Rheumatoid Arthritis

- Objectives:

By the end of this lecture student should be able to:

- Recognize which patient is likely to have RA
- Know the different modes of presentation of RA
- Develop a plan of investigation and management of RA

Introduction

Rheumatoid arthritis is a chronic systemic inflammatory disease that predominantly affects the joints. It can affect other systems in the body.

Early recognition and treatment can prevent joint destruction and disability.

Rheumatoid Arthritis

Systemic chronic inflammatory disease

Mainly affects synovial joints

- Variable expression
- Prevalence about 3%
- Worldwide distribution
- Female:male ratio 3:1
- Peak age of onset: 25-50 years

Rheumatoid Arthritis

- Autoimmune disorder of Unknown etiology
  - Genetics
  - Environmental
  - Possible infectious component

RHEUMATOID ARTHRITIS = AUTOIMMUNE

GENETICS

* Human Leukocyte Antigen
  HLA-DR1 & HLA-DR4

ENVIRONMENT

* CIGARETTE SMOKE
* PATHOGEN
  (E.g. Gut bacteria)

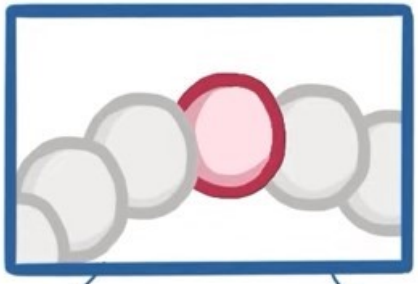
MODIFICATION OF OUR OWN ANTIGENS

CITRULLINATION

Susceptibility Genes

HLA-DR1

HLA-DR4



Amino Acids

ARGININE

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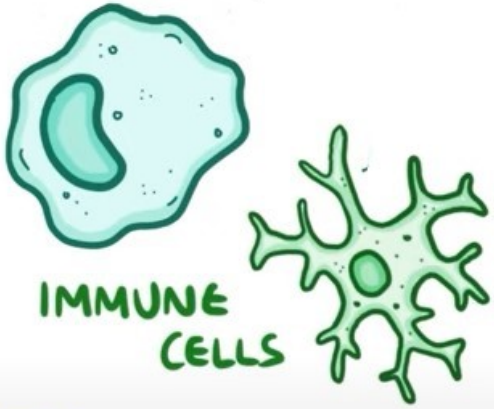
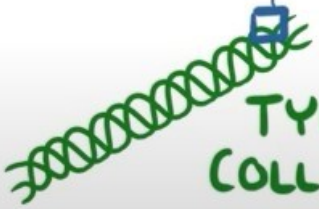
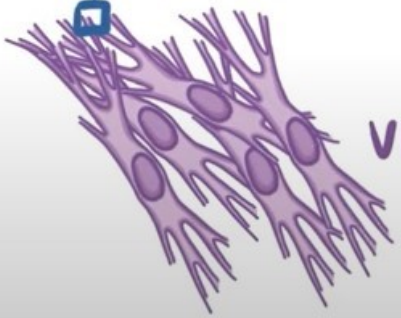
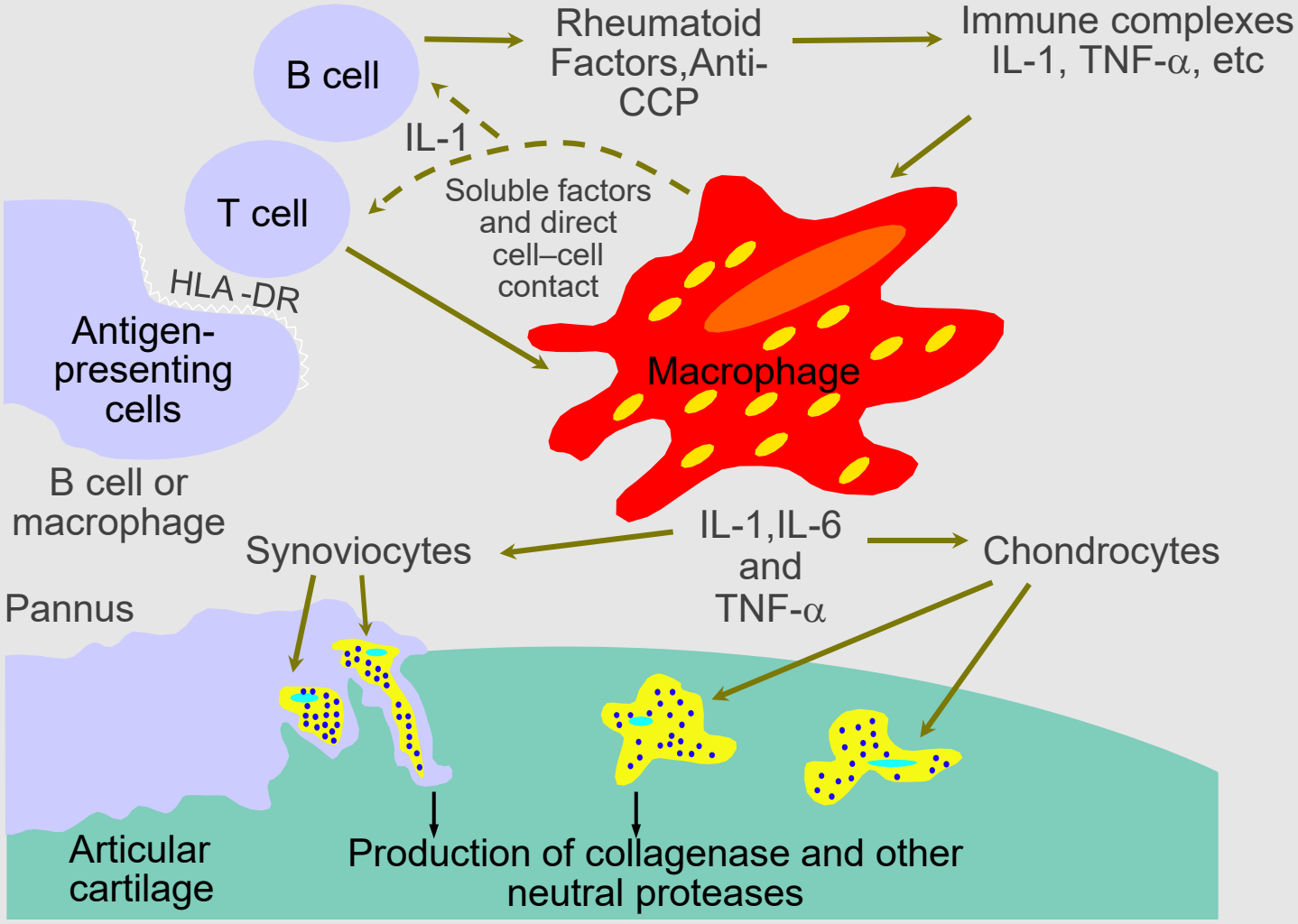
CITRULLINE







Numerous Cellular Interactions Drive the RA Process

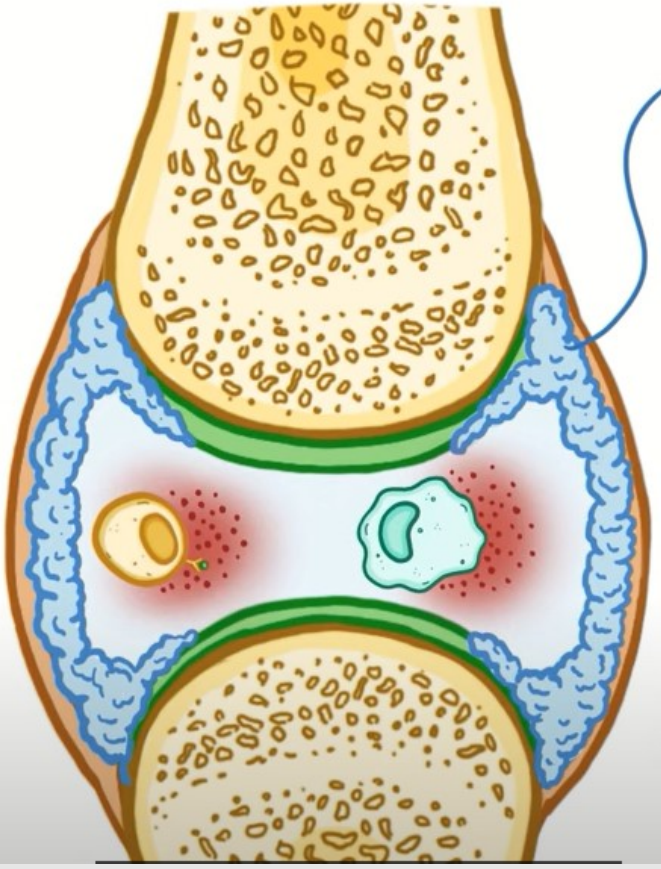


Arend W. *Semin Arthritis Rheum.* 2001;30(suppl 2):1-6.

T-CELLS
Secrete
CYTOKINES
- INTERFERON-γ
- INTERLEUKIN-17

↓

Recruits
MACROPHAGES
which produce
MORE CYTOKINES
- TNF-α
- INTERLEUKIN-1
- INTERLEUKIN-6



SYNOVIAL CELLS PROLIFERATE

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PANNUS

Thick, swollen synovial membrane with

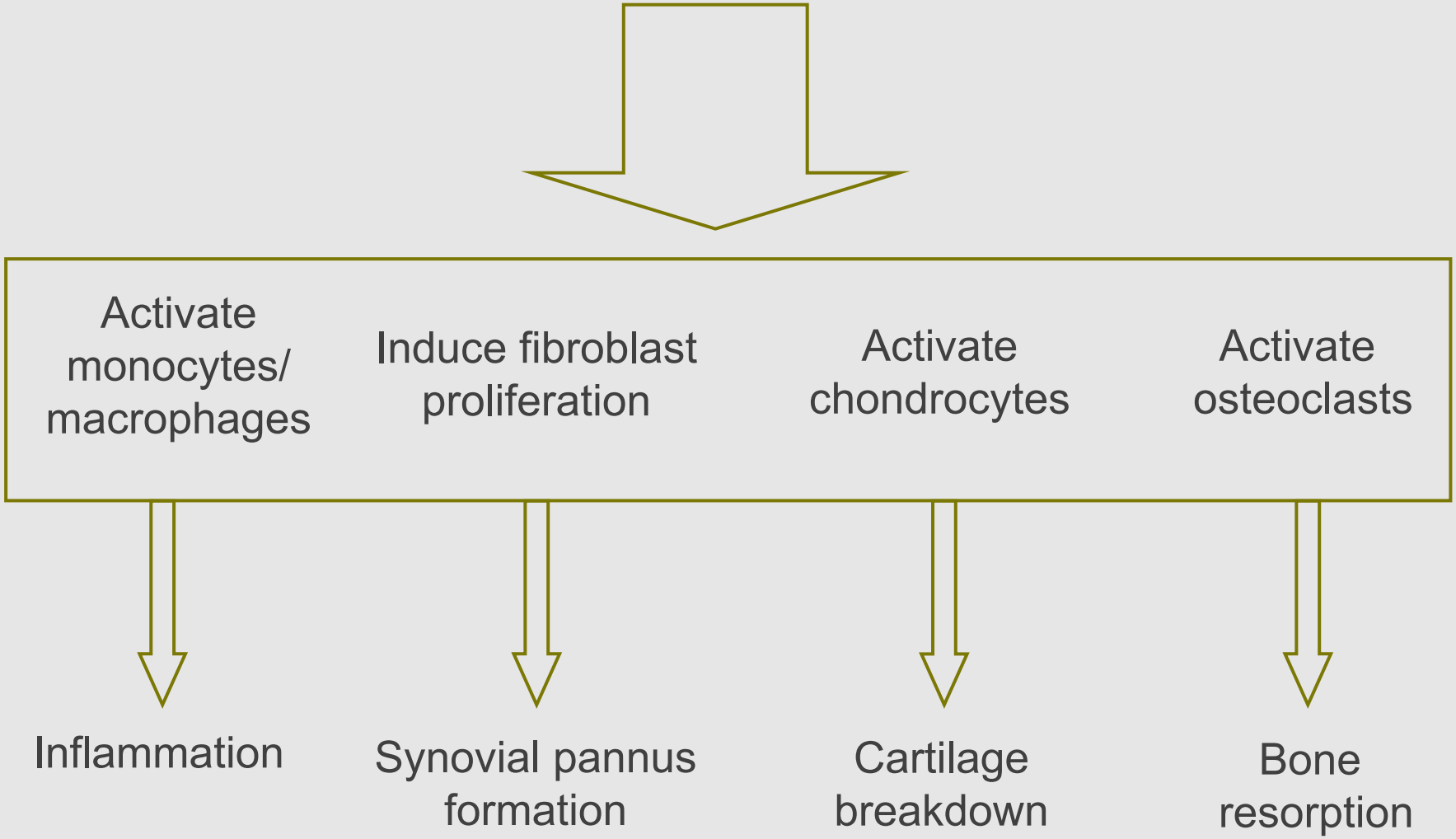
GRANULATION TISSUE

FIBROBLASTS

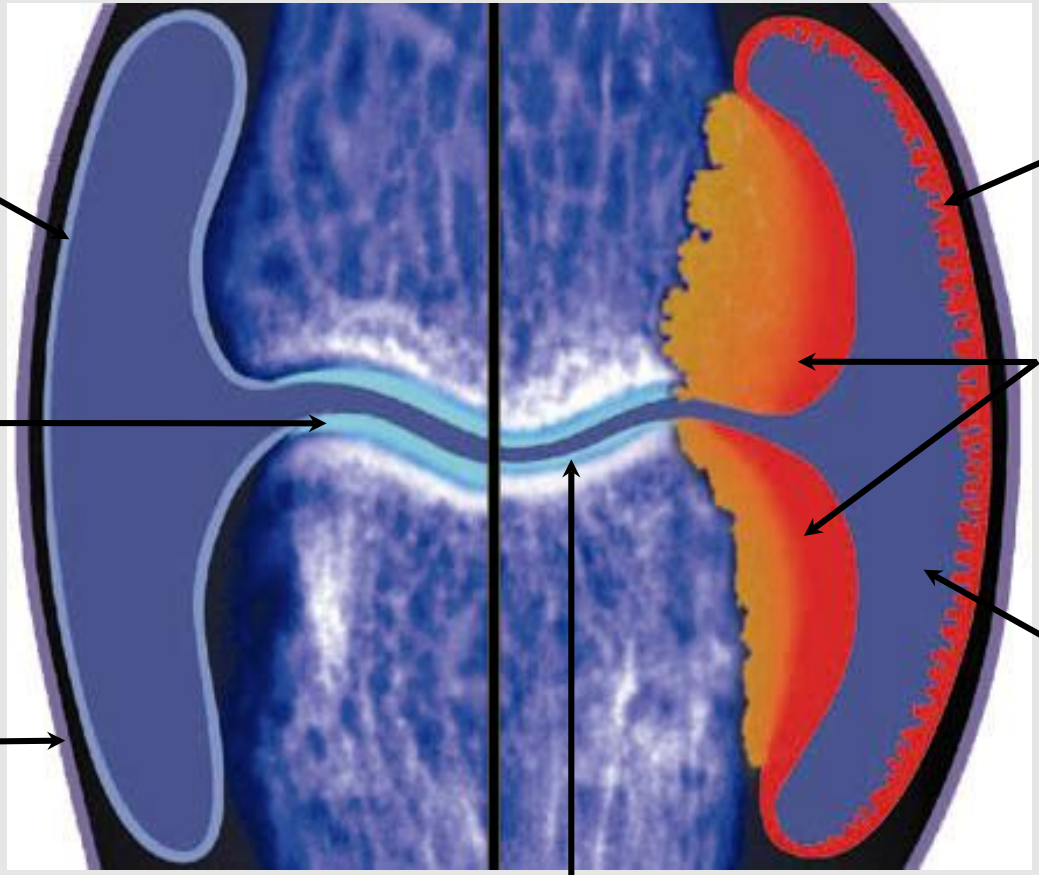
INFLAMMATORY CELLS

MYOFIBROBLASTS

Cytokines Play a Pivotal Role in the Inflammatory and Destructive Processes of RA



RA Is Characterised by Synovitis and Joint Destruction



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

Signs and Symptoms

- Joint inflammation
  - Tender, warm swollen joints
  - Symmetrical pattern
- Pain and stiffness
- Symptoms in other parts of the body
  - Nodules
  - Anemia
- Fatigue, occasional fever, malaise

JOINT INVOLVEMENT ON PRESENTATION OF RA

Polyarticular	**75%**	**Monoarticular**	**25%**
Small joints of hands and feet	60%	Knee	50%
Large joints	30%	Shoulder } Wrist } Hip } Ankle } Elbow }	50%
Large and Small joints	10%		

Articular features seen in the Rheumatoid Hand

WRIST:

- Synovitis
- Prominent ulnar styloid
- Subluxation and collapse of carpus
- Radial deviation

MCPs:

- Synovitis
- Ulnar deviation
- Subluxation

PIPs:

- Synovitis
- Fixed flexion or extension deformities
- (Swan neck or boutonniere deformity)

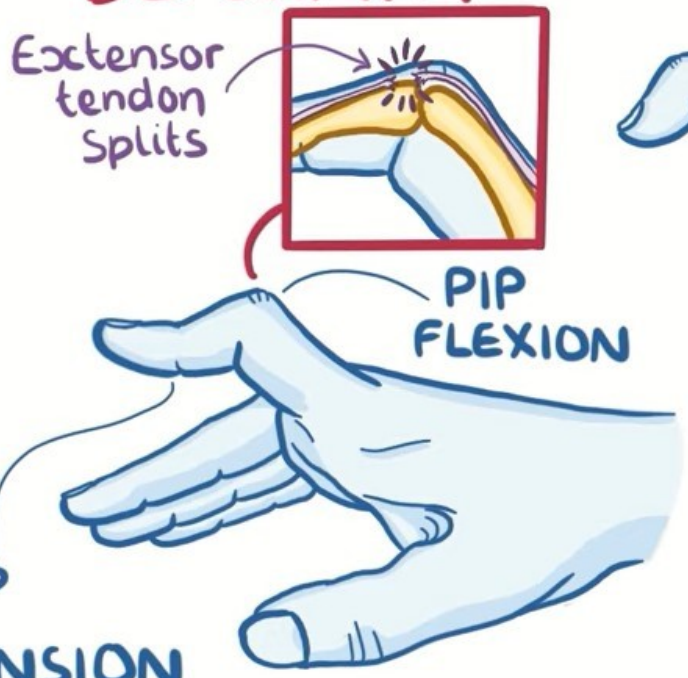
THUMBS:

- Synovitis
- ‘Z’ deformity

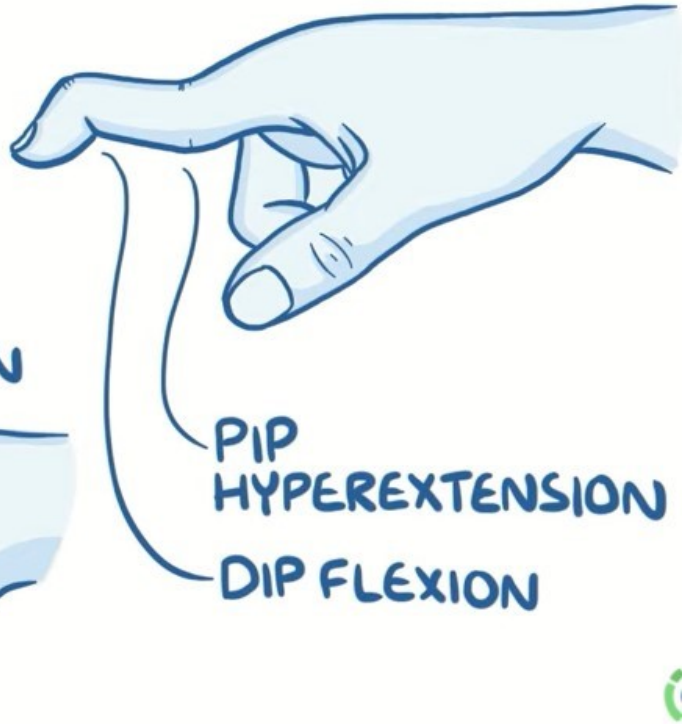
Specific Deformities

Ulnar Deviation

Boutonniere "Buttonhole" Deformity



Swan Neck Deformity

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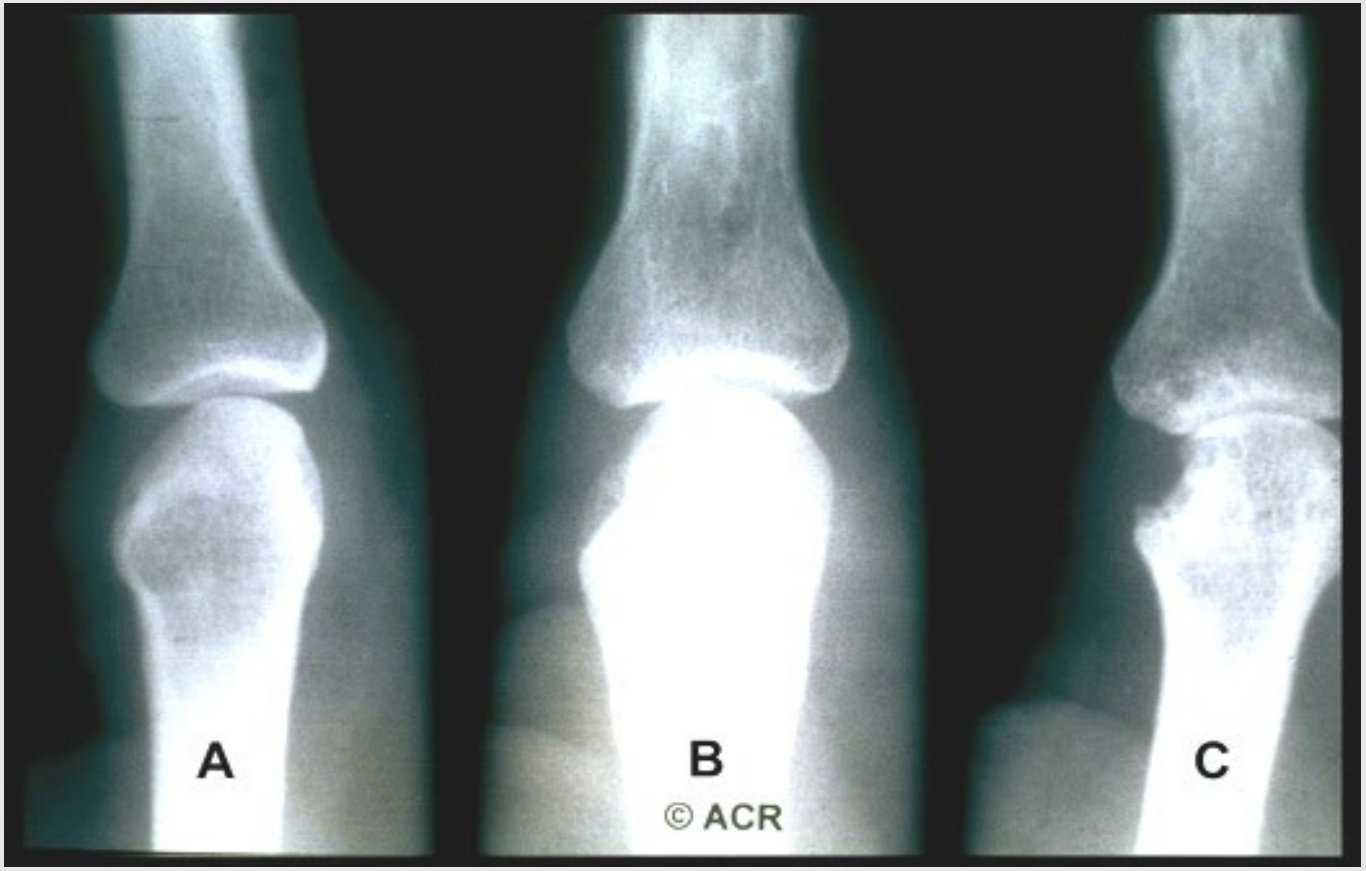
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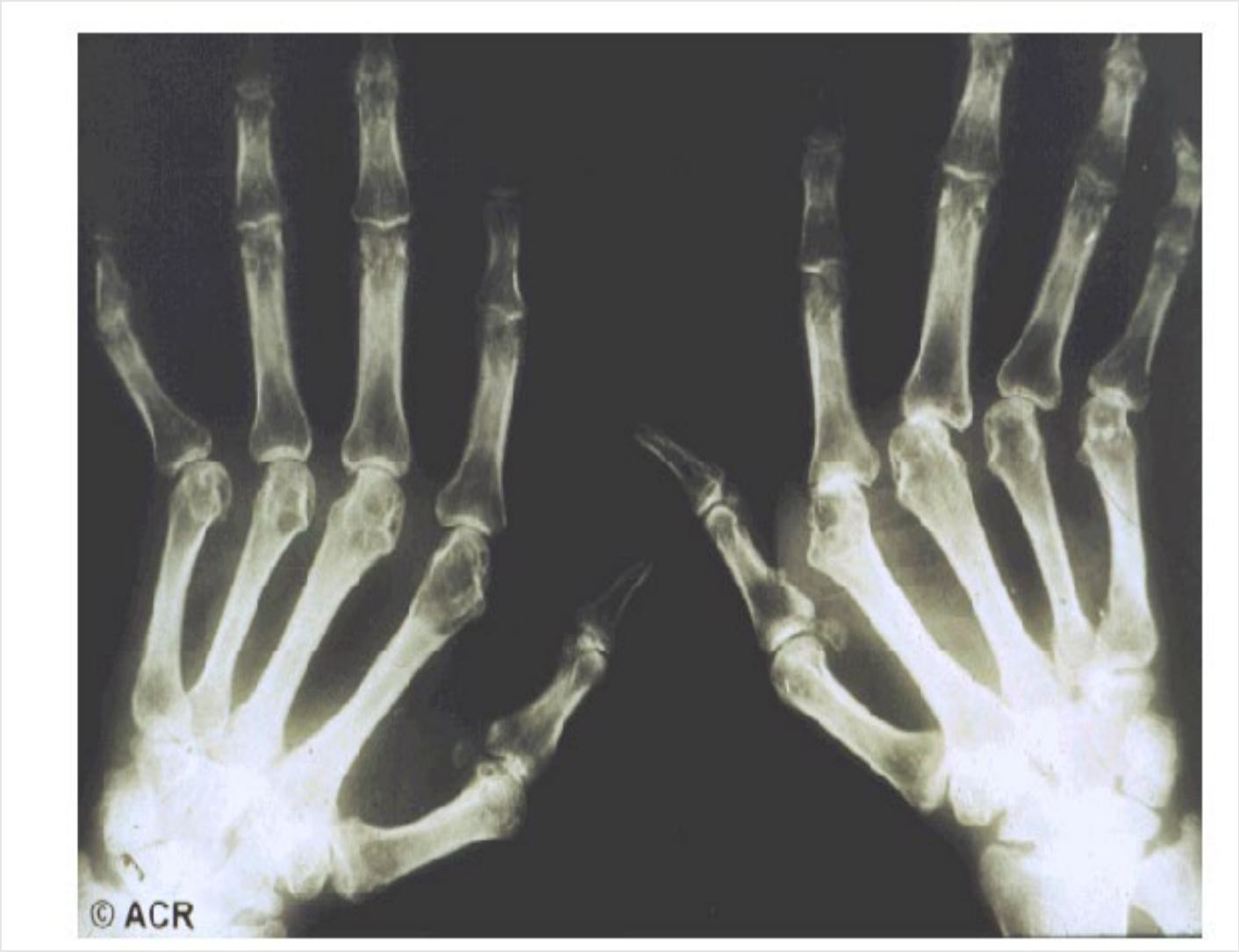
Joint Destruction



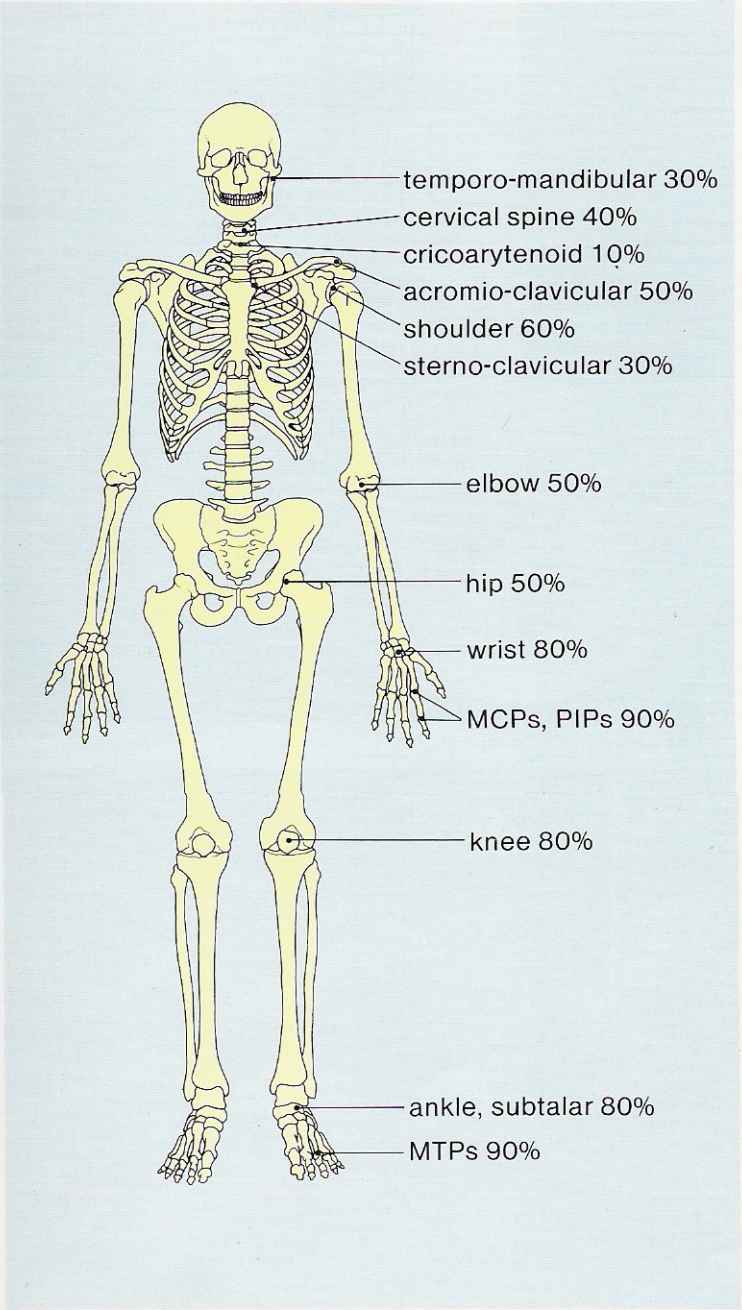


Fig. 3.6 Frequency of involvement of different joint sites in established RA.

INFLAMMATORY CYTOKINES

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MULTIPLE ORGAN SYSTEMS

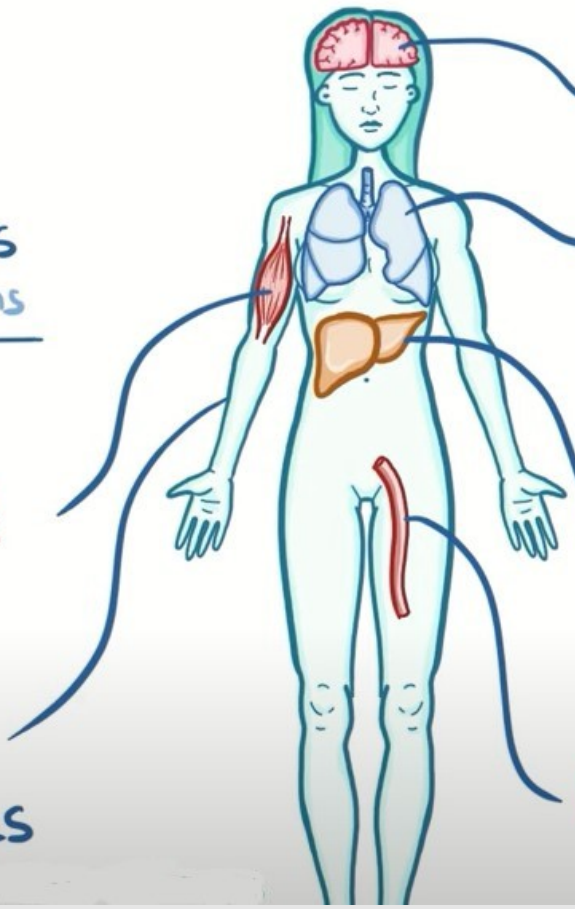
└ Extra-articular problems

SKELETAL MUSCLE

└ Protein breakdown

SKIN

RHEUMATOID NODULES



INTERLEUKIN 1 or 6

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BRAIN

Pyrogens → FEVER

LUNG

* **INTERSTITIUM**
  Fibroblasts → SCAR TISSUE
  ↓ Gas exchange
* **PLEURAL CAVITIES**
  Fill with fluid → PLEURAL EFFUSION

LIVER - HEPCIDIN

└ Causes ↓ iron by inhibiting absorption + trapping in macrophages / liver cells

BLOOD VESSELS

Atheromatous plaques

Extra-articular manifestations

- General
  - fever, lymphadenopathy, weight loss, fatigue
- Dermatologic
  - palmar erythema, nodules, vasculitis
- Ocular
  - episcleritis/scleritis, scleromalacia perforans, choroid and retinal nodules

Extra-articular manifestations

- Cardiac
  - pericarditis, myocarditis, coronary vasculitis, nodules on valves
- Neuromuscular
  - entrapment neuropathy, peripheral neuropathy, mononeuritis multiplex
- Hematologic
  - Felty's syndrome, large granular lymphocyte syndrome, lymphomas

Extra-articular manifestations

- Pulmonary
  - pleuritis, nodules, interstitial lung disease, bronchiolitis obliterans, arteritis, effusions
- Others
  - Sjogren's syndrome, amyloidosis


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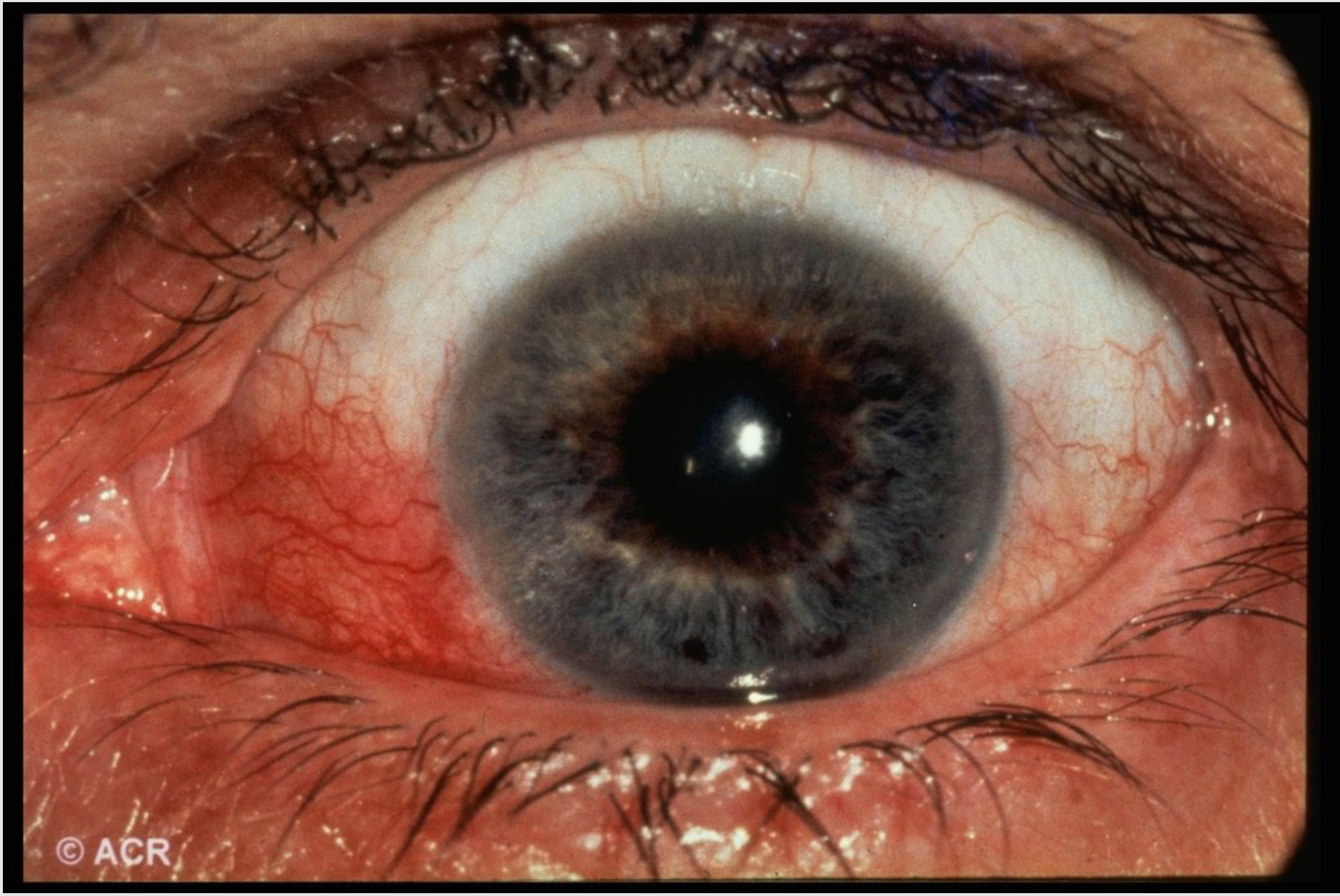
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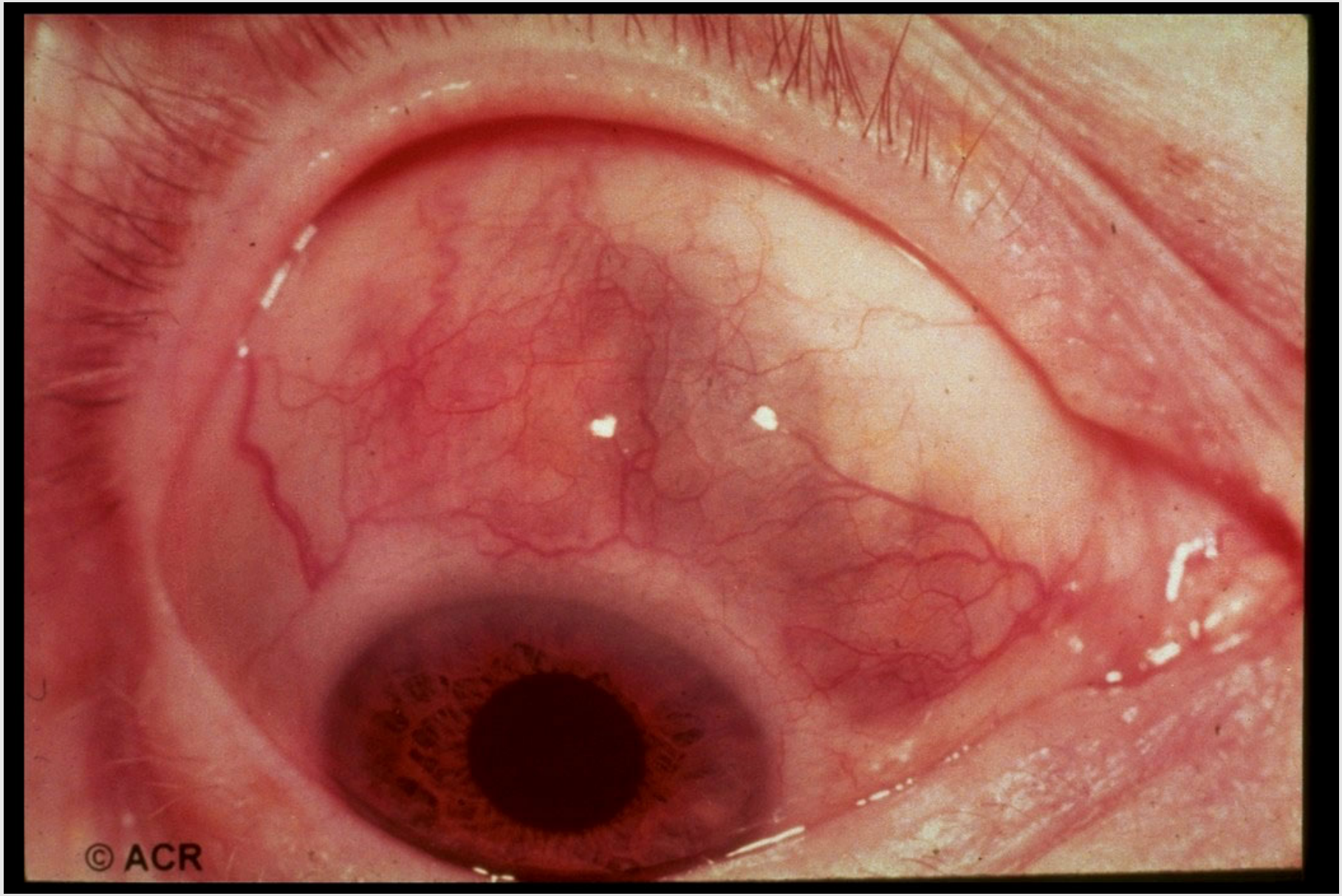
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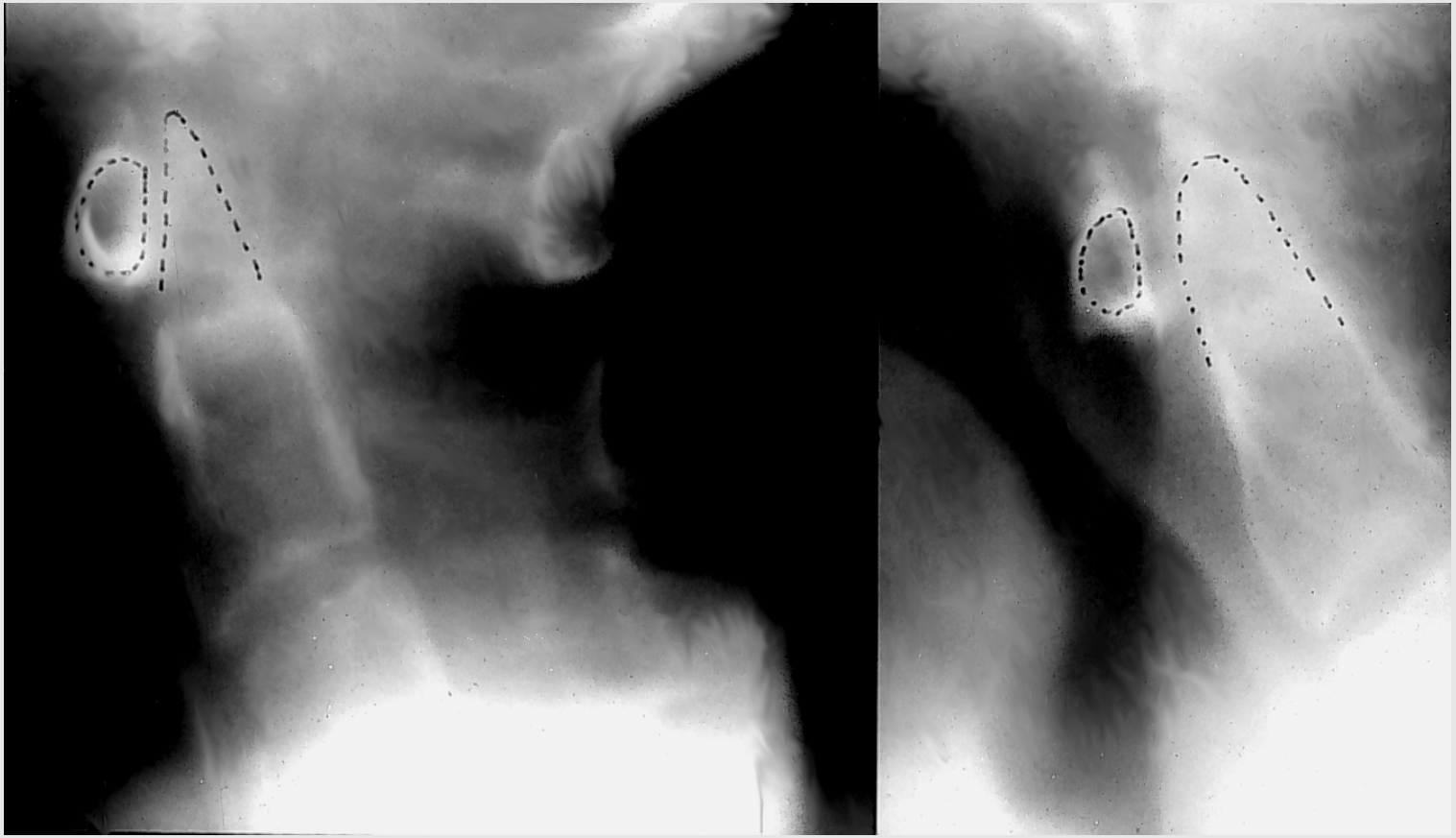


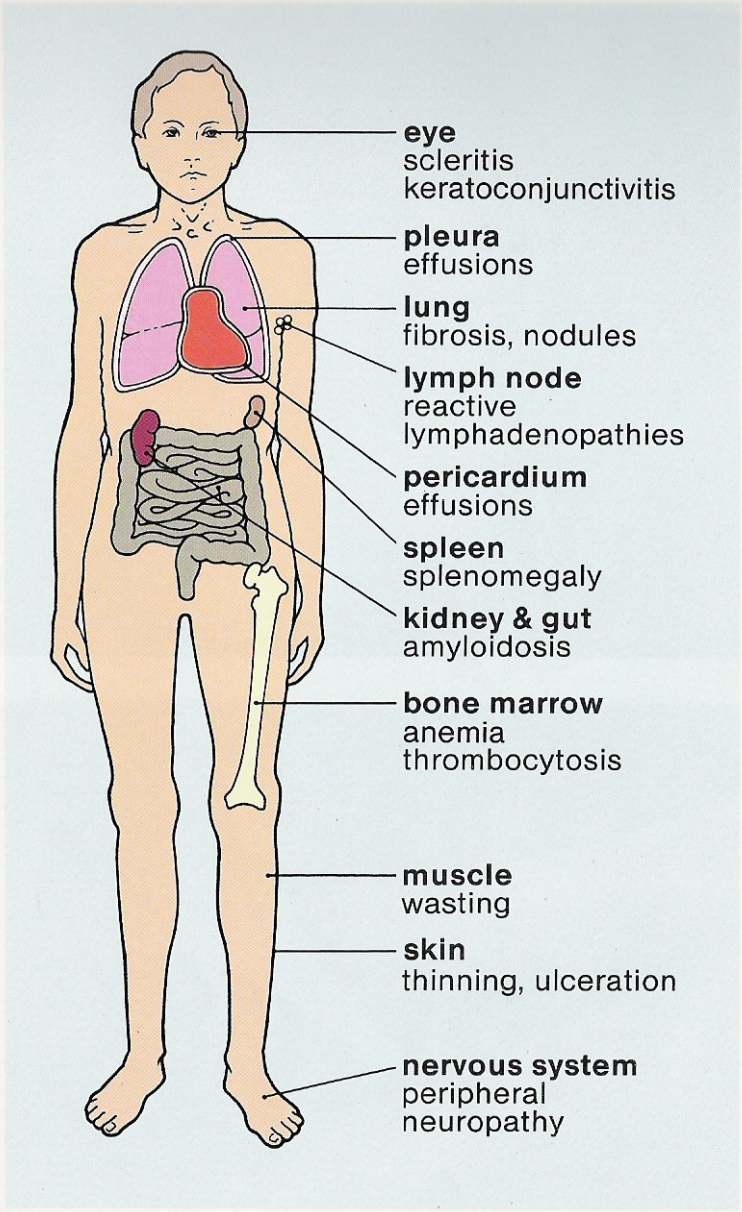


Fig. 3.27 Other organs commonly involved in rheumatoid disease.

Investigations:

- Hematology : CBC , ESR
- Biochemistry : LFT , Renal profile
- Serology : RF , Anti-CCP
- Radiography : Joints , Spines ,Chest

DIAGNOSIS

BLOOD TESTS

* Rheumatoid factor
* Anti-citrullinated peptide (Anti-CCP) antibody

IMAGING - X-RAY

↓ Bone density

Soft tissue swelling

Narrowing of joint space

Bony erosions

ACR 1987 Classification Criteria for Rheumatoid Arthritis

Patients Must Have Four of Seven Criteria:

- Morning Stiffness Lasting at Least 1 Hour*
- Swelling in 3 or More Joints*
- Swelling in Hand Joints*
- Symmetric Joint Swelling*
- Erosions or Decalcification on X-ray of Hand
- Rheumatoid Nodules
- Abnormal Serum Rheumatoid Factor

* Must Be Present at Least 6 Weeks.

The 2010 ACR / EULAR classification criteria for rheumatoid arthritis

Target population (Who should be tested?): Patients who

1) have at least 1 joint with definite clinical synovitis (swelling)
2) with the synovitis not better explained by another disease

Add **A–D**; a score of 6/10 is needed to classify patient as having definite RA

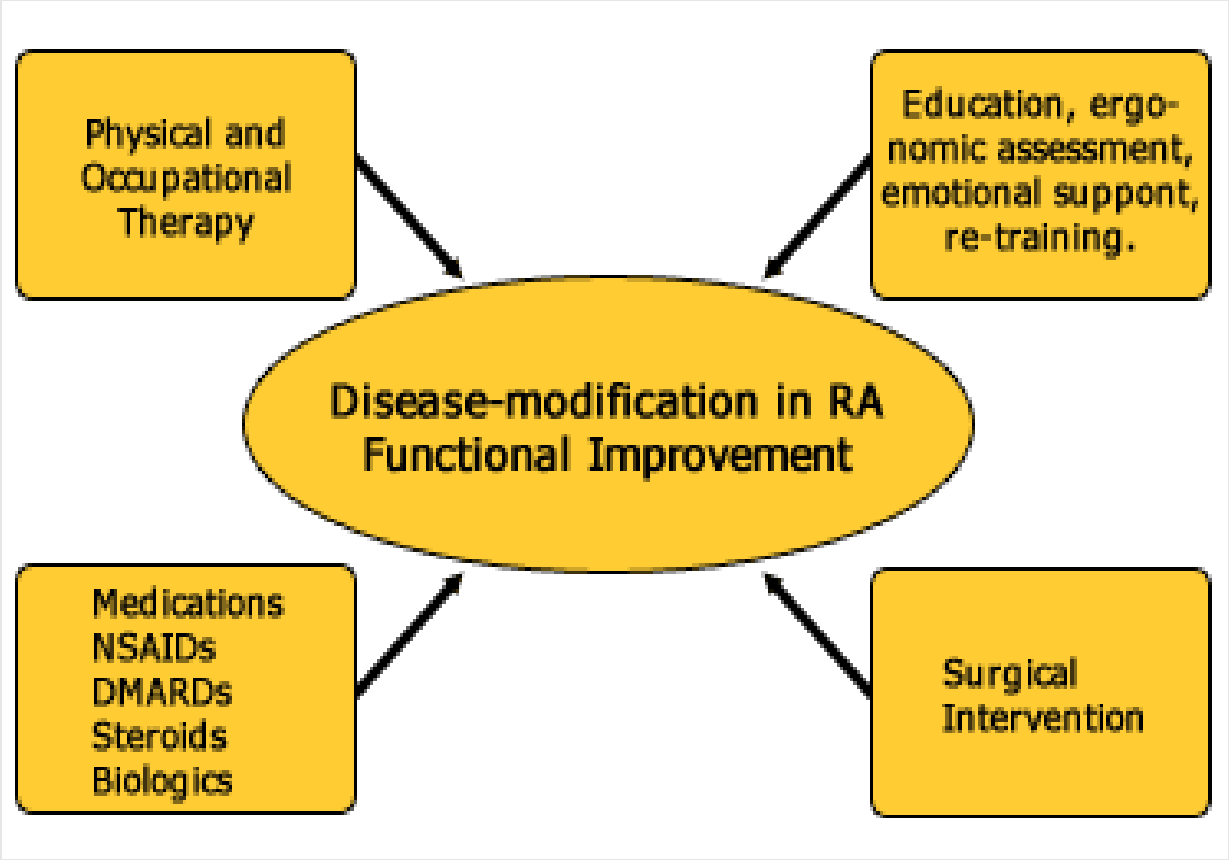
A. Joint involvement	
1 large joint.	**0**
2-10 large joints	**1**
1-3 small joints (with or without involvement of large joints)	**2**
4-10 small joints (with or without involvement of large joints)	**3**
3-10 joints (at least 1 small joint)	**5**
B. Serology (at least 1 test result is needed for classification)	
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 reactants (1 test result is needed for classification)	
Normal CRP *and normal ESR*	***0***
Abnormal CRP *or abnormal ESR*	***1***
D. Duration of symptoms	
6 weeks	**0**
>6 weeks	**1**

Treatment Goals

- Relieve pain
- Reduce inflammation
- Prevent/slow joint damage
- Improve functioning and quality of life

Treatment Approaches

- Lifestyle modifications
- Rest
- Physical and occupational therapy
- Medications
- Surgery


Physical and Occupational Therapy
Education, ergo-nomic assessment, emotional suppont, re-training.
Disease-modification in RA
Functional Improvement
Medications
NSAIDs
DMARDs
Steroids
Biologics
Surgical Intervention

Rationale for the Early Treatment of R.A.

- Erosions develop early in the disease course
- Destruction is irreversible
- Disease activity is strongly associated with joint destruction later in the disease course
- Early treatment can slow down radiographic progress
- Disease activity must be suppressed maximally in its early stages to prevent destruction and preserve function

Drug Treatments

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Disease-modifying antirheumatic drugs (DMARDs)
- Biologic response modifiers
- Corticosteroids

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Traditional NSAIDs

- Aspirin
- Ibuprofen
- Ketoprofen
- Naproxen

COX-2 Inhibitors

- Celecoxib
- Etericoxib

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

- To relieve pain and inflammation
- Use in combination with a DMARD
- Gastrointestinal side effects

Disease-Modifying Antirheumatic Drugs (DMARDs)

- Hydroxychloroquine (eye exam)
- Sulfasalazine (CBC, LFTs)
- Methotrexate (CBC, LFTs)
- Leflunomide (CBC, LFTs)

Disease-Modifying Antirheumatic Drugs (DMARDs)

- Control symptoms
- No immediate analgesic effects
- Can delay progression of the disease (prevent/slow joint and cartilage damage and destruction)
- Effects generally not seen until a few weeks to months

Biologic Response Modifiers

- **TNF Inhib:**
  etanercept,infliximab,Adalimumab
- **IL6 receptor inhib:**
  tocilizumab
- **T Cell costimulation modulator:**
  abatacept
- **Anti-CD20 - Rituximab**

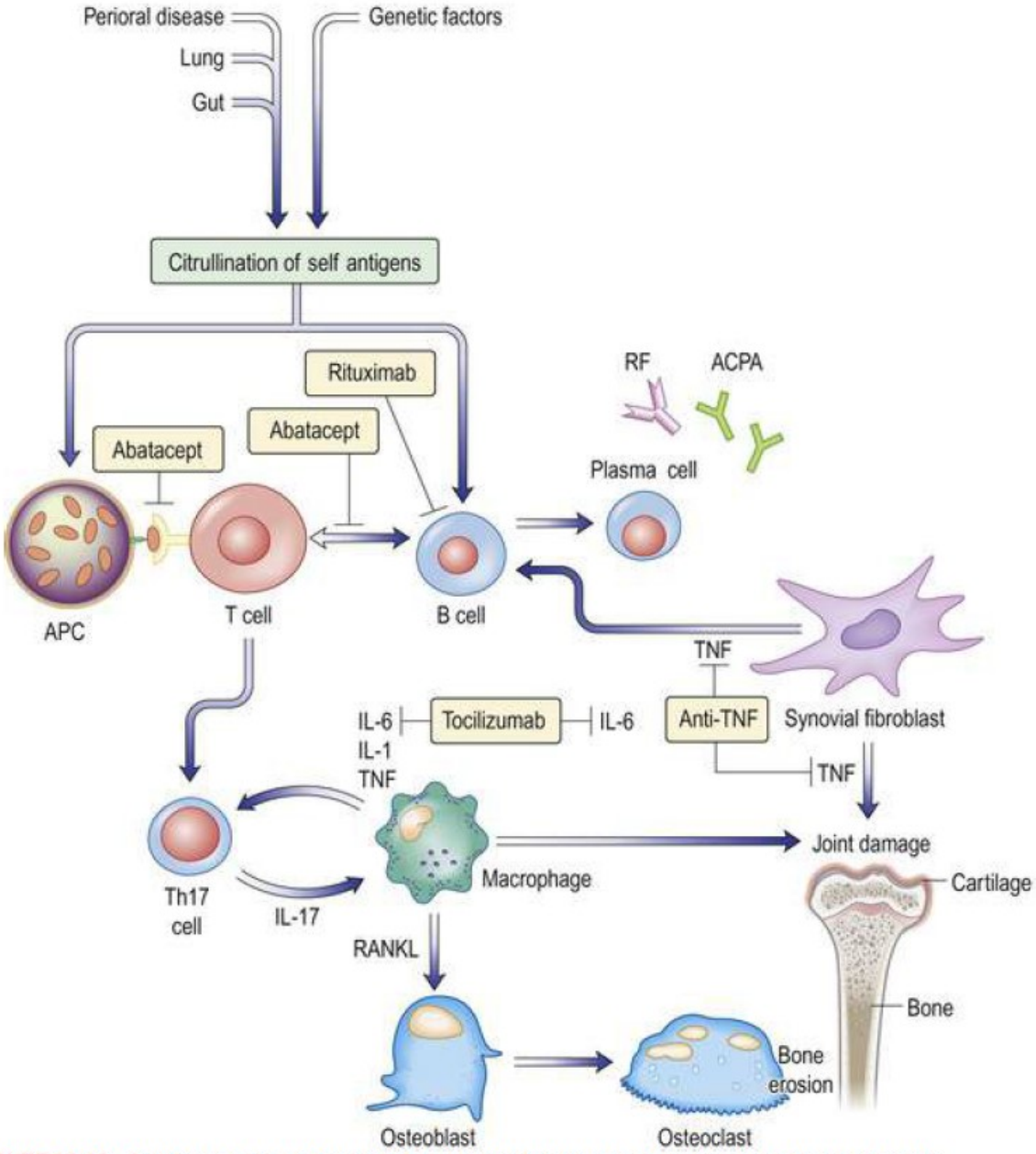


FIGURE 18.19 Pathogenesis of rheumatoid arthritis. Environment–gene interactions promote citrullination of self proteins, which can then be detected by T and B cells; this leads to a loss of tolerance and promotion of the inflammatory response, resulting in joint damage. Targeted therapy is also shown. ACPA, anti-citrullinated peptide antibody; APC, antigen-presenting cell; IL, interleukin; RANKL, receptor activator of nuclear factor kappa B ligand; RF, rheumatoid factor; Th, T helper; TNF, tumour necrosis factor.

Take home message:

Early diagnosis and treatment of RA can prevent joint destruction and preserve function.

THANK YOU