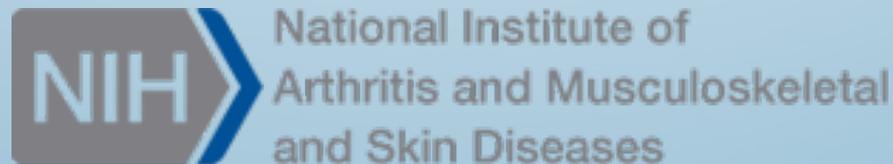


DEMYSTIFYING AUTOIMMUNE DISEASE

4/23/19

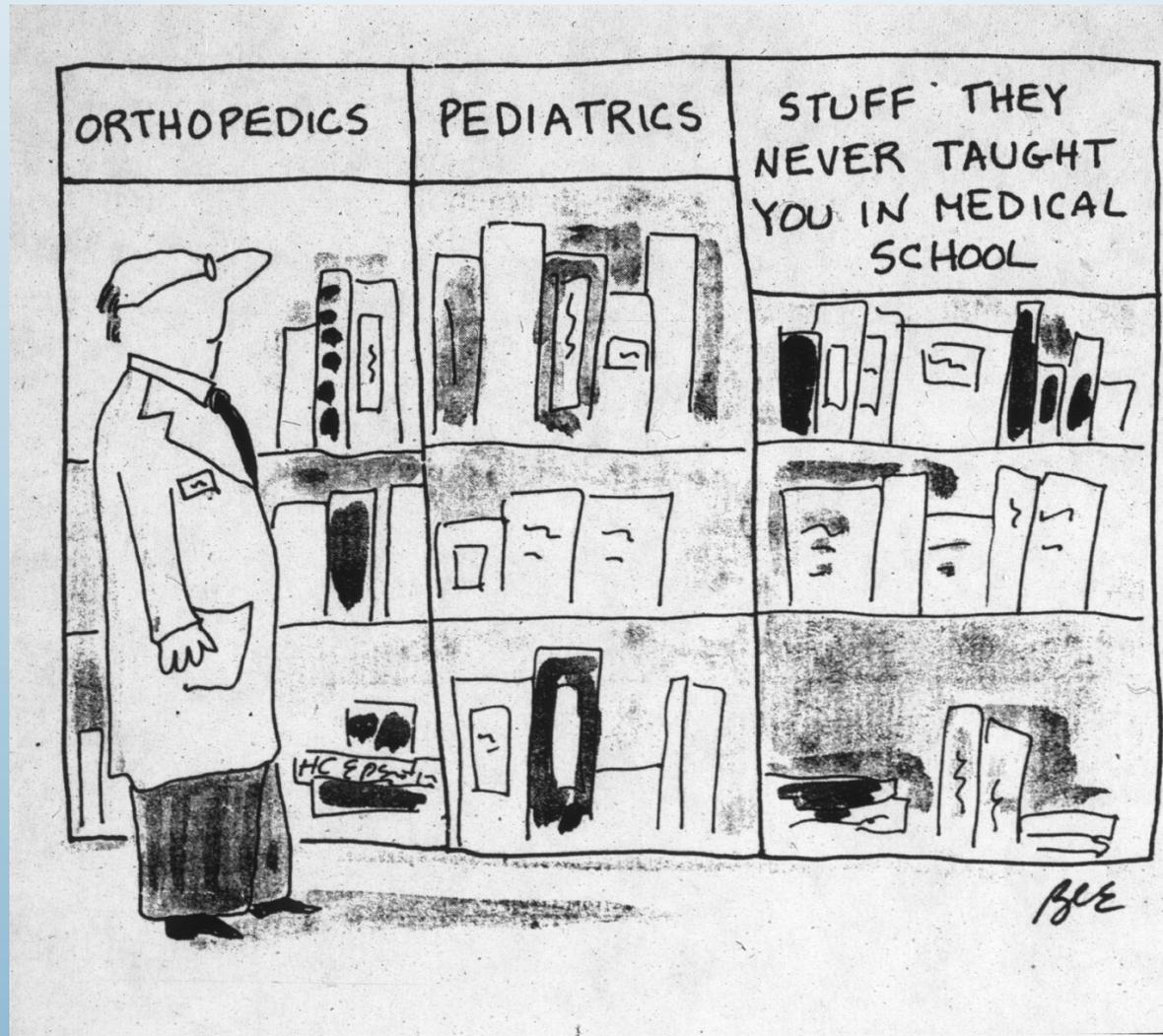
James D. Katz, MD



NONE

A red, rectangular stamp with rounded corners and a double-line border. The word "DISCLOSURE" is written in a bold, sans-serif font across the center of the stamp. The stamp is tilted slightly upwards to the right and is set against a light gray background.

LEARNING OBJECTIVES:



EDUCATIONAL INTERLUDE....



THE LANGUAGE OF PAIN

- necessarily comparative in nature
- metaphor uses language of substitution (e.g., “like walking on broken glass”)
- metonymy uses language of displacement (e.g., “I’m normally a strong person and I can’t even...”)

MYTH OF PERSONAL HEROISM

- we function in ever-present denial and pain is a threat that may undermine hope and force confrontation with mortal fears
- “Now I know what it feels like to get old.”

***LES DEUX SOEURS (SUR LA
TERRASSE): 1881***



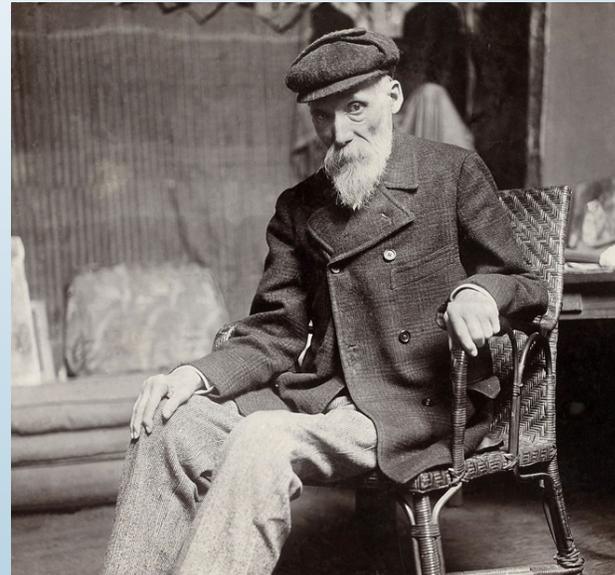
PIERRE-AUGUSTE RENOIR



IMPRESSIONIST STYLE



LONG BATTLE WITH 'RHEUMATISM'



OIL ON CANVAS 68 X 35 IN.
(172.7 X 88.9 CM)



LIMITED SHOULDER RANGE OF MOTION



RHEUMATOID ARTHRITIS IS...



- **Unhappy joints.**
- **Systemic disease of multifactorial origin, including a genetic predisposition, and characterized by immune-driven, chronic inflammation**

RHEUMATOID ARTHRITIS

- variable course of disease activity.
- chronic and progressive.
- results in disability.



RENOIR WAS AGE 47 WHEN HIS RA STARTED

- Peak age: 4th - 6th decades
- Sex distribution- (F:M) 2.5:1
- Prevalence rate - 1% in N. America
- Geography - Increased in some Native American populations; lowest rates found in oriental populations and rural Africans.

GENETIC ASSOCIATIONS

- HLA-DRB1 (within HLA-DR4 region) is a marker for disease severity
- Higher concordance rate in monozygotic versus dizygotic twins (relative risk = 3.5)



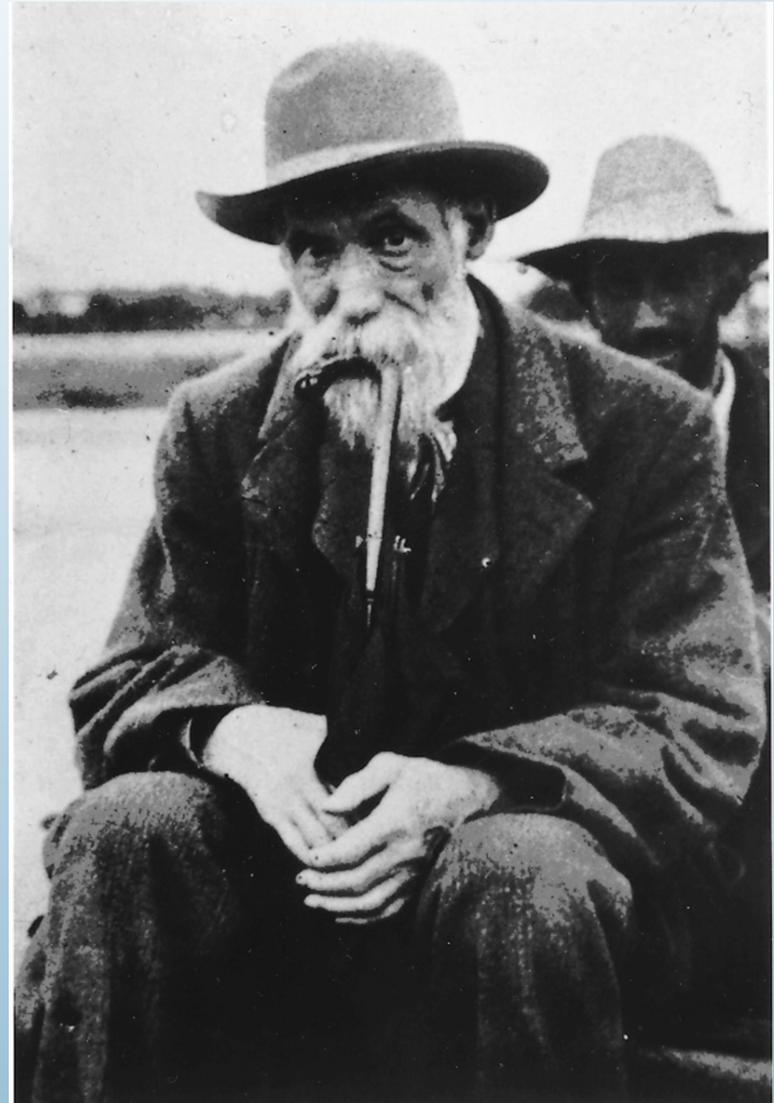
ENVIRONMENTAL CONSIDERATIONS

- Cigarette smoking is a strong risk factor
- Periodontal disease associated with RA
- Occupational exposures and silica associated with developing RA

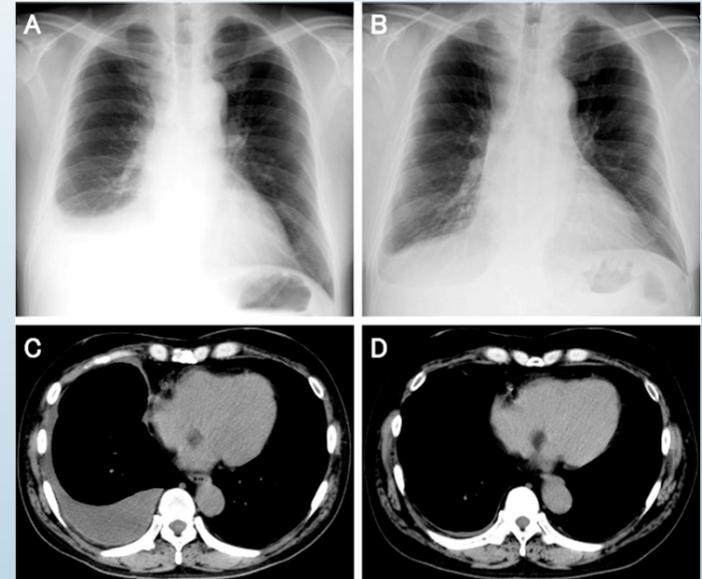


DIAGNOSIS

- Symmetric synovitis
- Longstanding duration
- Seropositive
- High sed rate



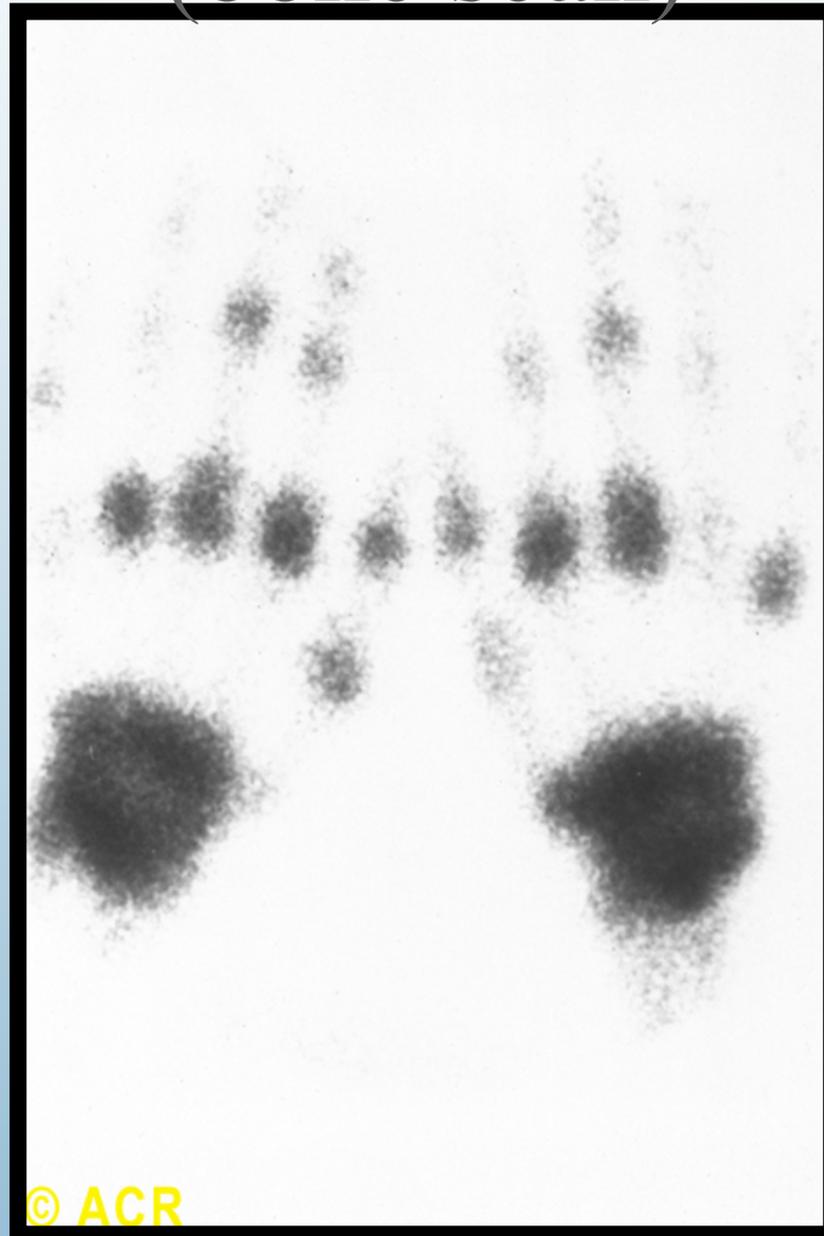
RENOIR HAD RHEUMATOID NODULES AND PLEURAL EFFUSIONS

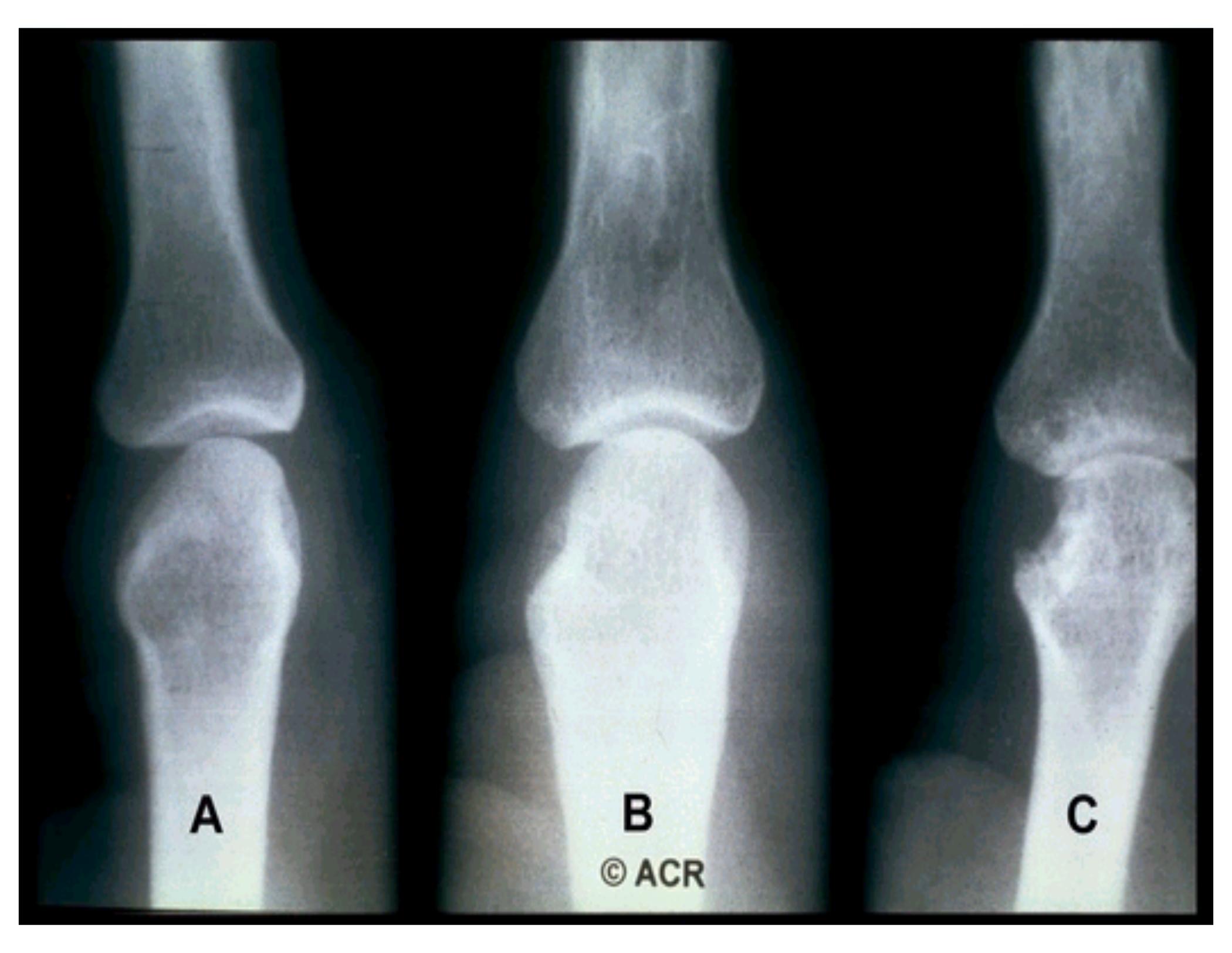


SYNOVIAL HYPERTROPHY



Rheumatoid arthritis: hand, inflammation (bone scan)





The image displays three sequential lateral radiographs of a knee joint, labeled A, B, and C from left to right. Each radiograph shows the distal femur at the top and the proximal tibia below it. In image A, the joint space is well-preserved. In image B, there is a noticeable narrowing of the joint space and the appearance of small, irregular bony spurs (osteophytes) at the joint margins. In image C, the joint space is significantly narrowed, and there are large, prominent osteophytes extending from the joint surfaces, characteristic of advanced osteoarthritis.

A

B

© ACR

C



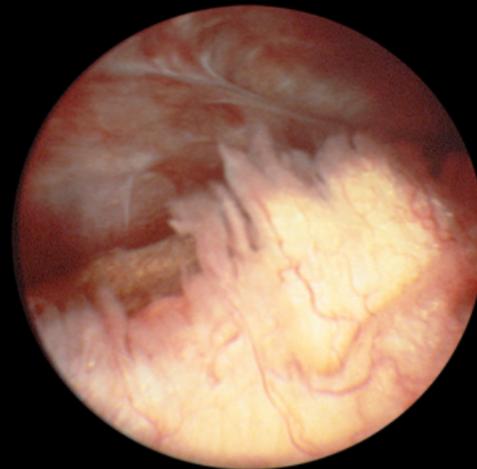
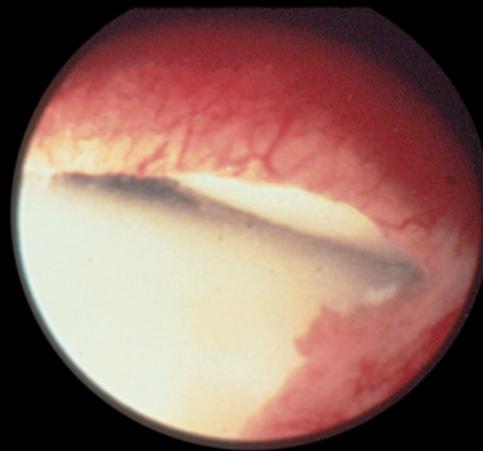
© ACR



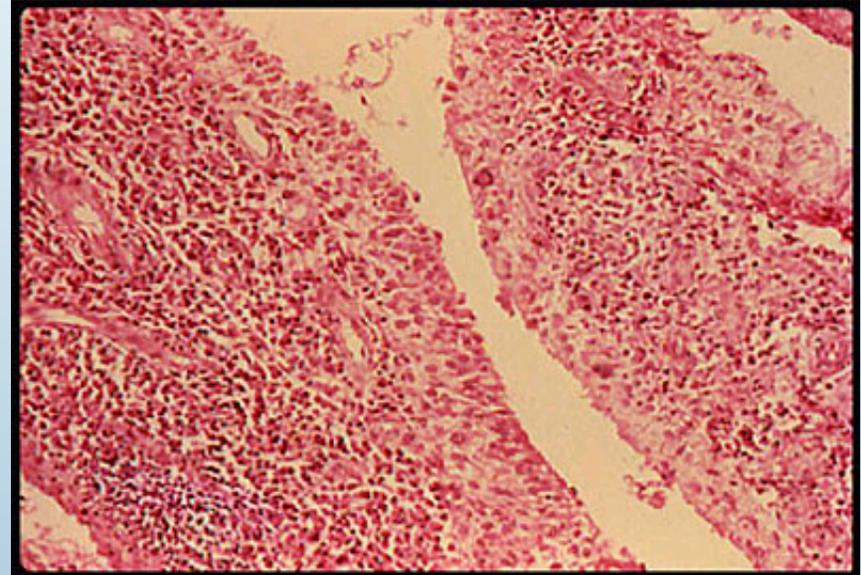
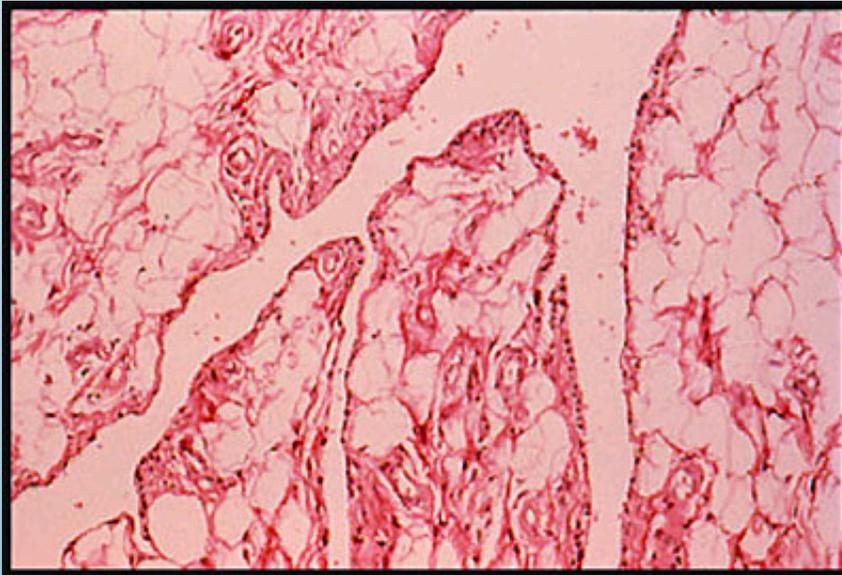
© ACR



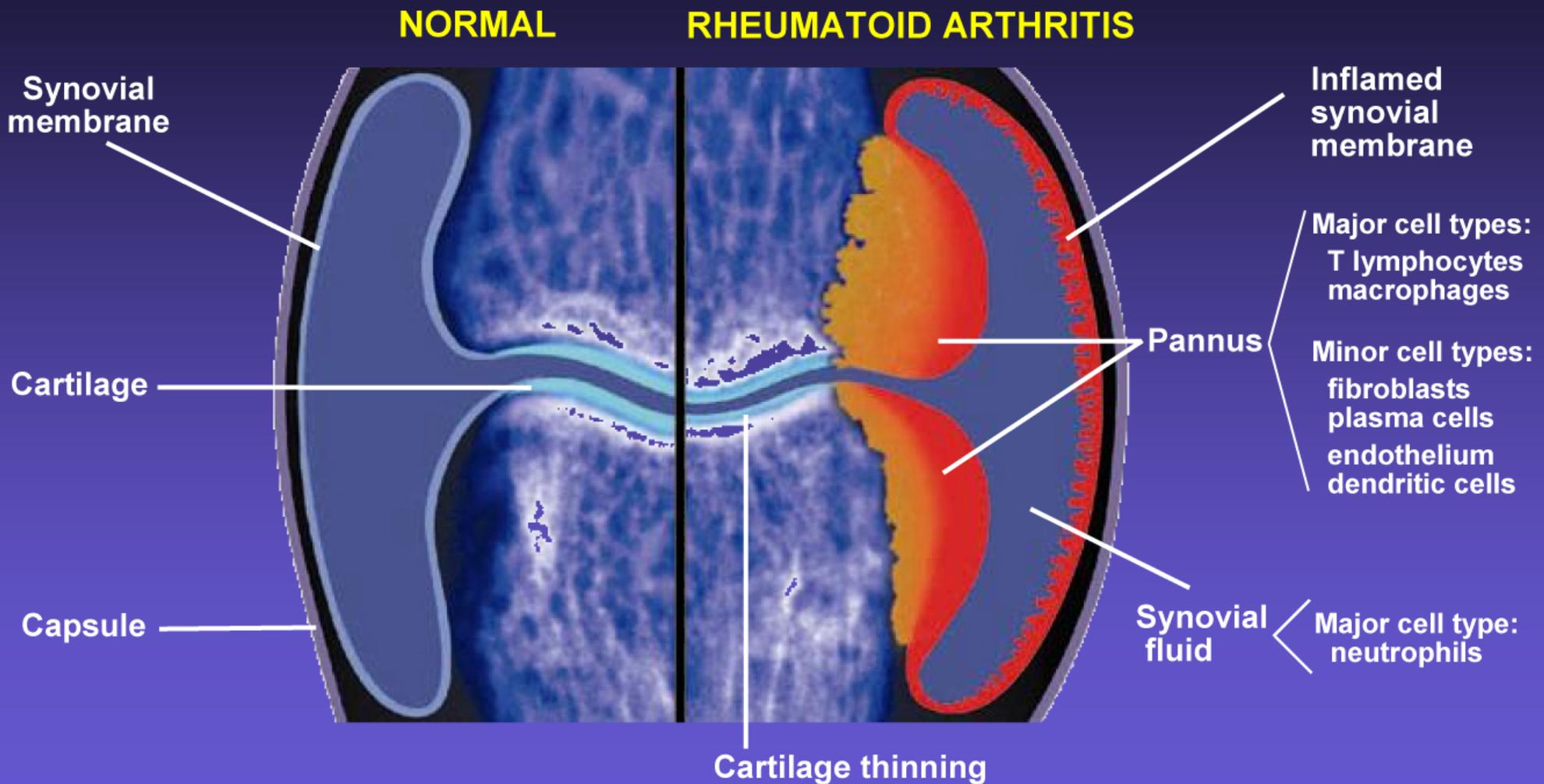
FIBROVASCULAR PROLIFERATION



PANNUS



The Pathogenesis of Rheumatoid Arthritis



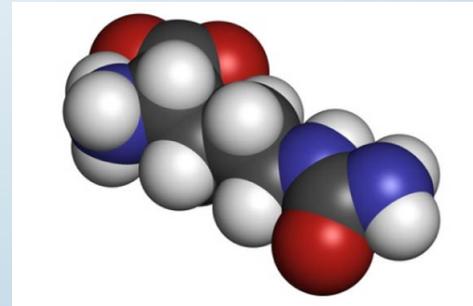
Adapted from Feldmann M, et al. *Annu Rev Immunol.* 1996;14:397-440.

IMMUNOLOGY

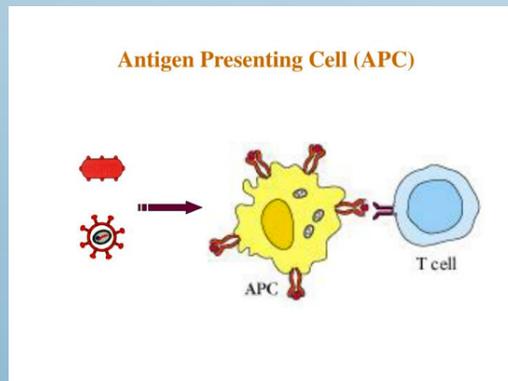
- Activation of innate immunity is probably the earliest process



- Followed by citrullination or carbamylation



- Loading of antigen-presenting cells (APCs) with autoantigens or altered native peptides in the joint



- Then migration to central lymphoid organs



THE T CELL ACTIVATION

- T cells constitute about 50 percent or more of cells in most RA synovia
- most of these are CD4+ with a memory phenotype
- preponderance of T cells of the Th1 and Th17 subset
- with deficiency of Th2 and regulatory T cells.

RENOIR TWICE BROKE HIS RIGHT ARM

- **osteoclasts secrete proteinases and create a local acidic environment that mediates bone destruction**
- **“Even the arm fractures could not prevent him from painting: Renoir became ambidexter.”**
 - **(Clin Cases Miner Bone Metab. 2012 Jan-Apr; 9(1): 59.)**

RHEUMATOID CACHEXIA

- **Reduced fat-free mass**
- **Excess of pro-inflammatory cytokines (e.g., TNF-alpha) is considered to be the central feature**



MANAGEMENT

Multidisciplinary approach

- Education
- Drug therapy
- Physical/occupational therapy
- Surgical intervention



“EARLY DIAGNOSIS/AGGRESSIVE MANAGEMENT”

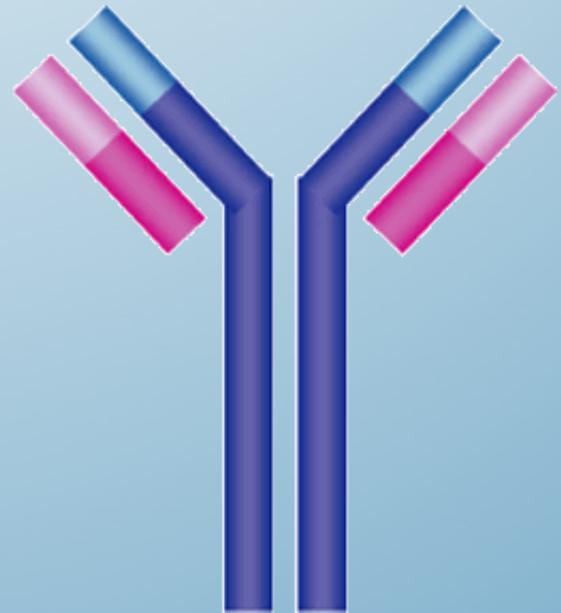
- **When RA is not detected and treated early, focal bone erosions progress rapidly and result in joint deformity and functional disability**

METHOTREXATE

- Dihydrofolate reductase inhibitor
- Long term resident in cells
- Potential lung, liver, and marrow toxicity

BIOLOGICS ARE THERAPEUTIC AGENTS

- Derived from human or animal sources or manufactured using recombinant DNA technology.
- May be proteins, monoclonal antibodies, recombinant receptors, or complex sugars.



ANTI-TNF ACTIONS ARE GOOD FOR RA

- **reductions in levels of C-reactive protein (CRP), IL-6, MMP-3, ICAM-1, and VEGF**



ANTI-TNF ALPHA

- **Etanercept (SC)**
- **Infliximab (IV)**
- **Adalimumab (SQ)**
- **Golimumab (SQ)**
- **Certolizumab pegol (SQ)**

OTHER BIOLOGICS

- **Abatacept**
- **Rituximab**
- **Anakinra**
- **Tocilizumab**



REFERENCES

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- (2010), *Scandinavian Journal of Immunology*, 72: 75–85
- *Arthritis Care & Research*; Volume 62, Issue 6, pages 805–810, June 2010
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- *Annals of Internal Medicine*, Platt et al, 2001; Vol 134(11) p. 1079. “Tell Me About Yourself”: The Patient-Centered Interview
- **How Renoir coped with rheumatoid arthritis.**
BMJ 1997;315:1704: **Annelies Boonen, et al**

THANK YOU

