Pathology Team

CLASS : 431

Non-infectious arthritis

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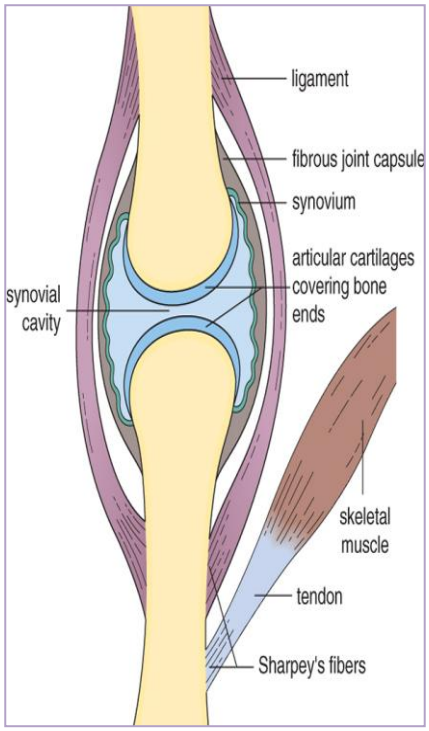
General structure of synovial joints: (out > in)

1. Outermost layer of muscles and ligaments
2. Dense fibrous capsule which is continuous with the periosteum
3. Lined by synovial membrane on the inner surface
4. Cavity containing synovial fluid
5. Articular (hyaline) cartilage directly covering bone ends



Arthritis and synovitis????

Causes of inflammation of joints:

Infection deposition	Degenerative	Autoimmunity	Crystal
Septic and tuberculous arthritis	Osteoarthritis	(age-related) Rheumatoid arthritis, SLE, Autoimmune rheumatic fever	(metabolic) Gout (uric acid) or pseudo-gout ($CaPO_4$)

All affect multiple joints EXCEPT infectious arthritis

Rheumatic fever:

Due to molecular mimicry usually caused by group A streptococcus microorganisms

The antibodies produced in response to the antigens of the bacteria begin to attack self-antigens which are similar in structure.

May cause permanent damage to: the heart, kidneys or joints.

Osteoarthritis:

A non-neoplastic disorder of progressive erosion of articular cartilage in which it's normally smooth surface becomesfragmented and fissured.

Also called degenerative joint disease.

Is the most common joint disorder, accounting for 80% of all arthritis cases.

Mostly affects the elderly, 50+ years. 80% of cases are seen in patients of 65 years.

Etiology:

Factors that may contribute to the development of osteoarthritis:

1. Age
2. Abnormal load on joints (mostly due to obesity)
3. Crystal deposition (as in gout)
4. Inflammation of joints

Pathogenesis:

It affects joints that are constantly exposed to "wear and tear" making it somewhat of an occupational disease; Fingers in typist and people who sew for a living
Knee joint in professional soccer players

Types:

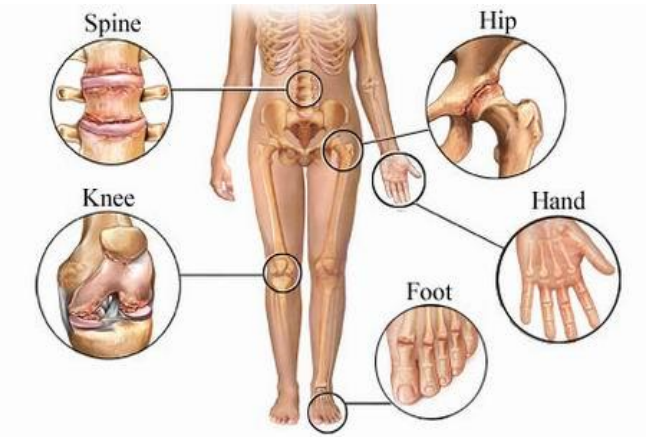
Primary Osteoarthritis	Secondary Osteoarthritis
appears insidiously with age	affects younger age group
unknown cause	usually due to predisposing conditions
affects few joints	
Most common	affects predisposed joints (1 or several)
	accounts for less than 5% of cases

Predisposing factors: developmental deformity, traumatic injury, underlying systemic diseases (diabetes), marked obesity, ochronosis (acid accumulation due to abnormal tyrosin metabolism), hemochromatosis (iron deposition in body due to lack of iron metabolism)

Common sites:

Usually affect one joint of the same joint bilaterally

Disease affects both genders equally, however, gender may affect the distribution of the disease; women are most likely affected in their knees and hands while men get affected mostly in the hips.



Pathological Changes:

Articular cartilage

Erosion and fibrillation causing degradation of matrix with obvious fissures on it's surface.
Causes narrowing of joint space
Unsymmetrical? Depending on weight on the different areas.
Eventually, entire loss of the cartilage layer in some areas.

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Bone

Subchondral bone is exposed and also faces erosion. This friction will cause the bone to be highly polished and smooth [Eburnation].
Next, small cysts will develop just beneath this eburnated surface.
Then, irregular bony outgrowths called osteophytes will develop, specially at the periphery of the joint.

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Synovium & Joint Capsule

Bone and cartilage debris will irritate them resulting in their thickening and inflammation.

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Muscles

Loose bodies, cartilage fragments, which separate and swim in the synovial fluid, along with inflammation will cause pain. Disuse and immobility of the joint will lead to the atrophy in the surrounding muscles.

Clinical Features:

- Usually gradual onset
- Deep aching pain; exacerbates by use and limits movement.
- Morning stiffness (not very significant)
- Osteophyte impingement on the spinal foramina can cause nerve root compression resulting in: radicular pain, muscle spasms, muscle atrophy and neurological deficits
- Heberden nodes in the fingers of affected women only which represent osteophytes in the distal interphalangeal joints.

Rheumatoid Arthritis:

A chronic systemic autoimmune disorder that affects the synovial lining of joints, bursae and tendon sheaths as well as the skin, blood vessels, heart, lungs and muscles.
(It is an auto-immune disease affects multiple sites in the body including joints).
Characterized by non-suppurative (no pus) proliferative inflammation. Systemic manifestations include: skin lesions, dry eyes, pulmonary fibrosis, osteoporosis, arthritis, drug-related stomach ulcers or drug-related renal damage.
May cause ankylosis:

1. fibrous ankylosis
2. bony ankylosis

Occurs at young ages, peaks at 10-29 years of age. Also common among menopausal women.
More common among women (75% of cases), because women are more susceptible to auto-immune diseases in general.

Etiology:

Rheumatoid arthritis is immunologically mediated. However, genetic and environmental factors may contribute by acting as triggers. It is believed that parvovirus B19 may be important in the pathogenesis of this disease. Genetic factors such as the finding of HLA-DR4 and DR1 are significant in 65& of patients.
Triggering of host by arthitogenic microbial antigen causes an autoimmune reaction in which T helper cells are activated and inflammatory mediators (TNF & cytokines) are released. Both of which result in joint destruction.
Circulating immune complexes, made up of rheumatoid factor bound to self antigen IgG, activate complement causing cartilage damage.

- In osteoarthritis, the disease starts at the joint itself, whereas in RA, the disease starts in the soft tissue and extends to joints.

Laboratory examinations:

80% of pateints are noted to have rheumatoid factor, an IgM auto-antibody, bound to the Fc portion of IgG molecules. However this test is not sensitive (some patients are negative to test but have disease) nor specific (other diseases may include same test result, elevated Abs)
increased neutrophil (acute stages) and proteins in synovial fluid
other antibodies including antikeratin antibody, a specific but not sensitive indication, antiperinuclear factor, anti-rheumatiod arthritis associated nuclear antigin (RANA)

Features of joints affected with chronic synovitis:

1. synovial hyperplasia and proliferation
2. angiogenesis and increased vascularity
3. dense perivascular inflammatory cell infiltrationincluding H helper cells, plasma cells and macrophages. Lymphoid follicles are freguently formed
4. neutrophil infiltration and aggregation of organizing fibrin on the surface
5. erosion of underlying bone due to increased osteoclast activity

6. pannus formation:
    - is formed by the proliferating synovial cells mixing with inflammatory cells, granulation and fibrous connective tissue.
    - Eventually, pannus will fill the entire joint space and will be followed by ankylosis: (at this stage it becomes irreversible)
        - Fibrous ankylosis: pannus becomes fibrous tissue.
        - Bony ankylosis: calcification of pannus causing the joint to become bone (loss of any trace of bone space > 2 bones join becoming one)

Clinical features:

- Symmetrical arthritis (Arthritis affecting same joints on both sides of the body)
- Affect small joints (fingers)
- Affects multiple joints (Usually in 3 or more areas)
- Morning stiffness? Lack of movement overnight > accumulation of cells
- Formation of rheumatoid nodules
- Rheumatoid factor in serum (in 80% of cases)
- Radiographical changes:

x-ray results include:

swan neck appearance of fingers: radial deviation at wrist + ulnar deviation of fingers
narrowing of joint space
destruction of surrounding tendons, ligaments and capsule
joint effusion and erosion
juxta-articular osteopenia (decrease in bone density but at a lesser extent than osteoporosis)

Clinical course:

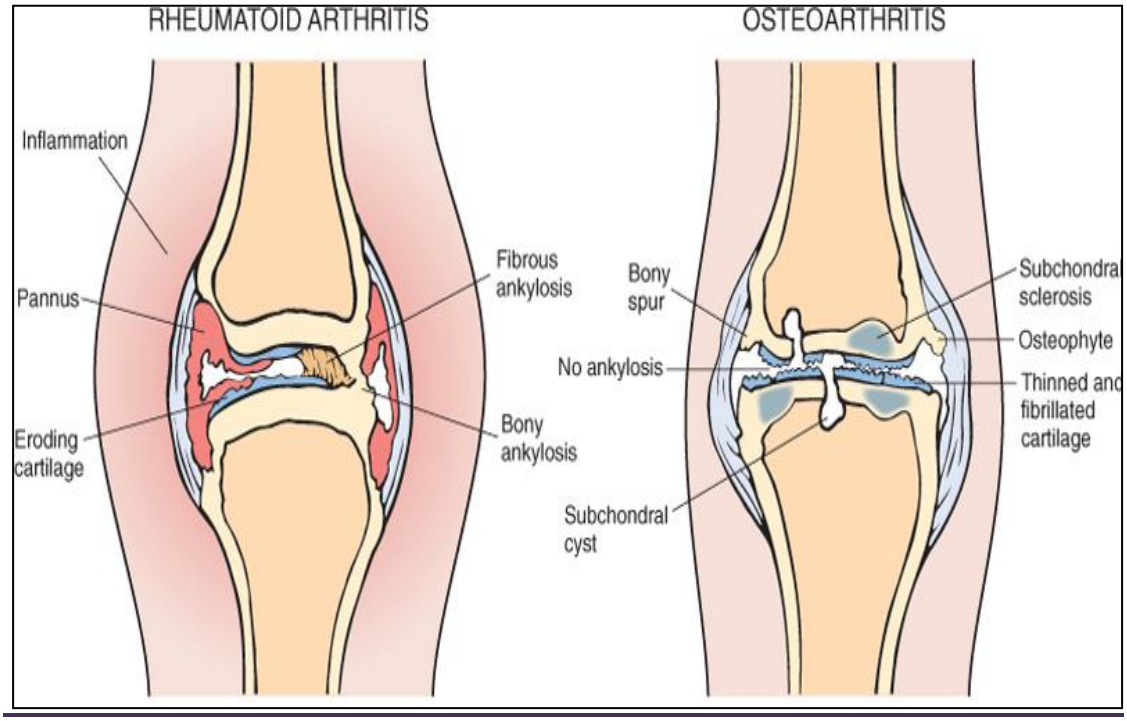
Is variable among patients
Begins with malaise, fatigue and musculoskeletal pain. Then, move on to joint involvement causing them to be warm, swollen, painful and stiff in the mornings.
Usually the course of the disease is prolonged, taking over months to years for the joint involvement to occur. However 10% of patients have an acute onset of the severe symptoms.
Spine involvement is seen in 50% of patients.

Prognosis:

Could be treated if caught early, prior to fibrous ankylosis formation.
Reduced life expectancy by only 3-7 years
Death is usually due to other aspects including amylidosis (deposition of amyloid protein causing renal failure), vasculitis which could be generalized and spread to the brain, GI bleeding from NSAIDs or infection by steroids.

Breif comparasion between Osteoarthritis and Rheumatoid arthritis:

Rheumatoid arthritis	Osteoarthritis
○ Autoimmune disease ○ Morning stiffness ○ Common in small joints ○ In finger joints	○ Degenerative disease ○ Stiffness occurs later in the afternoon ○ Common in large weight-bearing joints ○ In the knees ○ *No inflammation



Caused by: Immune complex formation, T-cell activation and cytokine release

Pathogenesis:
Synovium inflammation and proliferation
Infiltration of inflammatory cells
Erosion of articular cartilage and underlying bone
Pannus formation leading to fibrous of bony ankylosis

Unknown cause

Pathogenesis:
Erosion and fissuring of articular cartilage
Eburnation of underlying bone with cyst formation
Inflammation of synovium and joint capsule
Formation of osteophytes

Gouty Arthritis:

Transient attacks of acute arthritis initiated by crystallization of urates and neutrophils, followed by chronic gouty arthritis with tophi (Histological feature includes: foreign body+fibrosis+ foreign body reaction+neutrophils) in joints and urate nephropathy.

- It causes 2-5% of chronic joint disease **.**
- **Sites:** 50% have initial attack in first metatarsophalangeal joint; also ankles, heels, knees, wrists, fingers, elbows.

Types:

1- ***Primary gout (90%):*** idiopathic, with overproduction of uric acid or known enzyme defects.
2- ***Secondary gout (10%):*** increased nucleic acid turnover due to leukemia/lymphoma, chronic renal disease, inborn errors of metabolism**.**

Mechanism:

- deposition of monosodium urate crystals in joints and viscera and uric acid kidney stone formation. For this deposition to occur, the serum urate must be higher than 7 mg/dl.

Risk Factors:

- age > 30 years.
- Familial history of gout.
- Alcohol use.
- Obesity.
- Thiazide administration.
- Lead.

Arthritis:

- Synovial fluid is poorer solvent for sodium urate than plasma, so with hyperuricemia:
    - crystals develop in synovial lining cells, stimulate formation of antibodies, complement, generates C3a, C5a, attracts more neutrophils,
    - releases free radicals, releases lysosomal enzymes which eventually causes acute arthritis that last days to weeks without treatment.
- repeated attacks of acute arthritis cause chronic arthritis and formation of tophi in synovial membranes and periarticular tissue, which eventually damages joints.

Aspiration (sterile needle and syringe are used to drain fluid from the joint) :

- white-gray and granular; strongly birefringent needle-shaped crystals under polarized light with foreign body giant cells.

In case of chronic disease:

- Urate deposits may be present in soft tissue, ligaments, skin
- Gouty deposits may be surrounded by fibrous tissue and be rimmed by histiocytes and giant cells**.**

Psuedogout:

The only difference from the proper gout, is the deposits are calcium pyrophosphate crystals, and it starts with knee.

Good Luck …