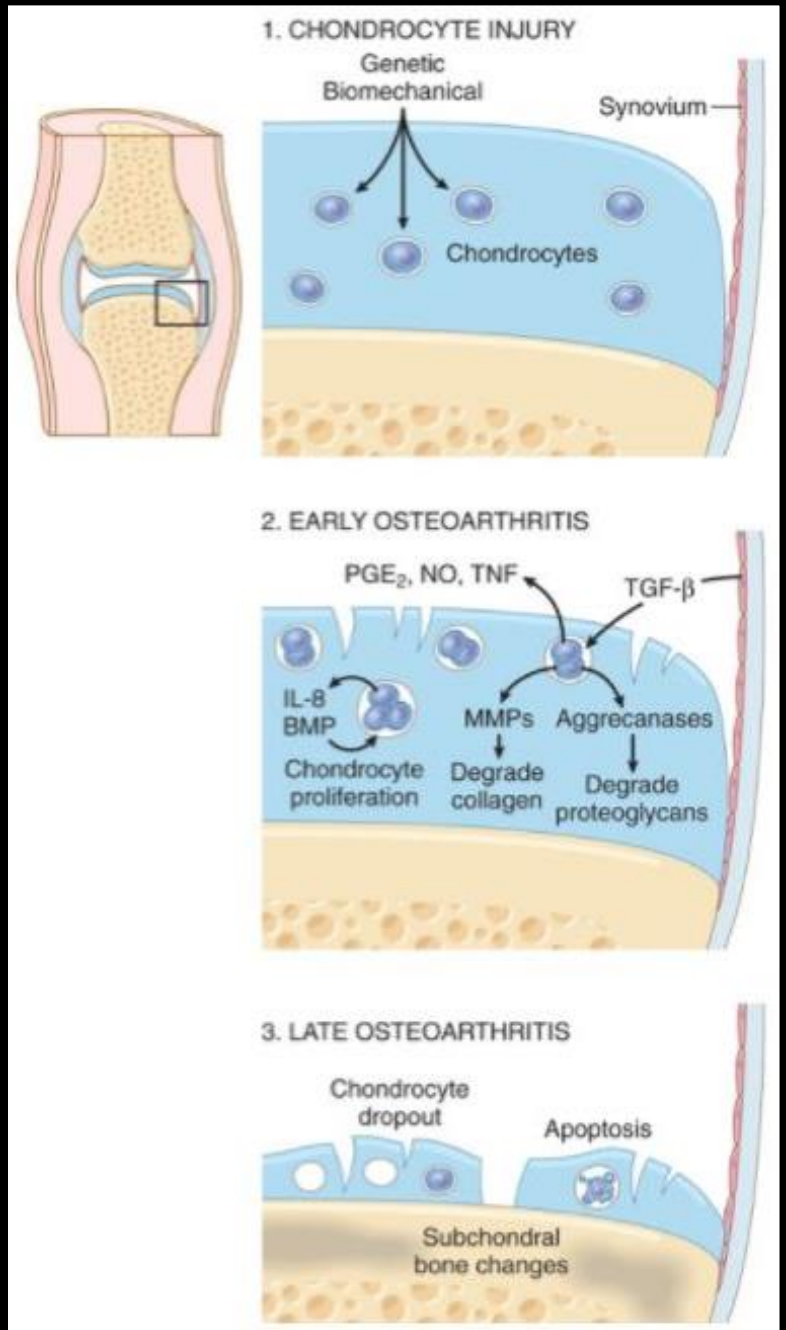
Lecture 7

JOINTS (BASIC KNOWLEDGE):

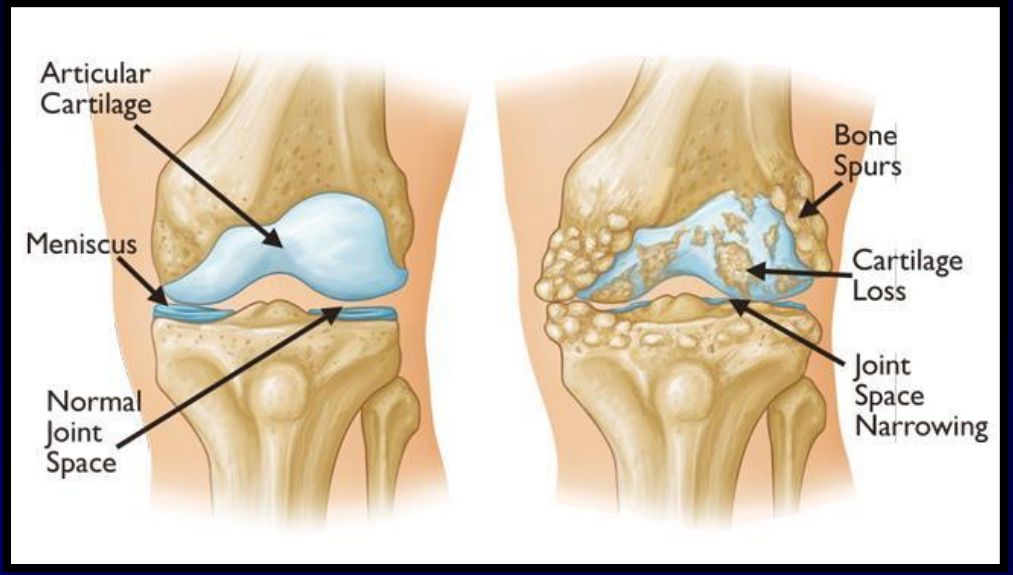
- **Provide motion & stability to our skeleton**
- **Synovial (cavitated): synovial joints, wide motion (knee, elbow…)**
- **Non synovial (solid): synarthrosis, minimal movement (skull, sternum…)**
- **Synovial joints covered by hyaline cartilage (70% water, 10% type II collagen, 8% proteoglycans + chondrocytes**
- **Synovial membrane contains: A synoviocytes (diff. macrophages), and B synoviocytes fibroblast-like**
- **Synov membrane lacks basement membrane**
- **Hyaline cartilage: no blood supply, no nerves, no lymphatics (shock absorber)**

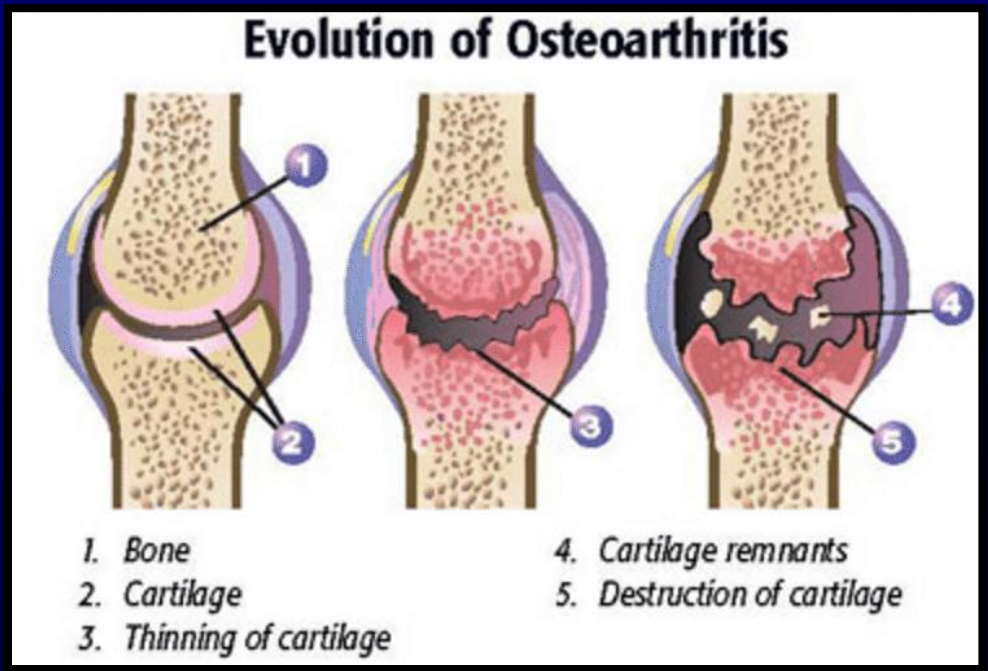
OSTEOARTHRITIS (DJD):

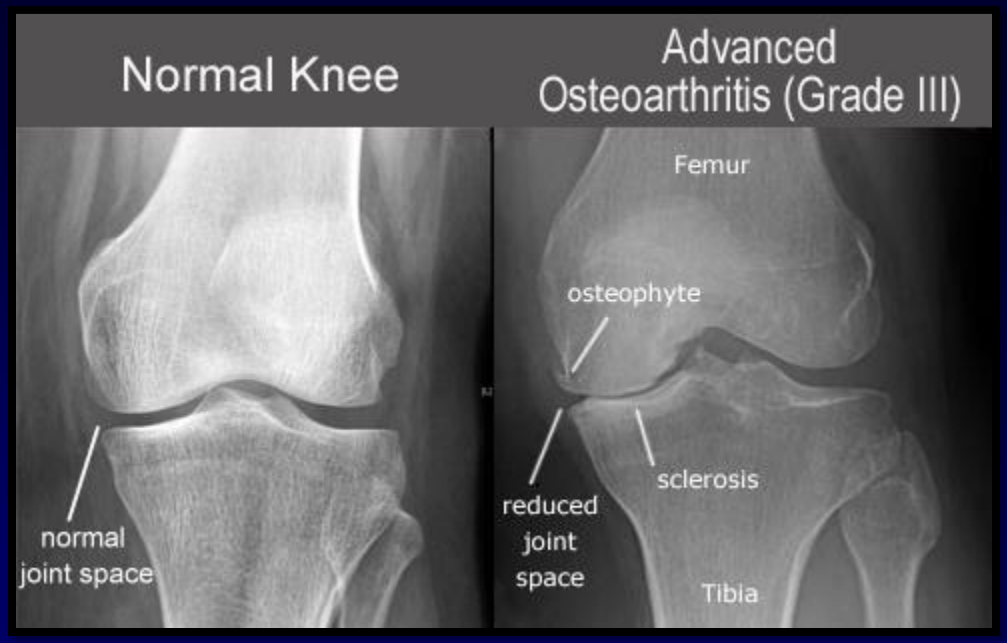
- **Degeneration of cartilage, not true – *ITIS***
- **Primary or idiopathic: aging process; few joints**
- **Secondary: due to pre existing diseases**
- **Insidious; increase with age (>50 yr); 40% of people > 70 years are affected**
- **Degeneration of cartilage >> repair and proliferation**



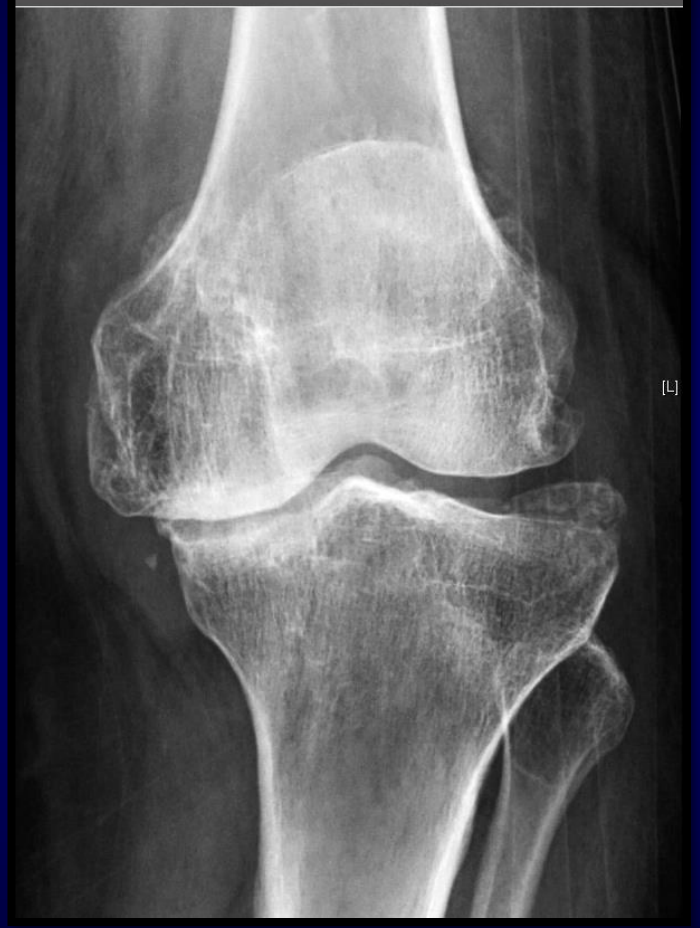
Schematic view of osteoarthritis (OA). OA is thought to be initiat

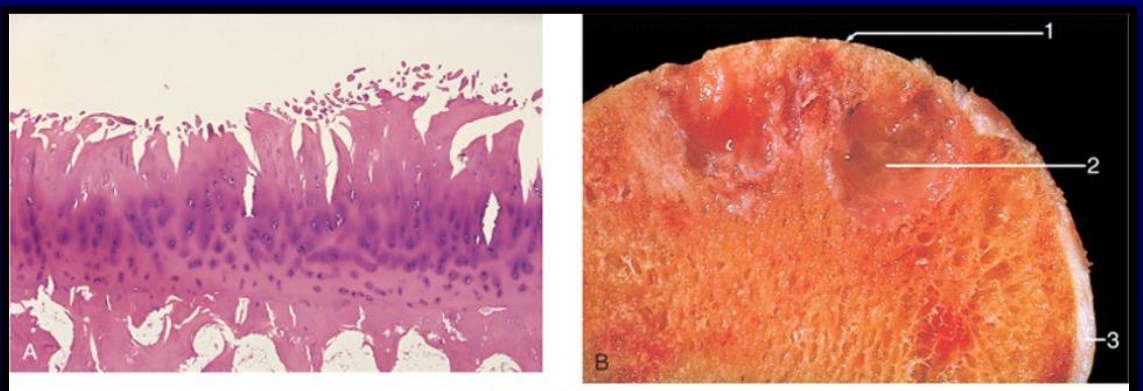






Very Advanced Osteoarthritis (Grade IV)





- Osteoarthritis. **A,** Histologic demonstration of the characteristic fibrillation of the articular cartilage. **B,** Severe osteoarthritis with 1, Eburnated articular surface exposing subchondral bone. 2, Subchondral cyst. 3, Residual articular cartilage

OA (DJD) CLINICALLY:

- Joint pain worsens with use, morning stiffness, crepitus & range limitation, radicular pain, osteophytes impingement on vertebrae, muscle spasm & atrophy
- No magic preventive strategies (wt loss?)
- Trx: pain control, decrease inflammation (NSAIDs), intra-articular steroids, or joint replacement for severe cases
- Large health cost on countries

RHEUMATOID ARTHRITIS:

- **Chronic inflammatory disease; autoimmune in nature; attacks joints with nonsuppurative proliferative and inflammatory synovitis; leading to destruction of joints and adhesions (ankylosis); systemic disease (skin, heart, vessels & lungs).**
- **1% prevalence in USA; F:M = 3:1; 4^{th}-5^{th} decade**
- **Genetic predisposition + environmental factors plays a role in the development, progression and chronocity of the disease**

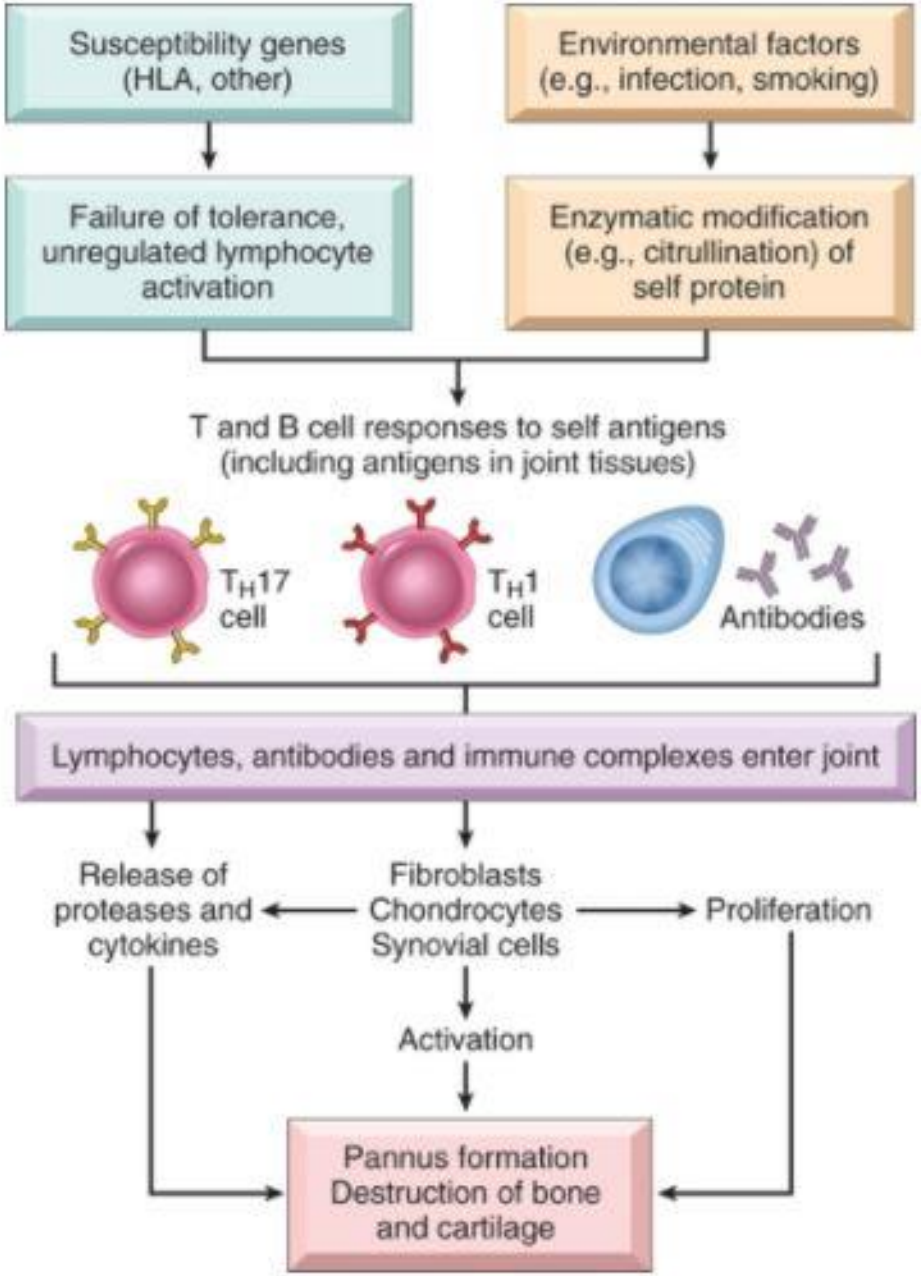


FIG. 21.36 Major processes involved in the pathogenesis of rheumatoid arthritis.

PATHOGENESIS:

IFN-γ from T_H1	Activates macrophages & synovial cells
IL-17 from T_H 17	Recruits neutrophils and monocytes
RANKL from T cells	Stimulates osteoclasts & bone resorption
TNF & IL-1 from macrophages	Stimulates residents synoviocytes to secrete proteases that destroy hyaline cartilage

80% of patients with RA have autoantibodies IgG & IgM against the Fc portion of their own IgG [Rheumatoid factor]

70% of patients with RA have Anti-Citrulliniated Protein Antibodies (ACPA)

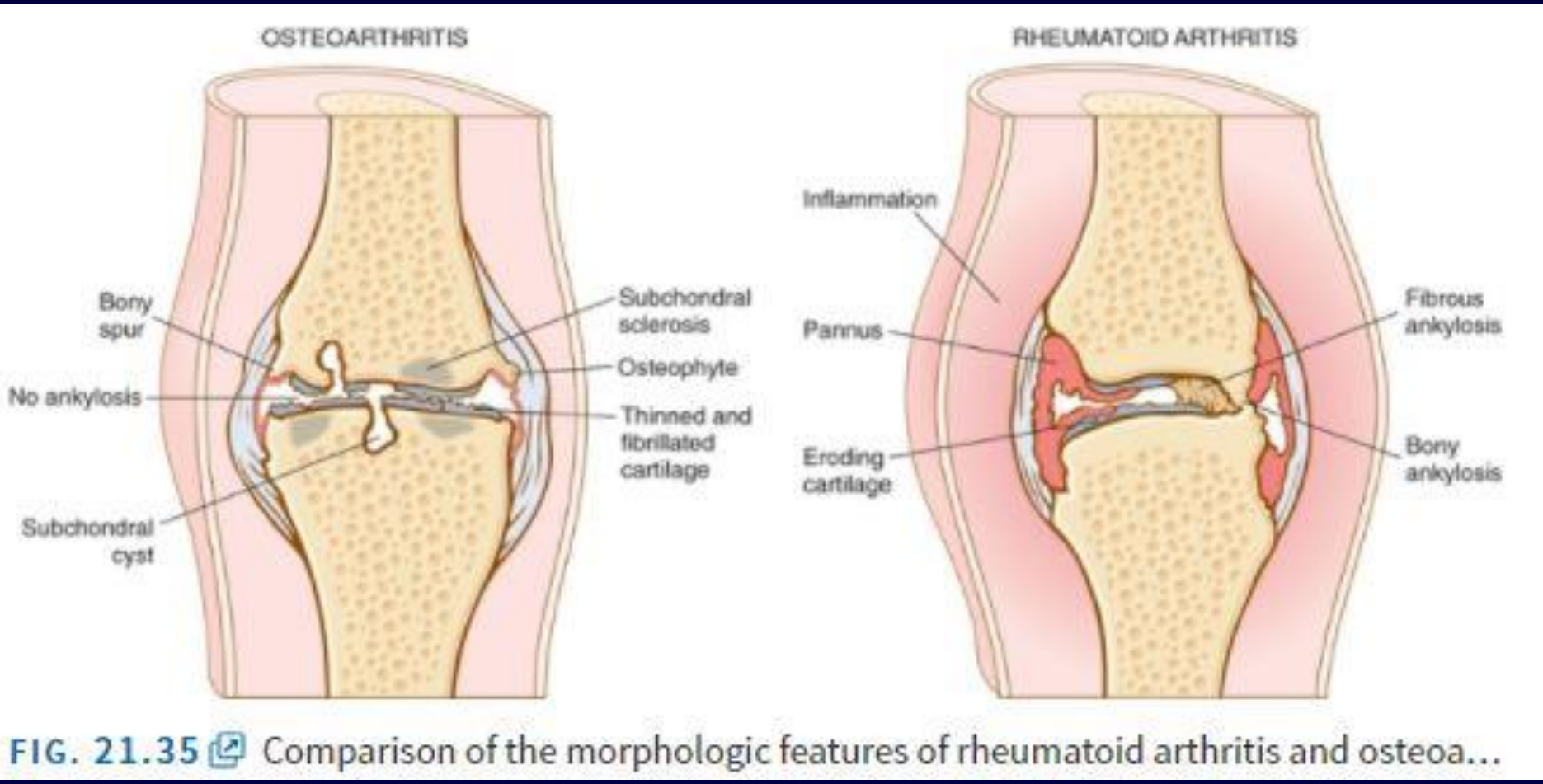
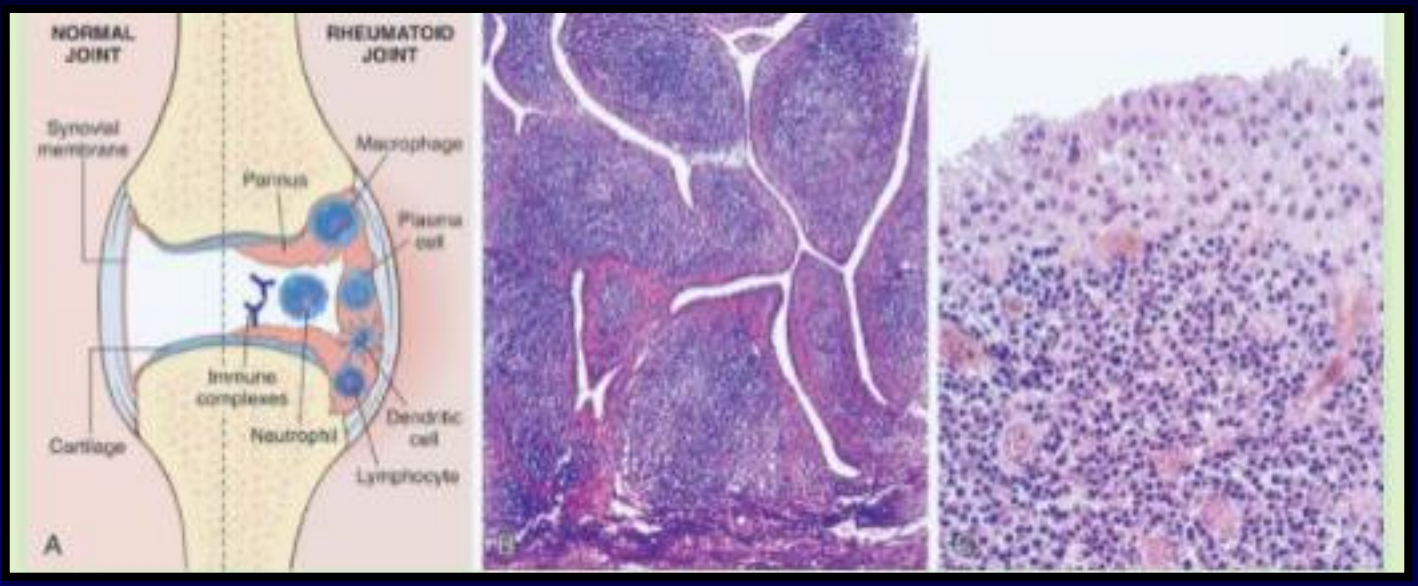
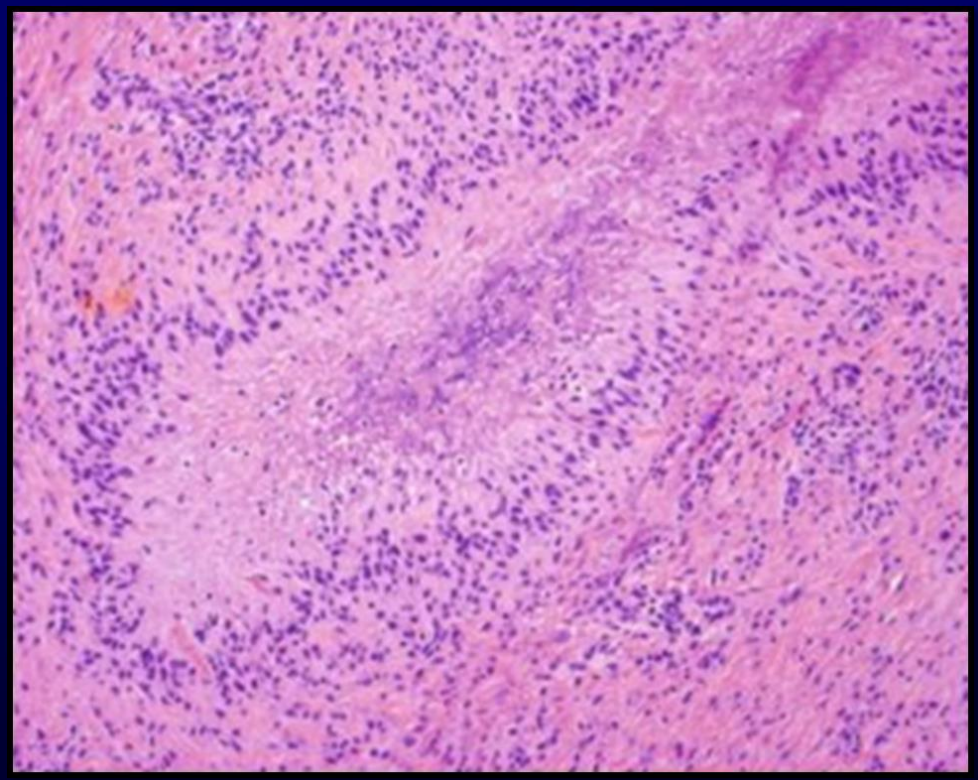


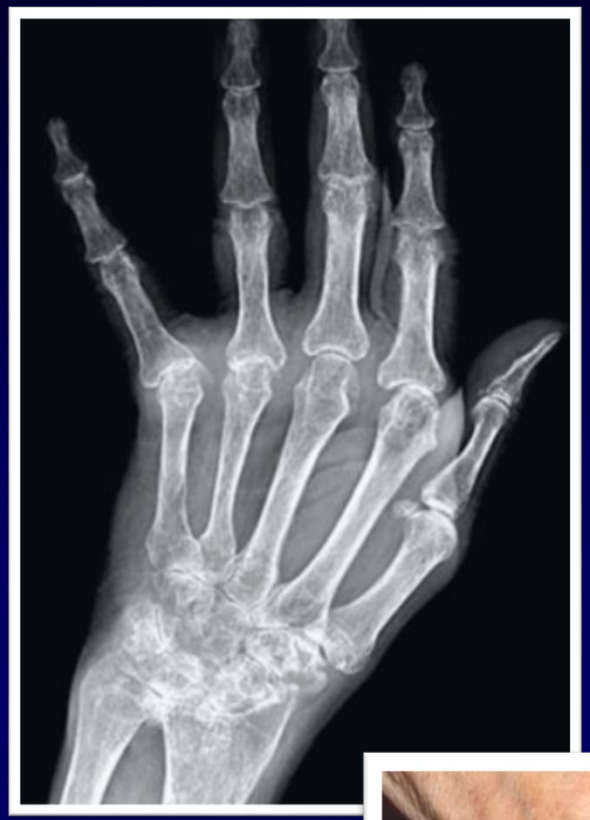
FIG. 21.35 Comparison of the morphologic features of rheumatoid arthritis and osteoa...

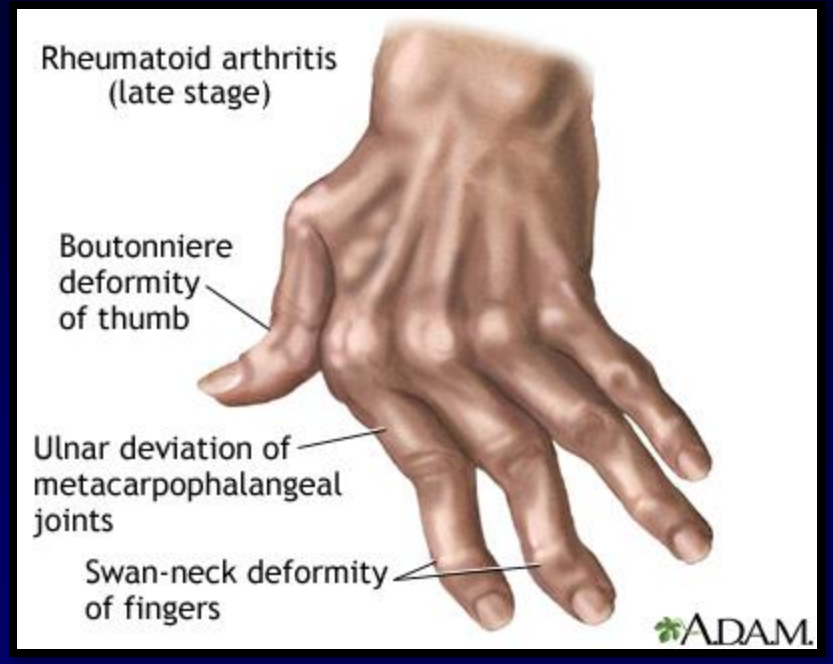

NORMAL JOINT
RHEUMATOID JOINT
Synovial membrane
Pannus
Macrophage
Plasma cell
Immune complexes
Neutrophil
Dendritic cell
Lymphocyte
Cartilage
A

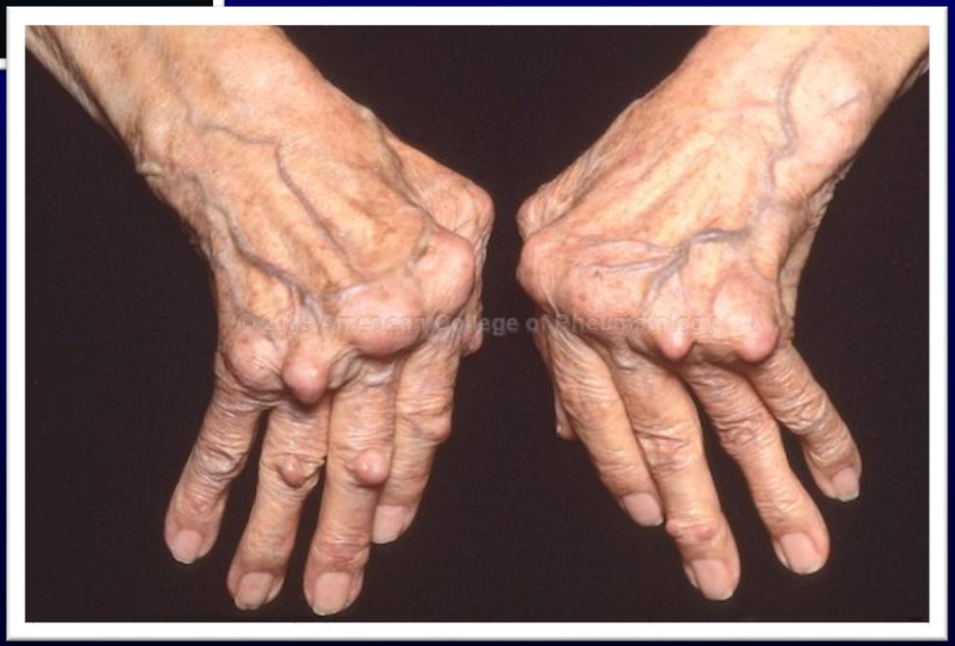


CLINICAL COURSE OF RA:

- Begins slowly and insidiously, polyarthritis
- Symmetrical joints: hands, feet, wrists, ankle, MCP and proximal IPJ are commonly affected
- Joints: warm, swollen & painful
- Stiffness when inactive and in the morning
- Waxing and waning chronic
- Ulnar deviation
- Trx: Steroids, MTX, Anti-TNF




Rheumatoid arthritis
(late stage)
Boutonniere
deformity
of thumb
Ulnar deviation of
metacarpophalangeal
joints
Swan-neck deformity
of fingers
A.D.A.M.



JUVENILE IDIOPATHIC ARTHRITIS (JIA):

- Heterogeneous group; arthritis of unknown cause ; <16 years for at least 6 weeks
- Pathogenesis is similar to adult RA
- Prognosis variable; only 10% will have serious functional disability

IN CONTRAST TO ADULTS RA; JIA IS CHARACTERIZED BY:
Oligoarthritis is more common
Systemic disease is more common
Large joints are affected more than small joints
Rheumatoid nodules and Rheum Factor are usually absent
Anti Nuclear Antibody seropositivity is common

SERONEGATIVE

Autoimmune T cell response to unidentified antigen (possibly infectious agent) that cross react with self musculoskeletal antigens

HETEROGENOUS GROUP THAT SHARE THE FOLLOWING FEATURES:
Absence of rheumatoid factor
Ligaments pathology rather than synovium
Sacroiliac joints mainly
Association with HLA-B27
Bony ankylosis (fusion)

- Ankylosing spondylitis: most common prototype.
- Destructive arthritis and bony damage and ankylosis of sacroiliac joint, main joint involved.
- 90% HLA-B27
- Anti IL-17 has shown some efficacy as treatment

SERONEGATIVE SPONDYLOARTHROPATHIES:

- **Ankylosing Spondylitis:**
  - Adolescent boys, HLA B27, axial joints (sacroiliac)
- **Reiter Syndrome:**
  - Triad of arthritis, urethritis/cervicits & conjuctivitis
  - Autoimmune but initiated by bacterial infection.
- **Enteropathic Arthritis:**
  - Secondary to bowel infections (salmonella, shigella)
  - HLA B27 positive
- **Psoriatic Arthritis:**
  - 5% of patients, starts in DIP joints, similar to RA.

Spondyloarthropathies: Subtype Classification

Ankylosing Spondylitis	Psoriatic Arthritis	Enteropathic (IBD-associated)	Reactive Arthritis	Undifferentiated SpA
Most common subtype along with uSpa 2.5:1 male:female Gradual onset of IBP Acute anterior uveitis most common extra-articular manifestation Can lead to sacroiliac fusion and spinal syndesmophyte formation	Between 10% and 40% of patients with psoriasis develop PsA, depending on study population and psoriasis severity Most phenotypically diverse SpA with 5 subtypes Skin disease precedes joint disease in approximately 70% of cases	5% to 29% of patients with IBD develop arthritis Peripheral arthritis (not axial) can parallel bowel inflammation and can occur in up to 20% of patients Spondylitis occurs in 3% to 6%	Typical acute asymmetric oligoarticular (<4 joints) arthritis 1-3 months after gastrointestinal and genitourinary infection Characteristic triad of urethritis, conjunctivitis, and arthritis seen in < 35% of patients Keratoderma blennorrhagica and circinate balanitis	Most common subtype along with AS Typically used to describe patients not fulfilling criteria of any one SpA but presenting with IBP and other extra-articular SpA manifestations Up to 50% of uSpA will develop into AS

uSpA = undifferentiated SpA; IBP = inflammatory back pain; PsA = psoriatic arthritis; IBD = inflammatory bowel disease; AS = ankylosing spondylitis