ACOI BOARD REVIEW 2019 RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

Robert DiGiovanni, DO FACR, FACOI
robdsimc@tampabay.rr.com
Slides prepared by Ryan Eaton, DO, Rheumatology Fellow
and Jeanine Martin, DO

Disclosures

- NONE

Learning Objectives

- By the end of the session you should be able to:
  - *Understand how Rheumatoid arthritis and osteoarthritis are diagnosed*
  - *Appreciate the need for early initiation of treatment of Rheumatoid Arthritis*
  - *Be aware of some extra-articular manifestations of Rheumatoid Arthritis*
  - *Recognize the types of treatment strategies that are used.*
  - *Name some common DMARD and Biologic drugs*

Case #1

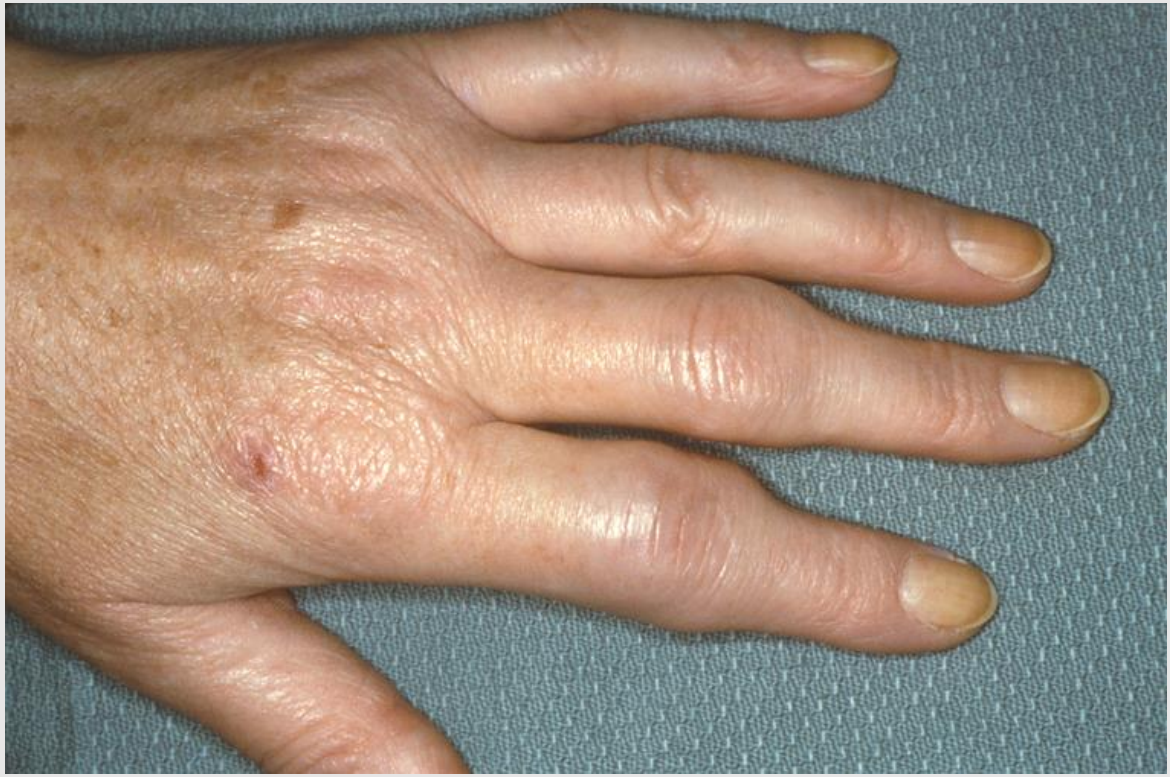
- A 34 year old female presents to your outpatient IM clinic complaining of worsening stiffness and aching in her hands for the last 3 months.
- She reports that the symptoms are worst when she wakes up in the morning at around 0700.
- By around 10:00, her joints are loosened up to where they will be for the day but will become stiff again if she sits still for too long.

- Past Medical History: Hashimoto Thyroiditis
- Social History: 10 Pack year cigarette smoker. No alcohol or drug use.
- Family History:
  - *Father-Psoriasis, Diabetes Mellitus*
  - *Mother-Rheumatoid Arthritis, Essential Hypertension*

- Labs:
  - *Rheumatoid Factor: Negative*
  - *Anti-Cyclic Citrullinated Protein: Positive*
  - *ANA: Positive 1:80 Speckled Pattern*
  - *ESR: 55 mm/hr*
  - *CRP: 4.9 mg/L*

Physical Examination

- Musculoskeletal exam:
  - *2+ synovitis across 2nd-5th Metacarpophalangeal (MCP) and Proximal Interphalangeal (PIP) joints bilaterally*
  - *Bilateral wrists with synovitis and reduced range of motion*
  - *Inability to fully make fist*
- Otherwise, she is a very healthy individual with unremarkable exam



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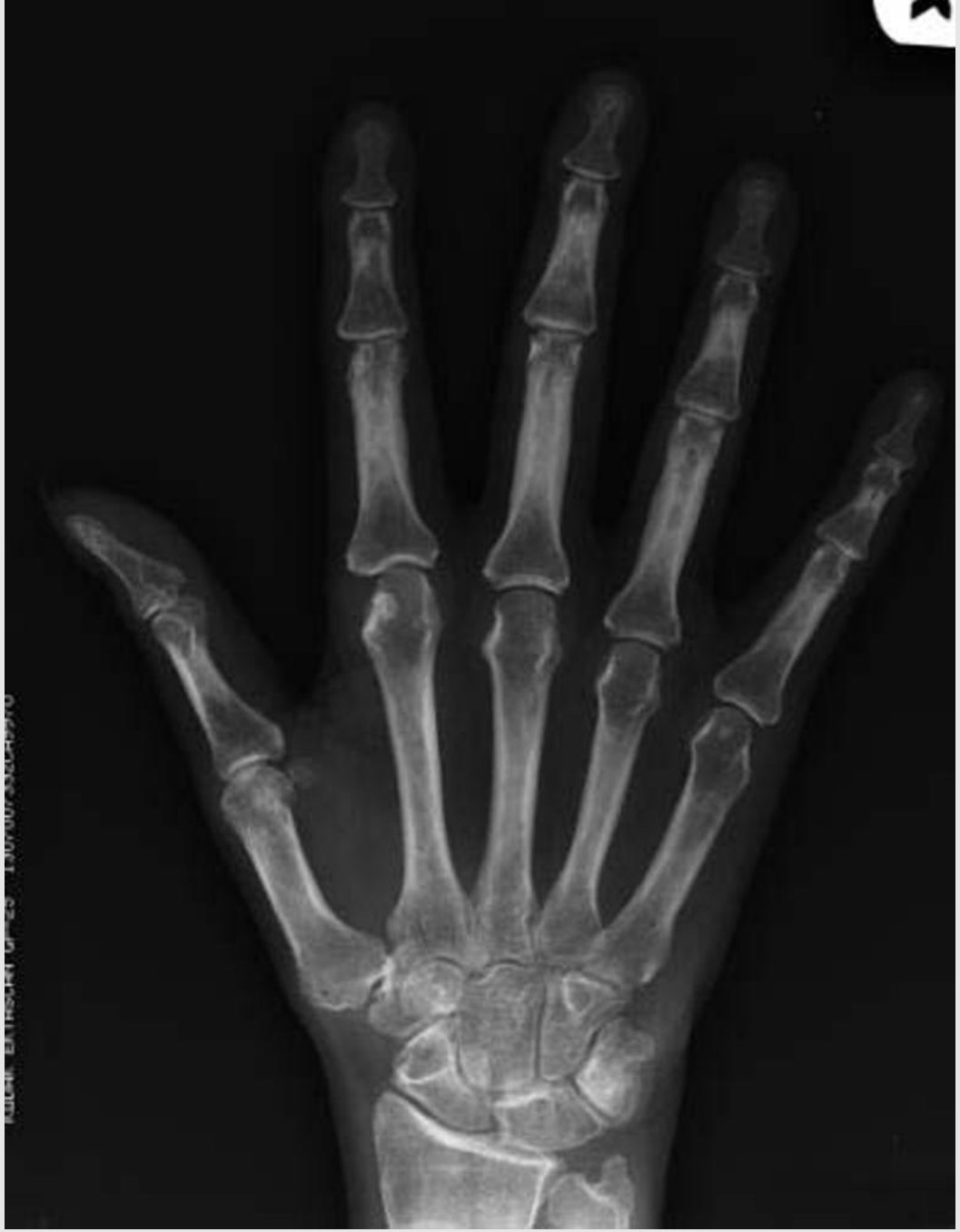
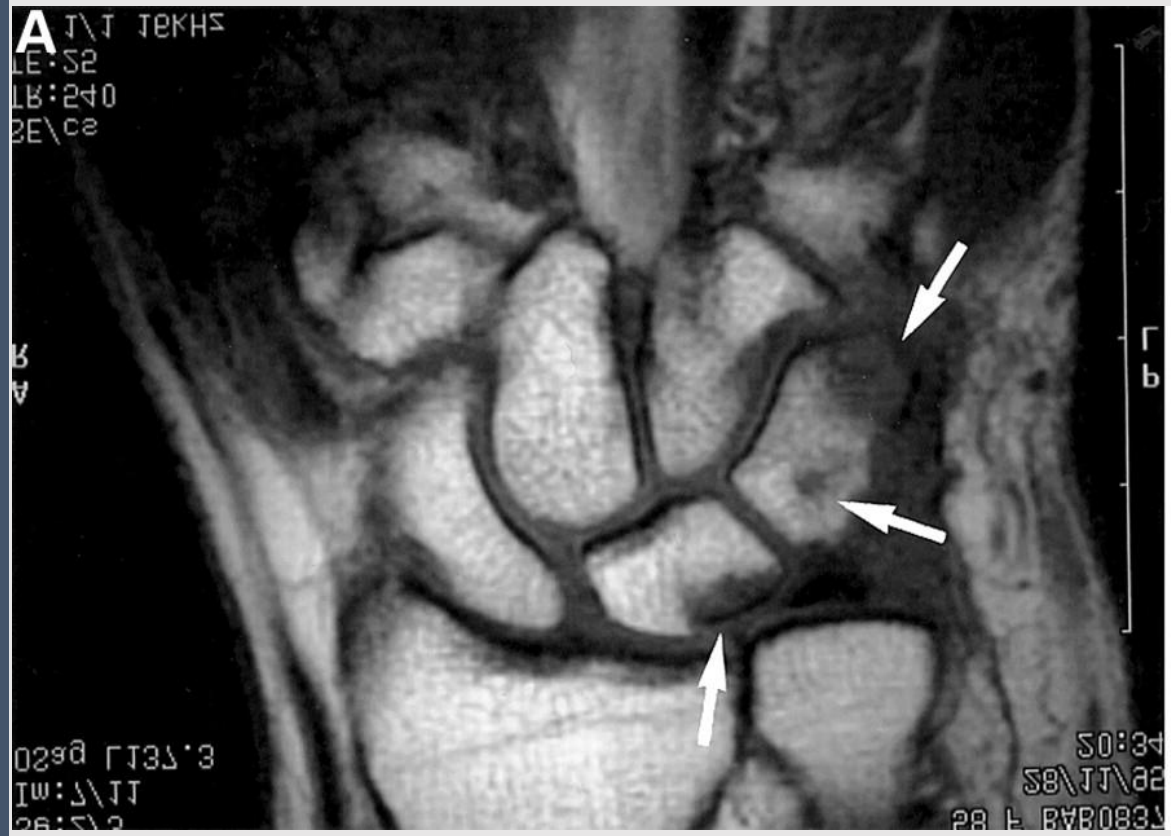
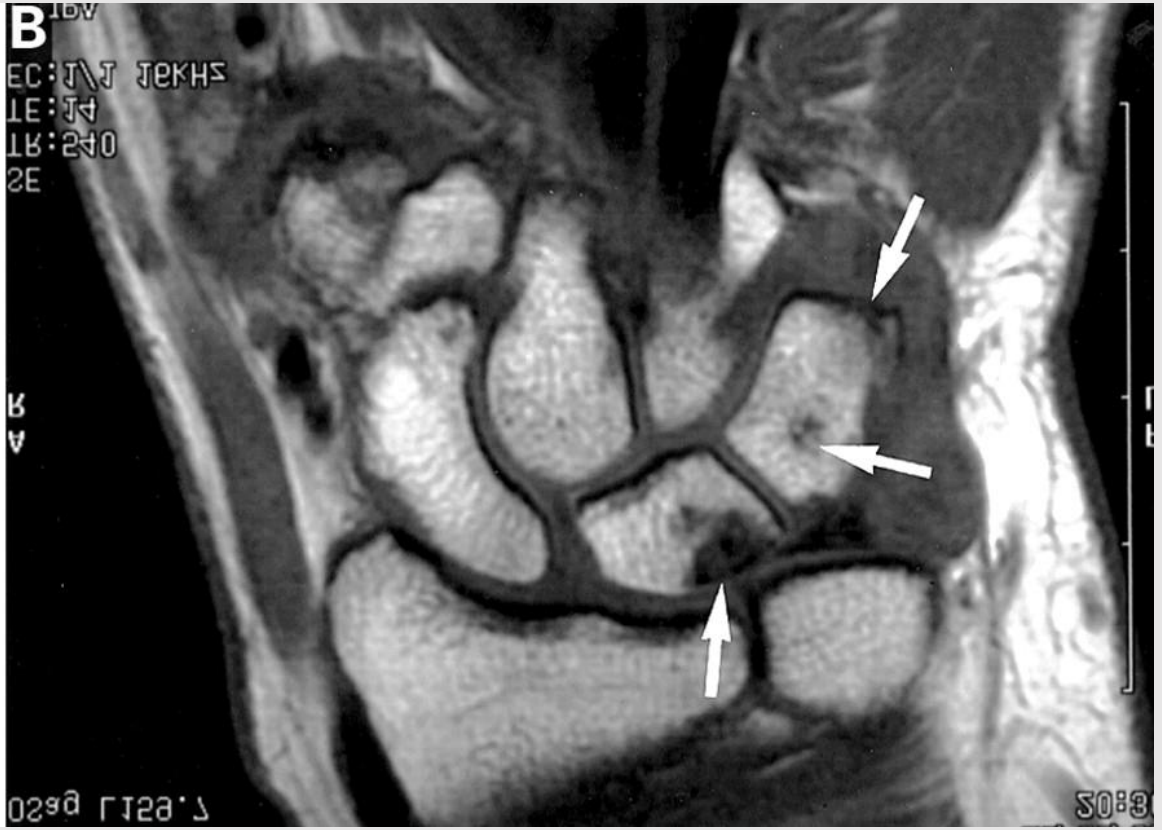


Image courtesy of Radswiki, Radiopaedia.org, rID: 11883





McQueen FM, Benton N, Crabbe J*, et al.* What is the fate of erosions in early rheumatoid arthritis? Tracking individual lesions using *x* rays and magnetic resonance imaging over the first two years of disease. *Annals of the Rheumatic Diseases* 2001;**60:**859-868.

Based on the above, what is the most likely diagnosis?

- Psoriatic arthritis
- Rheumatoid arthritis
- Osteoarthritis
- Viral arthritis
- Reactive arthritis

Rheumatoid Arthritis

- Chronic systemic inflammatory autoimmune disease, often insidious in onset, symmetric, and involving the small joints of hands, wrists, and feet
- Worldwide, the annual incidence of RA is approximately 3 cases per 10,000 population
- Prevalence is approximately 1%, increasing with age and peaking between the ages of 35 and 50 years
- Women are affected 3 times more often than men

https://emedicine.medscape.com/article/331715-overview

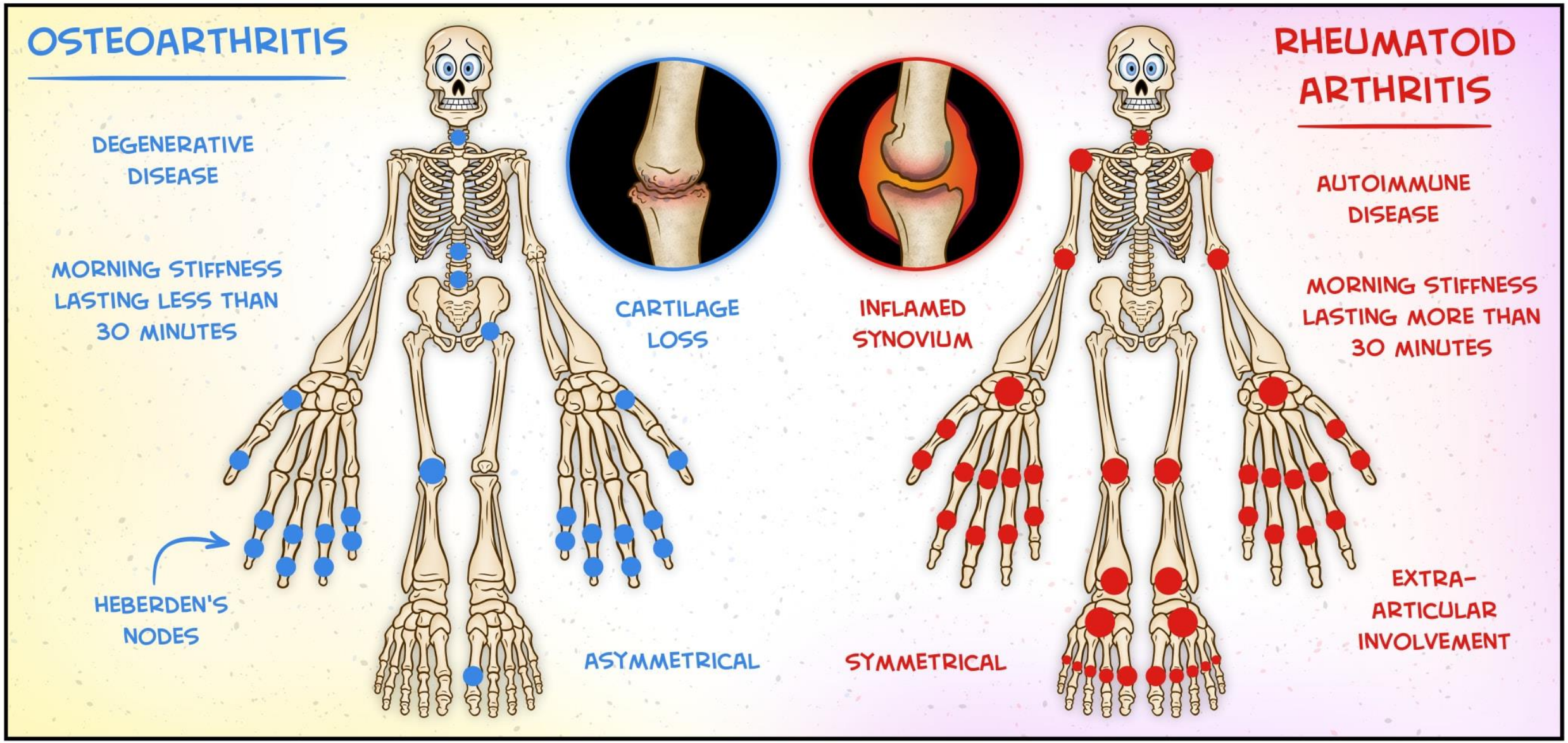


Image Courtesy of Jorge Muniz, Medcomic.com

Serologies

- Rheumatoid Factor: IgM antibody that recognizes the Fc portion of an IgG molecule.
  - *70% are RF+ at disease onset, with 10-15% become RF + within the first 2 years after onset*
  - *+RF without clinical evidence does NOT suggest RA: hepatitis C, SLE, Sjogren's, bacterial endocarditis (recall DUKE minor criteria)*
- Anti-citrillunated peptide antibody (CCP or ACPA):
  - ***Highly specific 98%***
  - *Seen in 70% of RF+ patients, and 33% of RF- (seronegative) RA patients.*
- ANA: positive in 30% of RA patients

Kroot EJ, de Jong BA, van Leeuwen MA, Swinkels H, van den Hoogen FH, van't Hof M, van de Putte LB, van Rijswijk MH, van Venrooij WJ, van Riel PL. The prognostic value of anti-cyclic citrullinated peptide antibody in patients with recent-onset rheumatoid arthritis. Arthritis Rheum. 2000 Aug;43(8):1831-5. PubMed PMID: 10943873.

2010 ACR/EULAR Classification Criteria for RA

JOINT DISTRIBUTION (0-5)	
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 (0-3)	
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
SYMPTOM DURATION (0-1)	
<6 weeks	0
≥6 weeks	1
ACUTE PHASE REACTANTS (0-1)	
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1

≥6 = definite RA

What if the score is <6?

Patient might fulfill the criteria...

→ **Prospectively** over time (cumulatively)

→ **Retrospectively** if data on all four domains have been adequately recorded in the past

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Assuming no contraindications, what is the most appropriate medication to initiate?

- Prednisone 60mg daily
- Ibuprofen 800mg TID
- Methotrexate 15mg weekly with folic acid 1mg daily
- Hydroxychloroquine 200mg daily
- Sulfasalazine 1500mg BID

Traditional DMARDs

- **Sulfasalazine:**
  - *Metabolized by intestinal bacteria to 5-aminosalicylic acid (5-ASA) and sulfapyridine (SP)*
- **Methotrexate:**
  - *Antimetabolite, inhibits **dihydrofolic acid reductase** which is an enzyme needed for synthesis of purine nucleotides*
  - *Comcomitant use with **Trimethoprim** can lead to **agranulocytosis***
  - *Must supplement with 1mg daily folic acid*
- **Leflunomide:**
  - *Interferes with **dihydroarotate dehydrogenase**, inhibiting pyrimidine synthesis, DNA synthesis*
- **Azathioprine:**
  - *Is an Imidazoylyl derivative of 6-mercaptourine and will metabolize to 6-mercatopurine (6-MP)*
- **Hydroxychloroquine:**
  - *Inhibits stimulation of the toll-like receptor (TLR) 9 family receptors*
  - *Inhibits IL-1*
- **Cyclosporin A:**
  - *Inhibits production of IL-2 by helper T cells thereby blocking T cell activation and proliferation*

Klippel, J.H.; Stone, J.H.; Crofford, L.e.J.; White, P.H. (Eds.) *Primer on the Rheumatic Diseases*, Arthritis Foundation, 2001, 13th ed. 2008, pg 155-141.

Biologics

- **Anti-TNF**
  - *Enbrel- Etanercept (1997)*
  - *Remicade- Infliximab (1998)*
  - *Humira - Adalimumab (2002)*
  - *Simponi- Golimumab (2009)*
  - *Cimzia- Certolizumab (2009)*
- **T-cell co-stimulatory specific**
  - *Orencia -Abatacept (2005)*
- **B-cell depletion:**
  - *Rituxan –Rituximab (RA 2006)*
- **IL-6 inhibition:**
  - *Actemra - Tocilizumab (2010)*
  - *Kevzara - sarulimab (2017)*
- **Small Molecules: Jak inhibitor**
  - *Xeljanz - Tofacitanib (2012)*
  - *Olumiant - Baricitinib (2018)*

Medscape

Case #2

- A 73 year old female with severe, longstanding seropositive (+RF and +CCP) Rheumatoid Arthritis presents to the hospital for elective cholecystectomy.
- Preoperative Chest Radiographs were remarkable for multiple 1cm lung nodules which were relatively unchanged compared to prior xrays.
- Brief preoperative physical exam reveals significant rheumatoid deformities of bilateral hands with large rheumatoid nodules on bilateral elbows.

- The surgery itself goes well with no immediate surgical complications.
- However, in the Post-Anesthesia Care Unit, she cannot wean off the ventilator due to failure to initiate breaths.
- She is also awake but unable to move her extremities.

Which of the following tests should have been performed pre-operatively?

- Left Heart Cath
- MRI Brain
- Hemoglobin A1c
- Radiographs of cervical spine with flexion and extension views

Spinal Involvement

- Major complication in advanced RA is atlantoaxial subluxation from tenosynovitis of the transverse ligament of C1 which stabilizes odontoid process
- RA Spares thoracic, lumbar, and SI joints

da Côrte FC, Neves N. Cervical spine instability in rheumatoid arthritis. Eur J Orthop Surg Traumatol. 2013 Jun 27. [Epub ahead of print] PubMed PMID: 23807394.

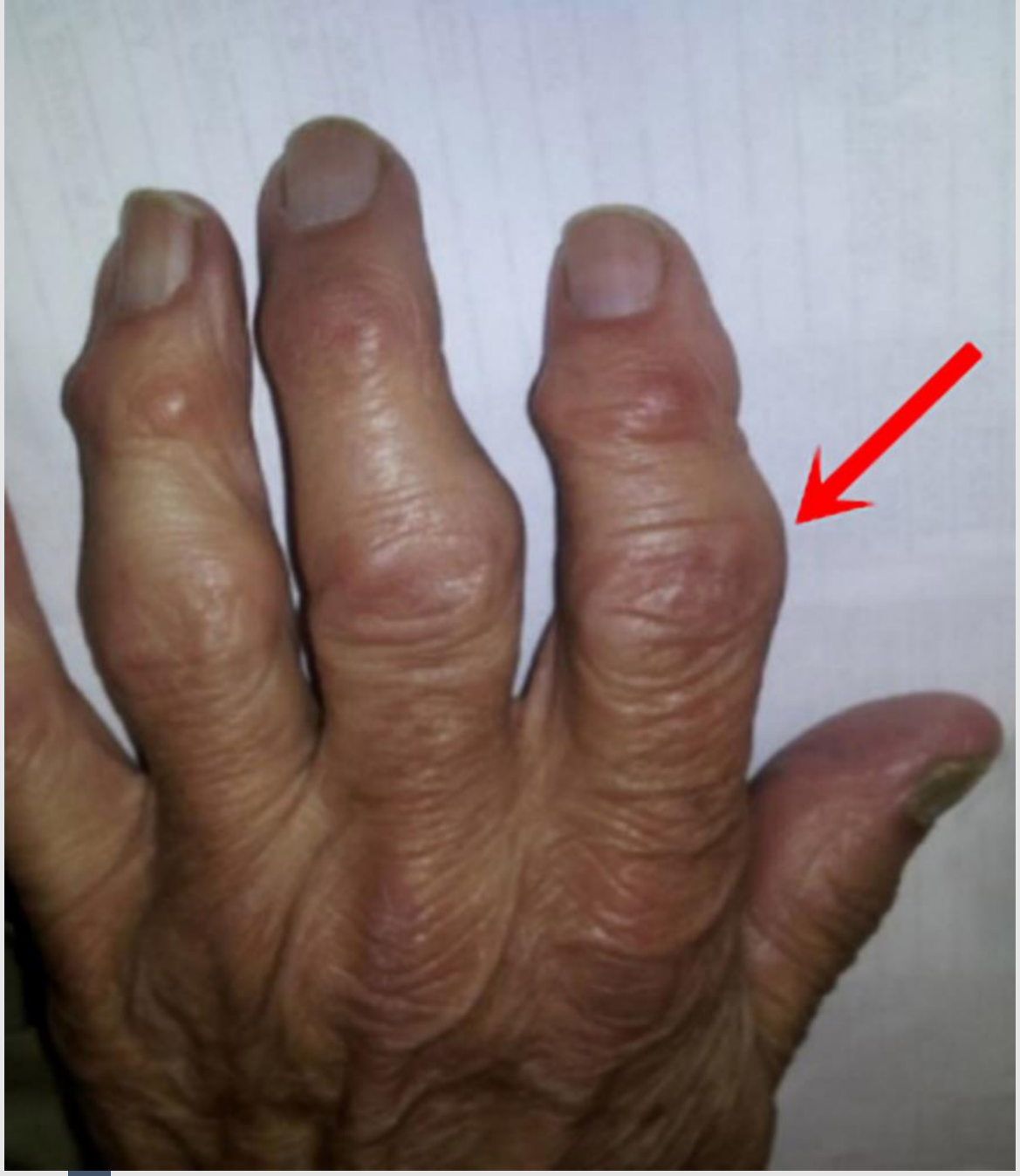
Remember, RA is a Systemic Disease

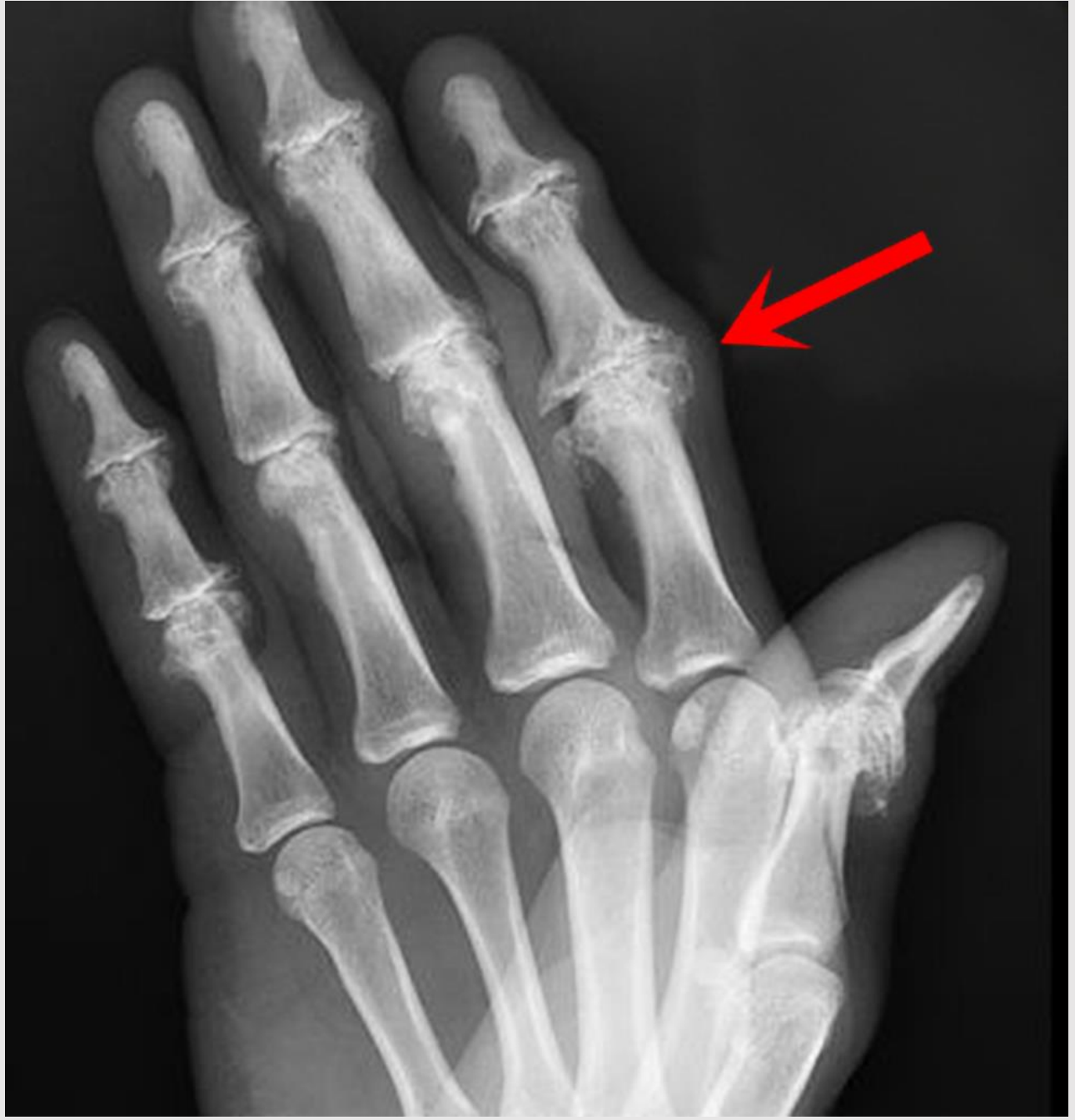
- Notable Systemic Manifestations:
  - *Lungs*
    - Rheumatoid nodules in lungs (necrobiotic nodules)
    - ILD (Rheumatoid Lung)
    - Pleural Effusions with Extremely low glucose levels
  - *Heart*
    - Patient's with RA have a 2-3x higher risk of Myocardial Infarction than age-matched controls
    - "Bread and Butter" Pericarditis

Luthra HS. Extra-articular manifestations of rheumatoid arthritis. Minn Med. 1979 Oct;62(10):743-4. PubMed PMID: 502991.

Case #3

- A 72 year old retired mechanic presents to your office with worsening bilateral hand pain
- Pain is most pronounced at PIPs and DIPs of bilateral hands and 1st CMC bilaterally
- Pain is worse for about 5 minutes upon awakening in the morning or with prolonged activity
- Prior History of Left knee arthroplasty and Right hip arthroplasty for osteoarthritis





Case courtesy of Dr Benoudina Samir, Radiopaedia.org, rID: 43417

What is the most likely diagnosis?

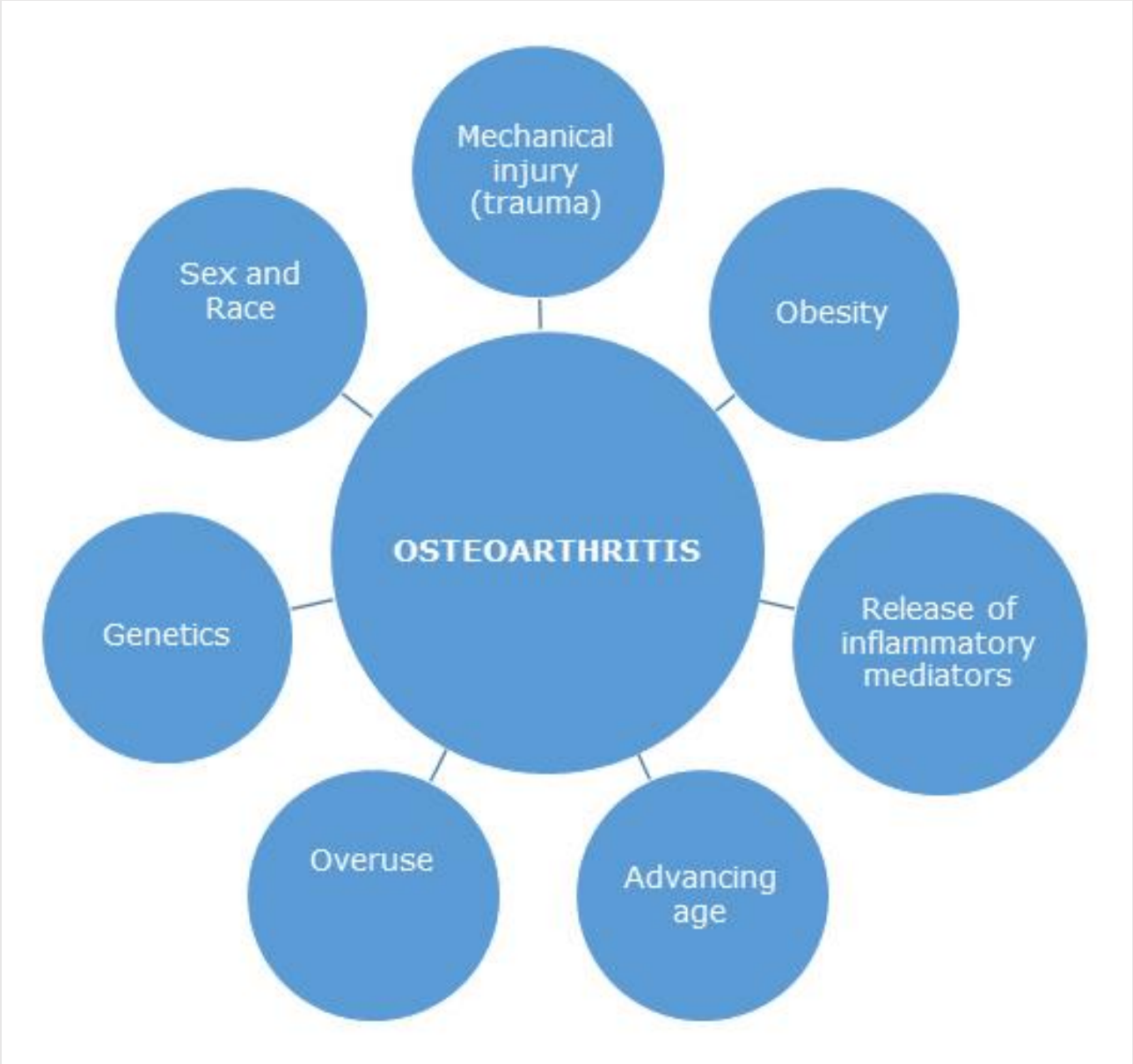
- Rheumatoid arthritis
- Osteoarthritis
- Hemachromatosis
- Wilson’s disease
- Gouty arthropathy

Osteoarthritis

- Most common type of joint disease, affecting more than 30 million individuals in the United States alone
- 80-90% of adults over age 65 have radiographic evidence of osteoarthritis
- Radiographic features:
  - *Joint space narrowing*
  - *Osteophytes*
  - *Subchondral sclerosis*
  - *Subchondral cysts*

https://emedicine.medscape.com/article/330487-overview

Risk Factors



https://www.wikidoc.org/index.php/Osteoarthritis_risk_factors

Treatment

- **Non-Pharmacologic**
  - *Reduce strain on joints when feasible*
  - *Physical therapy*
  - *Splinting or bracing*
  - *Ice or heat*
- **Pharmacologic**
  - *NSAIDs (either oral or topical), acetaminophen*
  - *Intra-articular corticosteroids*
- **Surgical**
  - *Joint arthroplasty generally reserved for large joints but can be*
  - *Joint arthrodesis (fusion) is sometimes used for severe pain*

https://www.uptodate.com/contents/management-of-hand-osteoarthritis

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