



RHEUMATOID ARTHRITIS (RA)

Dr. M Jokar

By: Dr. Mohammad Hasan Jokar



RA - Definition

- ◆ **chronic systemic inflammatory disorder**
- ◆ **unknown etiology**
- ◆ **diarthroidal joints**
- ◆ **synovium affected**
- ◆ **bone, cartilage, ligaments**
- ◆ **deformity**
- ◆ **extra-articular manifestations**



RA - Epidemiology

- ◆ **worldwide distribution**
- ◆ **all races**
- ◆ **female > male 3:1**
- ◆ **1% adults in U.S**
- ◆ **The most common Inflammatory disorder of joint**
- ◆ **All ages(peak 35-55)**

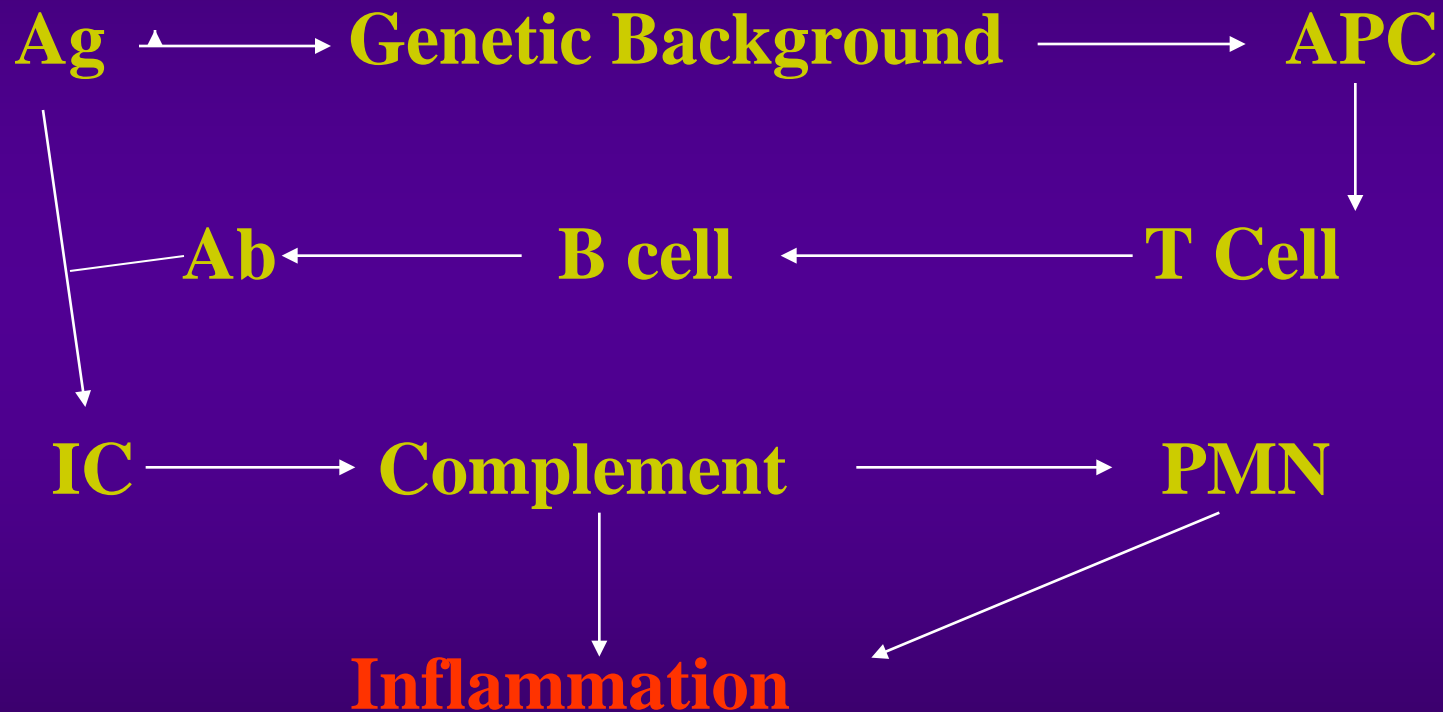


Causes

- ◆ **The cause of rheumatoid arthritis is unknown**
- ◆ **Several factors have been identified that may lead to its cause**
 - ◆ **Genetic factors**
 - ◆ **Environmental factors**
 - ◆ **Hormonal factors**



Pathophysiology





Ag

- ◆ **Bacterial**
- ◆ **Viral**
- ◆ **Foods**
- ◆ **HSP 65 KD**
- ◆ **Collagen type II**
- ◆ **Proteoglycans**

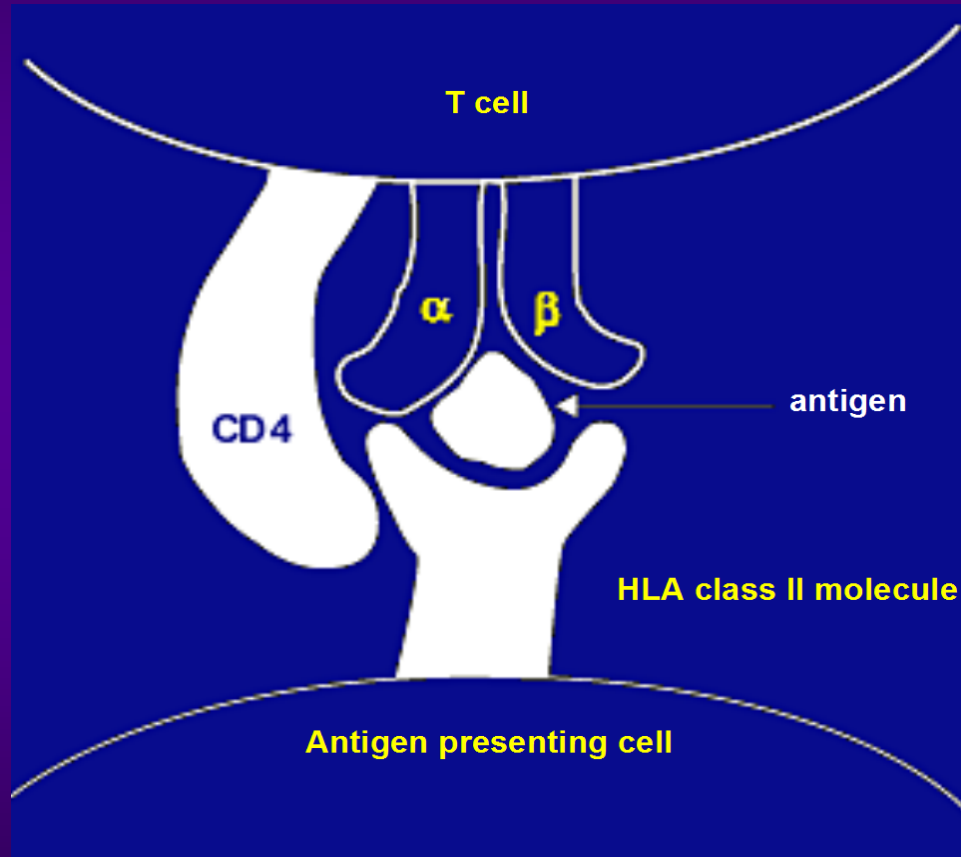


GENETIC BACKGROUND

- ◆ **First-degree relatives 3%**
- ◆ **Monozygotic twins 30%**
- ◆ **HLA-DR4 80%**
- ◆ **shared epitope (amino acids 70 to 74 of DR beta chains)**

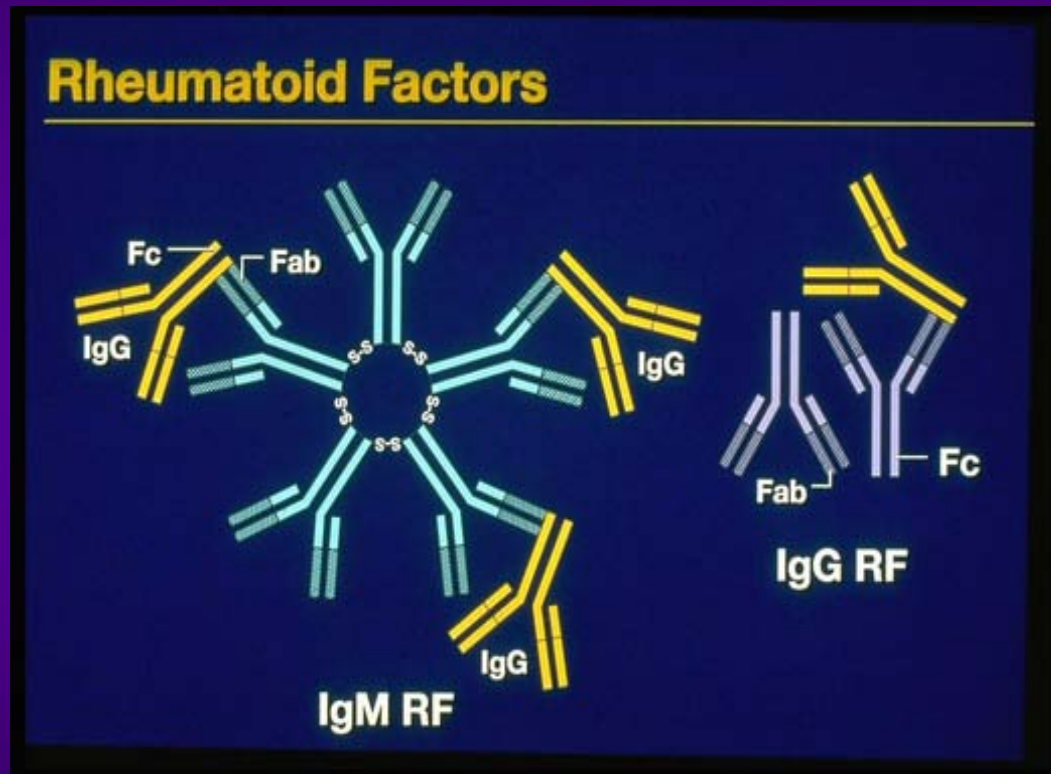


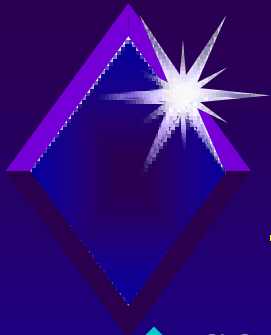
Ag presentation





B Cell → *RF*





Rheumatoid factor

- ◆ series of antibodies that recognize the Fc portion of an IgG molecule
- ◆ **any serotype**
- ◆ **most IgM**
- ◆ **many conditions associated with RF positivity - chronic inflammation**
- ◆ **70% RA positive at onset, overall 85% in first two years**
- ◆ **associated with more severe disease, extra-articular manifestations, mortality**



Anti-Cyclic Citrullinated Peptide Antibodies (AntiCCP)

- ◆ Sensitivity 80%
- ◆ Specificity 95%



Ag + Ab



Synovium



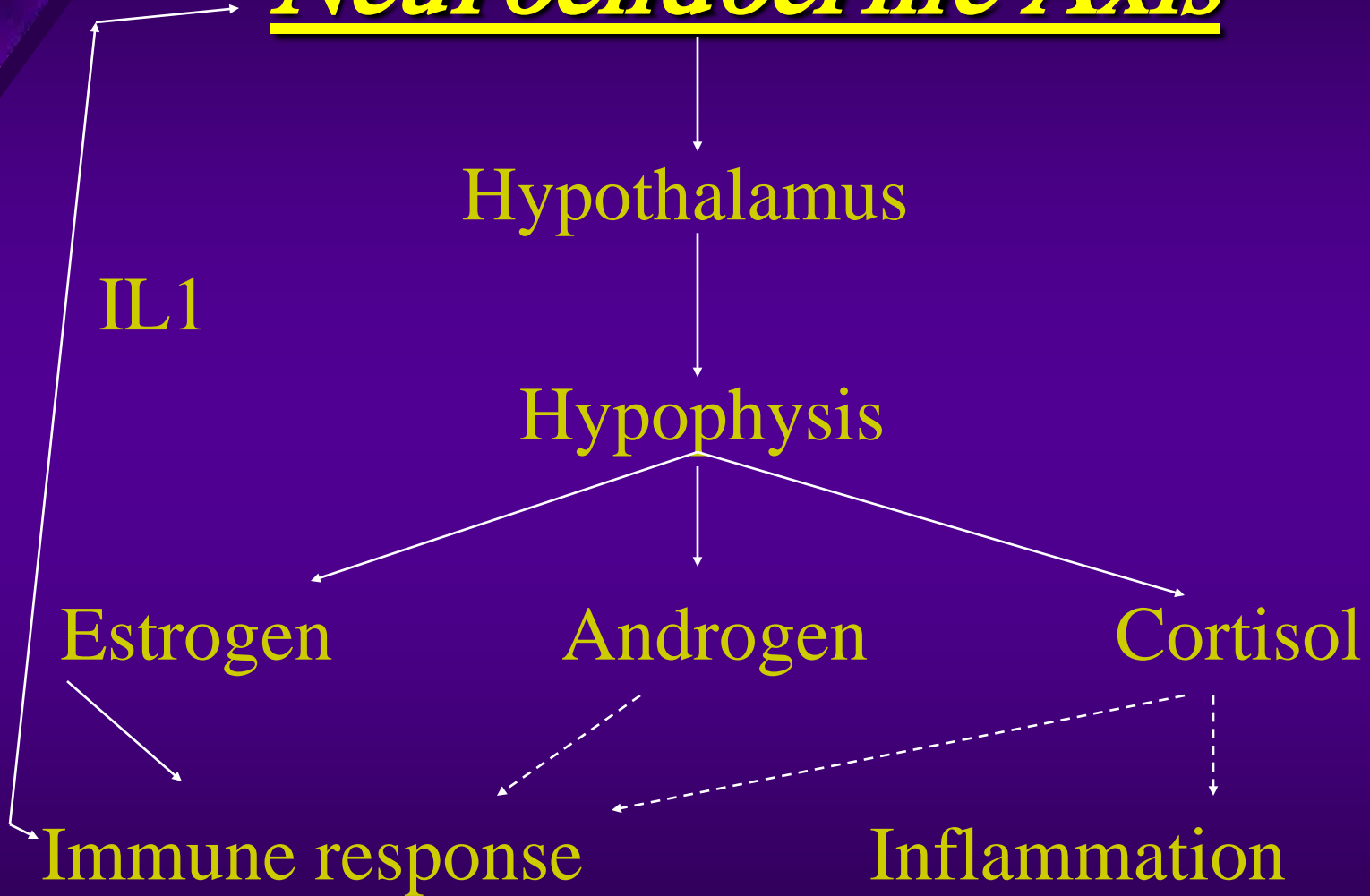
Inflammation



Inflammation

- ◆ Cellular
- ◆ PMN
- ◆ Lysosome
- ◆ Arachidonic acid
- ◆ Humoral
- ◆ Hageman factor
- ◆ Kinin system
- ◆ complement

Neuroendocrine Axis





Cytokines

◆ IL1

◆ IL6

◆ TNF



IL1

- ◆ **T Cell Activation**
- ◆ **Cartilage destruction**
- ◆ **Bone destruction**
- ◆ **Neuroendocrine system activation**
- ◆ **Fever**
- ◆ **Constitutional symptoms**
- ◆ **Acute phase reactants**



Clinical *manifestations*

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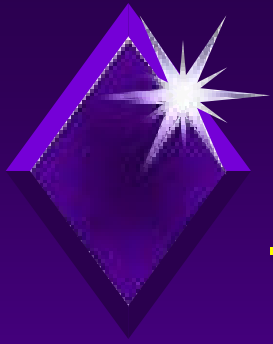
Onset

In **two thirds** the onset will begin with a prodromal illness lasting for weeks to months. The features of this illness are fatigue, anorexia, generalized weakness and vague musculo-skeletal symptoms.



Onset

In **10%** of people, the onset will be more acute, with rapid development of polyarthrititis, often accompanied by constitutional symptoms including fever, lymphadenopathy and splenomegaly.



Clinical manifestations

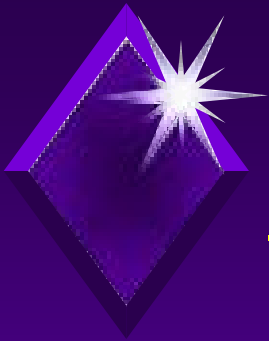
◆ Articular

◆ Nonarticular

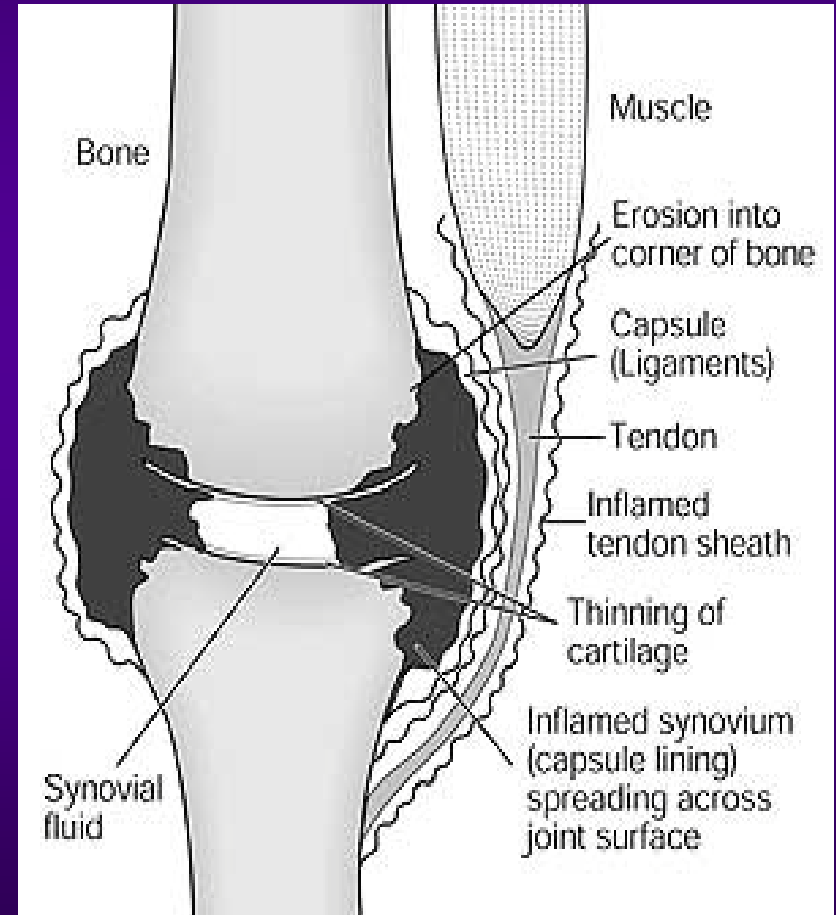
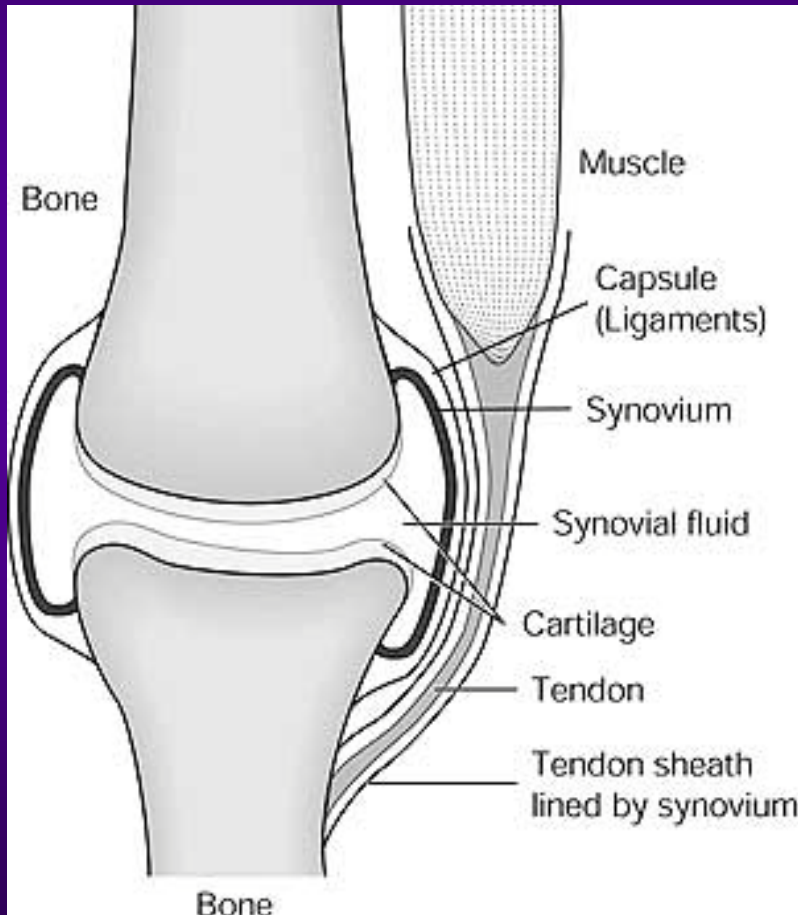


Articular Features

- ◆ Pain
- ◆ Swelling
- ◆ Tenderness
- ◆ Warmth (large joints)
- ◆ Stiffness (“gel phenomenon”)
- ◆ Deformity
- ◆ Redness is rare
- ◆ Symmetrical polyarthrititis



Normal versus Involved joint





Rheumatoid Arthritis



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Joints most commonly affected are:

- ◆ PIP
- ◆ Metacarpophalangeal (MCP)
- ◆ Carpal
- ◆ Elbows
- ◆ Metatarsophalangeal
- ◆ Feet
- ◆ Knees
- ◆ Upper cervical spine




Joints spared are:

- ◆ DIP
- ◆ Lumbar spine
- ◆ Sacro-iliac



Hands

- ◆ **Z deformity**
- ◆ **Swan neck**
- ◆ **Boutonniere**
- ◆ **Carpal tunnel syndrome**

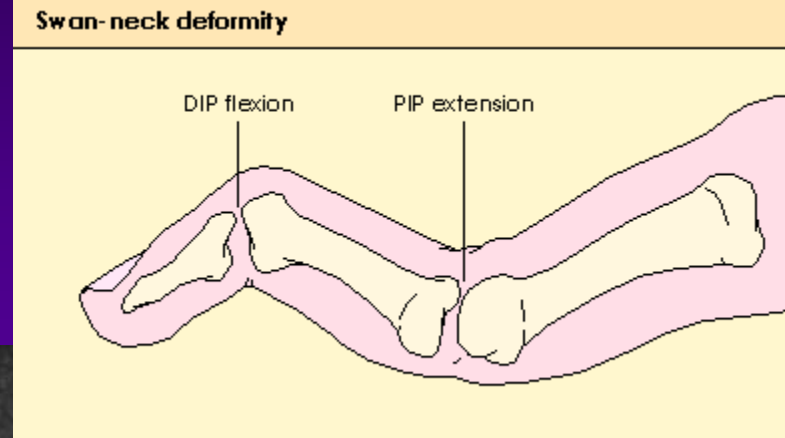


“Z deformity”; radial deviation at the wrist, ulnar deviation at MCP joints



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*Swan neck”; PIP extension, with
DIP flexion.*

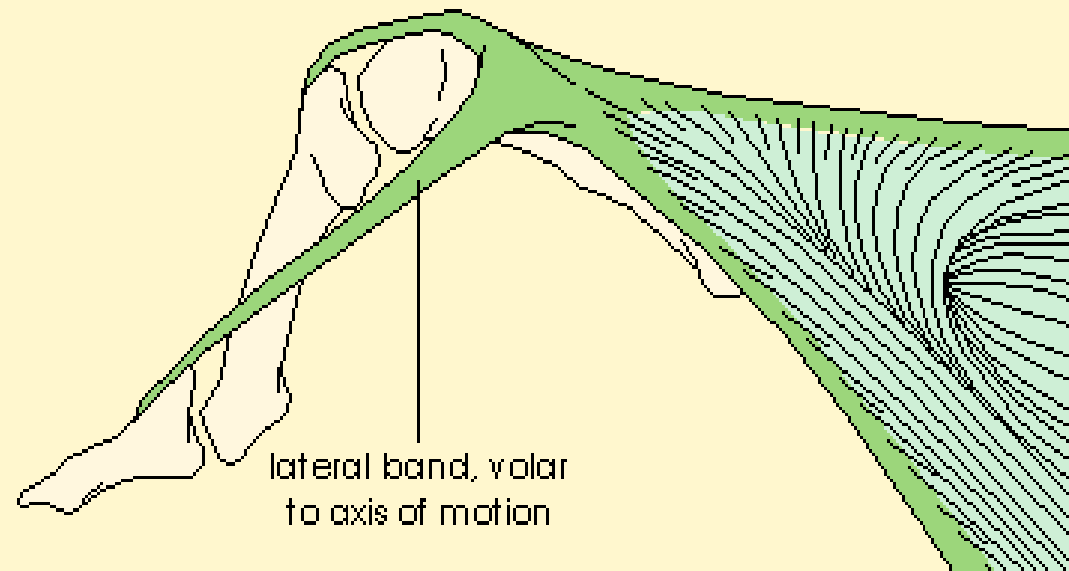




*“Boutonniere”; PIP flexion, with
DIP extension.*



Boutonniere deformity



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Extra-articular manifestations

◆ **General**

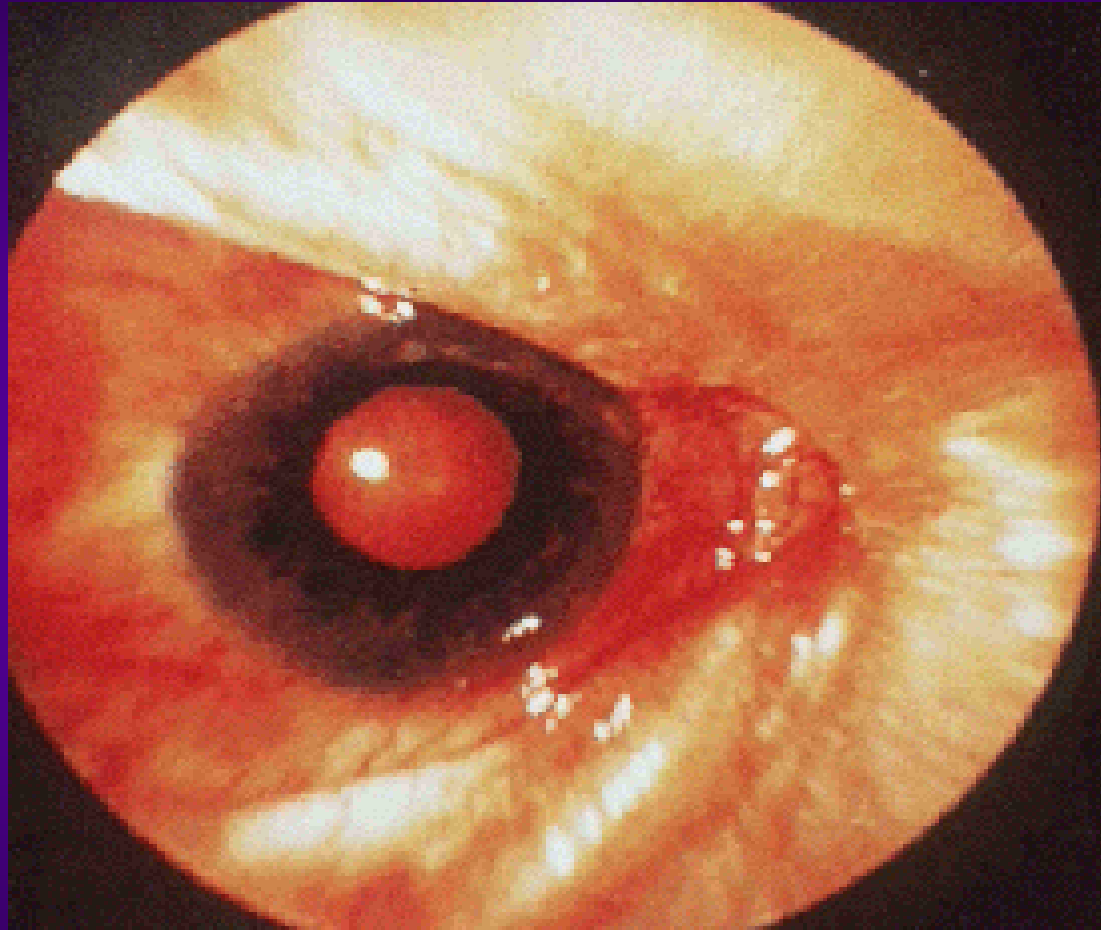
- ◆ fever, lymphadenopathy, weight loss, fatigue

◆ **Dermatologic**

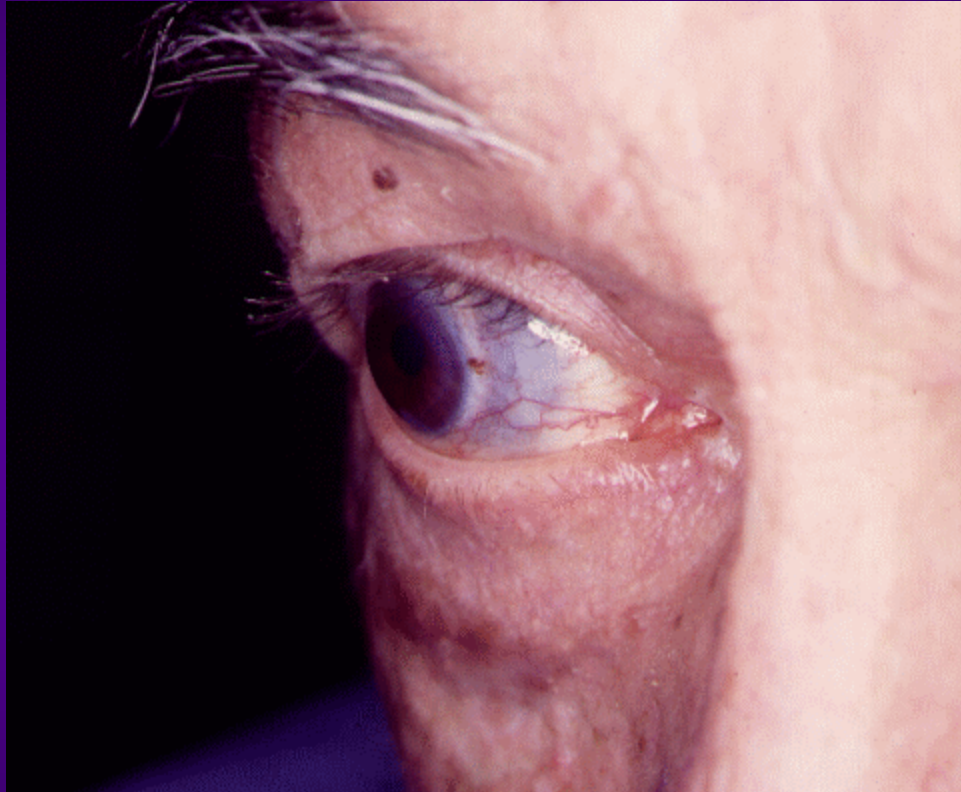
- ◆ palmar erythema, nodules, vasculitis

◆ **Ocular**

- ◆ episcleritis/scleritis, scleromalacia perforans, choroid and retinal nodules



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Rheumatoid nodule



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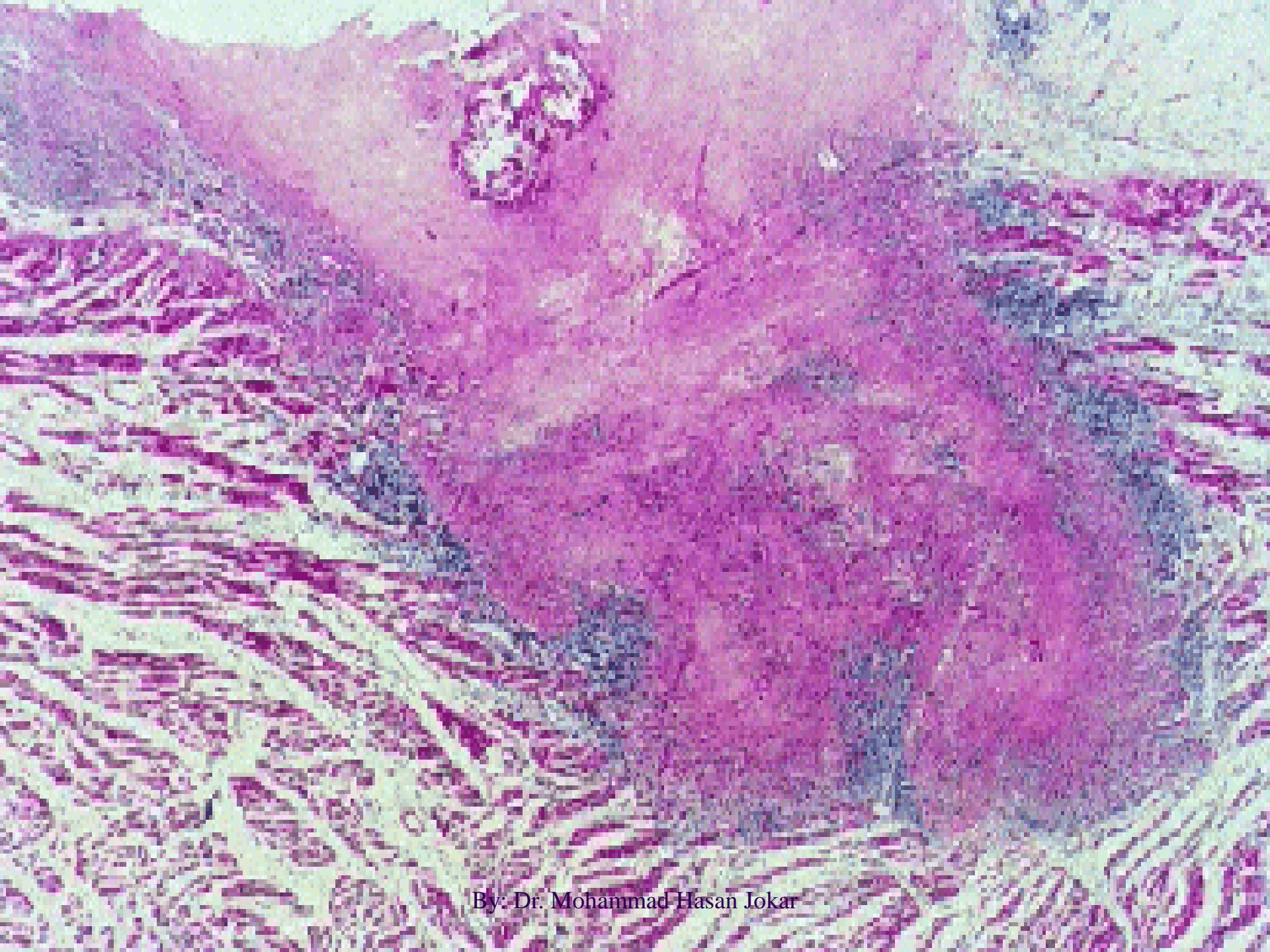


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Rheumatoid nodule

- ◆ Frequency
- ◆ Size
- ◆ Consistency
- ◆ Locations
- ◆ Symptoms
- ◆ Pathology
- ◆ RF+



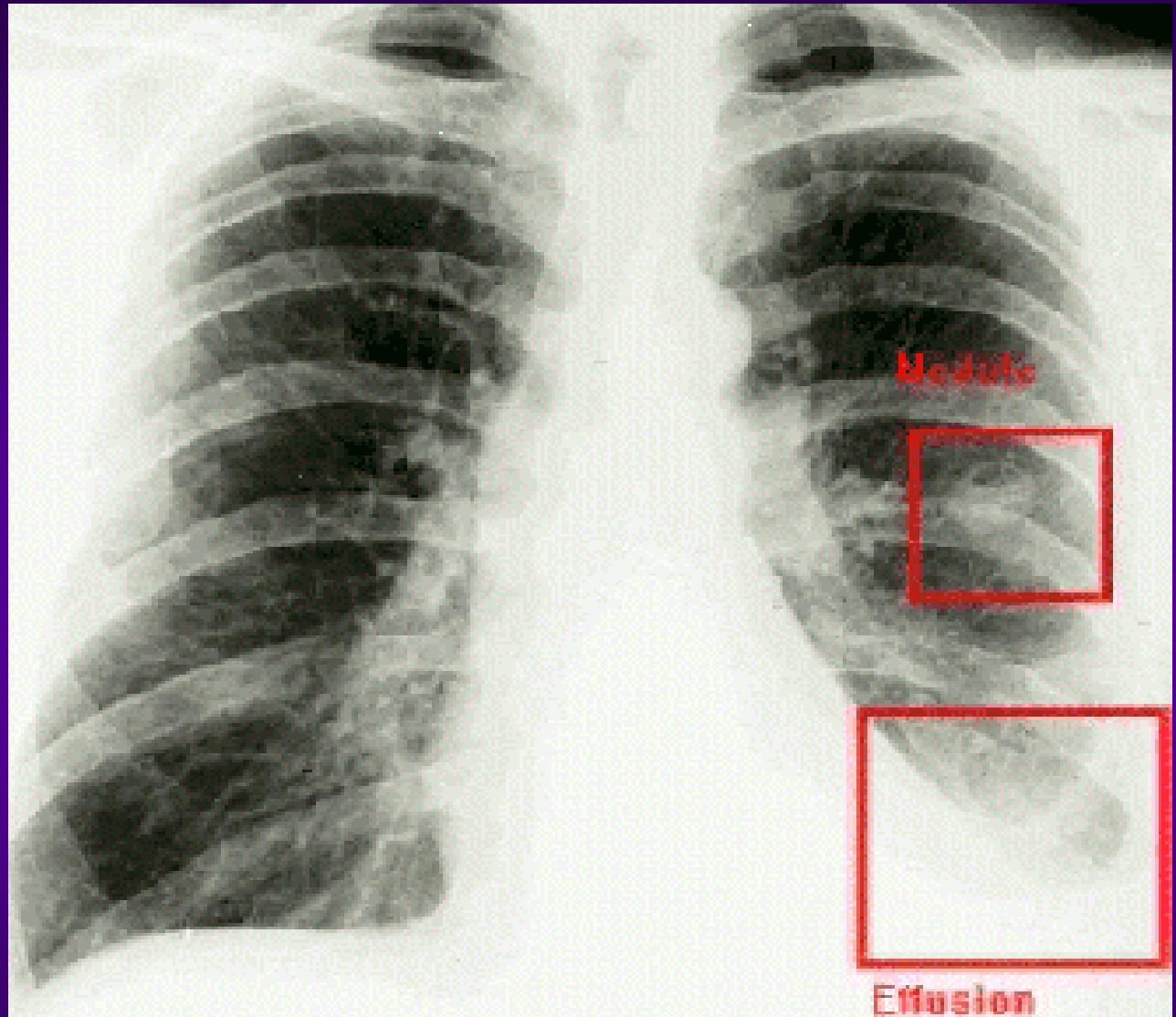
Extra-articular manifestations

◆ Pulmonary

- ◆ pleuritis, nodules, interstitial lung disease

◆ Others

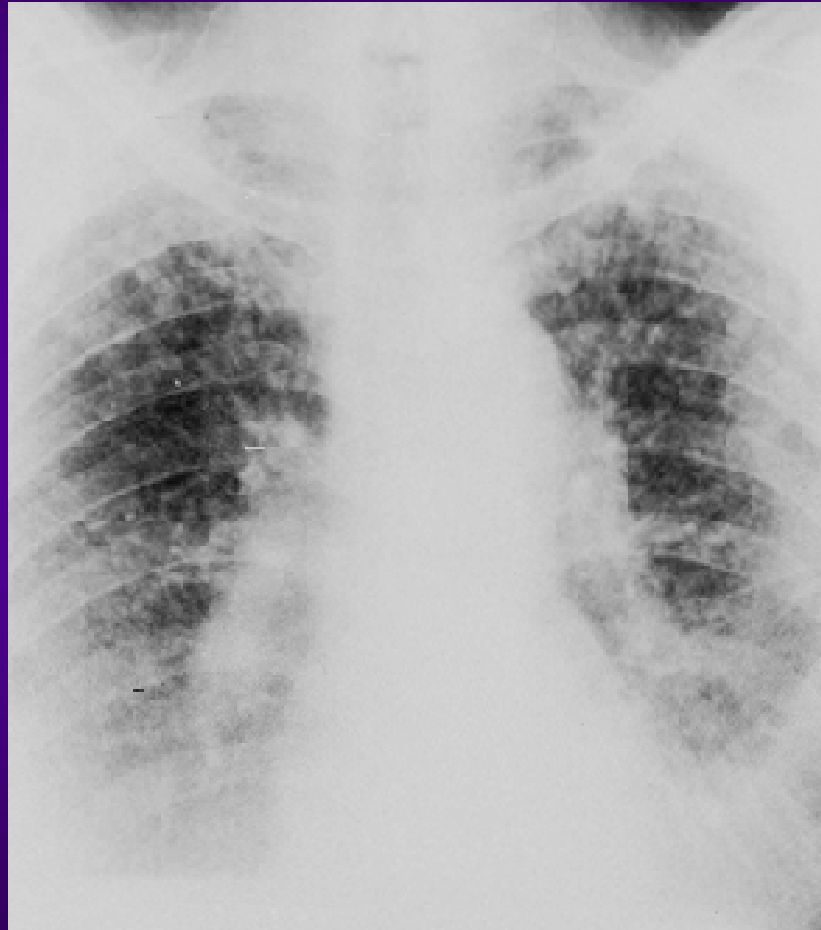
- ◆ Sjogren's syndrome, amyloidosis



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Caplan's syndrome



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Extra-articular manifestations

◆ Cardiac

- ◆ pericarditis, myocarditis, coronary vasculitis, nodules on valves

◆ Neuromuscular

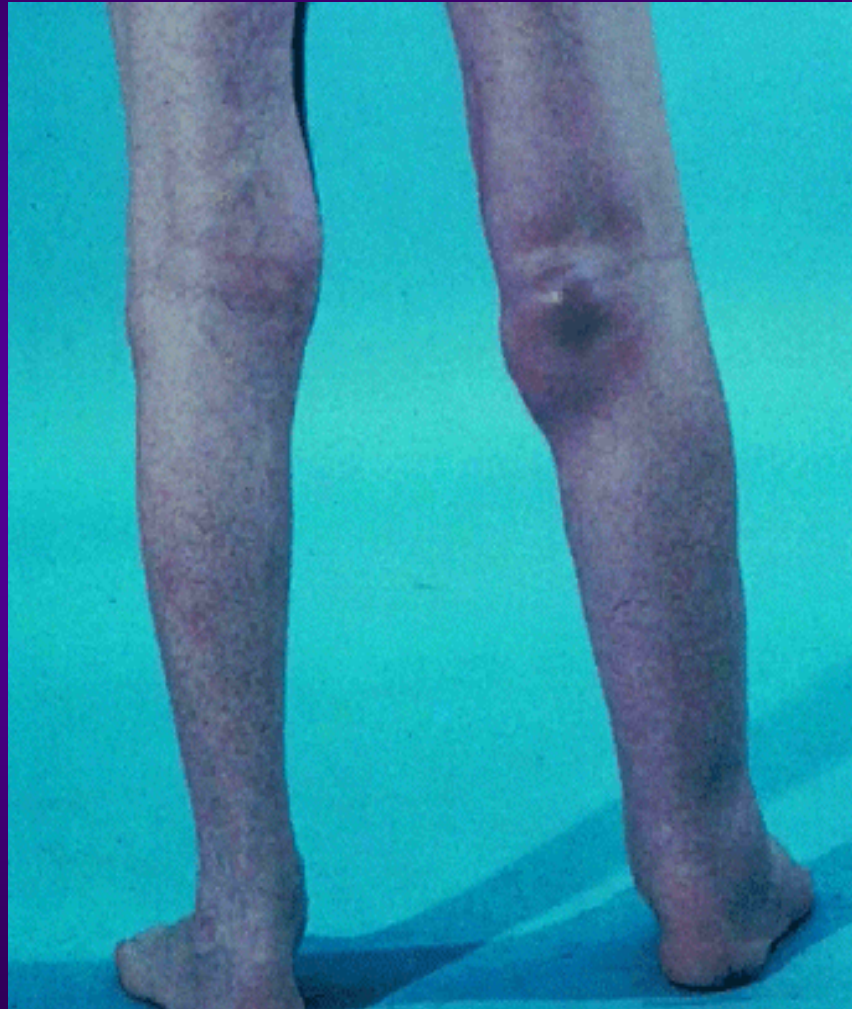
- ◆ entrapment neuropathy, peripheral neuropathy, mononeuritis multiplex

◆ Hematologic

- ◆ Anemia, Felty's syndrome, lymphomas



Backer's cyst



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Rheumatoid vasculitis



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Laboratory abnormalities

- ◆ anemia of chronic disease
- ◆ Leukocytosis
- ◆ thrombocytosis in active disease
- ◆ low white cell count in Felty's
- ◆ ESR
- ◆ CRP
- ◆ Rf




Unusual patterns of RA

- ◆ Adult-onset Still's disease
- ◆ Palindromic rheumatism
- ◆ Monoarticular



DDX of a positive RF

- ◆ normal - 1-4%, 10-25% over age 70
- ◆ systemic autoimmune diseases
- ◆ infections
- ◆ malignancy
- ◆ chronic liver disease
- ◆ pulmonary diseases



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.



RA - differential diagnosis

- ◆ spondyloarthropathies
- ◆ CTDs
- ◆ polyarticular gout
- ◆ CPPD
- ◆ viral infections
- ◆ fibromyalgia



RA - differential diagnosis

◆ Uncommon

- ◆ hypothyroidism
- ◆ SBE
- ◆ hemochromatosis
- ◆ hypertrophic pulmonary osteoarthropathy
- ◆ hyperlipoproteinemias
- ◆ hemoglobinopathies
- ◆ relapsing polychondritis

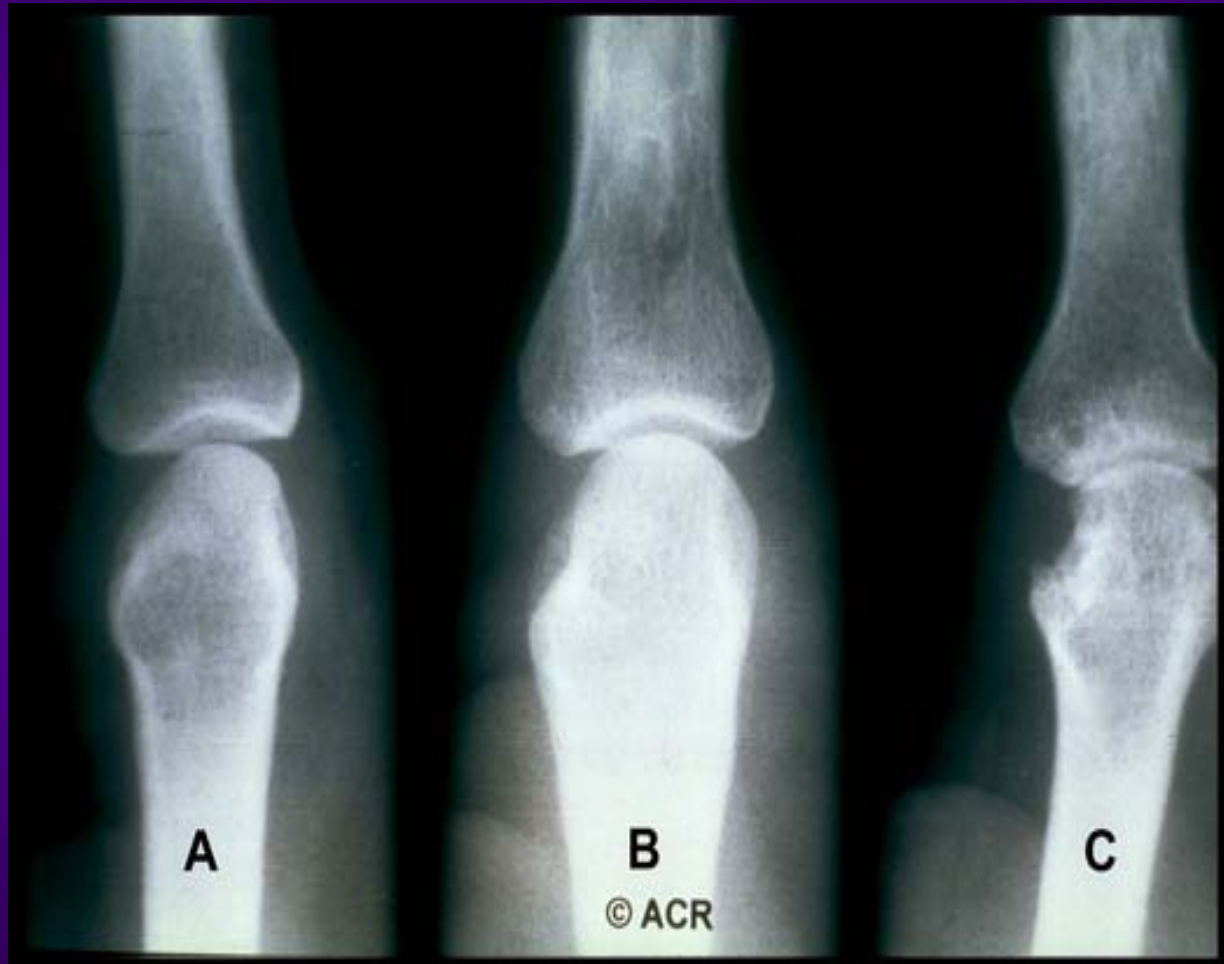


X - Ray

- ◆ **Soft tissue swelling**
- ◆ **Juxtaarticular osteoporosis**
- ◆ **Erosions**
- ◆ **Ankylosis**



RA: Erosion Progression



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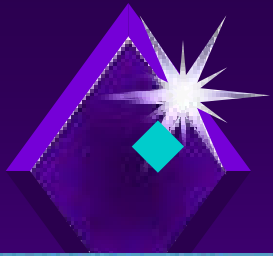
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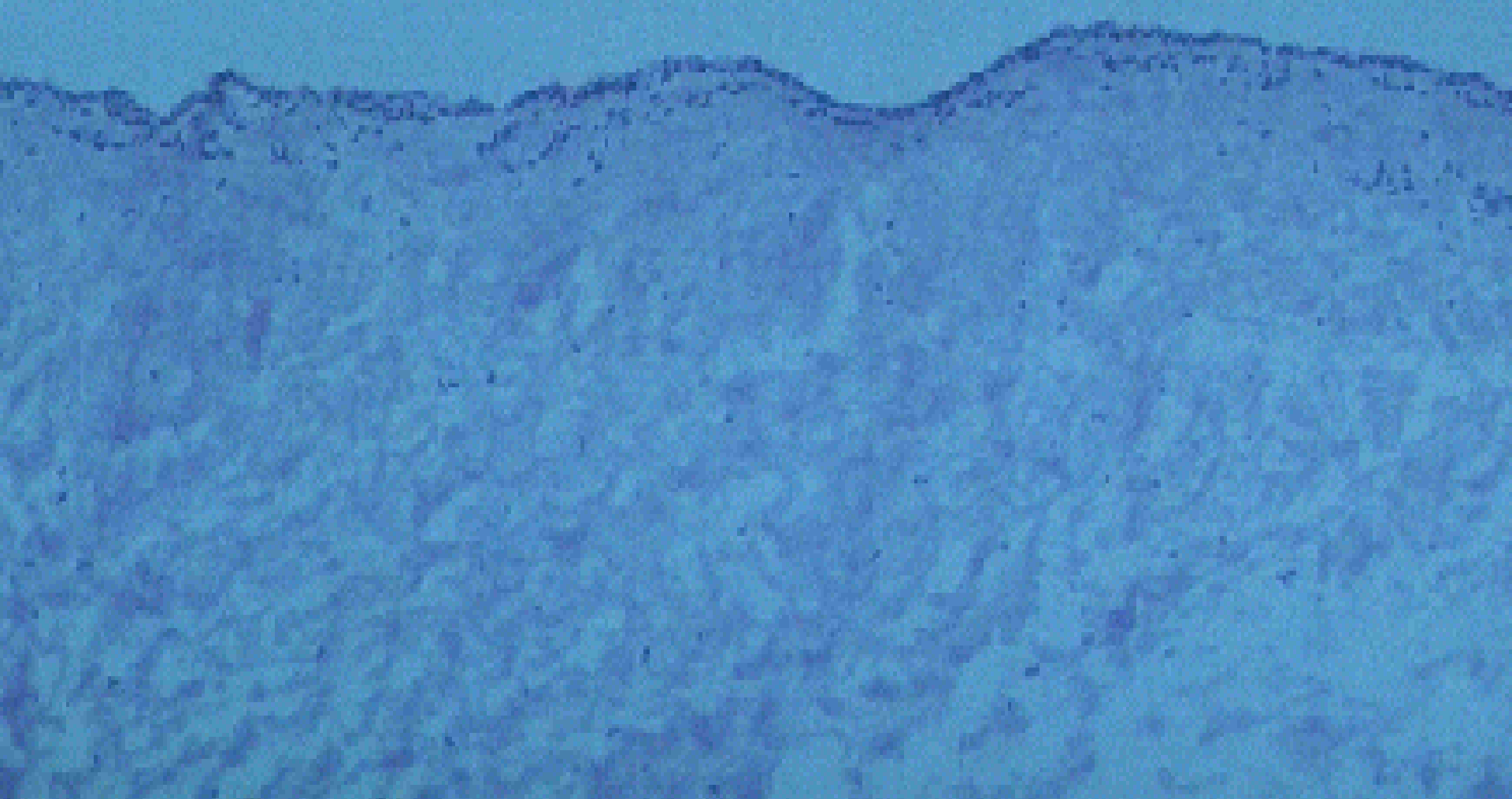


Pathology

- ◆ Synovial lining cell proliferation
- ◆ Subsynovial infiltrations
- ◆ Pannus formation

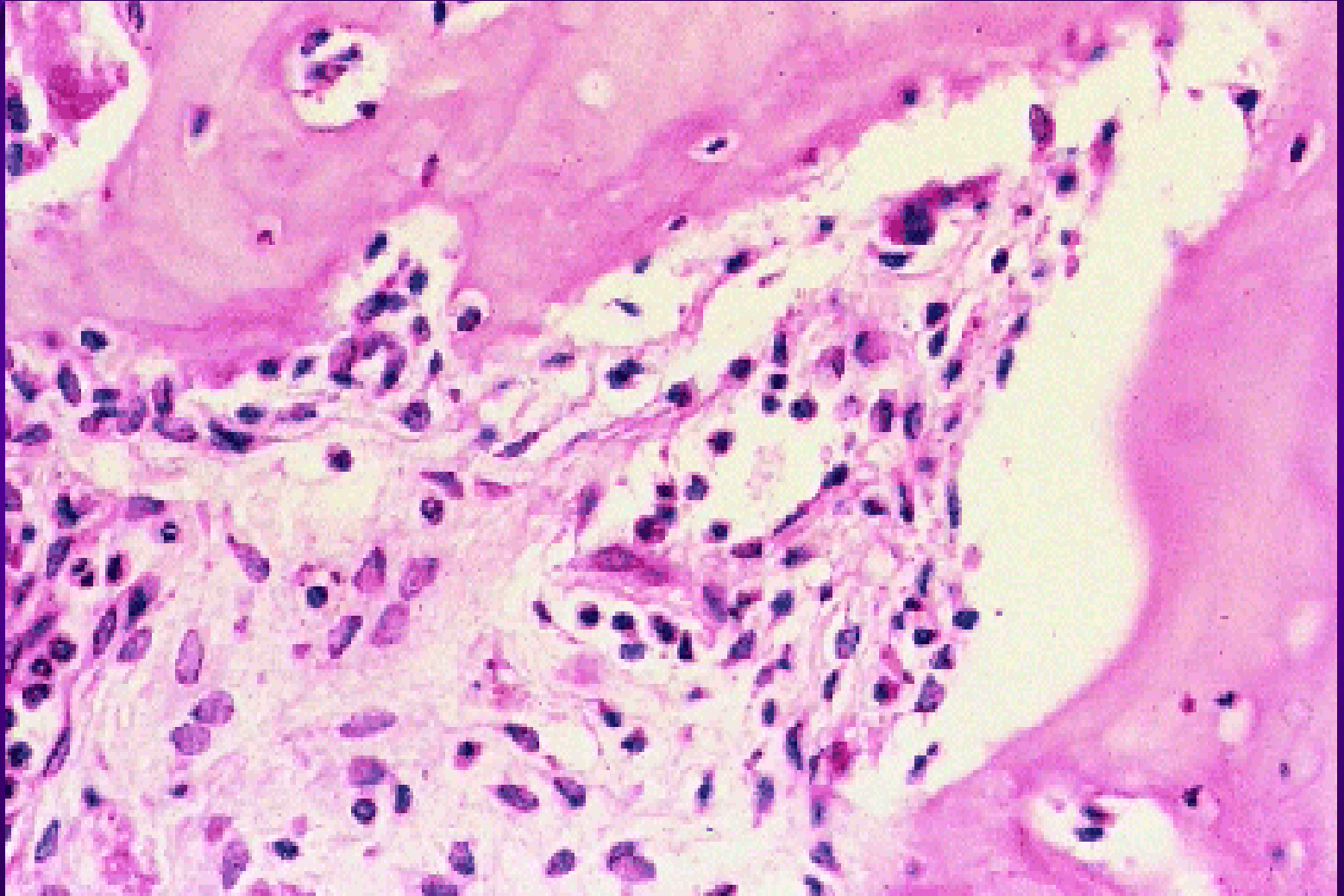


Synovial thickening



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Pannus



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Felty's syndrome

- ◆ classic triad
 - ◆ RA, splenomegaly, leukopenia
- ◆ generally a neutropenia ($<2000/\text{mm}^3$)
- ◆ thrombocytopenia may occur
- ◆ complications
 - ◆ infections, non-healing leg ulcers
- ◆ most require no additional treatment for cytopenias
- ◆ splenectomy?



RA - Management

◆ **Nonpharmacologic**

- ◆ **Patient education**

- ◆ **rest**

 - ◆ **splinting**

- ◆ **physical therapy**

 - ◆ **heat, cold, ultrasound, paraffin,
massage**

- ◆ **occupational therapy**



RA - Management

◆ Pharmacologic

- ◆ analgesics

- ◆ NSAIDs - full dose

- ◆ corticosteroids

 - ◆ prednisone at low dose

 - ◆ intra-articular steroids



Disease modifying agents

- ◆ ***every patient should be considered for at least one modifying agent***
- ◆ **Methotrexate**
- ◆ **Antimalaria**
- ◆ **Sulfasalazine**
- ◆ **Cytotoxic agents**



RA - long term prognosis

- ◆ **RA shortens survival and produces disability**
- ◆ **1/3 leave work force in five years**
- ◆ **aggressive DMARD TX can reduce disability by 30% in 10-20 years**