

# Historic City of Yazd

Iran  
(Islamic Republic of)

*IN THE NAME OF GOD*

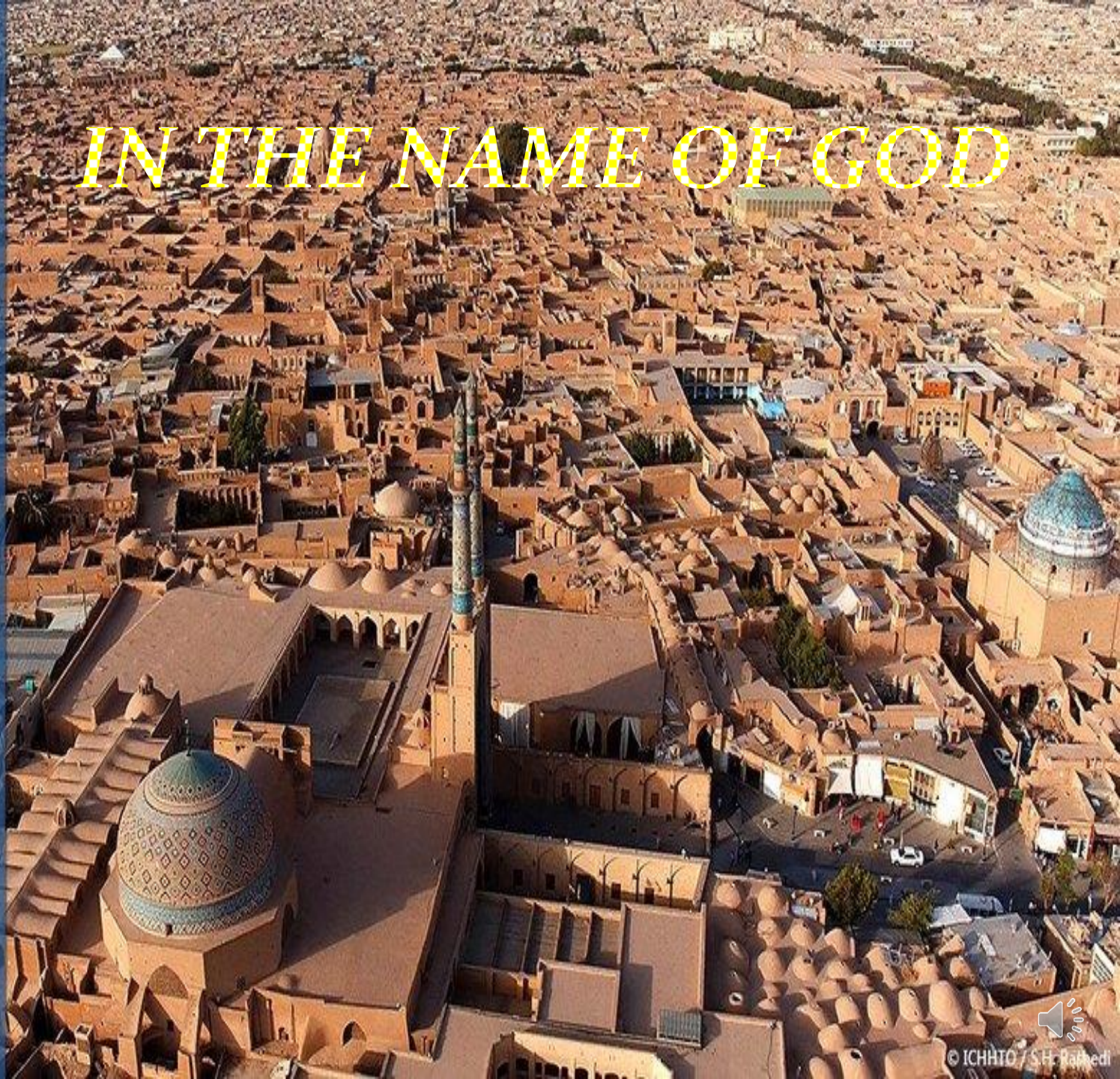


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# Rheumatoid Arthritis

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- A 35 y old women has presented with symmetric polyarthrititis (wrists, MCPs, PIPs, elbows and MTPs).
- She also has fatigue, low grade fever and weight loss.
- These joints are swollen, tender and warm.



# Rheumatoid Arthritis

- A chronic inflammatory disease
- A systemic disease
- Characteristic feature:
  - Persistent inflammatory synovitis
  - Peripheral joints
  - Symmetric
  - Cartilage damage and bone erosions → Destruction



# Epidemiology and Genetics

# Epidemiology

- Most common form of chronic inflammatory arthritis
- Prevalence: ~1% (range 0.3–2.1%)
- Annual incidence: 25 to 50/100,000
- Women: 2\_3 times more often than men

# Epidemiology

- ↑ Incidence between 25 and 55 y

# Genetics

- First-degree relative → 2-10 times > NL population
- Concordant in monozygotic twins → 15-20%



# Environmental factors

- Smoking
- Obesity
- Silica exposure
- Mineral oil
- Organic solvent



# Environmental factors

- Smoking:

More common environmental factor

Relative Risk: 1.5-3.5

↑ Severe RA with antibodies to CCP

↑ Extraarticular

In particular women (2.5 times)



# ONSET



# Onset

- In 2/3 of patients begins with:
  - Fatigue, anorexia, generalized weakness
- This prodrome may persist for weeks or months





# ARTICULAR SIGNS & SYMPTOMS



# Articular

- Most common manifestation:
  - Insidious onset of inflammatory pain
- An almost invariable feature:
  - Morning stiffness of >1-h



# Onset

- Specific symptoms appear gradually
  - Earliest joints: small joints of hands and feet
  - Especially: wrists, MCP and PIP joints
  - Symmetric
- 1/3 of patients ➡ Initially one or a few joints



# Articular

## ■ Synovial inflammation causes:

- Swelling
- Tenderness
- Limitation of motion
- Warmth
- Palpable synovium





# Articular

- Symmetric
- Certain specific joints:
  - Wrist joints
  - MCP, PIP
  - Elbow
  - Knee
  - Forefoot, ankles, and subtalar
  - Hip & shoulder



# Articular

DIP: rare (OA)

- Rarely affect → lumbar and thoracic spine

# Articular

- Synovial joints of C1-C2:
  - Atlantoaxial subluxation
  - Pain in the occiput
  - Rarely: compression of the cord



# Articular

- Characteristic joint changes:

- Hand:

- "Z" deformity → Radial deviation at wrist  
Ulnar deviation digits





# Articular

## ■ Characteristic joint changes:

### ● Hand:

- Swan-neck deformity → PIP hyperextension  
DIP Flexion



# Articular

- Characteristic joint changes:

- Hand:

- Boutonnière deformity → PIP flexion  
DIP extension



# Articular

- Characteristic joint changes:

- Hand:

- Thumb → Hyperextension of the first IP  
Flexion of the first MCP



# Articular

## ■ Characteristic joint changes:

### ● Foot:

- Hallux valgus
- Eversion at hindfoot
- Plantar subluxation of the metatarsal heads
- Widening of the forefoot
- Lateral deviation and dorsal subluxation of the toes





# EXTRAARTICULAR MANIFESTATION



# Extraarticular Manifestation

- RA is a systemic disease
- 40% of patients

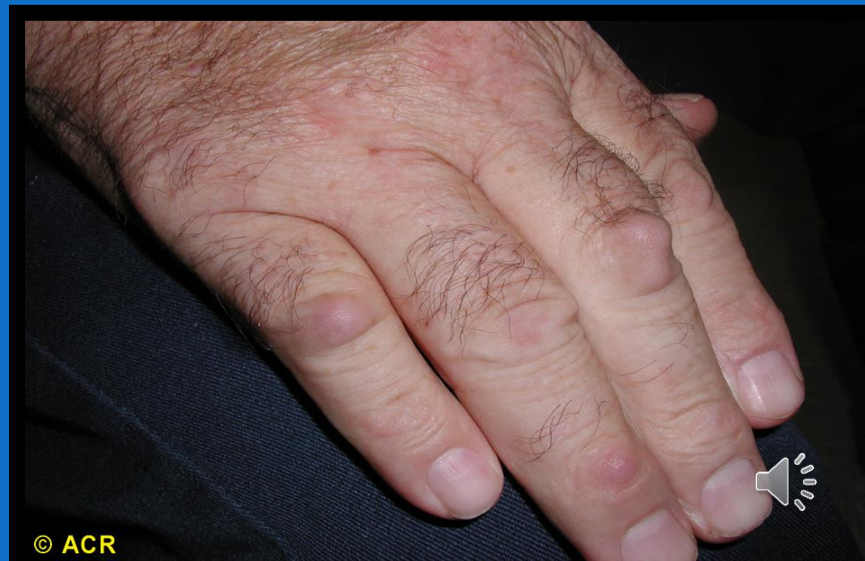
# Extraarticular Manifestation

- More commonly in:
  - History of smoking
  - Uncontrolled articular disease
  - RF or antiCCP positive



# Rheumatoid nodule

- In 30–40%
- On areas subjected to mechanical pressure
- Elsewhere
- Firm, nontender, adherent



# Rheumatoid nodule

## ■ Common locations:

- Olecranon bursa, proximal ulna, Achilles tendon, occiput



# Pleuropulmonary

## ■ Pleuritis:

- Most common pulmonary manifestation
- Autopsy → Common
- Symptomatic → Infrequent



# Pleuropulmonary

- ILD:
  - Dry cough
  - Progressive shortness of breath
- Pulmonary nodules



# Cardiovascular

## ■ Pericarditis:

- Asymptomatic
- 50% by echo

## ■ IHD

- Most common cause of death

-  Inflammatory markers





# Eye

- <1%
- Long-standing disease and nodules
- Episcleritis, scleritis
- Sjögren's syndrome (10%)



# Felty's syndrome

- Consists of:
  - Splenomegaly
  - Neutropenia
  - Nodular RA
- Leukopenia is selective neutropenia (PMN  $<1500$  cells/L)
- Late stage of severe RA

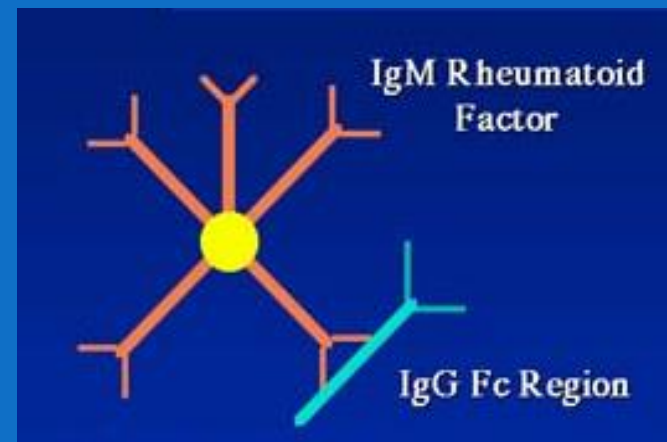


# LABORATORY



# Laboratory

- RF autoantibodies reactive with Fc portion of IgG
- 75\_80% of patients
- No specific
- 5% of healthy
- Rheumatic & infectiuse



# Laboratory

- Predictive value: low
- $<1/3$  of patients with a positive test for RF have RA
- Not useful as screening
- Prognostic
- Doesn't need to be repeatedly tested



# Laboratory

## ■ Anti-CCP:

- Sensitivity: 75\_80%%
- Specificity: 95%
- Prognostic
- 1.5% of population

# Laboratory

- Normochromic, normocytic anemia
- Anemia and thrombocytosis → disease activity
- ↑ ESR & CRP
- Synovial fluid: ↑ WBC



# Radiography

- Early: soft tissue swelling





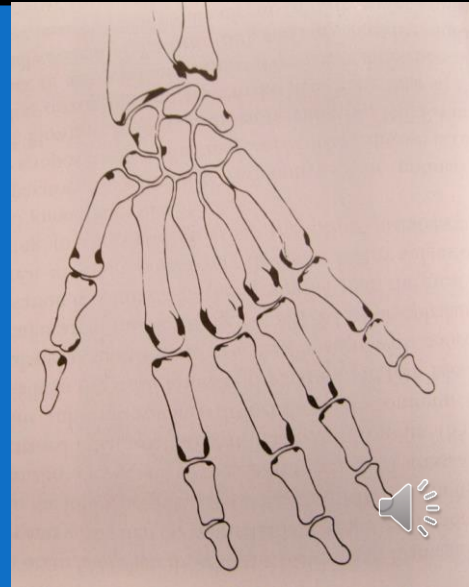
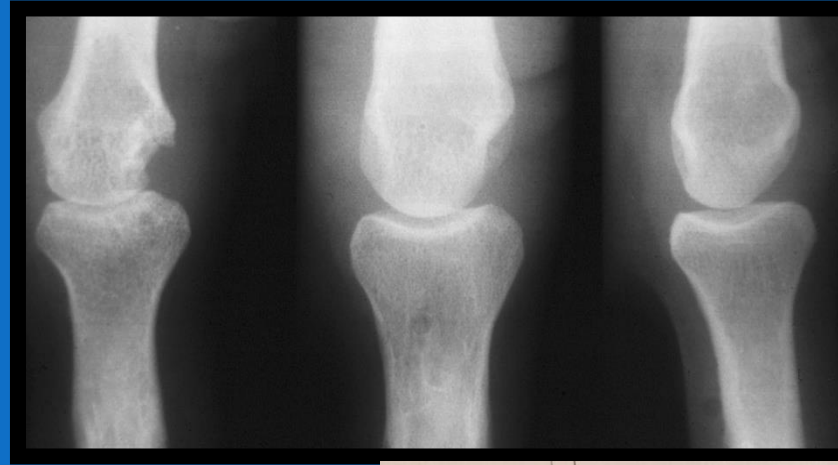
# Radiography

- Early: soft tissue swelling
- Juxtaarticular osteopenia



# Radiography

- Early: soft tissue swelling
- Juxtaarticular osteopenia
- Loss of articular cartilage
- Bone erosions



# Radiography



# Clinical course

- Persistent but fluctuating disease activity
- Early aggressive treatment



# Clinical course

- Poor prognostic factors:
  - High disease activity
  - Many joints involved
  - Increased inflammatory markers
  - High titers of RF and/or anti CCP
  - Tobacco use
  - Erosions on radiographs



# Diagnosis



# Diagnosis

- No pathognomonic finding in:

- Clinic
- Paraclinic

- Almost exclusively on:

- History
- Physical examination





# Diagnosis

- Typical picture:
  - Bilateral symmetric polyarthritis
  - Small and large joints
  - Upper and lower extremities
  - Sparing of the axial skeleton except cervical spine
- Constitutional features
- Morning stiffness
- Nodules
- ↑ RF & AntiCCP
- Radiography

# Treatment



# Treatment

## ■ Goals:

- ➡ Reduce pain
- ➡ Prevent deformity
- ➡ Normal joint function
- ➡ Normal social function

# Treatment

- NSAIDs

- Glucocorticoid

- DMARDs

- Biologic



# NSAIDs

- Short course
- Side effects:
  - Gastritis and peptic ulcer
  - Impairment of renal function
- Avoid chronic use



# Glucocorticoid

- Rapid control
- Low dose → Retard radiographic progression
- Side effects:
  - Osteoporosis
  - Avascular necrosis of bone
  - Obesity
  - Hypertension
  - Glucose intolerance



# DMARDs

■ Delayed onset of action ➡ 6-12 w

■ Methotrexate:

- First choice
- Once weekly
- Side effects:
  - Oral ulcers
  - Nausea
  - Hepatotoxicity
  - Cytopenia
  - Avoid pregnancy





# DMARDs

## ■ Leflunomide:

- Efficacy: similar to MTX
- Monotherapy or combination
- Avoid pregnancy



# DMARDs

## ■ Sulfasalazine:

- Side effect:
  - Nausea
  - Hypersensitivity
  - Bone marrow suppression

# DMARDs

## ■ Hydroxychloroquine:

- Early mild disease
- With other DMARD
- Ophthalmologic monitoring



# BIOLOGICS

# Anti-TNF

## ■ Infliximab:

- Chimeric (mouse & human) monoclonal Ab

## ■ Adalimumab & Golimumab:

- Humanized

## ■ Certolizumab:

- Pegylated

## ■ Etanercept: Fusion protein comprising TNF receptor



# Anti-TNF

- Monotherapy except Infliximab

- Avoided in:

- Active infection
- Hypersensitivity

- Screening for TB

# Rituximab

- Monoclonal Ab against CD20



# Tocilizumab

- Monoclonal Ab against IL-6 receptor
- Can be used as monotherapy



# Janus kinase (JAK) inhibitors

- Tofacitinib and baricitinib
- Shouldn't be used with biologic DMARDs due to increased risk of infections

# THANKS FOR YOUR ATTENTION

