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FULLY BOOKED

Friday, August 12, 2016

16:30 - 18:30 WS #53: Rheumatology Forum: Gout; Biologics; Stem Cells; Early Intervention in RA (120mins not repeated)

(Room 2)

Early Rheumatoid Arthritis

How to recognise it and why it matters

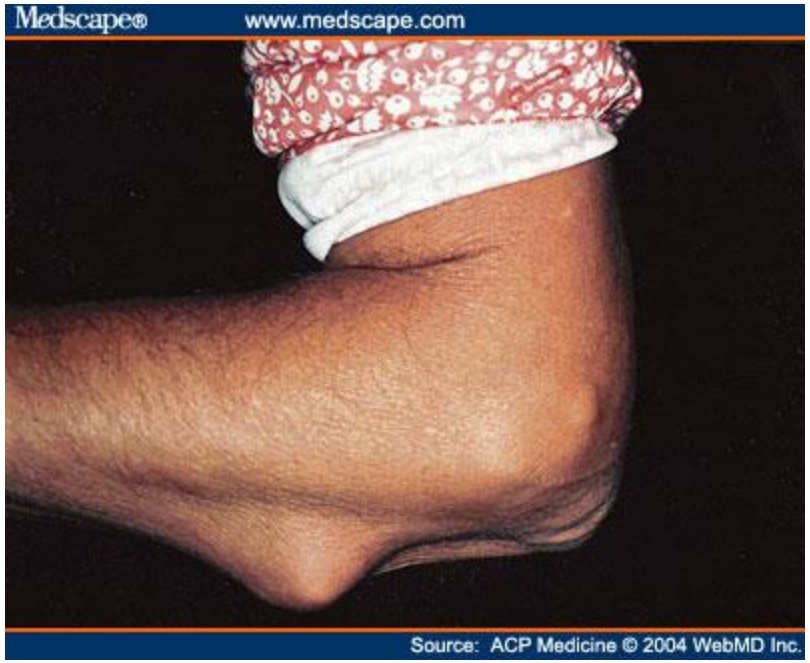
John Petrie

South GP CME General Practice Conference & Medical Exhibition

Early Rheumatoid Arthritis (ERA) messages

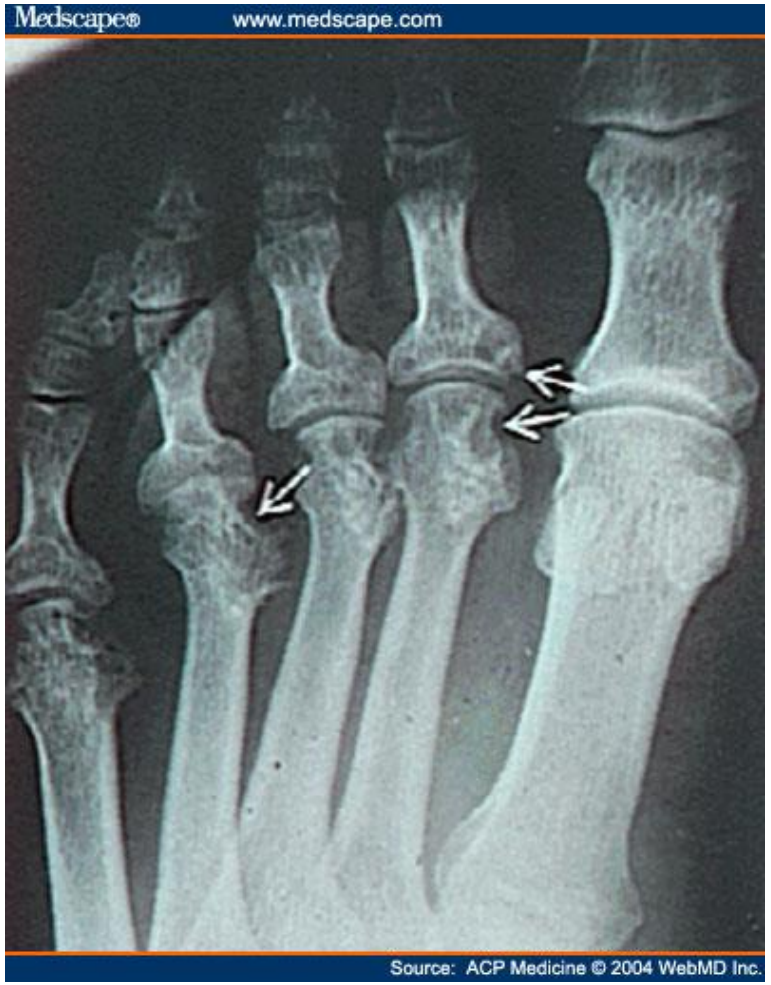
- Consider ERA when synovitis and morning stiffness present in peripheral joints
- The distribution of joint involvement is an important diagnostic aid
- Consider other medical conditions eg Psoriasis, IBD, Iritis
- Relevant serology includes ACPA, RhF and ANF
- Inflammatory markers can be deceiving (CRP, ESR)
- And REFER EARLY!!

Late Features of RA



Nodules

Erosions



Late Stages of RA

Table 3 – ACR criteria for the diagnosis of RA

At least 4 of the following 7 criteria must be met (criteria 1 through 4 must have been present for at least 6 weeks):

- Morning stiffness for at least 1 hour.
- At least 3 joint areas simultaneously had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician; the 14 possible areas are right or left PIP joint, MCP joint, wrist, elbow, knee, ankle, or MTP joint.
- At least 1 area swollen (as defined above) in a wrist, MCP joint, or PIP joint.
- Simultaneous involvement of the same joint areas on both sides of the body (bilateral involvement of PIP, MCP, or MTP joints is acceptable without absolute symmetry).
- Subcutaneous nodules over bony prominences or extensor surfaces or in juxta-articular regions, observed by a physician.
- Demonstration of abnormal amounts of serum RF by any method for which the result has been positive in < 5% of normal control subjects.
- Radiographic changes typical of RA on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (OA changes alone do not qualify).

ACR, American College of Rheumatology; RA, rheumatoid arthritis; PIP, proximal interphalangeal; MCP, metacarpophalangeal; MTP, metatarsophalangeal; RF, rheumatoid factor; OA, osteoarthritis.

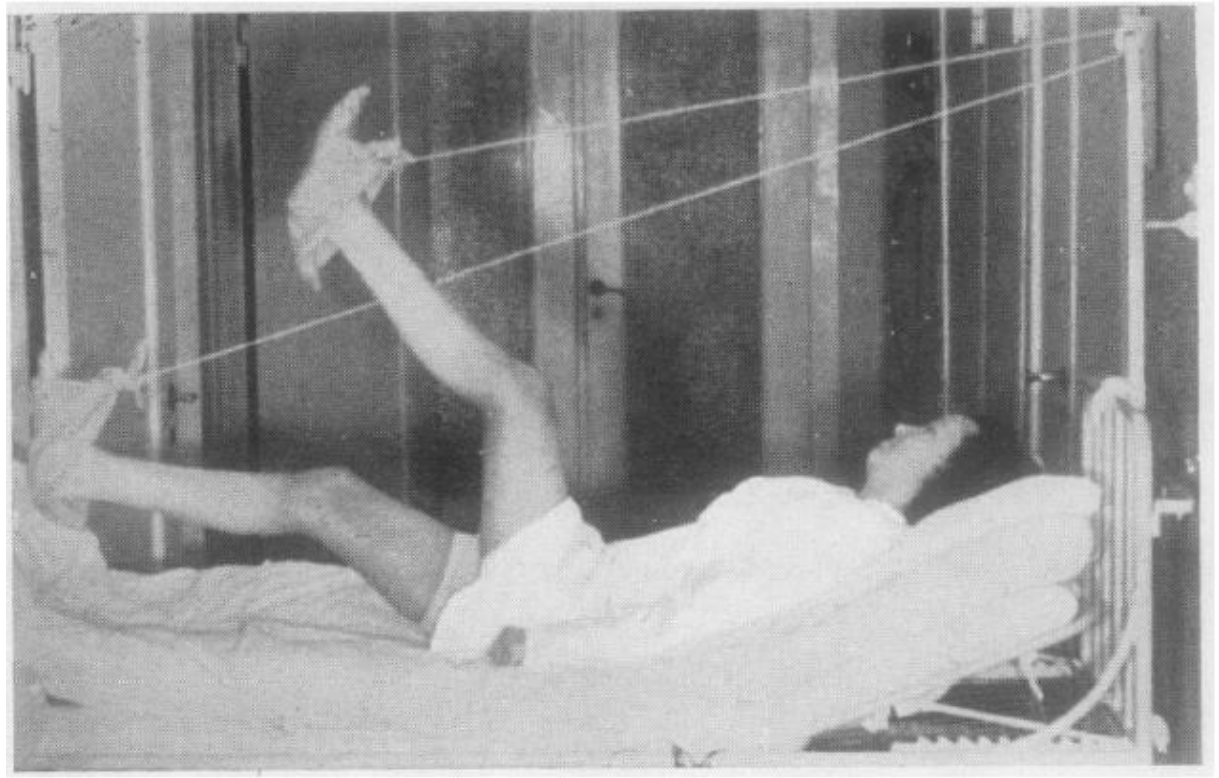
Adapted from Arnett FC et al. *Arthritis Rheum.* 1988.[6]

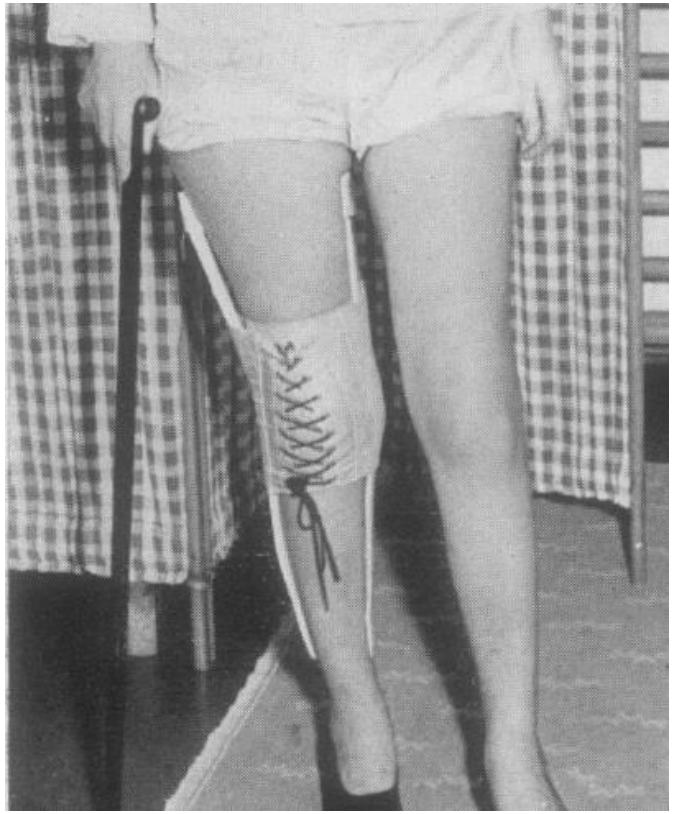
Features of the 1987 Criteria

- Developed to differentiate RA from other recognised arthritides
- Utilised characteristics of established disease
- Used in epidemiology and therapeutic research trials
- Relevant at a time when treatment goals were limited to diminishing disability

Treatment Options

- Medication
  - Aspirin, NSAID
  - Prednisone, penicillamine, gold injections
- Surgery
  - Wrist, ankle fusions
  - Excisions
  - Hip arthroplasty
- Physical
  - Bed rest, splintage, physiotherapy, hydrotherapy





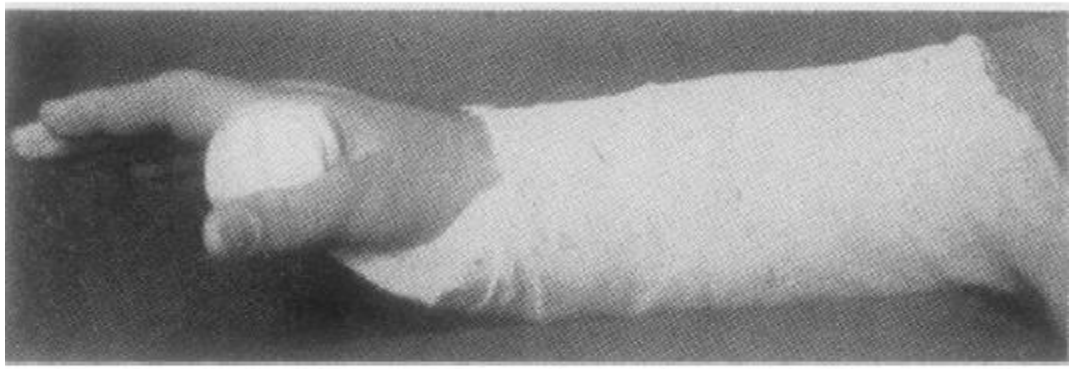
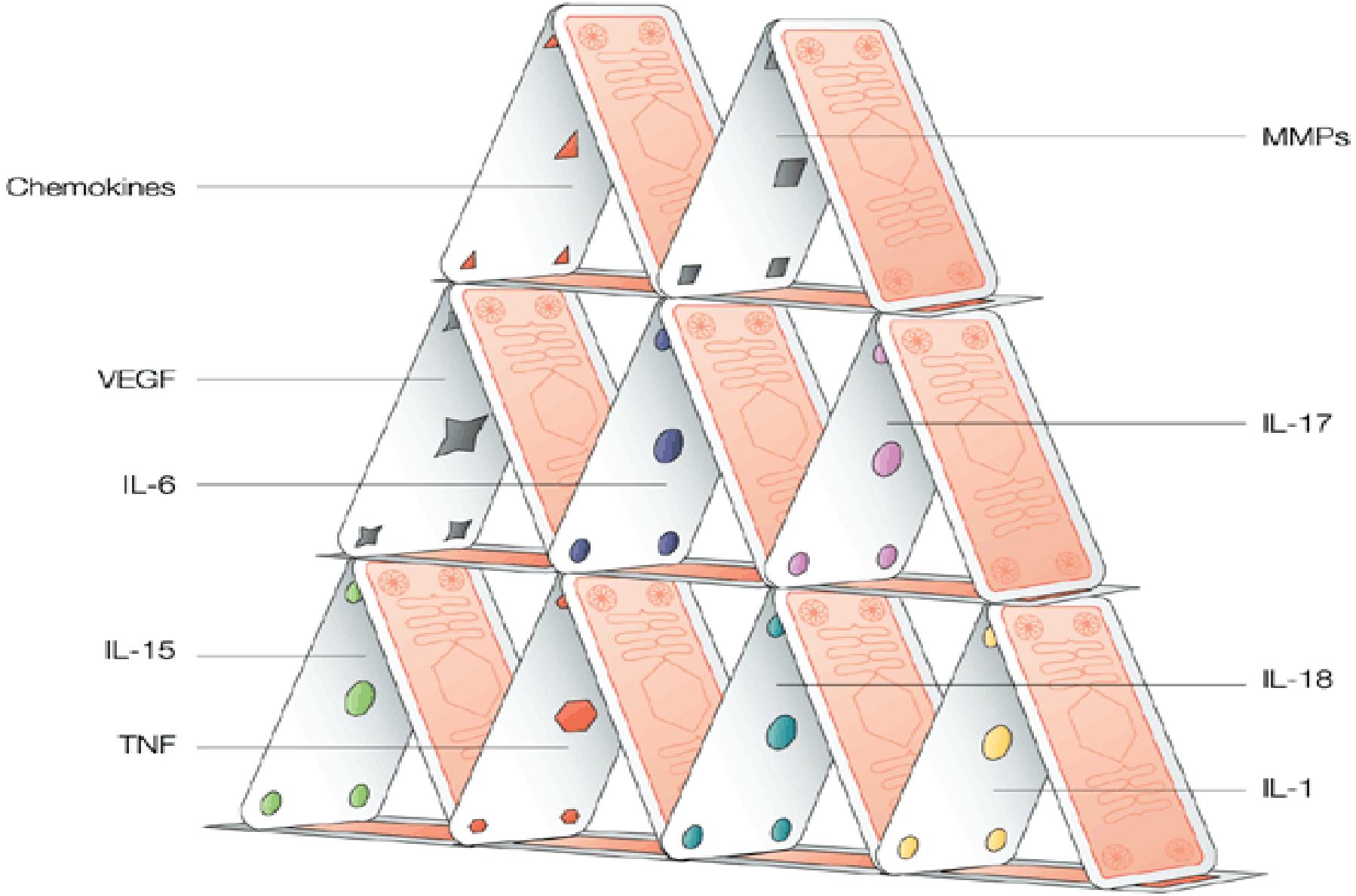


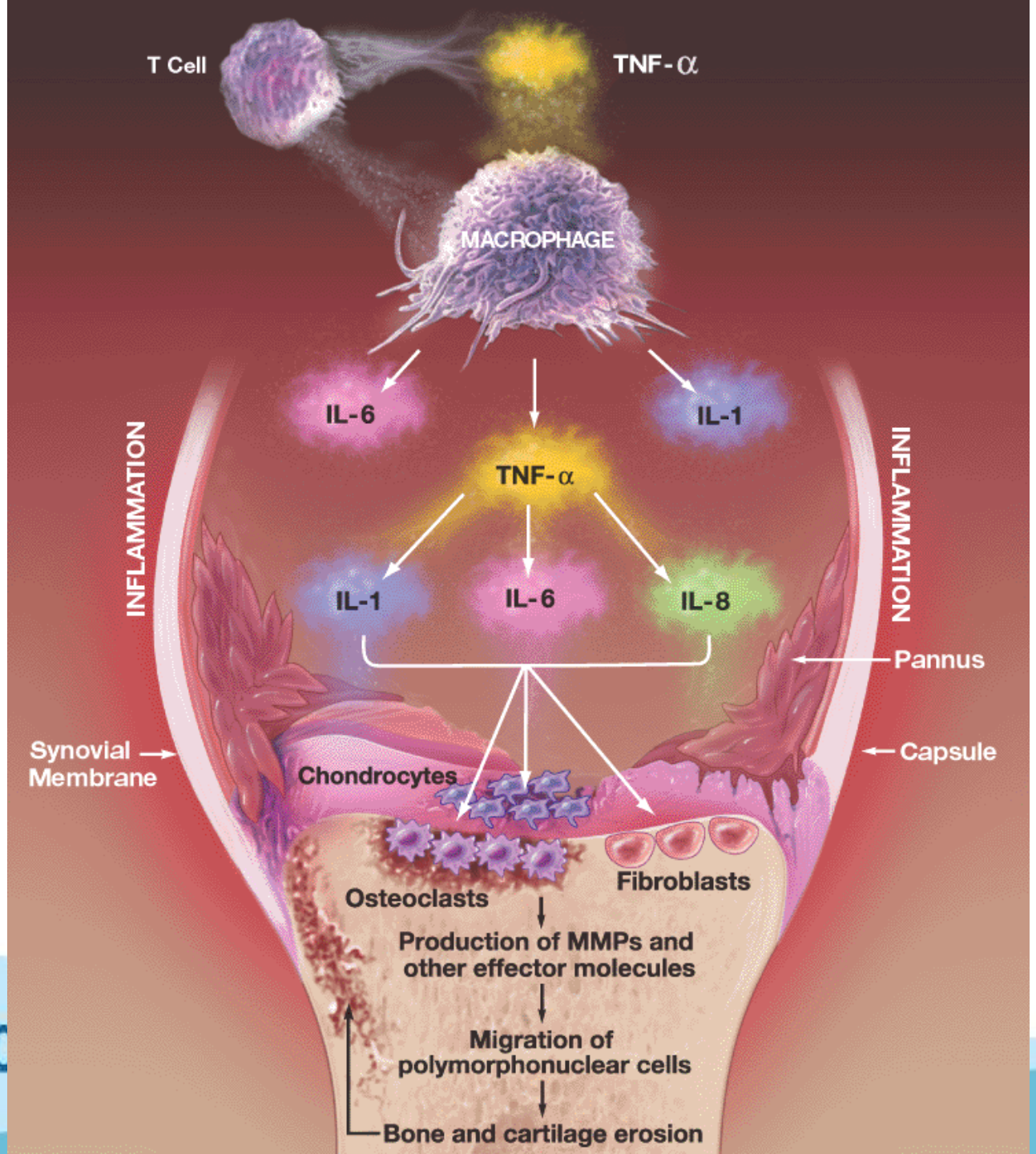
Fig. 5.—Night hand splint for the wrist (plaster of paris).

Impetus for Change

- Value of optimising DMARD use (MTX, GC)
- Benefits of early intervention; improving clinical outcomes and reducing disability
- Availability of new “biological” agents
- Development of a new prognostic indicator (Anti Citrullinated Peptide Antibodies, ACPA or Anti-CCP)



Nature Reviews | Drug Discovery


T Cell
TNF-α
MACROPHAGE
IL-6
IL-1
TNF-α
INFLAMMATION
INFLAMMATION
IL-1
IL-6
IL-8
Pannus
Synovial Membrane
Capsule
Chondrocytes
Fibroblasts
Osteoclasts
Production of MMPs and other effector molecules
Migration of polymorphonuclear cells
Bone and cartilage erosion

EULAR & ACR Combine..

- Charged to develop a new set of classification criteria
- To identify those ***at risk*** of chronicity and joint damage
- To facilitate the study of patients earlier in the course of the disease
- And to stimulate earlier treatment, thus improving prognosis
- It is a new ***definition*** of Rheumatoid Arthritis

2010 ACR/EULAR RA Classification Criteria

- Target population (who should be tested?): patients who
- 1) have at least one joint with definite clinical synovitis (swelling)
- 2) with the synovitis not better explained by another disease
- A score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA

Categories A - D

- A: JOINT INVOLVEMENT

  Large, small, 1-10 or more — Score 0-5

- B: SEROLOGY

  RhF, Anti-citrullinated peptide Ab — Score 0-3

- C: ACUTE PHASE PROTEINS

  CRP/ESR normal/abnormal — Score 0-1

- D: DURATION OF SYMPTOMS

  < 6 weeks, ≥6 weeks — Score 0-1

A: Joint Involvement

• 1 large joint	0
• 2–10 large joints	1
• 1–3 small joints (with or without involvement of large joints)	2
• 4–10 small joints (with or without involvement of large joints)	3
• >10 joints (at least one small joint)	5

B: Serology

- Negative RF *and* negative ACPA 0
- Low-positive RF *or* low-positive ACPA 2
- High-positive RF *or* high-positive ACPA 3

C: Acute Phase Proteins

- Normal CRP *and* normal ESR 0
- Abnormal CRP *or* abnormal ESR 1

D: Duration of Symptoms

- <6 weeks 0
- ≥6 weeks 1

Target Population of the Criteria

Two requirements:

(1) Patient with at least one joint with definite clinical synovitis (swelling)

(2) Synovitis is not better explained by "another disease"

Differential diagnoses differ in patients with different presentations.

If unclear about the relevant differentials, an expert rheumatologist should be consulted.

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Classification vs. Diagnosis

- We **don't have diagnostic criteria** for RA
- Typically in rheumatic diseases, criteria are labeled as **"classification" criteria**
  - These are helpful in defining homogeneous treatment populations for study purposes
- A **clinical "diagnosis"** has to be established by the physician (rheumatologist)
  - It includes many more aspects than can be included in formal criteria
  - Formal classification criteria might be a guide to establish a clinical diagnosis

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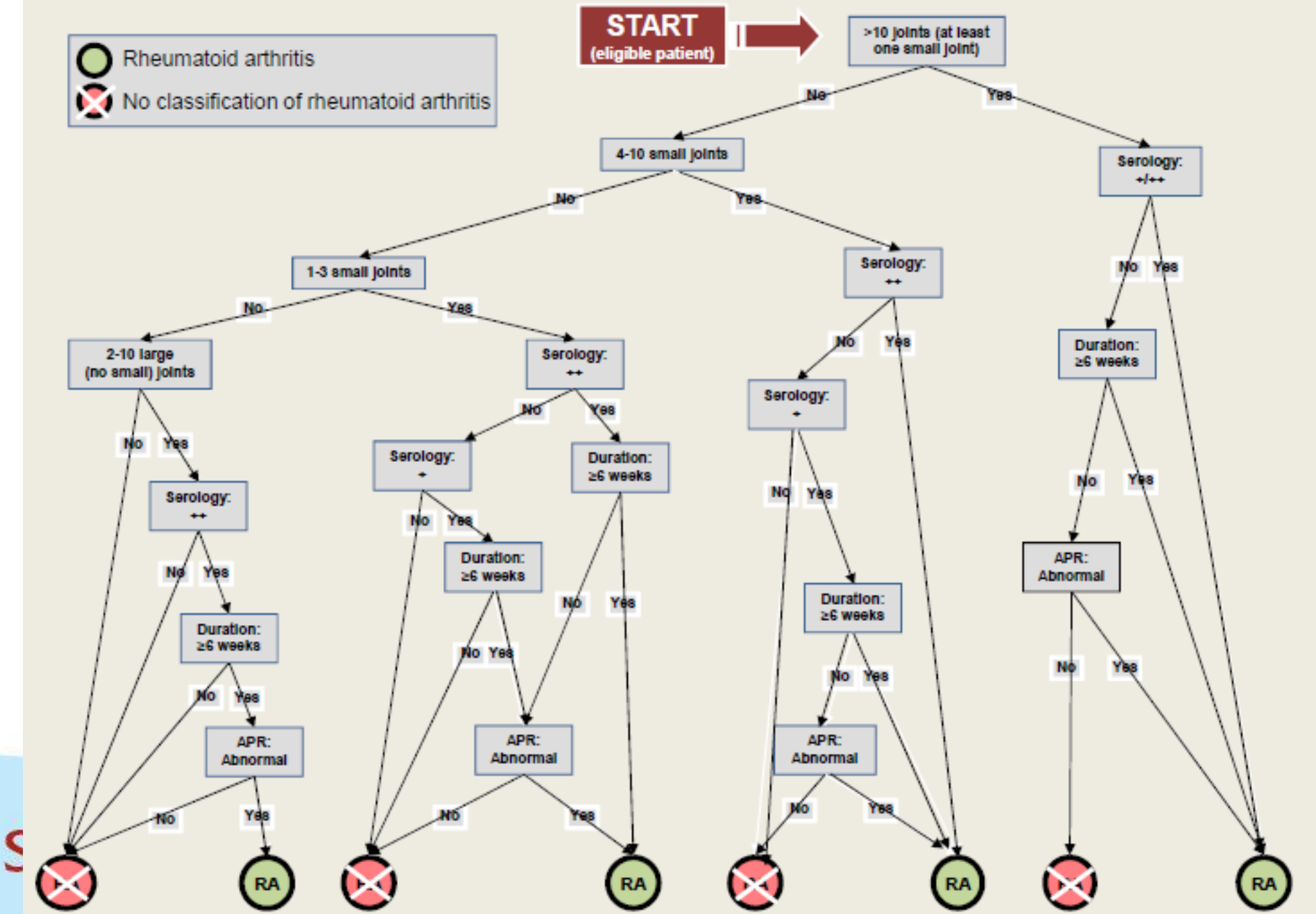
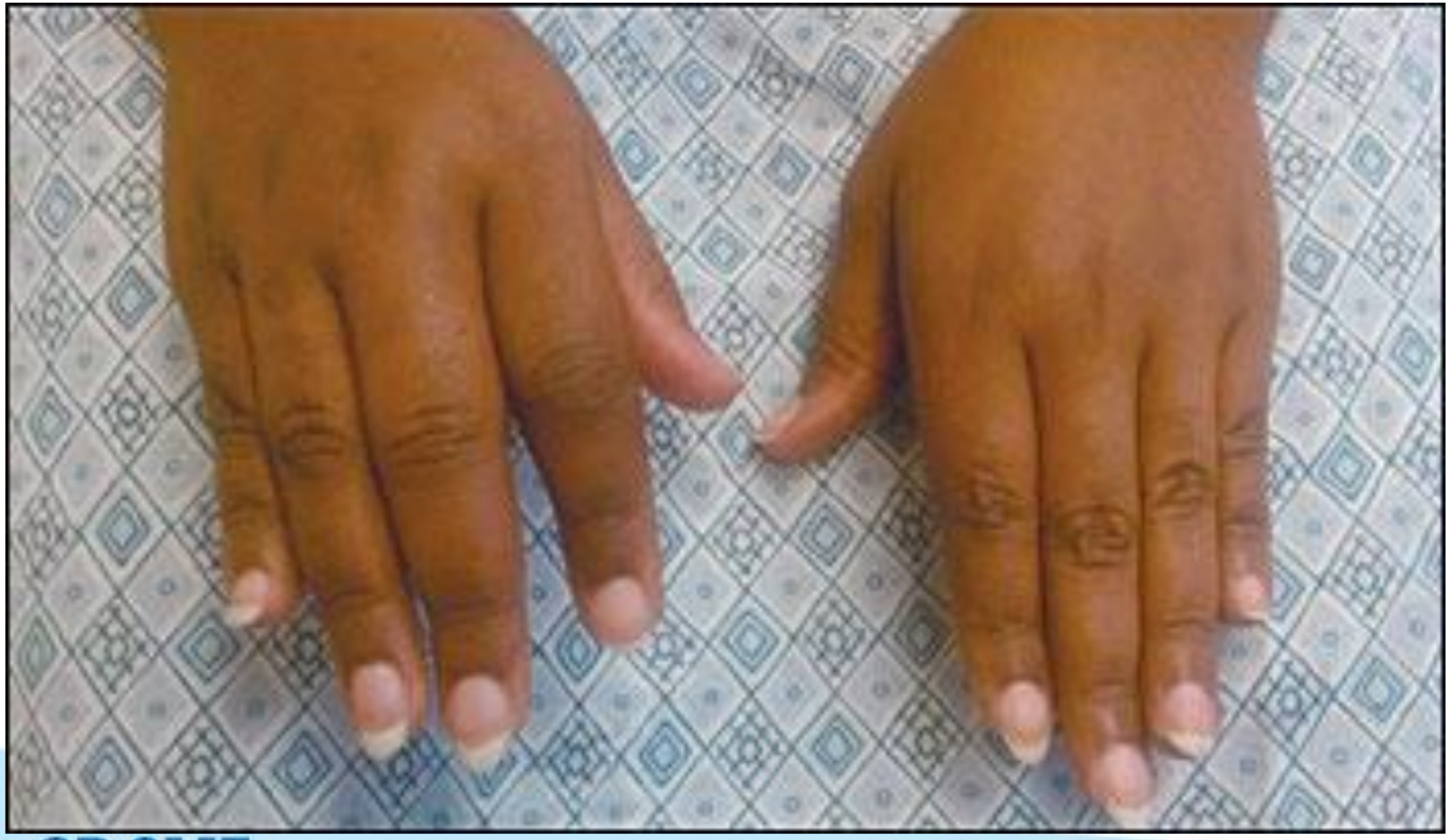
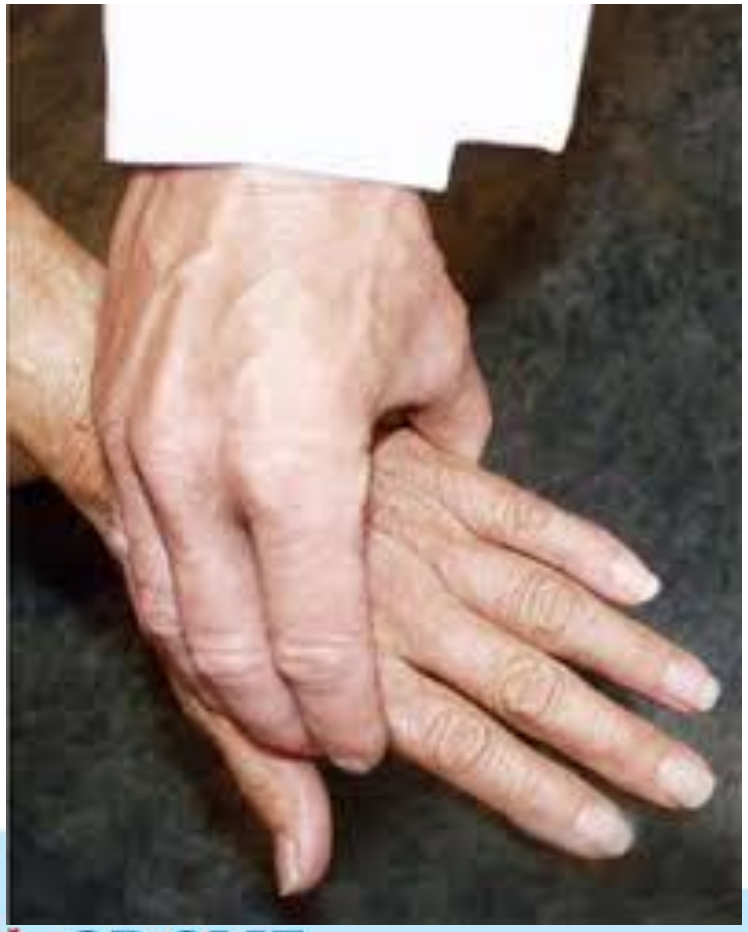
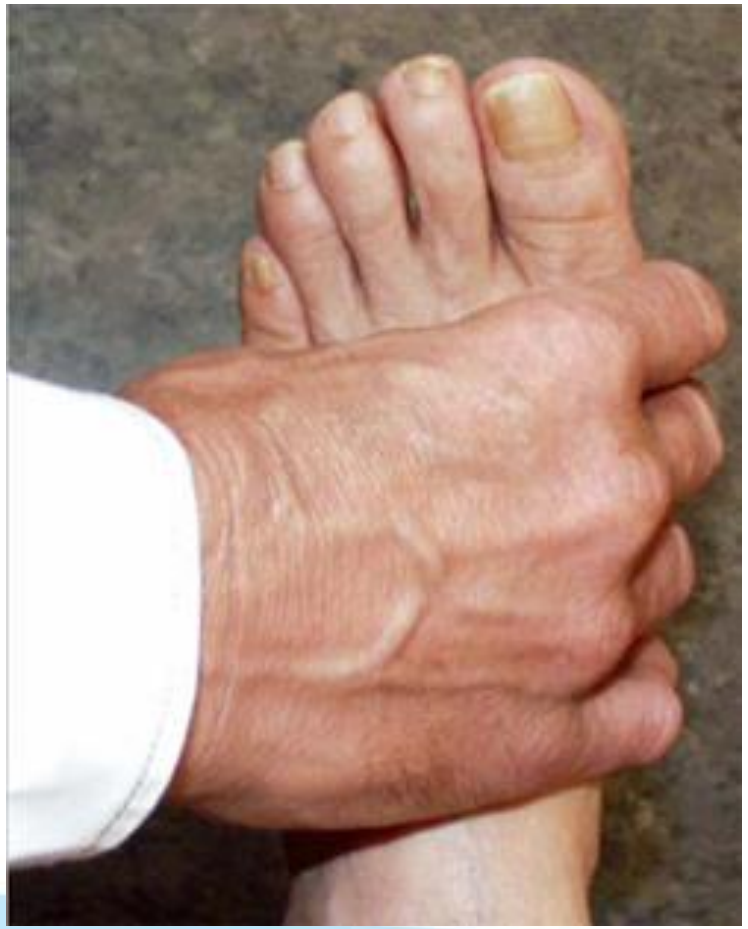

Rheumatoid arthritis
No classification of rheumatoid arthritis
START
(eligible patient)
>10 joints (at least one small joint)
4-10 small joints
1-3 small joints
2-10 large (no small) joints
Serology: ++
Serology: +
Duration: ≥6 weeks
APR: Abnormal
Serology: +/++
No
Yes
RA

Asymmetrical MCPJ/PIPJ synovitis

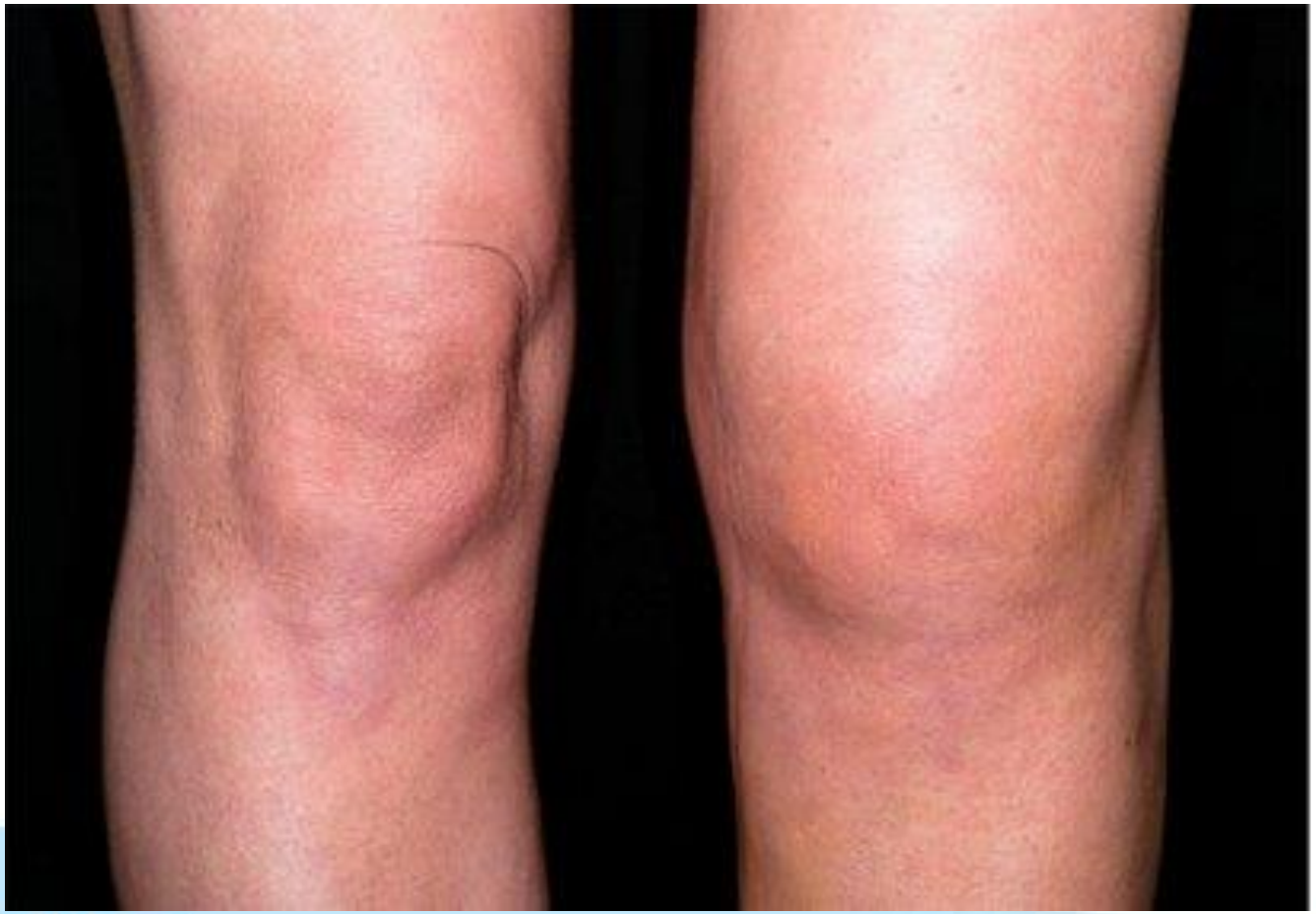


Squeeze Test





Knee Synovitis



Early Treatment options: DMARDs

- Methotrexate
  - Drug of choice
  - Extreme care with potential pregnancy
- Glucocorticoids
- Alternative DMARDs
  - Leflunomide
  - Sulfasalazine
  - Hydroxychloroquine

Types of Biologic Therapies

- TNF inhibition (Humira, Remicade, Enbrel)
- Il 1 inhibition (Anakinra)
- Il 6 inhibition (Tocilizumab)
- Costimulation blockade (Abatacept)
- B cell depletion (Rituximab [mabthera])
- Il 12/23, Il17

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- Consider other medical conditions eg Psoriasis, IBD, Iritis
- Relevant serology includes ACPA, RhF and ANF
- Inflammatory markers can be deceiving (CRP, ESR)
- And REFER EARLY!!

Early Intervention, Aim at Remission