RHEUMATOID ARTHRITIS

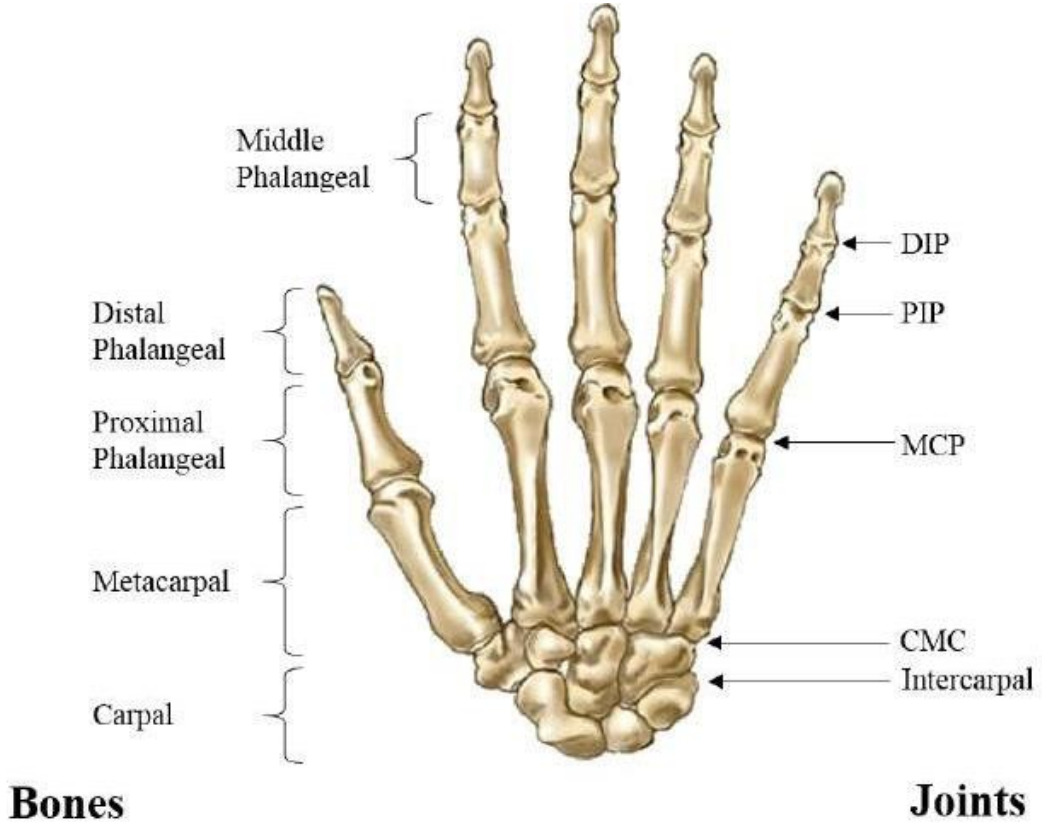
Internal Medicine CME Update

Blair Solow, MD, MSc

2021

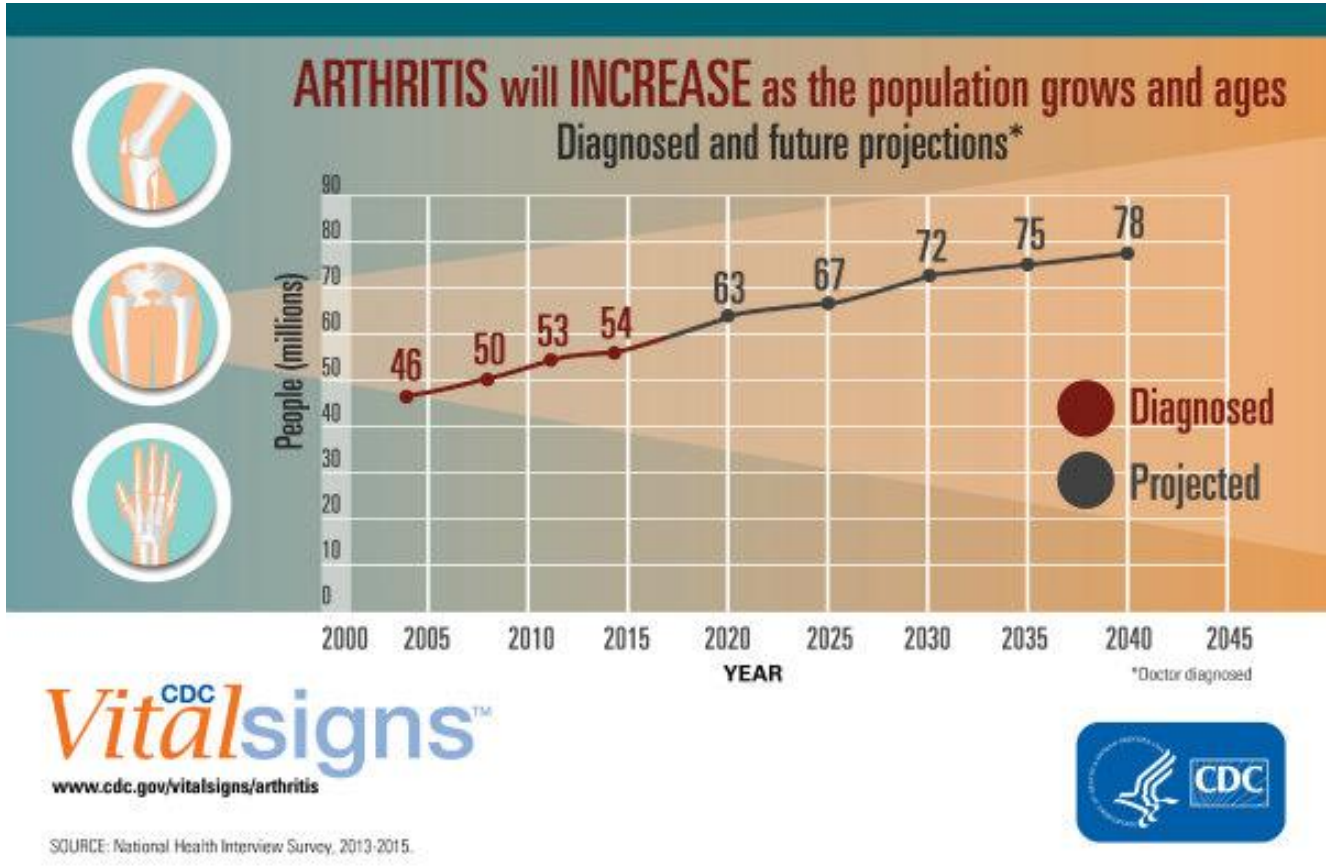
OUTLINE

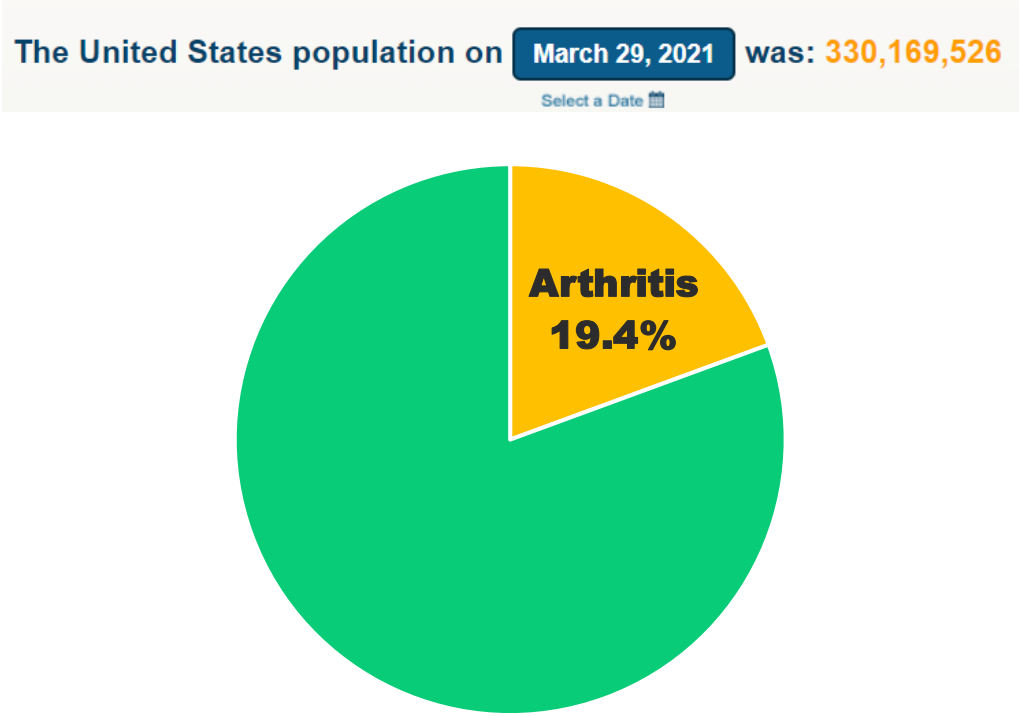
- Cases in the differential of Rheumatoid Arthritis
- RA Pathogenesis
- Therapy in RA
- Concluding Remarks



Picture from Abdallah et al., IJSSIS 2017

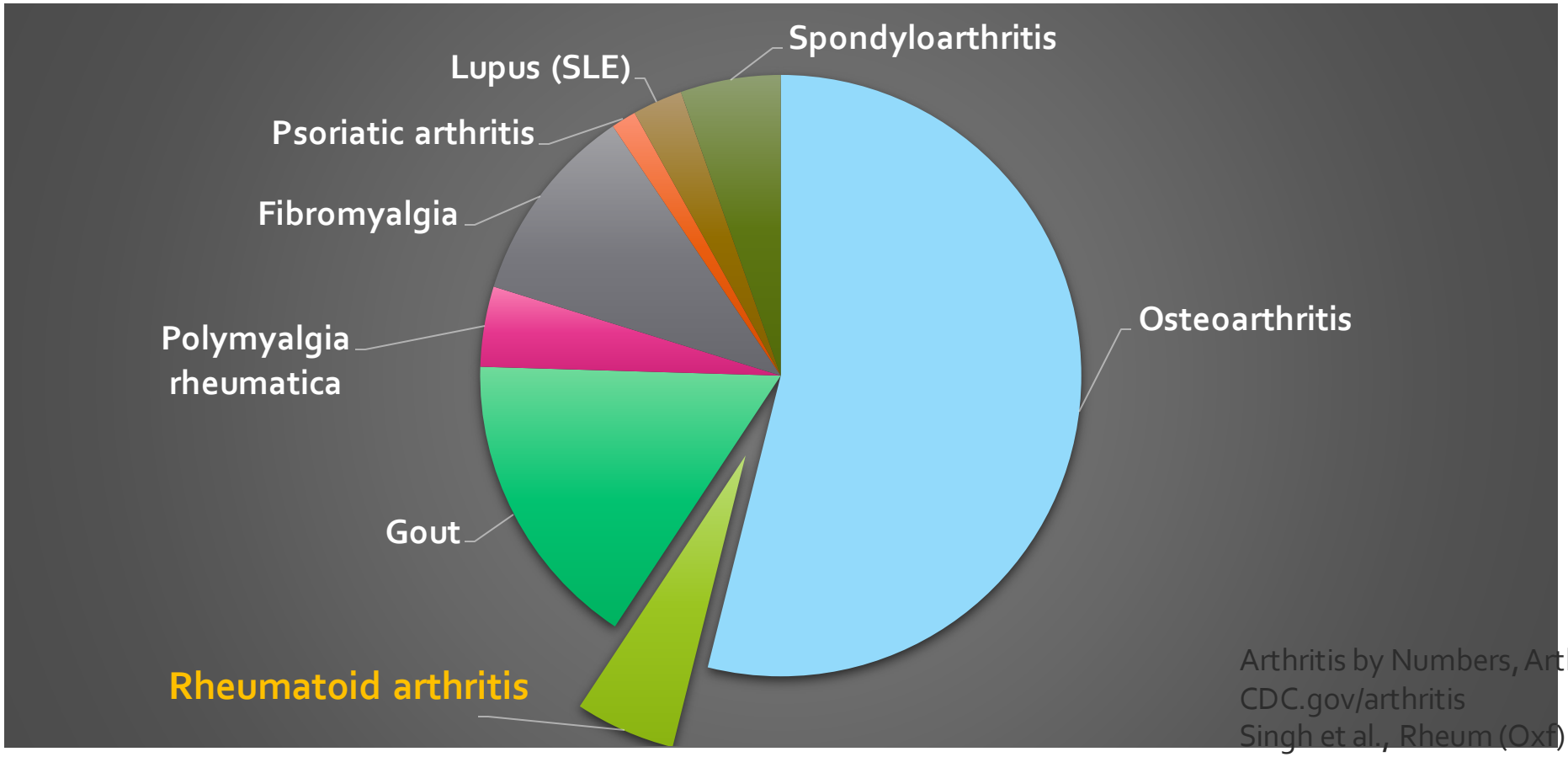
ARTHRITIS ON THE RISE





https://www.cdc.gov/arthritis/data_statistics/arthritis-related-stats.htm#projected
https://www.census.gov/popclock/

PROPORTIONS



Arthritis by Numbers, Arthritis Foundation 2020
CDC.gov/arthritis
Singh et al., Rheum (Oxf) 2019
Crowson, et al., Semin Arth Rheum 2017
Ogdie, et al., Rheum Disc Clin N Amer 2015

CASE 1

- A 59-year-old male presents to your office with worsening pain in his hands, wrists, and knees over the past 9 months. He feels stiff in the morning for 15 minutes and notes occasional swelling in his knees after prolonged walking or standing.
- He works as a bus mechanic and does not smoke or drink. When working he reports more pain in hands and knees at the end of the day.
- His mother and brother have "arthritis".

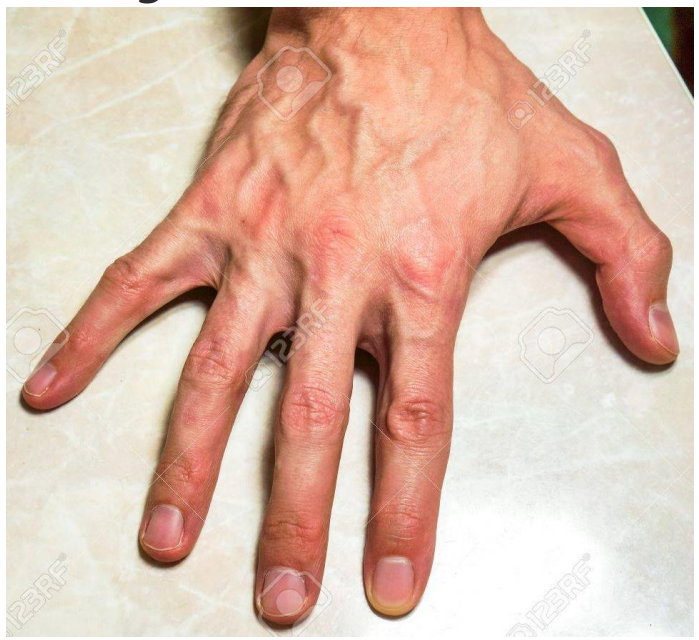


Photo from 123RF.com

CASE 1

- Labs:
  - Normal CBC
  - Normal creatinine
  - Liver mild elevation AST: 45 ALT: 52
  - ESR 20, CRP normal
  - Rheumatoid Factor 66 (nl<14 IU/ml), anti-CCP 28 (nl<20 U/ml)
  - Hepatitis C positive, Hepatitis B negative

- Xray of hands and knees shows mild degenerative changes

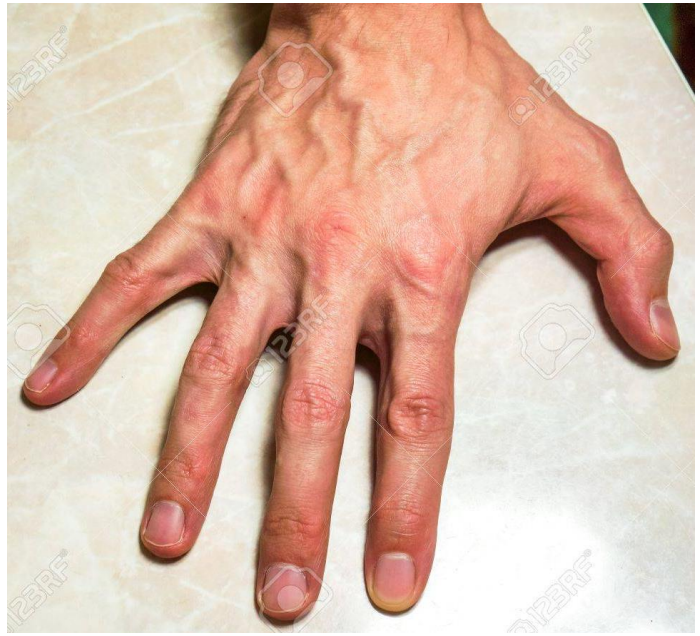


Photo from 123RF.com

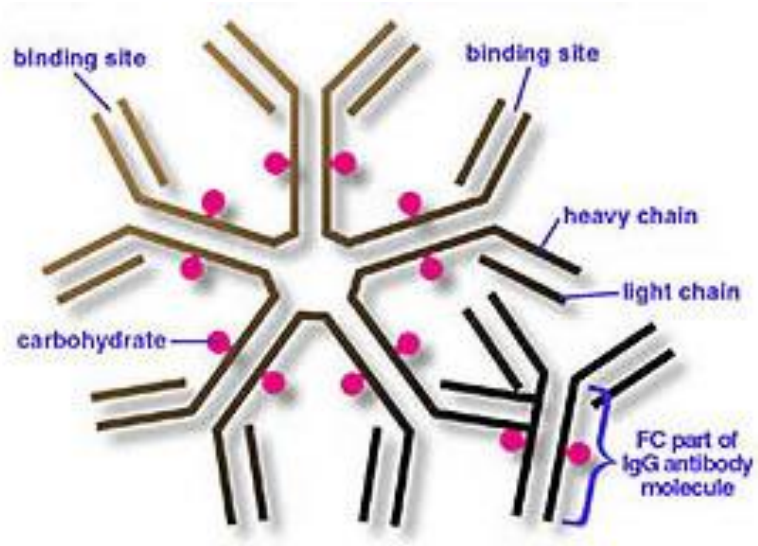
CASE 1: HEPATITIS C - ASSOCIATED ARTHROPATHY

- Prevalence of Hepatitis C: ~1.7 %
- Prevalence of HepC associated arthropathy: 2-20 %
- RF in Hepatitis C: 10-70%
- Anti-CCP in Hepatitis C: 0-20% (low levels)

Hofmeister, MG, et al. Hepatology March 2019
Zengin, O, et al. Adv Clin Exp Med Sept 2017
Lienesch D, et al. J Rheum 2005
Clifford, BD, et al. Hepatology 1995

ANTIBODIES: RHEUMATOID FACTOR

Normal	Individuals, especially with **age**
Arthritis	Rheumatoid arthritis (85%), Sjögren's, Lupus
Viral Infections	Hepatitis C, mononucleosis, HIV
Bacterial Infections	Endocarditis, TB, leprosy, syphilis
Parasites	Trypanosomiasis, malaria
Other	Sarcoidosis, pulmonary fibrosis, liver disease



Tedesco, A. Pathological and therapeutic antibodies, 2008

CASE 2

- A 75-year-old woman presents to your office with worsening joint pain for the past 1 year.
- She wakes with 10 minutes of stiffness diffusely and reports swelling in her fingers. She reports pain in her hands, wrists, shoulders, knees and feet. She cannot open bottled water anymore and keeps dropping her coffee cup.
- She works part-time in accounting and exercises regularly.
- She mentions her mother had "deformed hands" and severe arthritis. Her sister was recently diagnosed with arthritis too.
- She smokes 10 cigarettes per day.

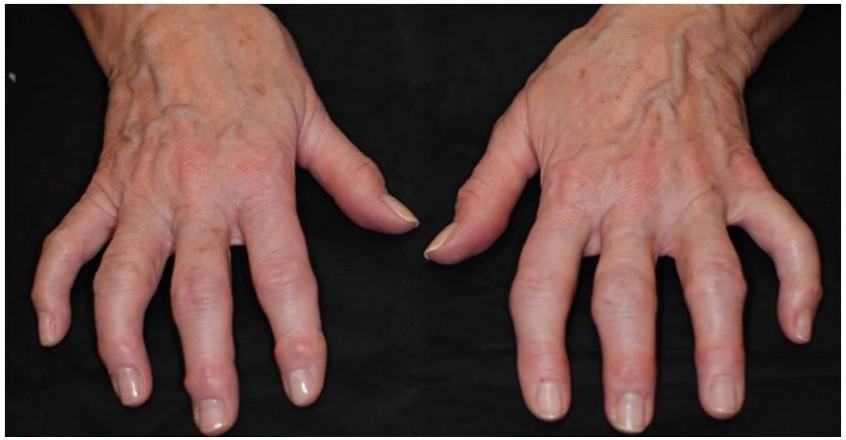


Image from ACR Image bank

CASE 2

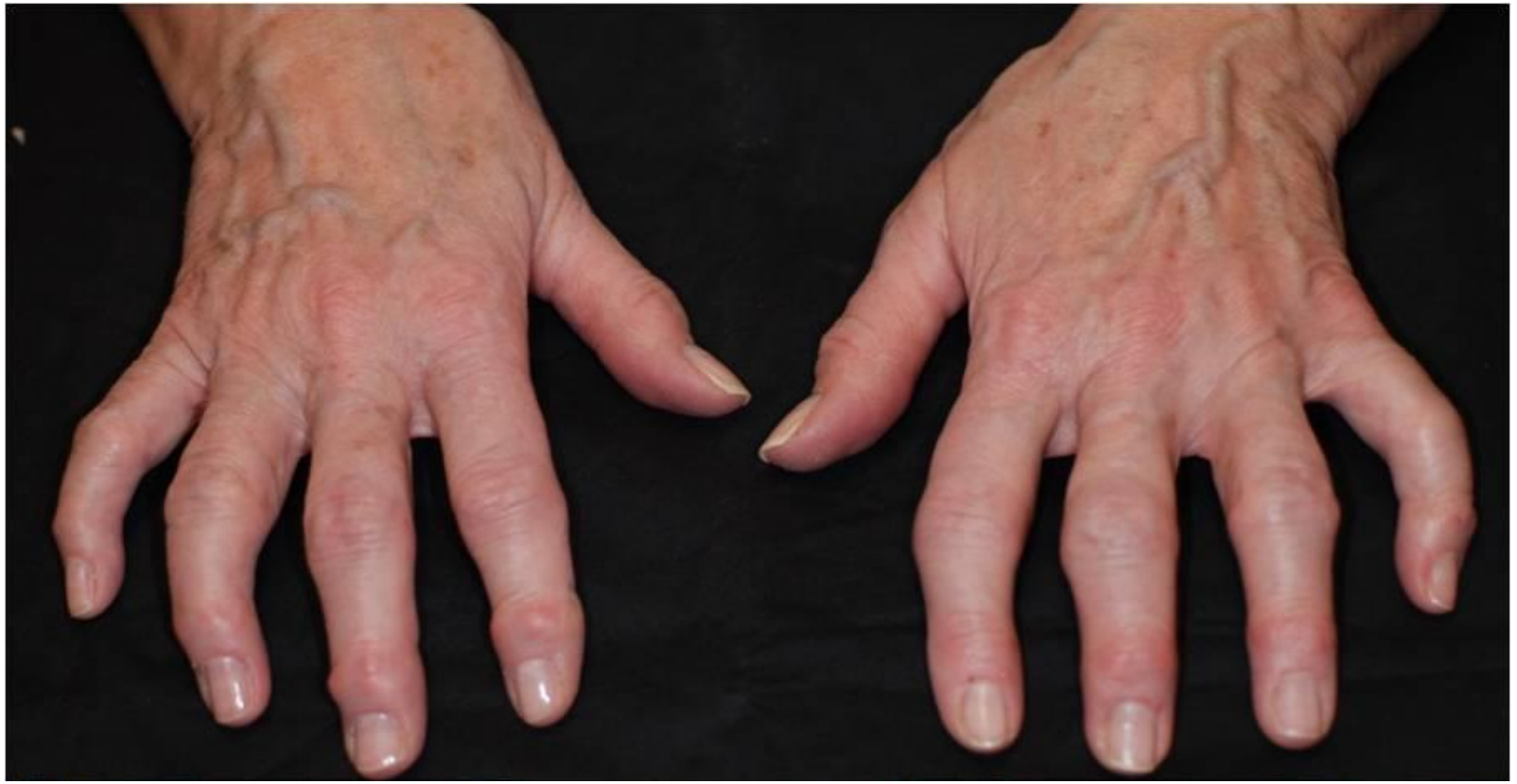
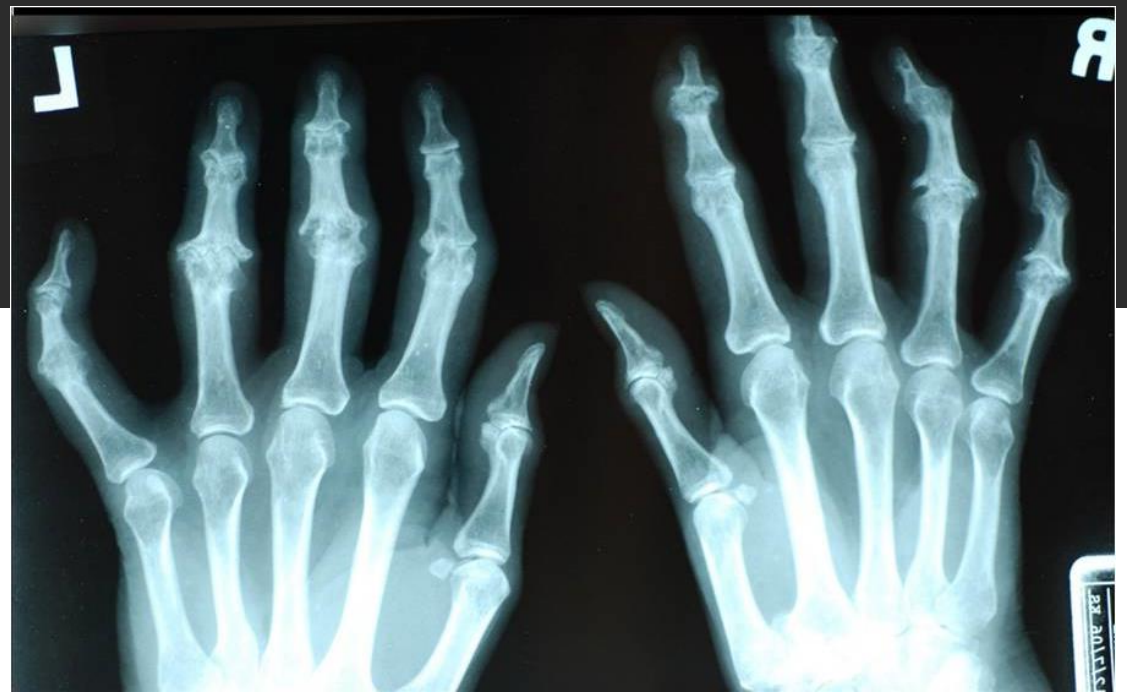


Image from ACR Image bank

CASE 2



- Labs:
  - Normal CBC
  - Normal liver and creatinine
  - ESR 15
  - CRP normal
  - Rheumatoid Factor 23 (nl<14 IU/ml), anti-CCP 45 (nl<20 U/ml)

- Xray of hands and knees reveal joint space narrowing, gull-wing, (central) erosive changes

Image from ACR Image bank

CASE 2: EROSIVE OSTEOARTHRITIS

- Erosive Osteoarthritis (EOA)

- Why it's not RA:
  - No inflammatory symptoms or labs
  - Exam with bony changes, no synovitis
  - Xray erosive changes related to EOA in PIP and DIP

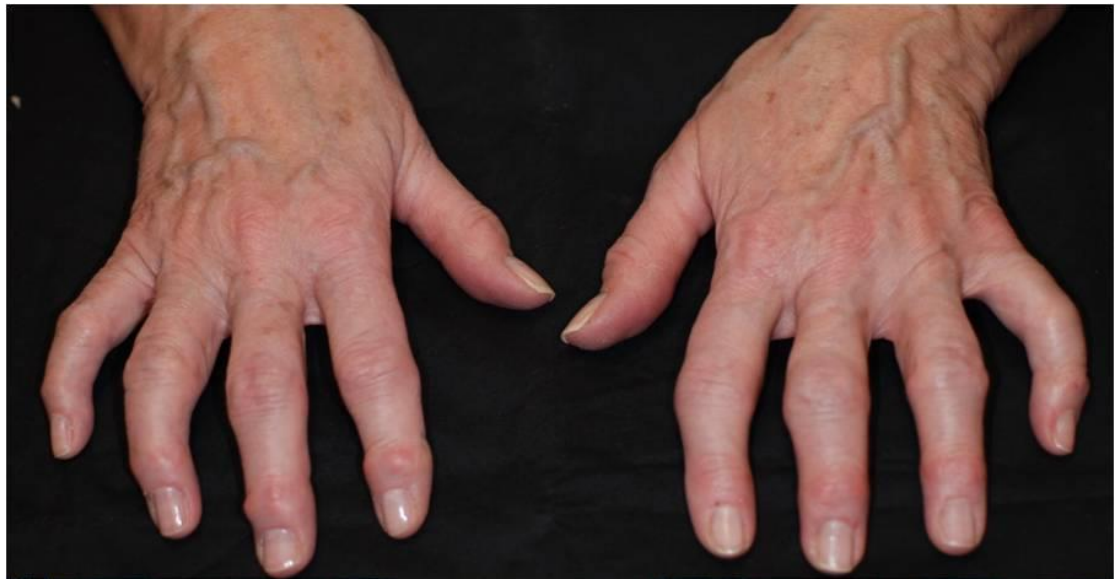
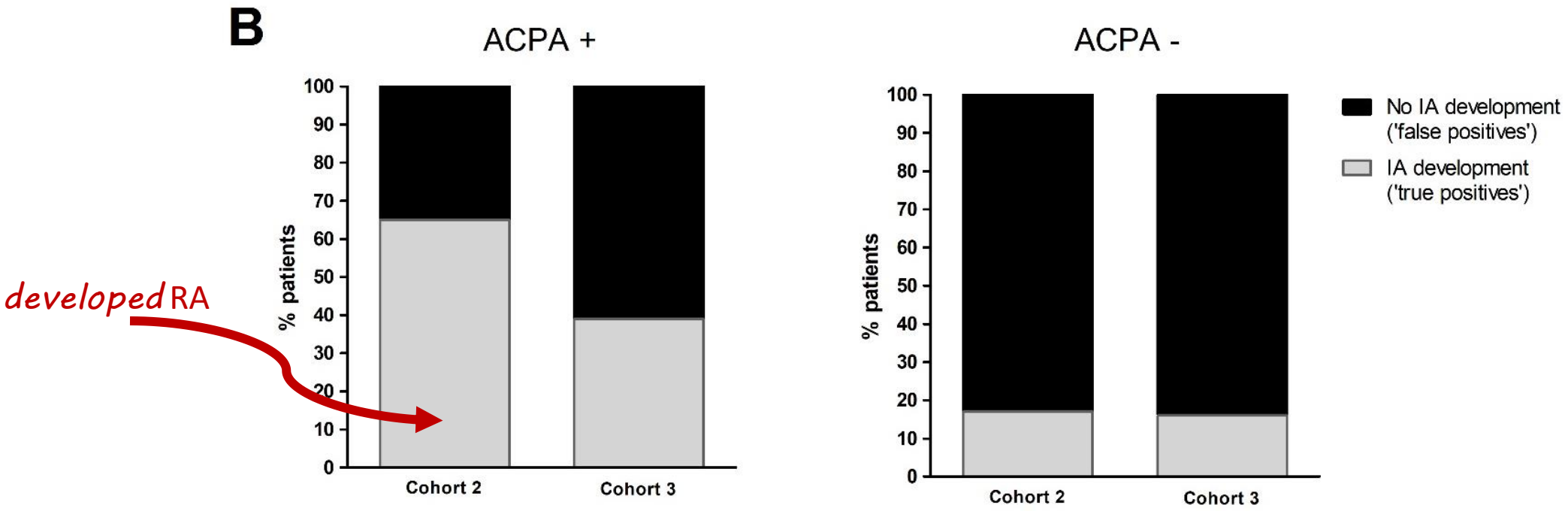


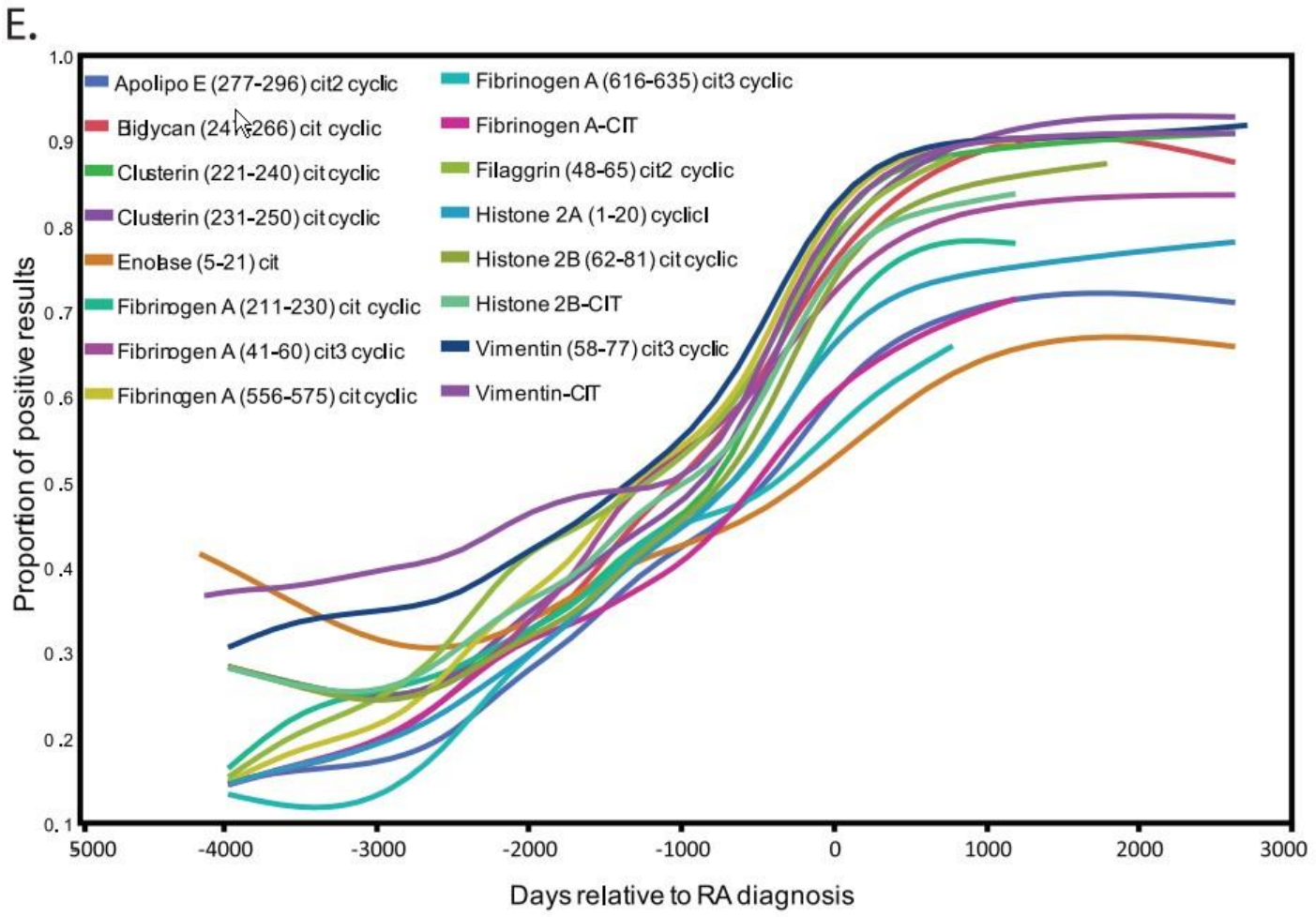
Image from ACR Image bank

ANTI-CCP AND RISK OF RA



Lee, et al., AnnRheum Dis, 2003
Demouruelle, et al., A&R, 2013
Rogier, et al., A&R supp, 2020

ANTIBODIES: ACPA



Sokolove Plos One 2012

RHEUMATOID ARTHRITIS

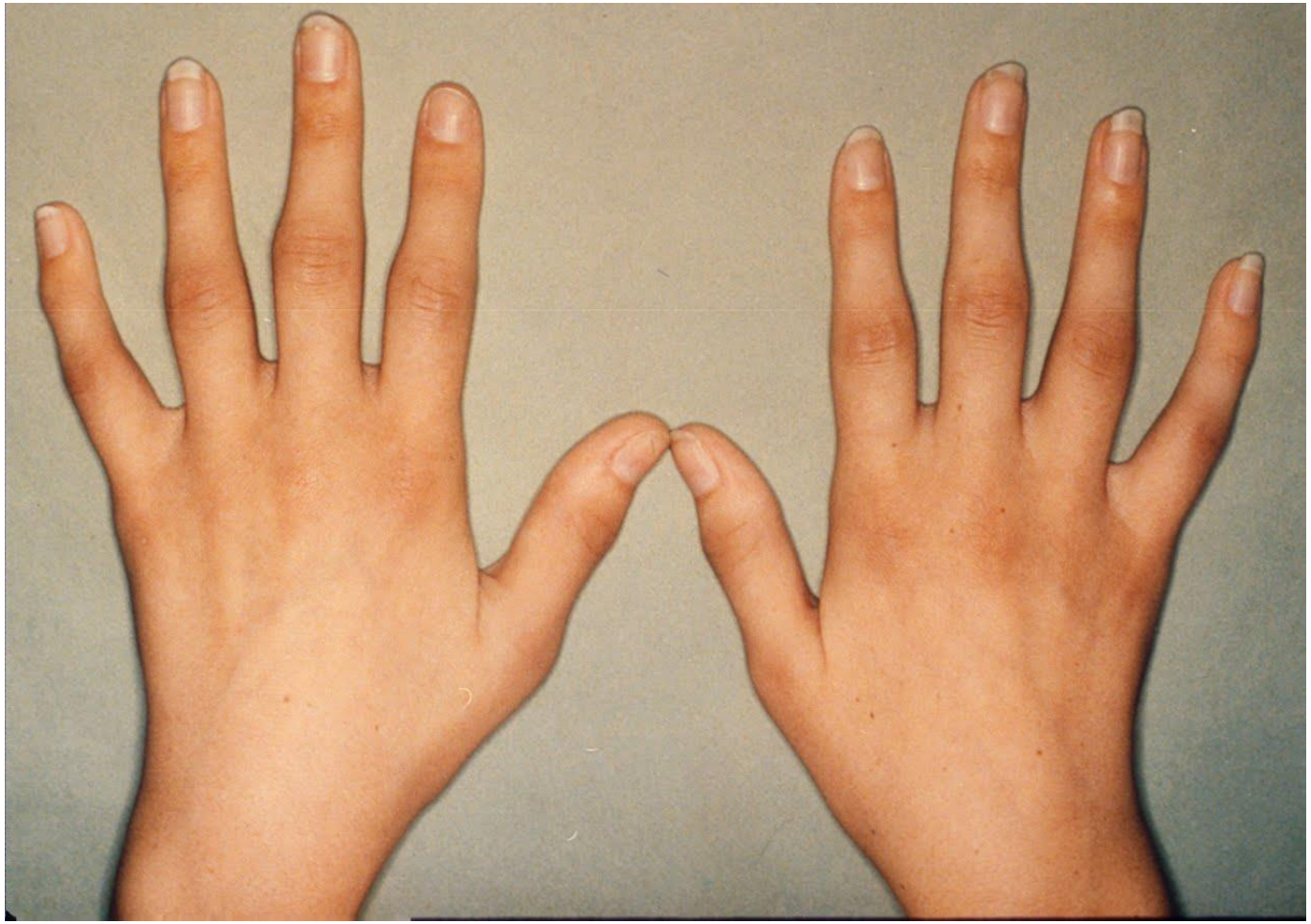
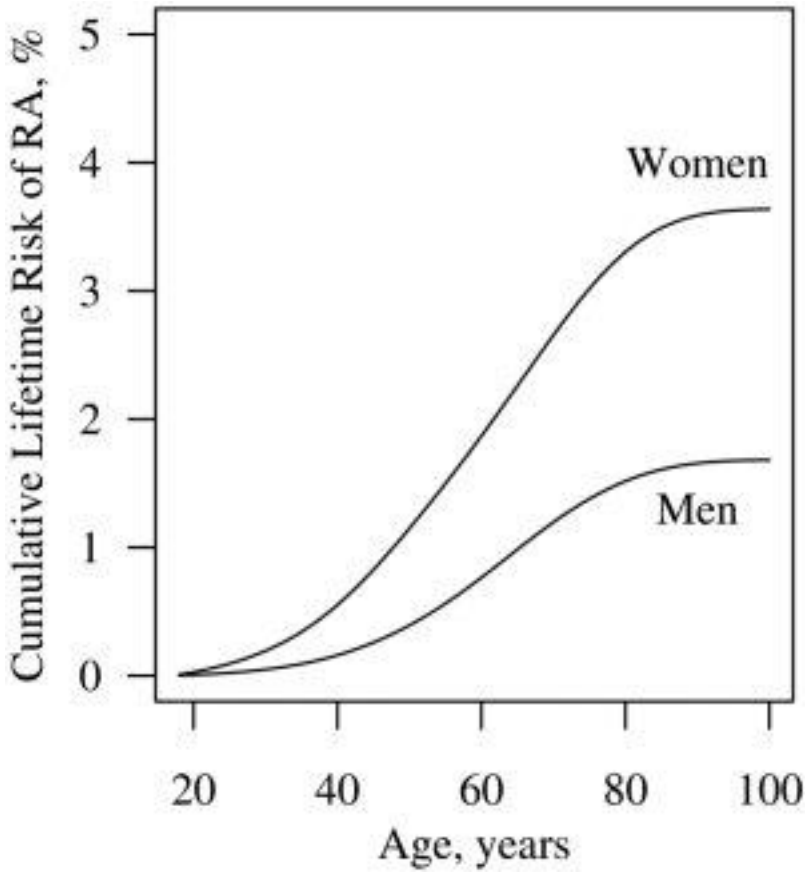


Image from ACR Image bank

RHEUMATOID ARTHRITIS

Incidence 3.6%* and Prevalence 1 %

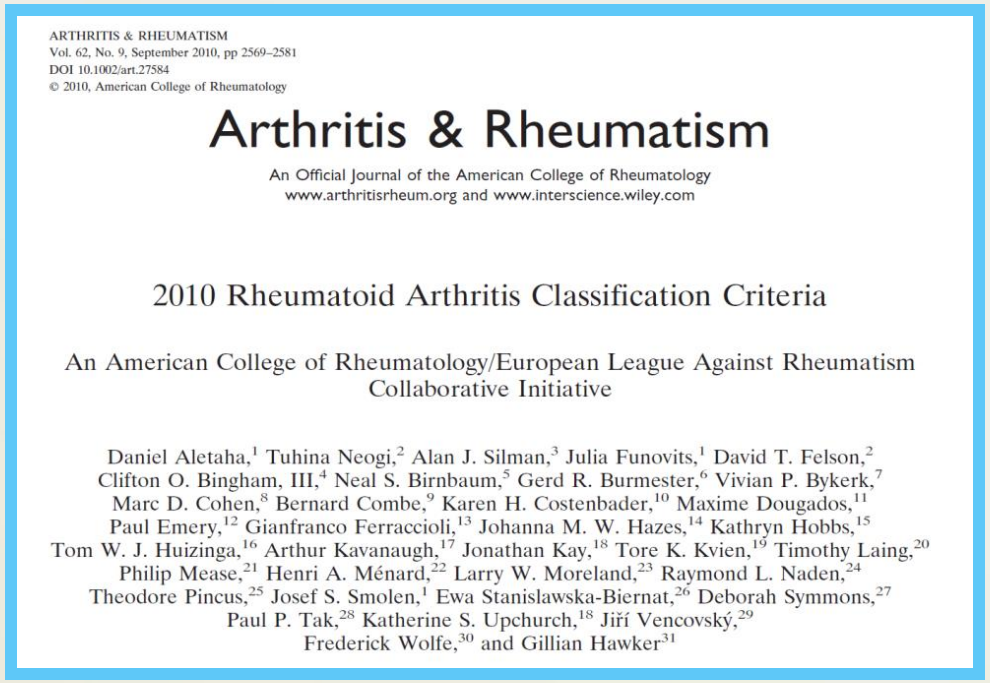


Gabriel, et al., A&R, 2011

Classification

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



ARTHRITIS & RHEUMATISM
Vol. 62, No. 9, September 2010, pp 2569–2581
DOI 10.1002/art.27584

Arthritis & Rheumatism
An Official Journal of the American College of Rheumatology
www.arthritisrheum.org and www.interscience.wiley.com

2010 Rheumatoid Arthritis Classification Criteria

An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative

Daniel Aletaha,[1] Tuhina Neogi,[2] Alan J. Silman,[3] Julia Funovits,[1] David T. Felson,[2] Clifton O. Bingham, III,[4] Neal S. Birnbaum,[5] Gerd R. Burmester,[6] Vivian P. Bykerk,[7] Marc D. Cohen,[8] Bernard Combe,[9] Karen H. Costenbader,[10] Maxime Dougados,[11] Paul Emery,[12] Gianfranco Ferraccioli,[13] Johanna M. W. Hazes,[14] Kathryn Hobbs,[15] Tom W. J. Huizinga,[16] Arthur Kavanaugh,[17] Jonathan Kay,[18] Tore K. Kvien,[19] Timothy Laing,[20] Philip Mease,[21] Henri A. Ménard,[22] Larry W. Moreland,[23] Raymond L. Naden,[24] Theodore Pincus,[25] Josef S. Smolen,[1] Ewa Stanislawska-Biernat,[26] Deborah Symmons,[27] Paul P. Tak,[28] Katherine S. Upchurch,[18] Jiří Vencovský,[29] Frederick Wolfe,[30] and Gillian Hawker[31]

American College of Rheumatology
Education • Treatment • Research

eular

HISTORICAL PERSPECTIVES

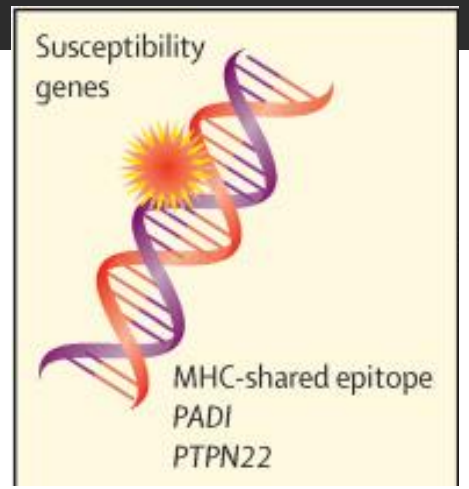
*1800 French medical resident Augustin Jacob Landré-Beauvais

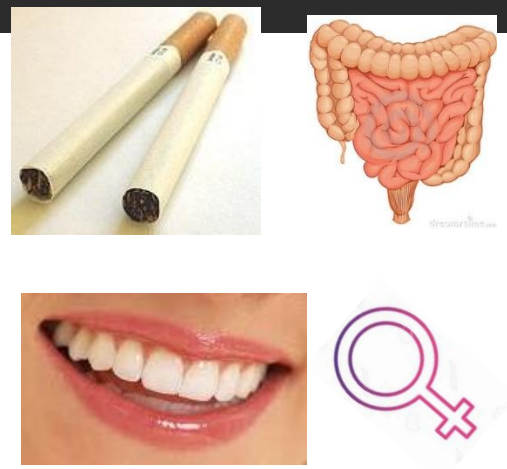
Paleopathological evidence controversial, may pre-date Landré-Beauvais by several hundred (?thousand) years

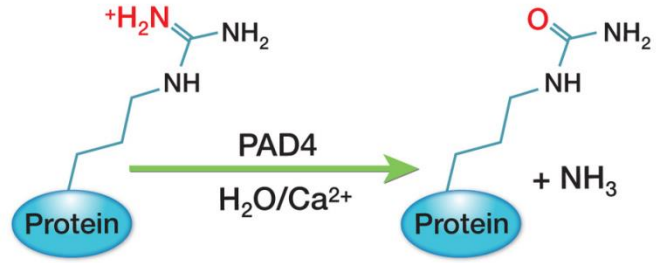
Old World > New World (1492 Columbus sailed the ocean blue)

Entezami, et al., Hand Clin, 2012
Stetka, et al., Medscape 2016
Panush, 2012 https://hippocratesinst.org/the-sugar-timeline

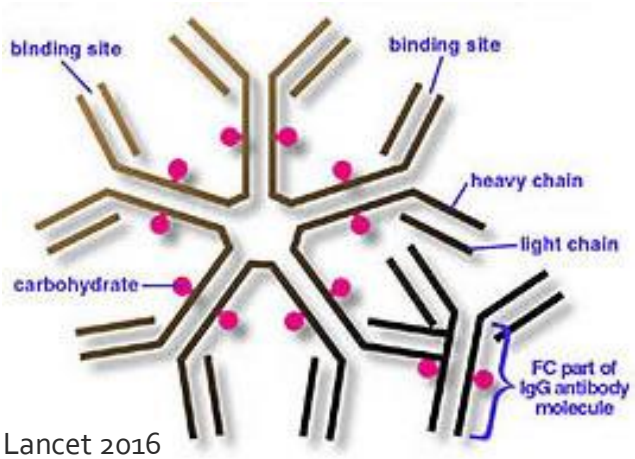
PATHOGENESIS



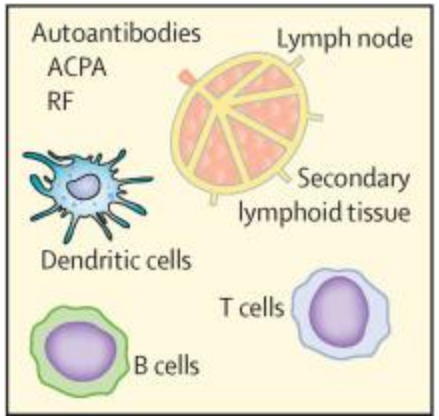


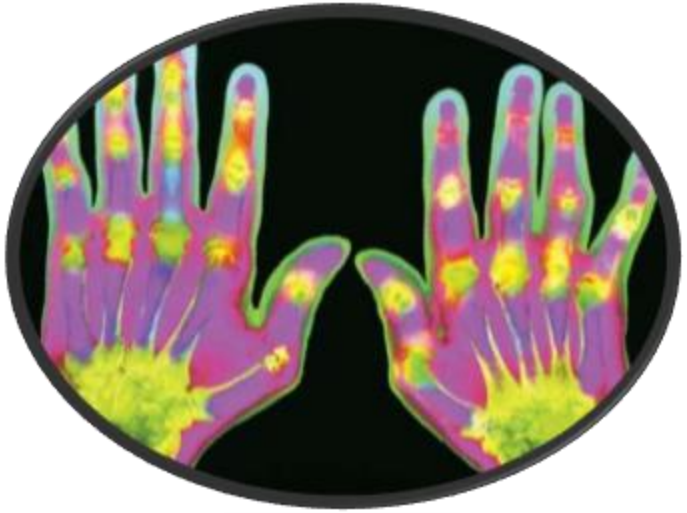


citrullination



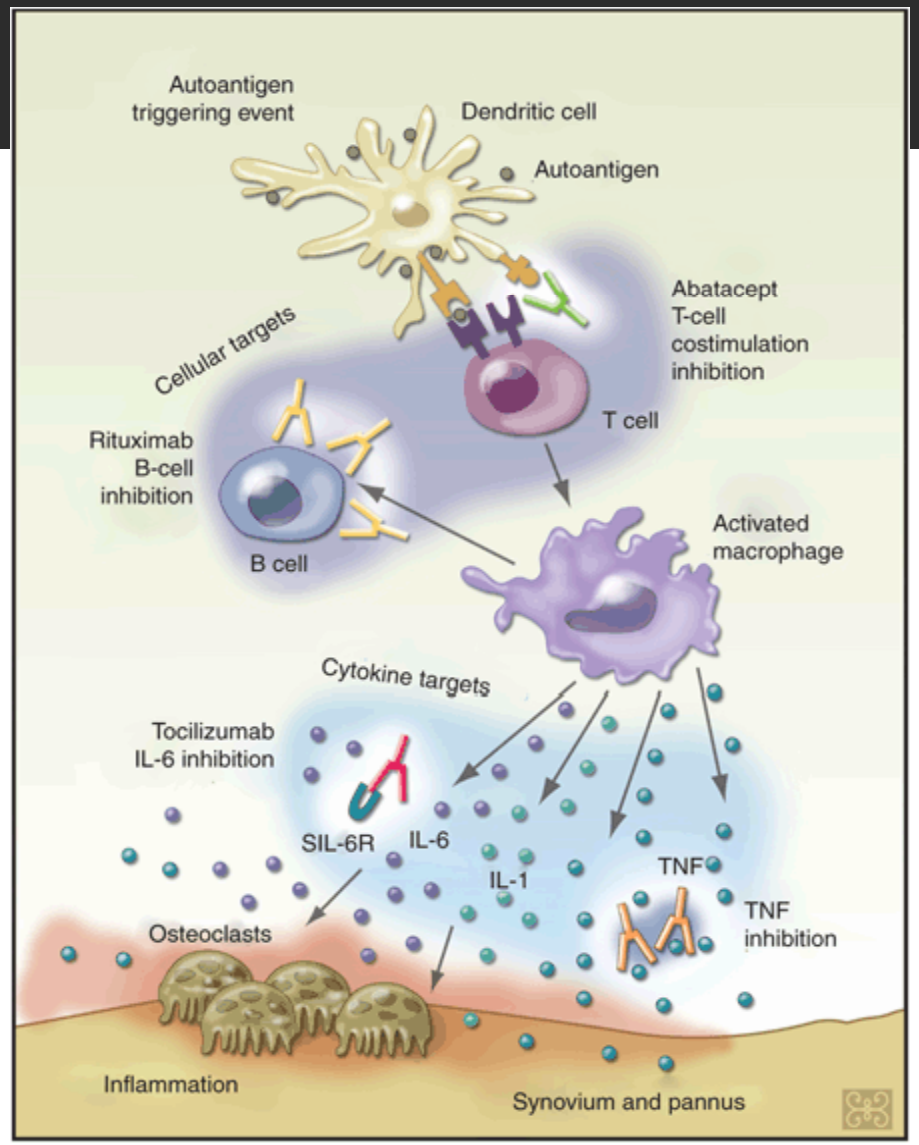
?





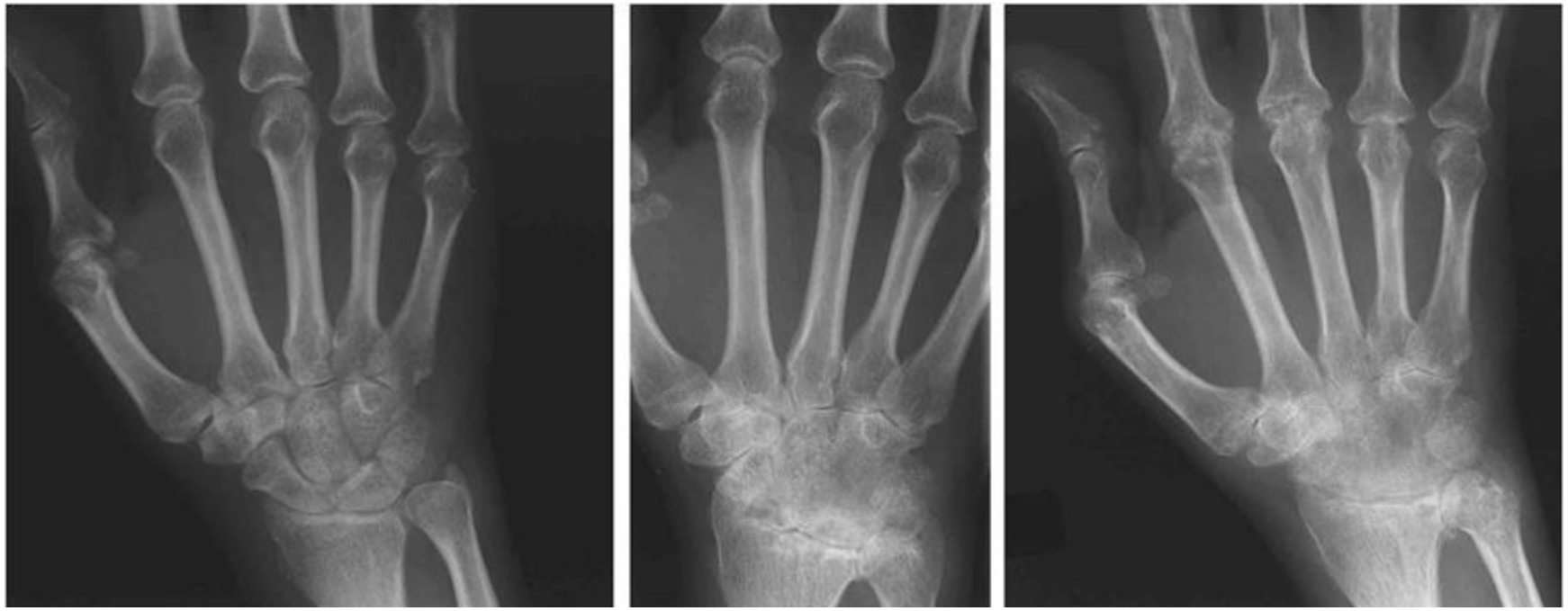
Smolen et al., Lancet 2016
Deane et al., Best Pract Res Clin Rheum 2017
Holers, et al., Nature Rev Rheum 2018

PATHOGENESIS

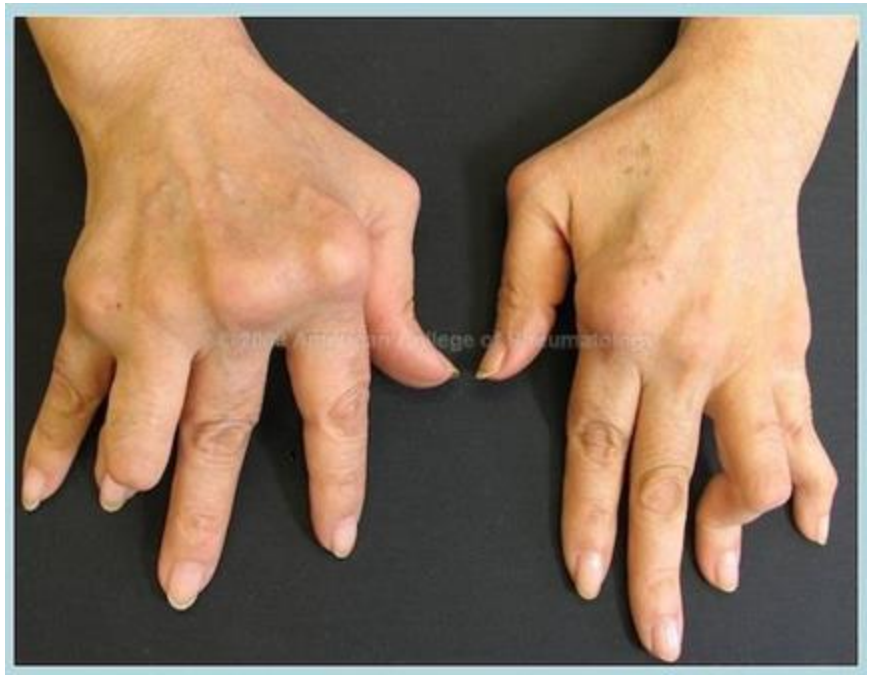


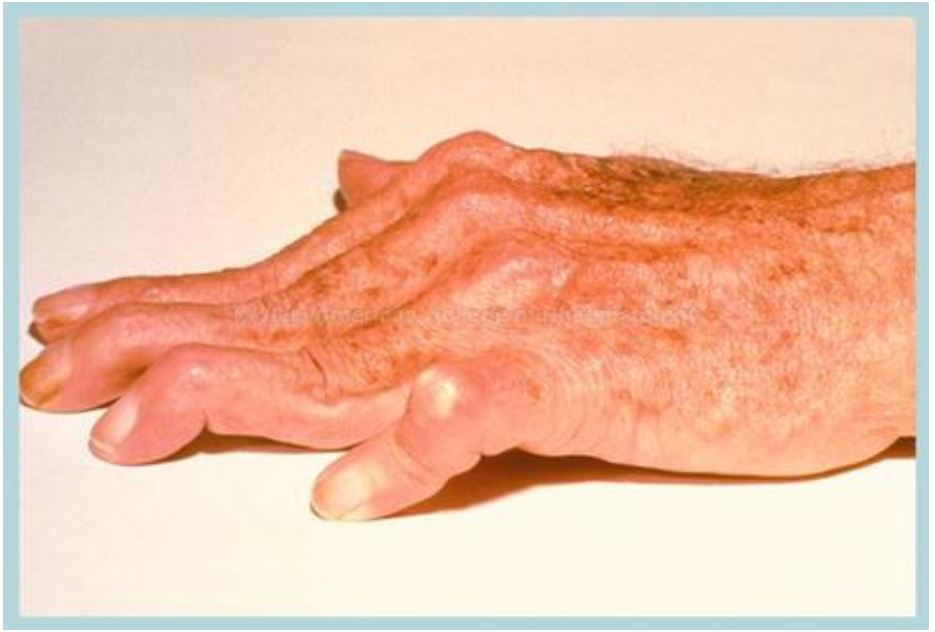
Scott Clin Pharm and Ther 2012 91(1)

RHEUMATOID ARTHRITIS XRAYS

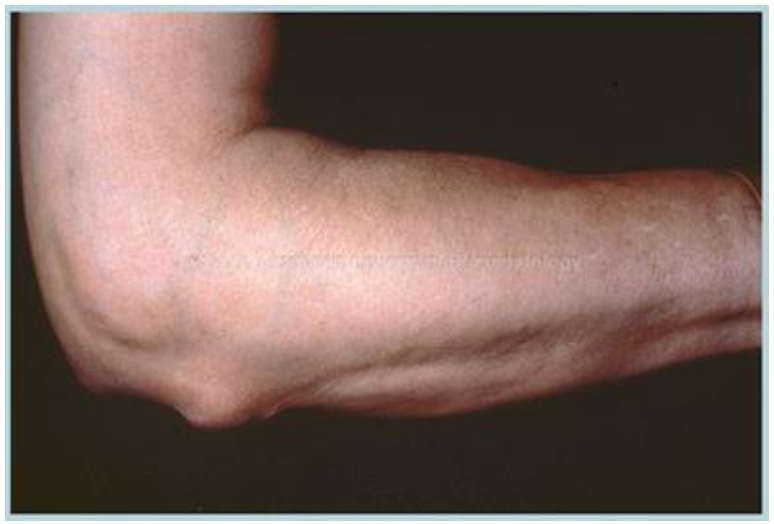


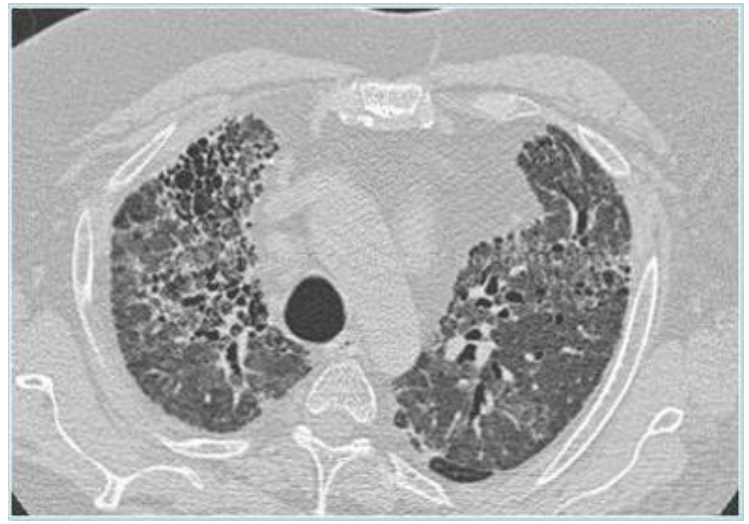
ARTICULAR MANIFESTATIONS



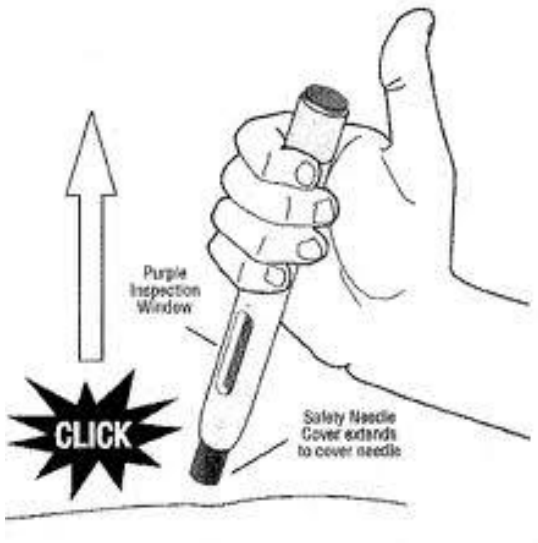


EXTRA-ARTICULAR FINDINGS





THERAPY


Purple
Inspection
Window
CLICK
Safety Needle
Cover extends
to cover needle

NSAIDS

Generic NSAIDs Available

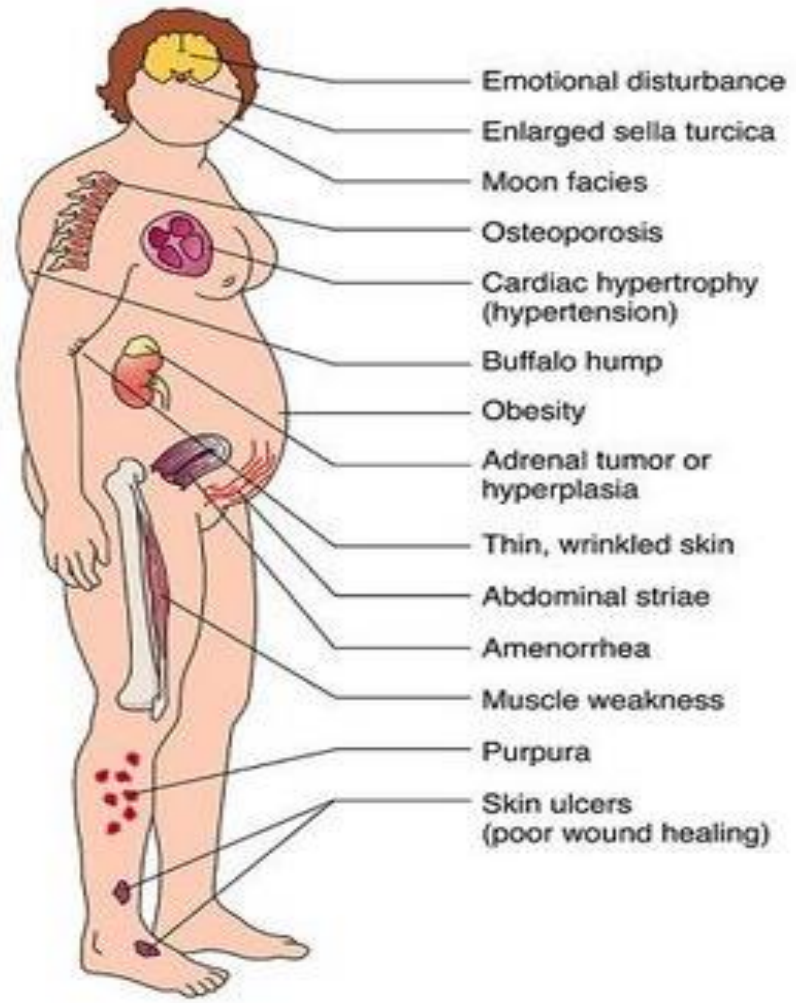
NSAID Class	Generic Name	NSAID Class	Generic Name
Salicylates	Salsalate	Acetic acids	Diclofenac potassium
Propionic acids	Fenoprofen		Diclofenac sodium
	Flubriprofen		Etodolac
	Ibuprofen		Sulindac
	Ketoprofen	Oxicams	Piroxicam
	Naproxen	Naphthyl-alkanones	Nabumetone
	Naproxen sodium		
	Oxaprozin		

Brand-only NSAIDs:

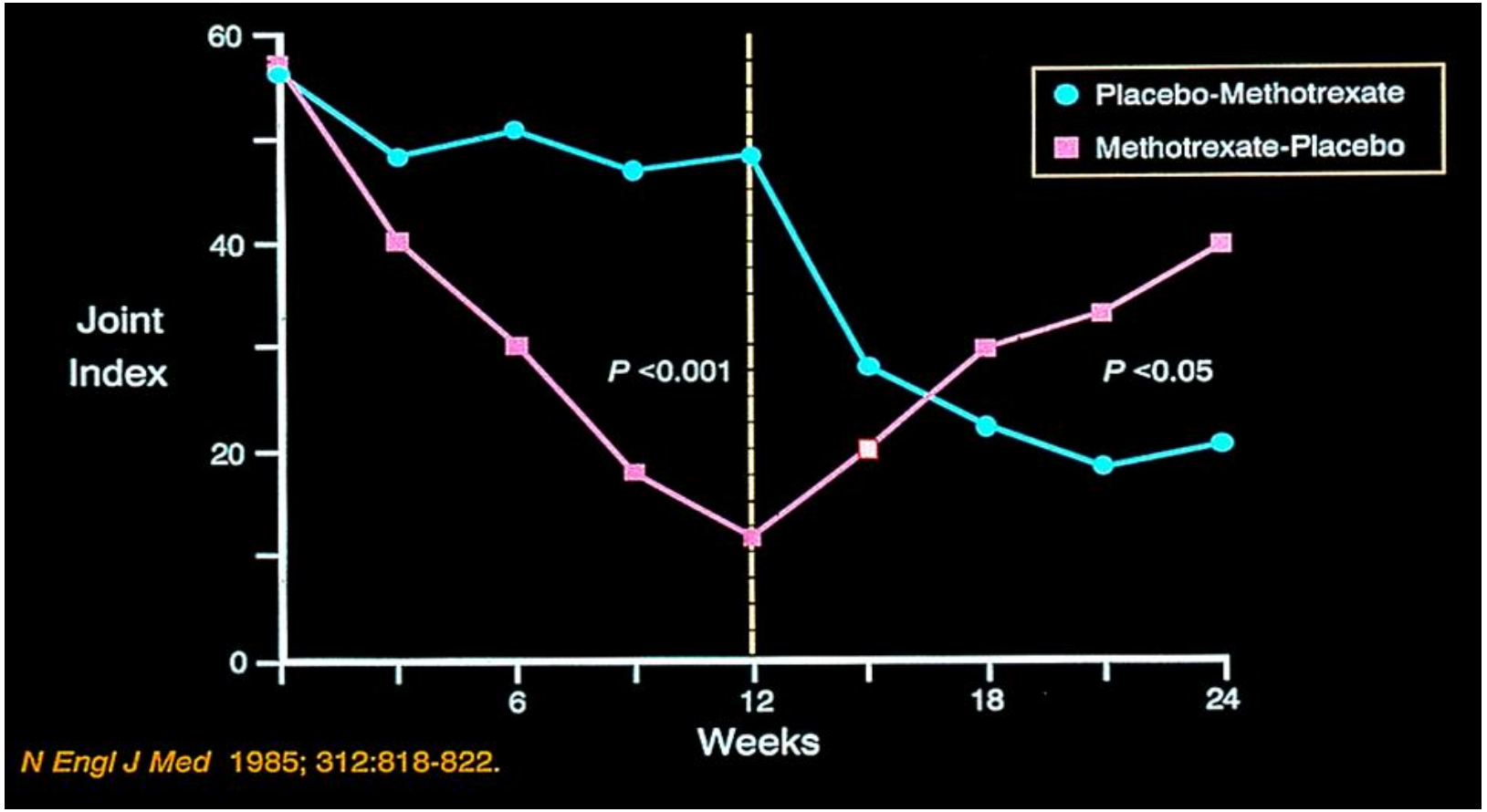
NSAID Class	Generic Name / Proprietary Name
Semi-selective COX-2 inhibitor	Meloxicam / Mobic®
Selective COX-2 inhibitor	Celecoxib / Celebrex®

CORTICOSTEROIDS / PREDNISONE

- Dosing: 5-10 mg per day
- Bone health + Vitamin D



METHOTREXATE

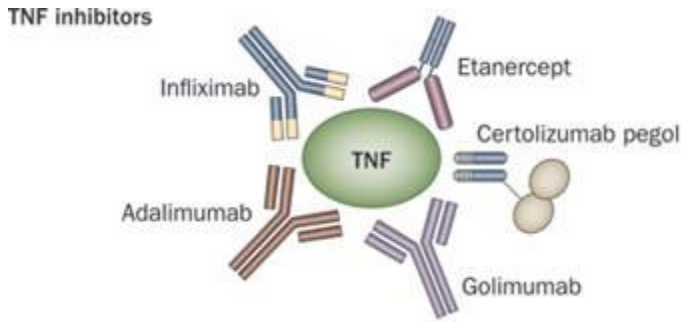


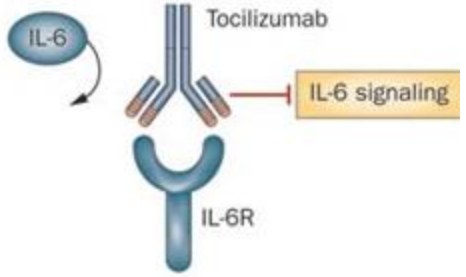
Slide courtesy of Drs. Gary Firestein and Michael Wienblatt

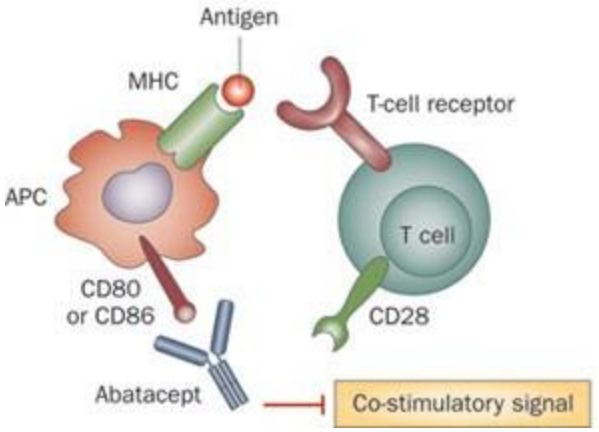
BIOLOGIC AND SMALL MOLECULE THERAPY

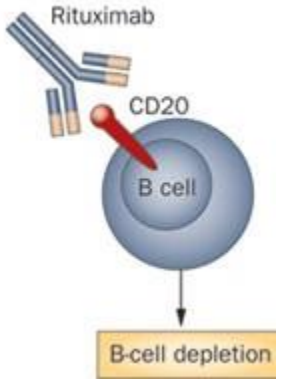
BIOLOGIC AND SMALL MOLECULE THERAPY

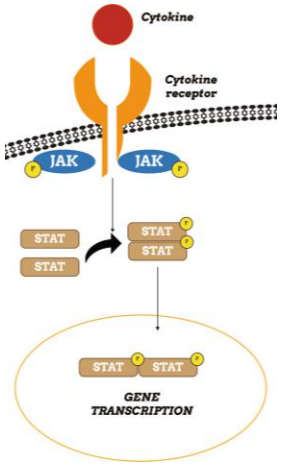
- Binding anti-TNFα
- Blocking T cell co-stimulation
- B cell depletion
- Targeting IL-6 / IL-6R
- Inhibiting Jak/Stat pathway











Woodrick, et al., Nature Rev Rheum 2011
Winthrop, Nat Rev Rheum 2017
Nogueira et al., Drugs 2020

OTHER TREATMENT MODALITIES

Deane, et al., Best Pract Res Clin Rheum 2017
Smolen et al., Nat Rev Dis Prim 2018
Coras, et al., Arth & Rheum 2020 (suppl 10)
Hahn, et al., Arth & Rheum 2020 (suppl 10)

IMMUNOSUPPRESSION AND VACCINATION

- Live virus vaccines should be avoided
- Response to the vaccine may be decreased in some immunosuppressed individuals
- Indicated inactivated Vaccines:
  - Influenza
  - Pneumococcal
  - Hepatitis B
  - Shingrex
  - Covid-19

Wolfe et al., Arthritis Rheum, 2007
Friedman, et al., Curr Opin Rheum 2016

SUMMARY

- RA is a common inflammatory, autoimmune disease affecting joints and other organs
- Genetics and environment play a role in the development of immune dysregulation
- Methotrexate is the anchor drug
- Biologics target specific immune system functions to reduce inflammation
- Smoking cessation, mediterranean-style diet, and healthy lifestyle may mitigate inflammation

THANK YOU

Renoir

Dance at the Moulin de la Galette (1876)
Musee d'Orsay, Paris