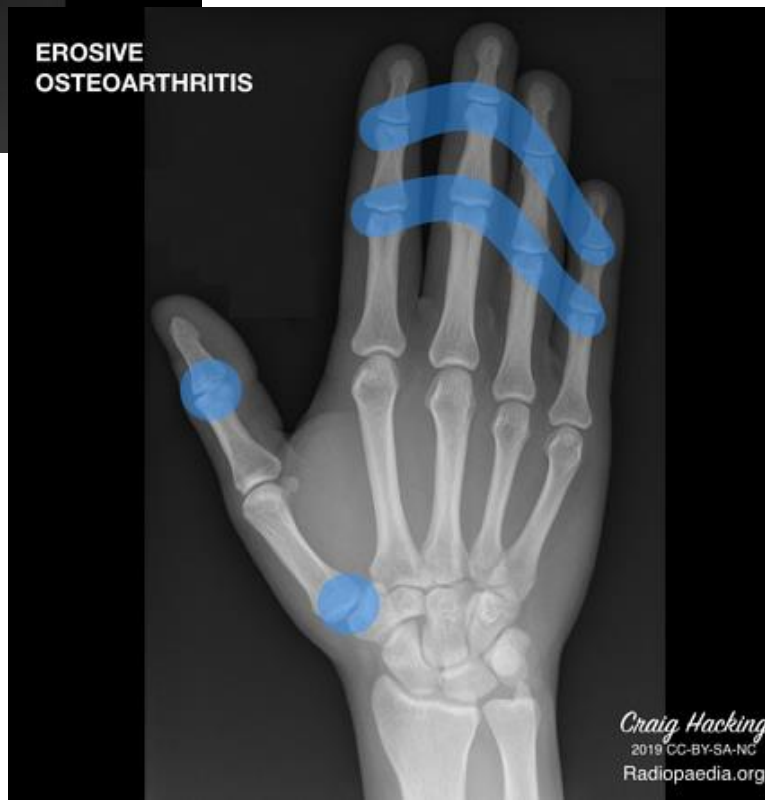
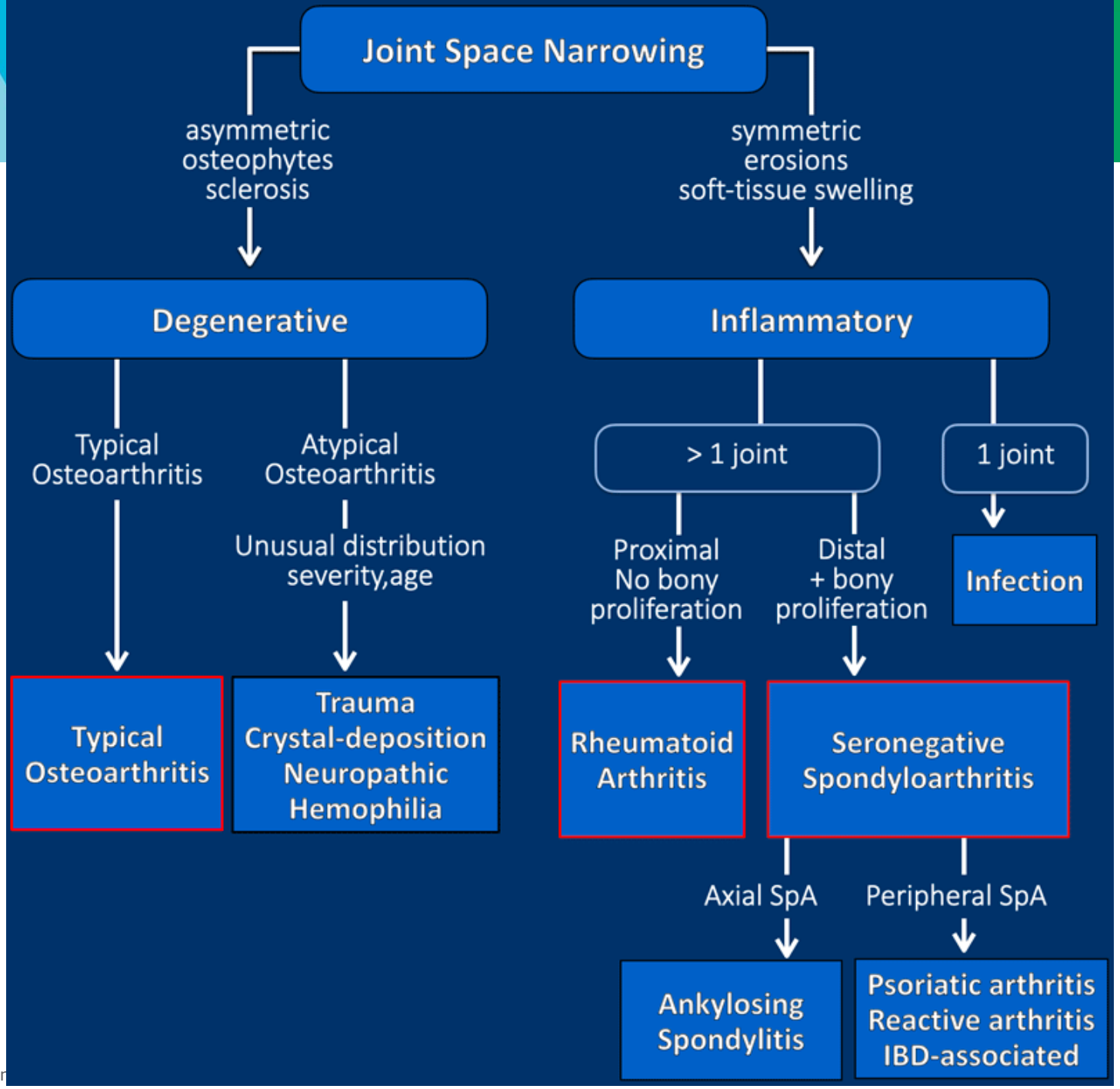
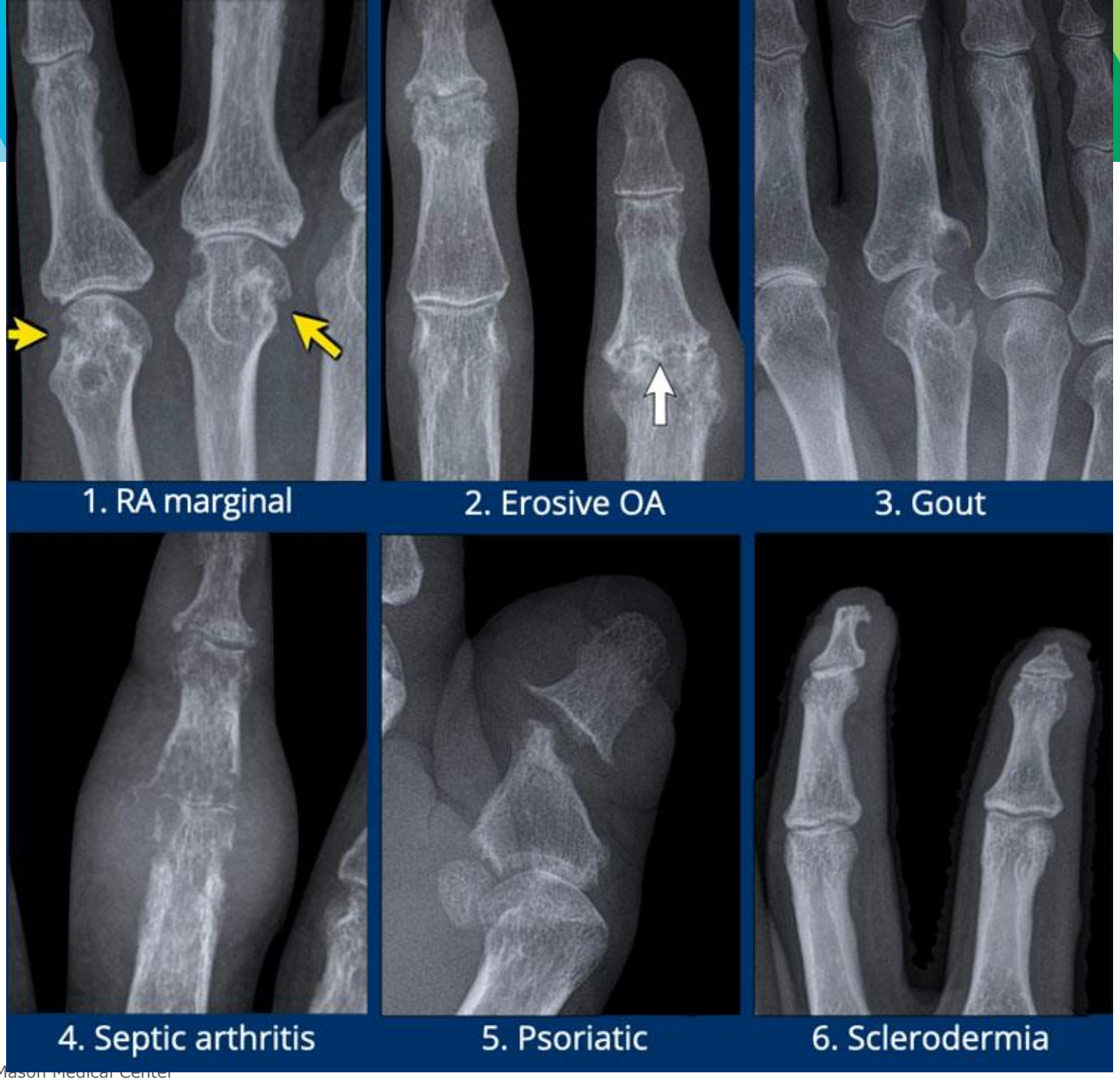
Radiopaedia.org


EROSIVE
OSTEOARTHRITIS
Craig Hacking
2019 CC-BY-SA-NC
Radiopaedia.org


Joint Space Narrowing
asymmetric
osteophytes
sclerosis
symmetric
erosions
soft-tissue swelling
Degenerative
Inflammatory
Typical
Osteoarthritis
Atypical
Osteoarthritis
> 1 joint
1 joint
Unusual distribution
severity,age
Proximal
No bony
proliferation
Distal
+ bony
proliferation
Infection
Typical
Osteoarthritis
Trauma
Crystal-deposition
Neuropathic
Hemophilia
Rheumatoid
Arthritis
Seronegative
Spondyloarthritis
Axial SpA
Peripheral SpA
Ankylosing
Spondylitis
Psoriatic arthritis
Reactive arthritis
IBD-associated



When to Order an ANA

- Do you think this patient has an ANA associated Rheumatologic condition?
    1. SLE / drug induced lupus
    2. Scleroderma
    3. Autoimmune Myositis
    4. Sjogren's

- Is this a young person with Raynaud's or older person with new Raynaud's

- New JIA diagnosis

Diseases associated with a positive ANA

	Percent with positive ANA
Systemic autoimmune diseases	
SLE	
Active	98 to 100 percent
Remission	90 percent
Scleroderma	95 percent
Rheumatoid arthritis	45 percent
Sjögren's syndrome	60 percent
Mixed connective tissue disease	100 percent
Drug-induced LE	80 to 95 percent
Raynaud's phenomenon	40 percent
Polymyositis/dermatomyositis	35 percent
Juvenile idiopathic arthritis	15 to 40 percent
Organ-specific autoimmune diseases	
Hashimotos thyroiditis	50 percent
Graves' disease	50 percent
Autoimmune hepatitis	70 percent
Primary biliary cirrhosis	50 to 70 percent
Infectious diseases*	
Viral:	
EBV	
HIV	
HCV	
Parvovirus 19	
Bacterial:	
SBE	
Syphilis	
Malignancies*	
Lymphoproliferative diseases	
Paraneoplastic syndromes	
Miscellaneous diseases*	
Inflammatory bowel disease	
Interstitial pulmonary fibrosis	

ANA: antinuclear antibodies; SLE: systemic lupus erythematosus; EBV: Epstein-Barr virus; HCV: hepatitis C virus; SBE: subacute bacterial endocarditis.

* Although positive tests of ANA are reported in these diseases more often than in healthy controls, precise estimates vary.

Courtesy of Donald B Bloch, MD.

UpToDate®

When not to order an ANA

- Known prior positive ANA
- Joint pain with no other concerning clinical or laboratory features for SLE, Sjogren's
- Concern for PMR or GCA
- Concern for fibromyalgia
- Concern for a spondyloarthropathy (ankylosing spondylitis, psoriatic arthritis, reactive arthritis)
- If you aren't sure which autoimmune

What to do with that + ANA

If you have a real clinical concern for SLE:

CBC, CMP, ds-DNA, C3, C4, UA with urine protein/Cr

Call Rheumatology

Young person with Raynaud's or older person with new Raynaud's + ANA:

Pulmonary screening

Prior to Rheumatology Referral

If you think the patient has an autoimmune/inflammatory arthritis:

- CBC with diff
- CMP
- ESR / CRP
- RF and CCP
- Uric acid
- XR of hands, feet and more painful joints
- HLA B27 (if you suspect spondyloarthropathy)
- Hepatitis B/C screening panel
- Quantiferon gold or PPD
- Relevant STI testing if indicated or concern for infectious etiology

When to order an **ANA**: if you think the patient has an ANA associated disease (lupus, scleroderma, autoimmune myositis, Sjogrens)

Questions?

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Hospital & Seattle Medical Center

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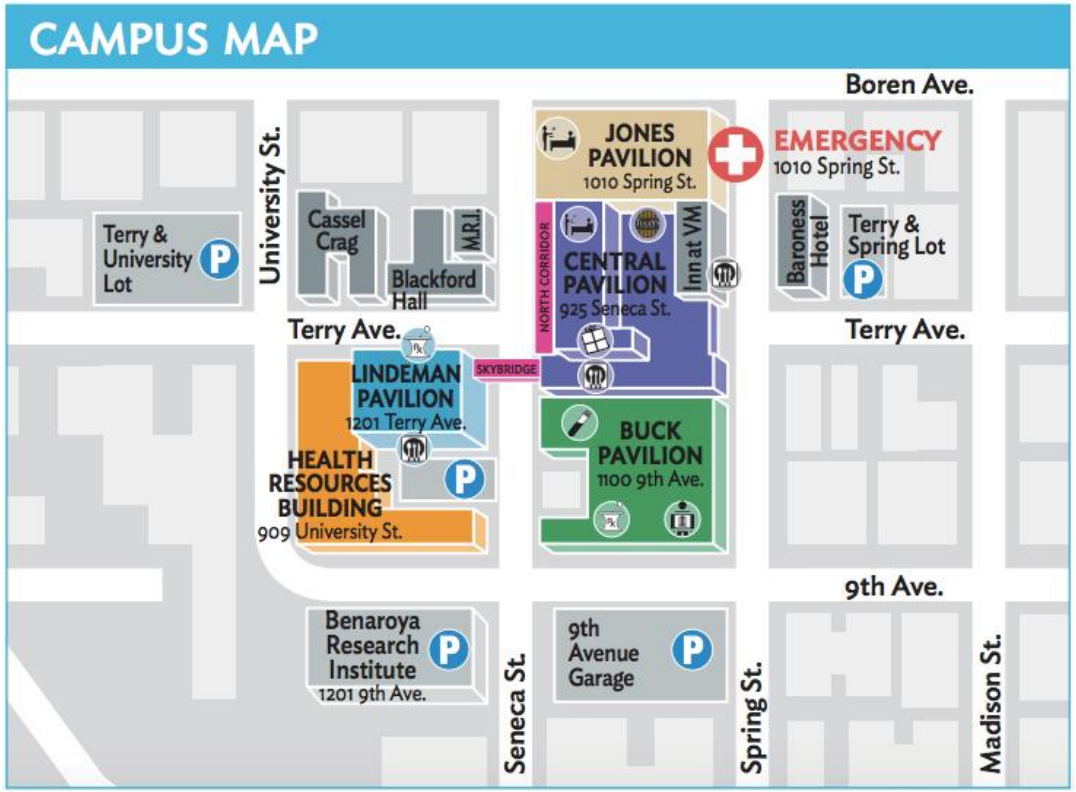

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