MSS

Musculoskeletal System

Doctor 2019 | Medicine | JU

7

Pathology

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Scientific correction:

Grammatical correction:

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Diseases of the Joints

In this lecture, we will talk about some diseases that affect the joints. Let's start by talking about the basic physiological and anatomical characteristics of joints:

Joints are extremely important structures in the locomotive system, they provide motion (flexion, extinction, or sideways movement) and stability to our skeleton (shock absorber). without joints, it will be difficult even to walk (like penguins).

Tow type of the major joint :

1. Synovial (cavitated): synovial joints, wide motion (knee, elbow…)
2. Non-synovial (solid): synarthrosis, minimal movement (skull, sternum…)

Synovial joints:

- ☑ covered by hyaline cartilage; an important structure for the motion and shock absorption. doesn't have blood, nerves, or lymphatics supply, composition: (70% water, 10% type II collagen, 8% proteoglycans + chondrocytes(cartilaginous primary cells)).
- ☑ The synovial membrane contains: A synoviocytes (different macrophages), and B synoviocytes fibroblast-like and lacks basement membrane(they don't have collagen IV in the laminin).

NOW, let's start talking about the diseases that affect the joints.

In this lecture we will talk about :

1. Osteoarthritis
2. Rheumatoid Arthritis
3. Juvenile Idiopathic Arthritis
4. Seronegative Arthropathies

Osteoarthritis (DJD)

It's not a true "ITIS" (not a true inflammatory process) rather, it's a **degenerative process** so it has a better pathologic term: **Degeneration of cartilage (DJD)**

Very common Insidious disease; increase with age (>50 years), 40% of people > 70 years are affected.

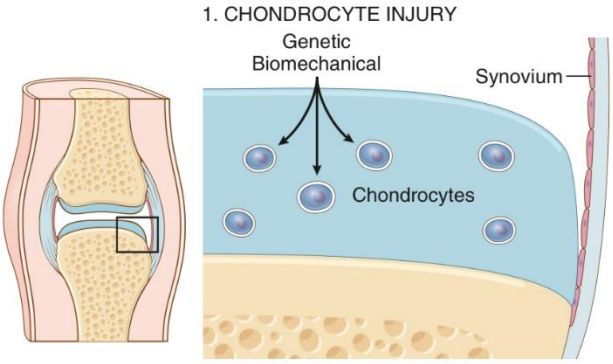
Happened mainly because of the imbalance between degeneration and repair of the cartilage.(degeneration >> repair and proliferation)

Osteoarthritis classified into:

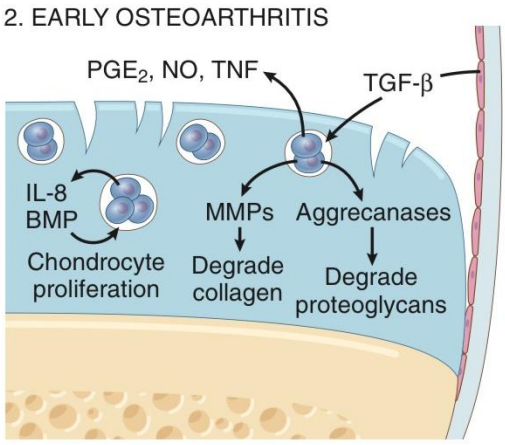
1. Primary or idiopathic: most common, the chance of incidence increasing with the age, affect few major joints (knee, elbow, and pelvis).

2. Secondary: less common, occurs due to preexisting diseases, so it may affect the right knee joint but not the left.

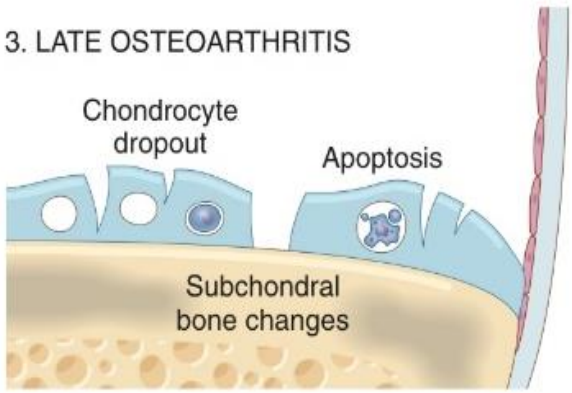
Pathogenesis timestamp (00:07:32)



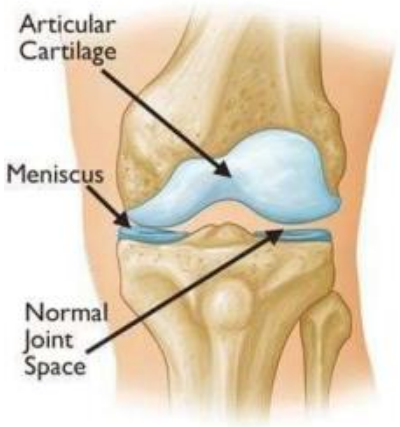
Genetic and biochemical predisposition with inciting trauma to the joint area causing injury to the chondrocytes.



In the early stage, it will cause lines of aberration, erosion of the articular cartilages, and anergy. Inflammatory mediators will release (TNF, NO, PGE2). The repair will be inset by stimulation of the synovial site (TGF-β). Multiple mediators will be involved (IL-8, BMP) for chondrocyte proliferation. This process takes weeks, months, or years.

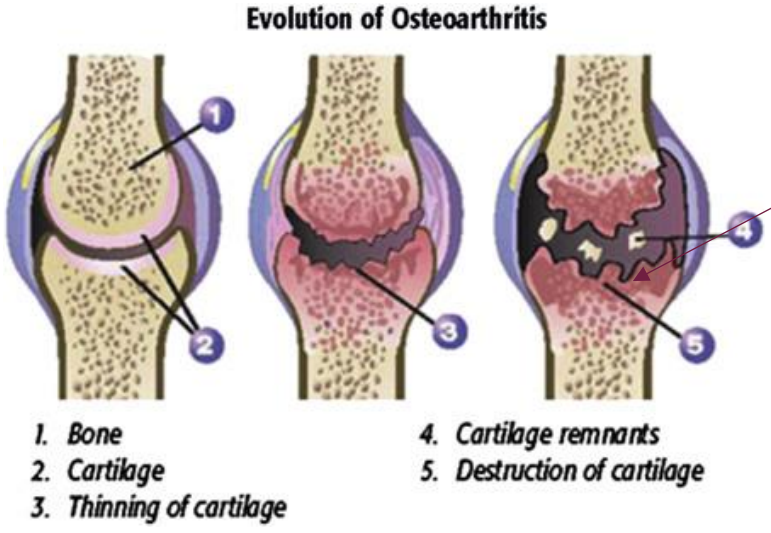


In the late stage, the inability of the articular cartilage to proliferate and repair leading to apoptosis (programmed cell death) and chondrocyte dropout. They will form a necked subchondral area lacking the proper thickness of cartilages (Spacing between the cartilages and irregular appearing thicker cartilages).



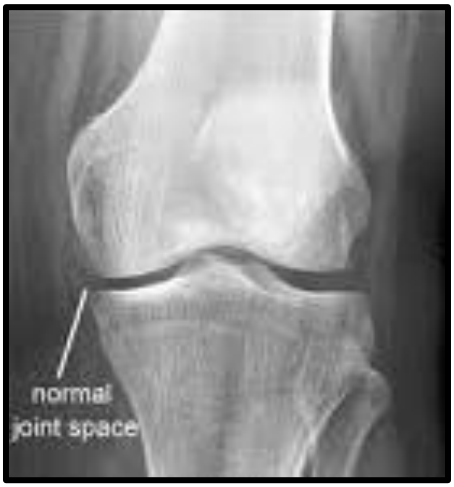
The pathogenesis of the previous process will impact the synovial space, especially in the large joints like the knee joint, the main feature will be:

1. Cartilage cap loss; eating up of the cartilages.
2. The bone underneath these areas will start reacting causing bone spurs.
3. sometimes these bone spurs released into the joint space causing loos bodies in between which causes more distraction to the cartilages and narrowing of the joint space.



The evolution of osteoarthritis goes through grades.

here, Very severe Osteoarthritis, which leads to subchondral reaction, subchondral sclerosis, and subchondral cyst formation with loos bodies in the space causing pain and stiffness of the joint.

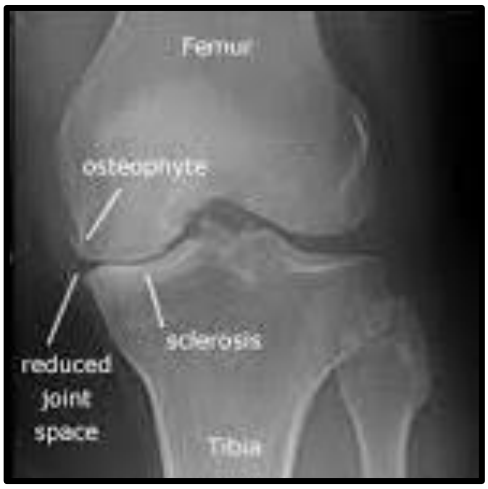


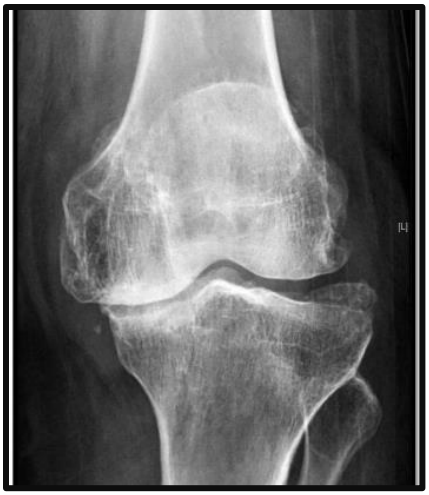
normal knee

notice the space between the bones, the edges of the bone and the structure of the bone, all of them are normal ones.

Advanced osteoarthritis (grade III)

the space between the bones is narrowed, there is sclerosing of the underlining bone which reduced the bone space, the bone spurs start to appear at the lateral side of the knee.



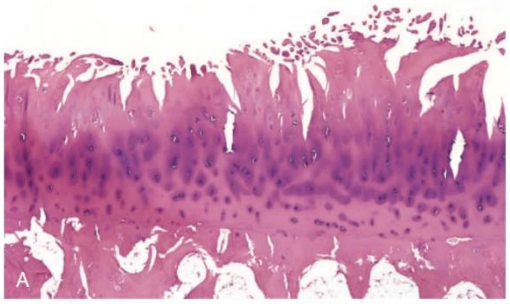


Sever osteoarthritis (grade IV)

sever narrowing, degeneration of the articular cartilages, sclerosis of the subchondral bone, multiple cyst formation, bone spurs in the medial side of the knee which narrowing of the joint space.

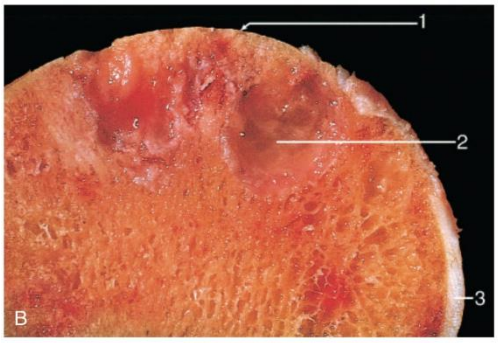
Histological features

this is a histologic section from the articular cartilage, notice here:



1. upper p: apoptotic cartilage
2. middle p: sclerosis of the subchondral bone
3. lower p: cyst formation

this is a gross apparent section to the bone, notice here:



1. complete loss of the cartilages
2. hemorrhage, cyst formation in the subchondral space, and some sclerosis in the bone.
3. Normal cartilages.

Osteoarthritis clinically

- ☑ Joint pain worsens with use.
- ☑ morning stiffness.
- ☑ crepitus; due to narrowing the joint space because of the presence of osteophyte or loose bodies in the joint space.
- ☑ range limitation.
- ☑ radicular pain; when the pain goes near to the neurons.
- ☑ osteophytes impingement on vertebrae, muscle spasm & atrophy.

preventive: No magic preventive strategies.

Treatment: Depends on the stage; pain control, decrease inflammation (NSAIDs), intra-articular steroids, or joint replacement for severe cases. If the patient is very obese, losing weight may help in relieving symptoms.

Osteoarthritis and its complications have a large health cost on countries.

Rheumatoid Arthritis

Chronic systemic inflammatory disease, autoimmune in nature, attacks joints with **nonsuppurative proliferative and inflammatory synovitis**, leading to the destruction of joints and adhesions (ankylosis).

Every single word is important. So again it's:

- ☑ Chronic
- ☑ Systemic → multi-organ disease, affect the skin, heart, vessels & lungs.
- ☑ inflammatory → true "itis"
- ☑ autoimmune → the immunity attacking and destroying the joint.
- ☑ nonsuppurative → there is no bacteria and pus formation.
- ☑ proliferative→ cause proliferation to the fibroblast.
- ☑ synovitis→ target the synovium of the joint.
  remember: DJD affects the articular cartilage but the rheumatoid mainly targets the synovium.

Prevalence: 1% in USA, F:M = 3:1; 4th-5th decade.

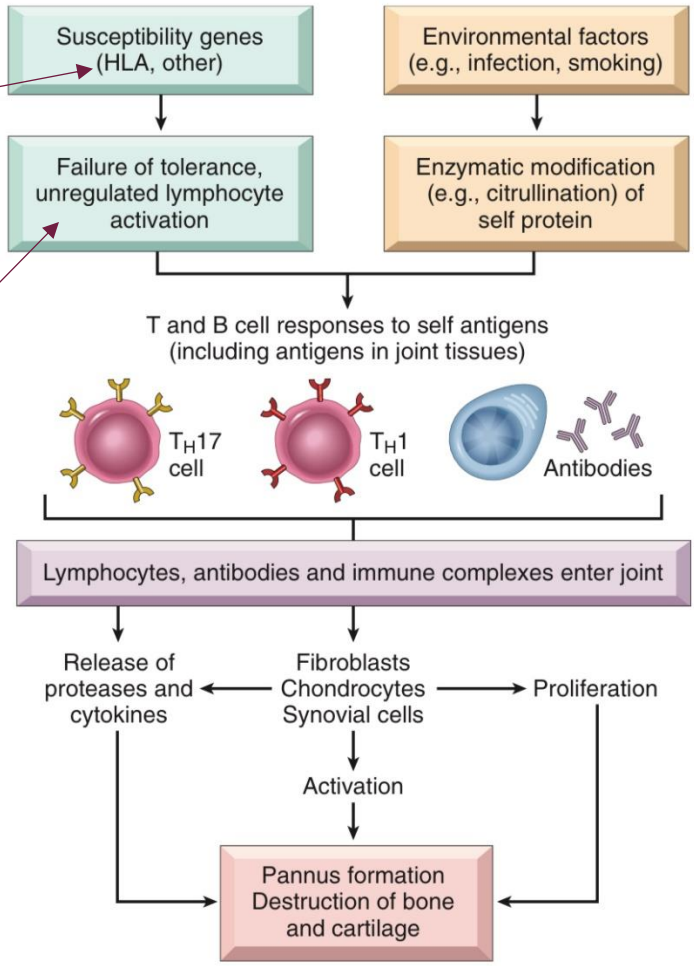
Etiology: compensation of both genetic predisposition + environmental factors play a role in the development, progression, and chronicity of the disease.

Treatment: Steroids, Anti-TNF, and methotrexate (immunosuppressor drug).

Pathogenesis: timestamp (00:22:19)

Human leukocyte antigen

failure of tolerance in the end stages of reparative process of the inflammation.



It's an autoimmune disease, so it's involved, multiple mediators:

IFN-γ from TH1	Activates macrophages & synovial cells
IL-17 from TH 17	Recruits neutrophils and monocytes
RANKL from T cells	Stimulates osteoclasts & bone resorption
TNF(major player) **& IL-1 from macrophages**	Stimulates residents synoviocytes to secrete proteases that destroy hyaline cartilage

Diagnosis

1. Rheumatoid factor

   A blood test to look for autoantibodies (IgG & IgM against the Fc portion of their own IgG). 80% of Rheumatoid Arthritis patients have a positive Rheumatoid factor.

2. Anti-Citrullinated Protein Antibodies (ACPA)

   70% of patients with RA have positive ACPA.

Comparison between Rheumatoid and Osteoarthritis:

Pay attention to the details on the figure!

Remember: Osteoarthritis is much common than RA.

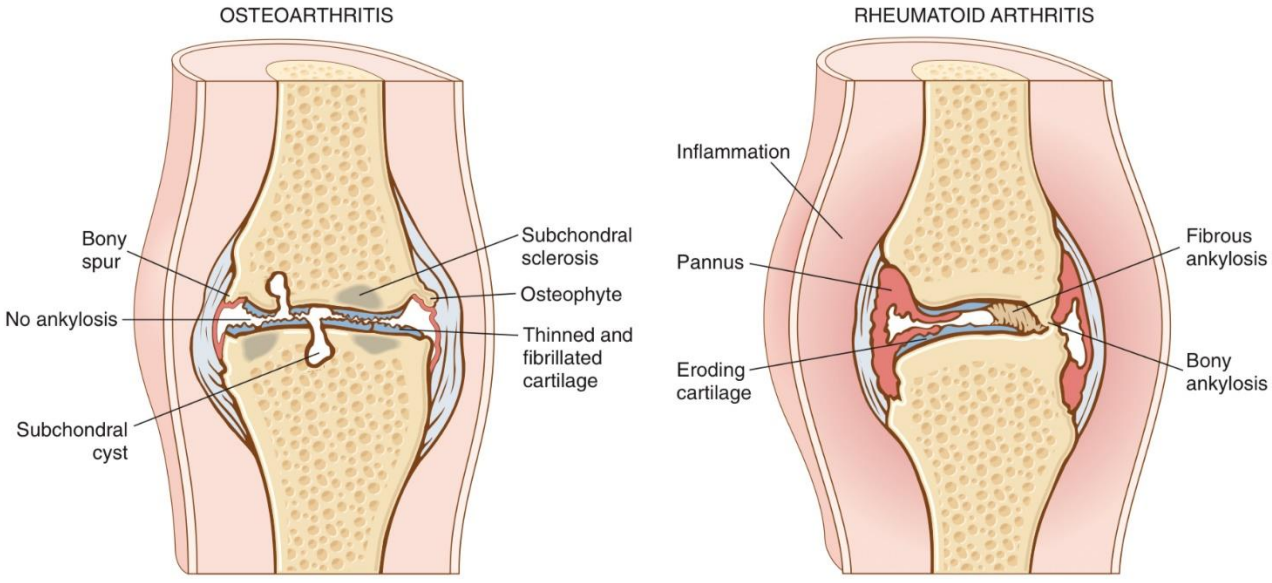
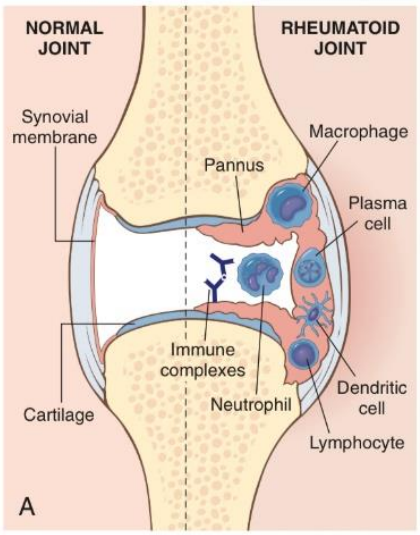
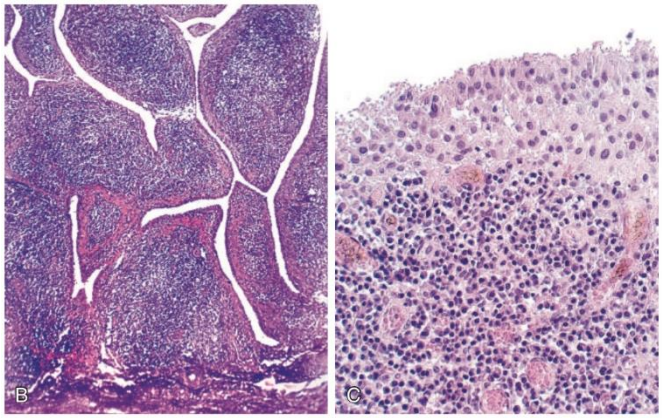


Fig. 21.35 Comparison of the morphologic features of rheumatoid arthritis and osteoarthritis.

Histological features

This figure explains the role of many inflammatory cells in RA, proliferative autoimmune synovitis with pannus formation leading to the distraction of the cartilages with narrowing and ankylosis of the joint space.





this is a biopsy taken from the synovium, shows a severe blue cell proliferation and infiltration.

sometimes RA leads to chronic granulomatous inflammation.

we can see in the figure: Rheumatoid nodules and Rheumatoid granulomas

Activated epithelioid histiocytes some time associated with central necrosis.

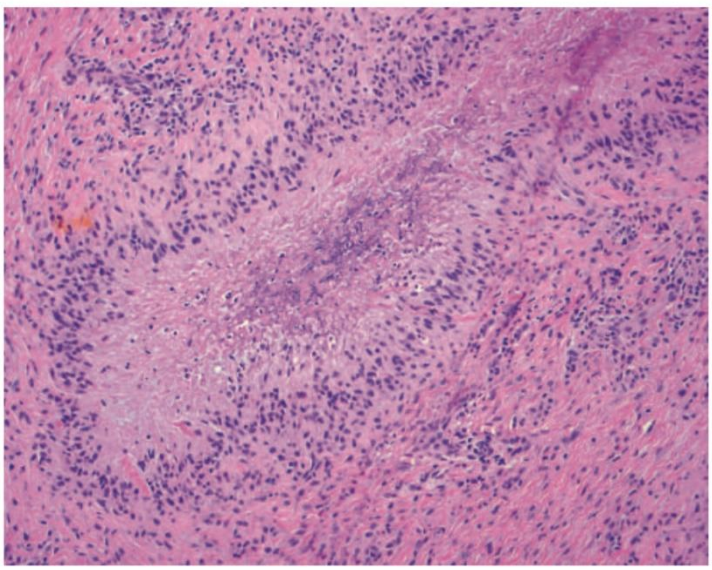
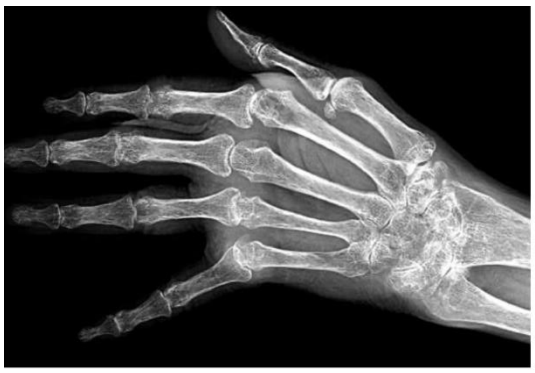
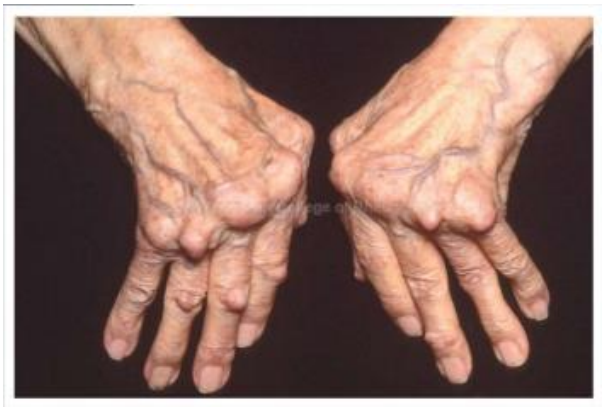


Fig. 21.38 Rheumatoid nodule composed of central necrosis rimmed by palisaded histiocytes.

Rheumatoid Arthritis clinically

- ☑ Begins slowly and insidiously.
- ☑ Polyarthritis; involves multiple symmetrical joints: hands, feet, wrists, ankles, metacarpophalangeal (MCP) and proximal interphalangeal (IP) joints are commonly affected.
- ☑ The Joints will be warm, swollen & painful.
- ☑ Stiffness when inactive and in the morning (opposite to DJD).
- ☑ Waxing and waning chronic.
- ☑ Ulnar deviation.

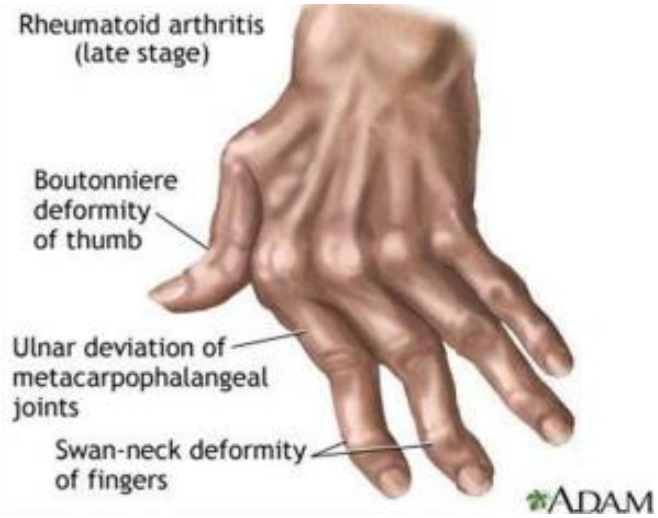




This is **Ulnar deviation**, affect the bananas formation of the small joint of the hand, both hands are affected.

IN THIS FIGURE:

- ☑ Boutonniere deformity of the thumb→ thumb is tended and the patient unable to hyperextend the IP joints.
- ☑ Ulnar deviation→ deviate of the MCP joint toward the ulnar side.
- ☑ Swan-neck deformity of fingers→ Hyperflexion in the distal IP Joint.



Juvenile Idiopathic Arthritis (JIA)

- ☑ Another form of RA that affects children.
- ☑ A heterogeneous group of diseases characterized by the presence of arthritis of unknown cause.
- ☑ Affect children less than 16 years.
- ☑ The symptoms should be last for at least 6 weeks before making up the diagnosis.
- ☑ Pathogenesis is similar to adult RA.
- ☑ Prognosis variable: only 10% will have a serious functional disability.

In contrast to adult RA, JIA is characterized by:

- ☑ Oligoarthritic 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 which is a simple screening test for autoimmune disease.

Seronegative Arthropathies

Family of joint disorders in which the patient doesn't have the same antibodies that a person who is "seropositive" has but has Arthropathies.

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

It's a heterogeneous group of disease share the following features:

- ☑ Absence of rheumatoid factor.
- ☑ **Ligament's** pathology rather than synovium
- ☑ Sacroiliac joints are mainly affected.
- ☑ They are strongly associated with HLA-B27.
- ☑ Bony ankylosis (fusion).

Examples of Seronegative Arthropathies:

1. **Ankylosing spondylitis**:
   - The most common prototype
   - destructive arthritis, bony damage, and ankylosis of sacroiliac joint (main joint involved).
   - 90% of the patient have HLA-B27
   - Anti IL-17 has shown some efficacy as a treatment

2. Ankylosing Spondylitis:
   Adolescent boys, HLA B27, axial joints (sacroiliac)

3. Reiter Syndrome:
   Triad of arthritis, urethritis/cervicitis & conjunctivitis
   Autoimmune but initiated by a bacterial infection.

4. Enteropathic Arthritis:

Secondary to bowel infections (salmonella, shigella)

HLA B27 positive

5. 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

Sorry for errors, if there was

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