Non-Infectious Arthritis

Editing File

Black: original content
Red: important
Green: ALRIKABI's notes
Grey: Explanation
Blue: Only in the boys slides
Pink: only in the girls slide

Reviewed by Razan AlRabah & Khalid Alkhanji

Objectives

- ➔ Know the pathogenesis and clinicopathological features of osteoarthritis (degenerative joint disease).
- ➔ Know the pathogenesis and clinicopathological features of rheumatoid arthritis.
- ➔ Know the pathogenesis and clinicopathological features of gout and calcium pyrophosphate arthropathy [pseudogout].

Normal cartilage

- Articular cartilage bears the brunt of the degenerative changes in Osteoarthritis.
- Normal articular cartilage performs **two functions**:

(1) Along with the synovial fluid, it provides virtually friction-free movement within the joint.

(2) In weight-bearing joints, it spreads the load across the joint surface.

These functions require the cartilage to be:

- Elastic (i.e., to regain normal architecture after compression)
- Have high tensile strength.

These attributes are provided by:

- Proteoglycans.
- Type II collagen.

Produced by chondrocytes

Structure of the joint:

The joint usually consist of the end of two bones, and the ends of These bones are covered with articular cartilage (usually Hyaline Cartilage and its rich in collagen type ll). There is a space between the cartilage which is the synovial space which contains synovial cells. If there is an accumulation of large amount of fluid in the joint then this is what we call Articular effusion or joint effusion (increase in the amount of fluid inside the joint.), we usually aspirate this fluid to study the cells and cytology, and most important we look for crystals in the fluid.

So we have the articular cartilage (covering the end of two bones), and the synovial cavity lined by the synovial membrane, and then we have ligament around it, and then the insertion of muscles, ALL OF THESE STRUCTURES CAN BE AFFECTED IN ANY JOINT DISEASE, part of them or all of them.

Inflammatory disease of joints (arthritis and synovitis)

Non-infectious arthritis: not caused by organisms like bacteria of viruses.

Four main causes:

- **Degeneration, e.g. osteoarthritis.**
- **Autoimmunity, e.g. rheumatoid arthritis, SLE.**
- **Crystal deposition, e.g. gout and other crystalline arthropathies.**
- **Infection, e.g. septic arthritis, tuberculous arthritis.**

Osteoarthritis

Osteoarthritis (degenerative joint disease) is the most common joint disease and is characterized by the progressive degeneration of articular cartilage in weight-bearing joints[(1)].

Osteoarthritis can be: primary or secondary

Primary[(2)]

- appears insidiously with age and without apparent initiating cause
- usually affecting only a few joints.

Secondary

- some predisposing condition, such as[(3)]:
  1- previous traumatic injury
  2- developmental deformity
  3- underlying systemic disease, e.g. diabetes
  4- hemochromatosis
  5- obesity
- Secondary osteoarthritis affects young.
- often involves one or several predisposed joints
- less than 5% of cases.

(1): e.g. knee & hip
(2): more common in females than males (because of the menopause)
(3): certain metabolic disorders (Mucoploysaccharidosis), certain congenital diseases like achondroplasia..

Osteoarthritis (Cont.)

1) Pathogenesis

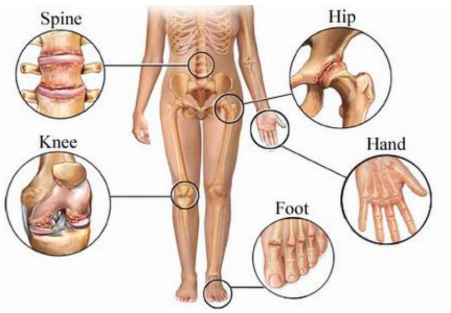
- Chondrocyte function is affected by a variety of influences: mechanical stresses, aging and Genetic factors.
- Regardless of the inciting stimulus, there is an **imbalance in:** the expression, activity, and signaling of cytokines and growth factors, **resulting in:** degradation and loss of matrix.
- Early osteoarthritis is **marked by** degenerating cartilage containing more water and less proteoglycan.
- The type II collagen network also is diminished, presumably as **a result of**: decreased local synthesis and increased breakdown.

the chondrocytes (the cell forming the cartilage) dies, and this will create inflammatory reaction (MILD INFLAMMATION), which is associated with certain cytokines especially Nitric oxide, Tumor growth Factor beta1 (TGF-B1), and Tumor necrosis factor (TNF), and this will enhance this deterioration.

Osteoarthritis Common sites:

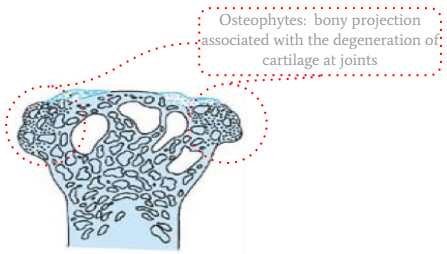
Gender has some influence:

- Women: knees and hands
- Men: Hips

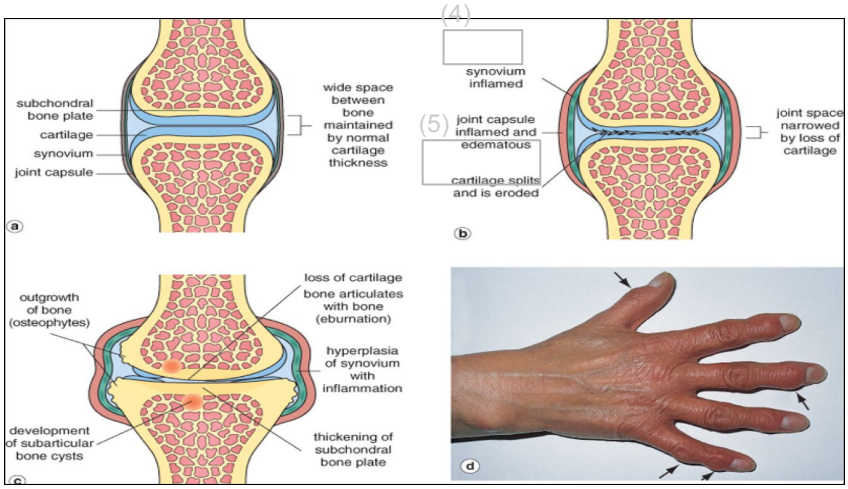


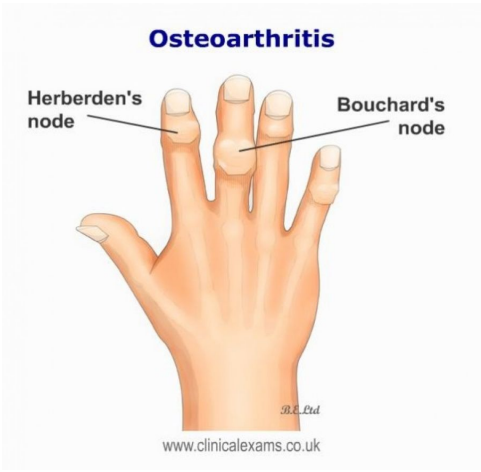
Osteoarthritis (Cont.)

IT AFFECTS THE CARTILAGE AND START IN THE CARTILAGE (the degeneration in the cells and matrix)

Normal articular cartilage	
Fragmentation of articular surface and thinning of cartilage(2).	
Calcification of cartilage margins. Patchy loss of cartilage revealing bare bone (eburnation(3)).	
Formation of lips of new bone (osteophytes) extensive loss of cartilage cystic degeneration of underlying bone.	

*constant friction of bone surfaces, leading to a polished ivory bony articular surface (eburnation).





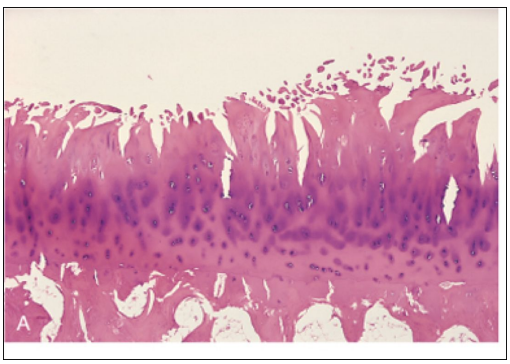
Heberden's nodes: osteophytes on the distal interphalangeal joints of the fingers.
Bouchard's node: osteophytes on the Proximal interphalangeal joints of the fingers. .(6)

(2): also called fibrillation & cracking of the matrix
(3): friction between two bones
(4): secondary pathological cause of osteoarthritis
(5): main pathological cause of osteoarthritis
(6): for easier memorizing: Bouchard's node >> proximal
or you could say the letter B (Bouchard's node) is before the letter H

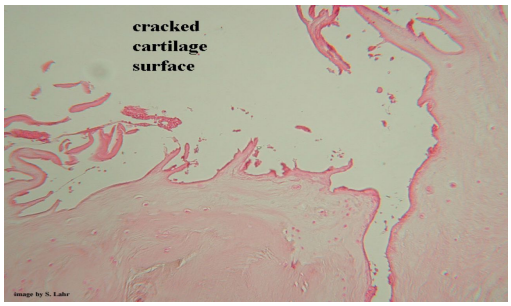
Osteoarthritis (Cont.)

2) Morphology

- fibrillation and cracking of the matrix occur as the superficial layers of the cartilage are degraded.
- Eventually, full-thickness portions of the cartilage are lost, and the subchondral bone plate is exposed and is smoothened by friction, giving it the appearance of polished ivory (bone eburnation).
- Small fractures can dislodge pieces of cartilage and subchondral bone into the joint, forming loose bodies (joint mice).
- The fracture gaps allow synovial fluid to be forced into the subchondral regions to form fibrous walled cysts.
- Mushroom-shaped osteophytes (bony outgrowths) develop at the margins of the articular surface.

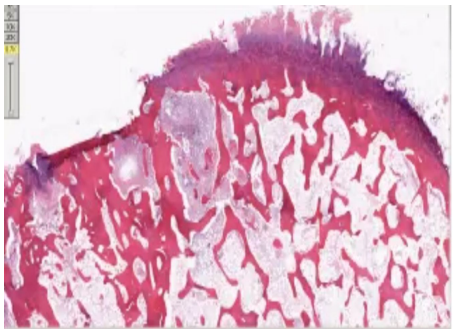


Osteoarthritis. : Histologic demonstration of the characteristic fibrillation of the articular cartilage.



Cracking and fibrillation of cartilage

1-Eburnated articular surface exposing subchondral bone.
2-Subchondral cyst.
3-Residual articular cartilage

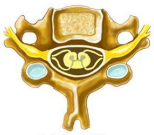


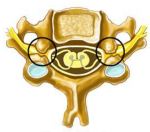
Osteoarthritis (Cont.)

3) Clinical course

- Characteristic **symptoms and signs** include:
  - deep, aching pain exacerbated (worsened) by use.
  - morning stiffness.
  - crepitus (grating or popping sensation & sounds in the joint).
  - limitation in range of movement.

- Osteophyte impingement on spinal foramina can cause nerve root compression with radicular pain and neurologic deficits.





- Commonly involves:
  - Hips
  - Lower lumbar and cervical vertebrae
  - Proximal and distal interphalangeal joints of the fingers
  - First carpometacarpal joints
  - First tarsometatarsal joints

Heberden nodes in the fingers are characteristic in women

4) course and prognosis

- Slow and progressive.

- With time, significant joint deformity can occur. Treatment usually is based on symptoms, with joint replacement in severe cases

Rheumatoid Arthritis

it affects many organs like the lung, lymph node, spleen, skin but it loves the joint

- Rheumatoid arthritis (RA) is a systemic, chronic inflammatory **autoimmune disease**[7] affecting many tissues but principally attacking the joints.
- It causes a nonsuppurative[8] proliferative synovitis that frequently progresses to destroy articular cartilage and underlying bone with resulting disabling arthritis.
- RA is a relatively common condition, with a prevalence of approximately 1%; it is three to five times more common in women than in men.
- The peak incidence is in the second to fourth decades of life, but no age is immune.

1) Pathogenesis

- interactions of genetic risk factors, environment, and the immune system.
- The pathologic changes are caused mainly by cytokine-mediated inflammation, with CD4+ T cells being the principal source of the cytokines.
- Many patients also produce **antibodies against cyclic citrullinated peptides (CCPs)**, which may contribute to the joint lesions In RA, antibodies to:

- citrullinated fibrinogen
- type II collagen
- α-enolase
- vimentin

بمعنى أن ال Anti CCPs anitbodies تهاجم هالأشياء بجسم المريض

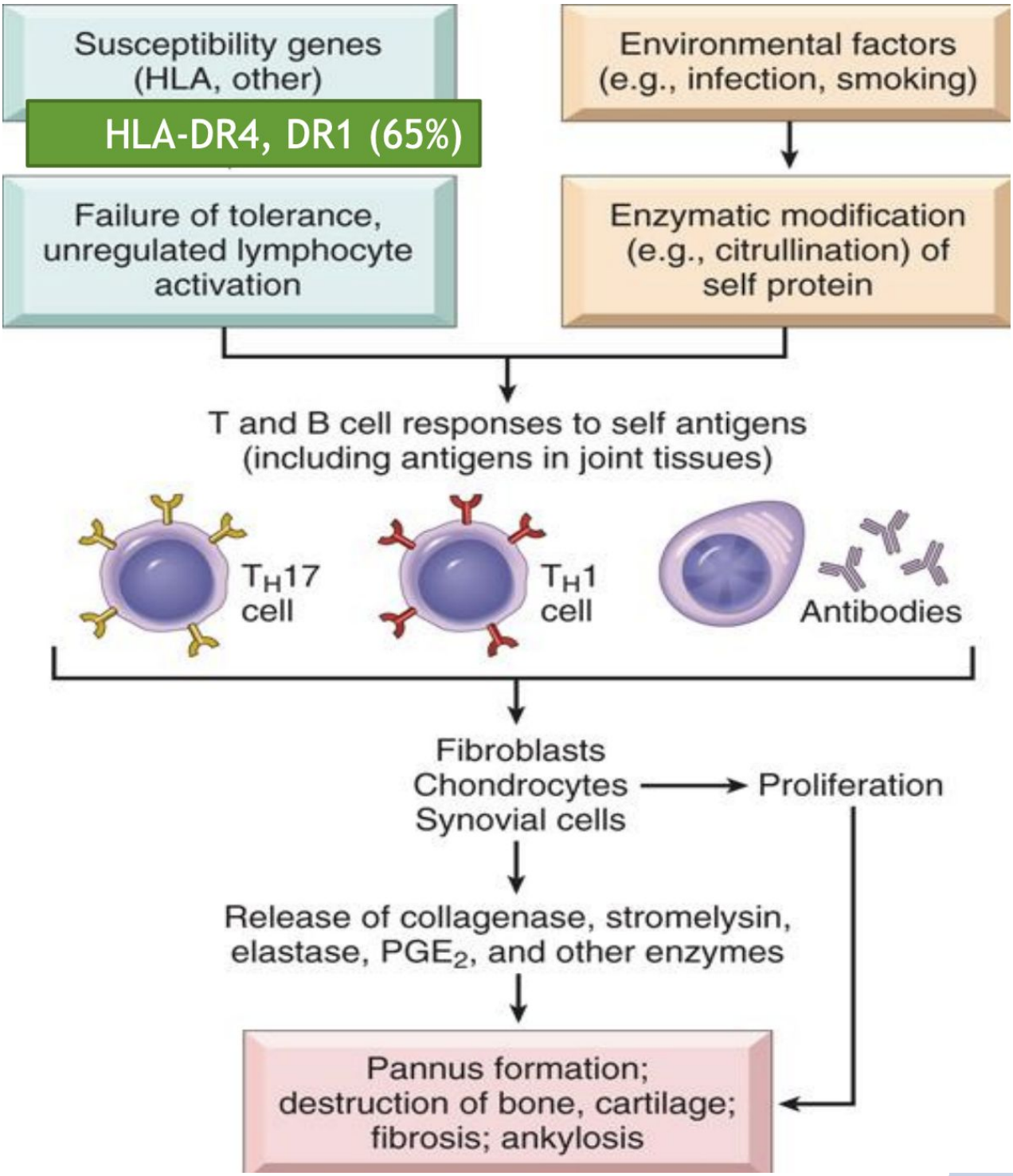
These antibodies are the most important and may form immune complexes that deposit in the joints. They are **diagnostic marker** for the disease and may be involved in tissue injury.

- **Genetic factors:** mainly involves HLA-DRB1
- **Environmental factors:** Many candidate infectious agents whose antigens may activate T or B cells have been considered, but none has been conclusively implicated.
- About 80% of patients have serum immunoglobulin M (IgM) (and, autoantibodies that bind to the Fc portions of their own (self) IgG. These autoantibodies are called rheumatoid factor. They may form immune complexes with self-IgG that deposit in joints and other tissues, leading to: inflammation and tissue damage[9].

(7): Since it is autoimmune, it will be more prevalent in women. (437)
(8): inflammation without pus formation
(9): However, the role of rheumatoid factor in the pathogenesis of the joint or extra articular lesions has not been established.

Rheumatoid Arthritis (Cont.)

- Antibodies against cyclic citrullinated peptides (CCP protein antibodies) is the most specific for a diagnosis of rheumatoid arthritis.



Rheumatoid Arthritis (Cont.)

2) Laboratory findings

- Rheumatoid factor: 80% have IgM autoantibodies that act on Fc portion of IgG
  It is NOT Specific , Although it is sensitive and can come out positive in almost 20% of patients.
- Anti-CCP (cyclic citrullinated peptides) protein antibodies for a diagnosis of rheumatoid arthritis (when the arginine is metabolized it produces citrulline, and rheumatoid arthritis patients they develop antibodies against citrulline. THIS TEST IS VERY SPECIFIC, because it is positive in more 70% of the patients)..
- ESR and C-reactive protein.

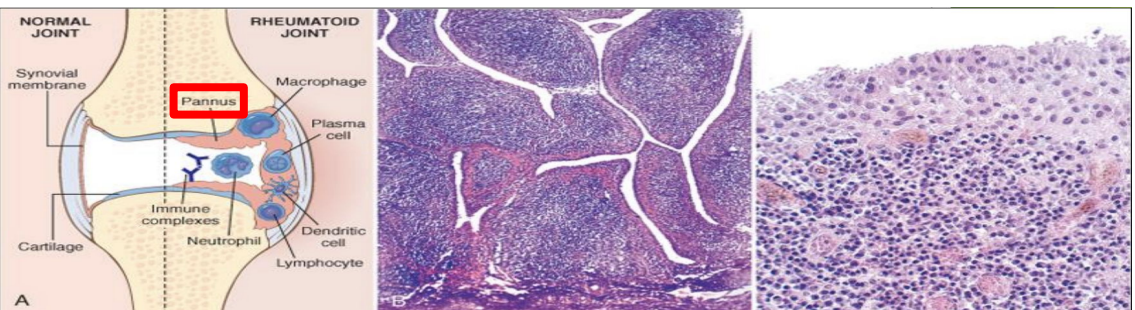
3) Pathological Feature

1. synovial cell hyperplasia and proliferation
2. Dense perivascular inflammatory cell infiltrates (Chronic synovitis) frequently forming lymphoid follicles in the synovium composed of : CD4+ T cells plasma cells macrophages
3. increased vascularity due to angiogenesis (Formation of new vessels)
4. neutrophils and aggregates of organizing fibrin on the synovial surface
5. increased osteoclast activity in the underlying bone →bone erosion

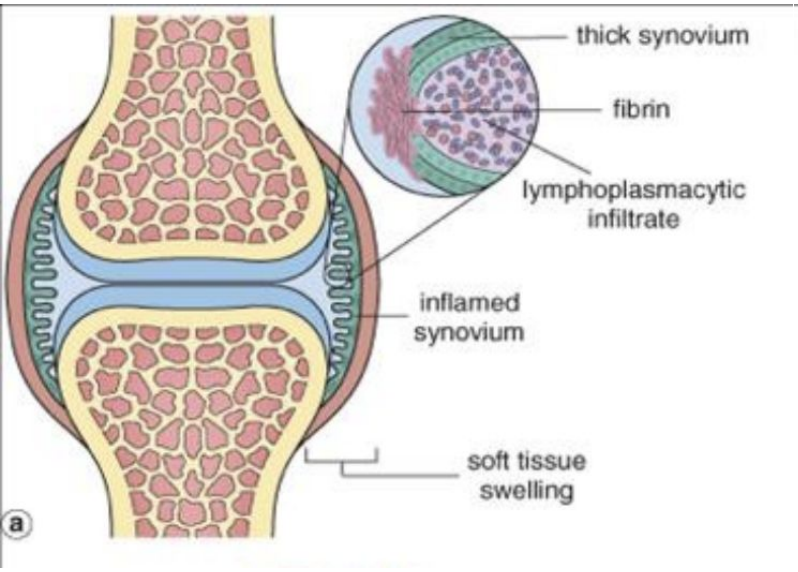
RA IS A DISEASE OF THE SYNOVIUM, it is not a disease of the cartilage, even if the cartilage and bone is affected, BUT IT ALWAYS START FROM THE SYNOVIUM. (Unlike osteoarthritis which starts in the cartilage).

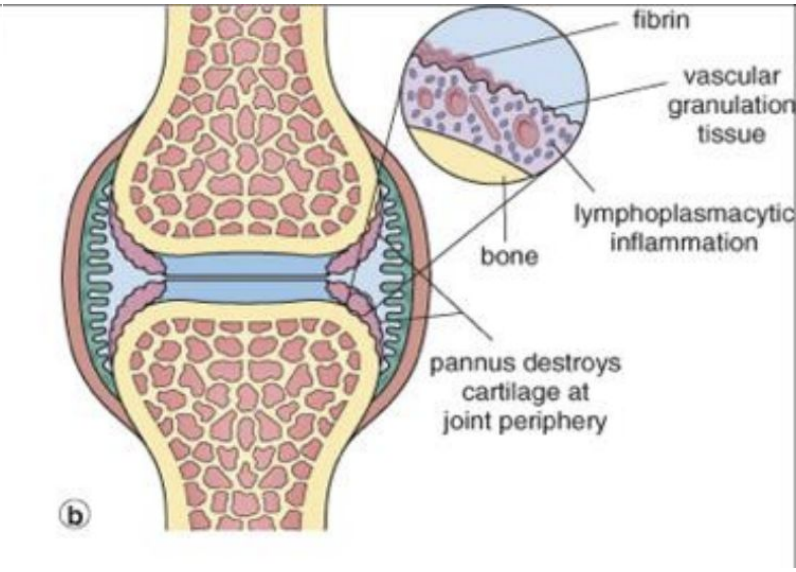
Pannus:

- An important pathological feature formed by proliferating synovial-lining cells admixed with inflammatory cells, granulation tissue, and fibrous connective tissue.
- Eventually the pannus fills the joint space, and subsequent fibrosis and calcification may cause permanent ankylosis (stiffness and immobility of joint).



Rheumatoid Arthritis (Cont.)





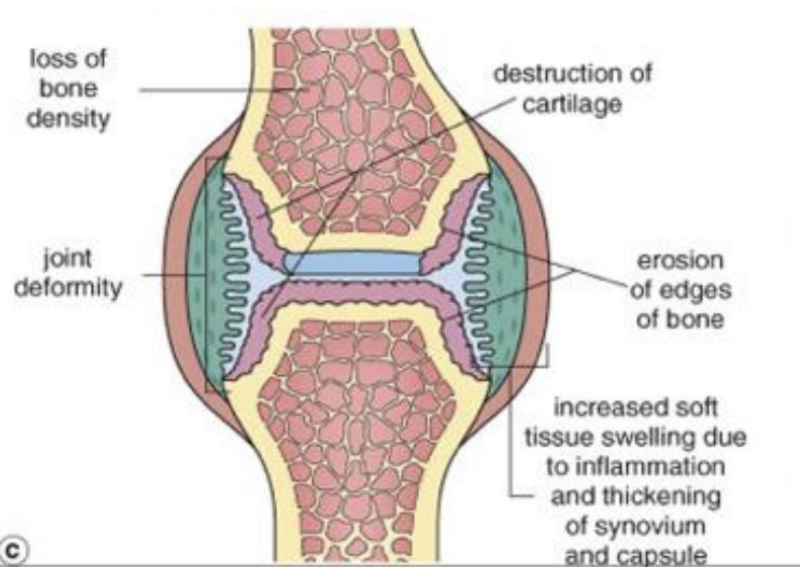
Dense inflammatory cell infiltrates

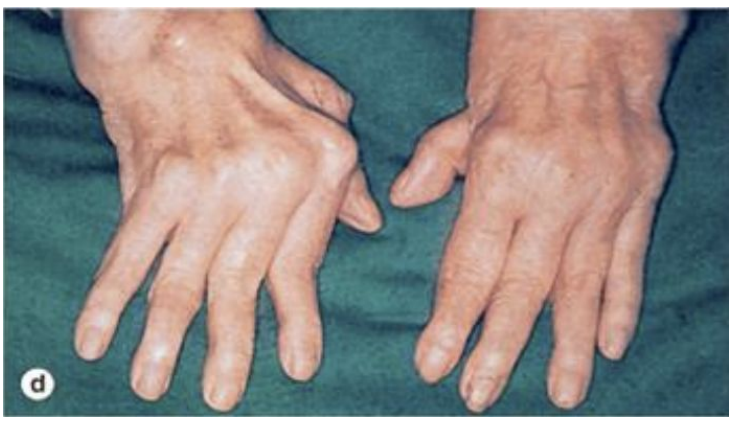
Neutrophils and aggregates of organizing fibrin on the synovial surface

Synovial cell hyperplasia and proliferation

Increase vascularity

Pannus formation





Swan neck figure

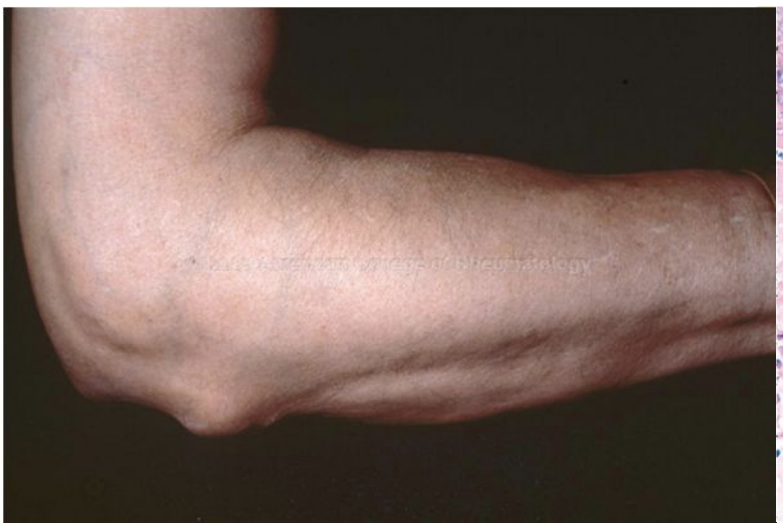
increased osteoclast activity in the underlying bone ➔ bone erosion

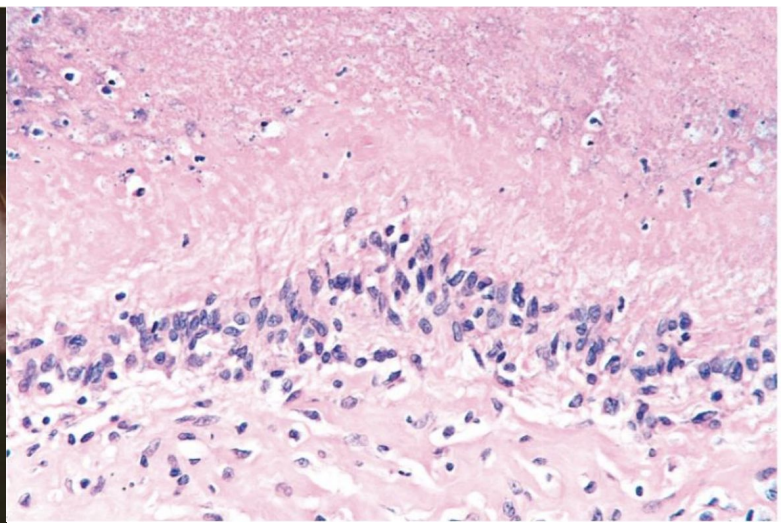
Swan : بجعة

Rheumatoid Arthritis (Cont.)

3) Rheumatoid subcutaneous nodules

- Develops in about one fourth of patients.
- Occuring along the extensor surface of arm.
- Rheumatoid nodules are firm, non-tender, oval or rounded masses as large as 2 cm in diameter.
- They are characterized microscopically by a central focus of fibrinoid necrosis surrounded by a palisade of macrophages, which in turn is rimmed by granulation tissue and lymphocytes.





When the rheumatoid arthritis affects the skin it is called **Rheumatoid nodules**, it can cause vasculitis, and it can cause interstitial lung disease, it can affects also the spleen and this will cause splenomegaly (enlarged spleen), and enlarged lymph nodes. They are RARELY seen in rheumatoid arthritis, but when they are seen it means that the disease is very severe and advanced.

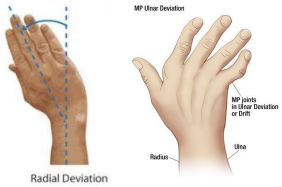
Rheumatoid Arthritis (Cont.)

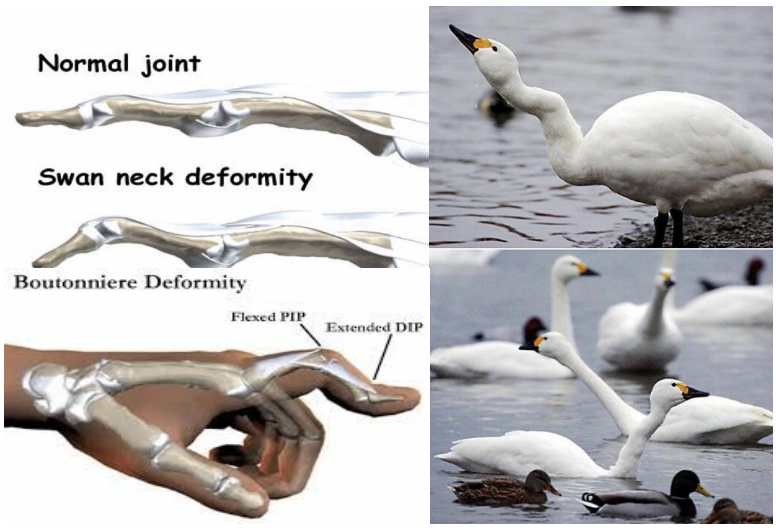
4) Clinical features

- symmetric arthritis[10], principally affecting the small joints of the hands and feet, ankles, knees, wrists, elbows, and shoulders.
- Most often, the proximal interphalangeal and metacarpophalangeal joints are affected, but distal interphalangeal joints are spared.
- Axial involvement, when it occurs, is limited to the upper cervical spine; similarly, hip joint involvement is extremely uncommon
- Weakness , low grade fever
- aching and stiffness of the joints, particularly in the morning
- As the disease advances, the joints become enlarged, motion is limited

❑ characteristic derformities develop. These include:

- Radial deviation at the **wrists**.
- Ulnar deviation at the **fingers**.
- Flexion and hyperextension deformities of the fingers **(swan neck and boutonniere deformities).**



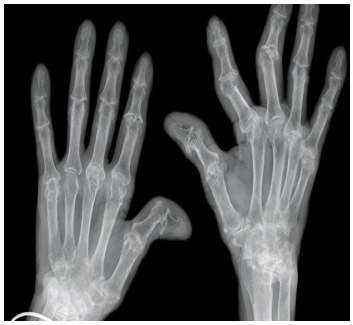


(10): both hands are affected in the same way

Rheumatoid arthritis (Cont.)

X-ray:

- Loss of articular cartilage leading to narrowing of the joint space.
- Joint effusions.
- Erosions.

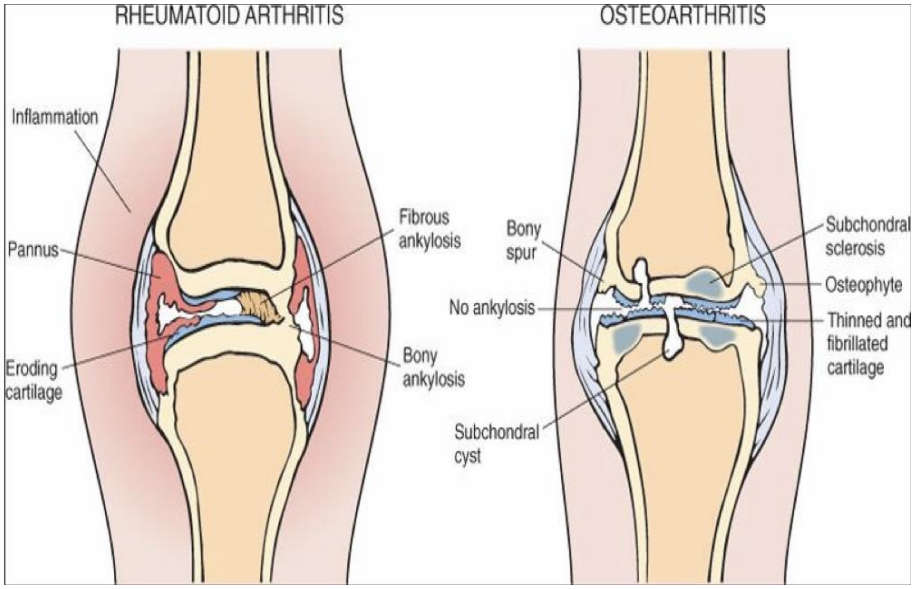


5) Prognosis

- The clinical course of RA is highly variable.
- In a minority of patients, the disease may stabilize or even regress.
- in most patients it pursues a chronic, remitting-relapsing course[11].
- progressive joint destruction leading to disability after 10 to 15 years. The outcome has been dramatically improved by recent advances in therapy.
- RA is an important cause of **reactive amyloidosis**, which develops in 5% to 10% of these patients, particularly those with long-standing severe disease.

(11): يكون بخير فترة ثم يرجع ينتكس

Comparison of the morphologic features of RA and osteoarthritis



	Osteoarthrosis	Rheumatoid Arthritis
Basic process	Degenerative	Immunologic, inflammatory
Site of initial lesion	Articular cartilage	Synovium
Age	50 plus	Any, but peaks at age 20–40 years
Sex	Male or female	Female > male
Joints involved	Especially knees, hips, spine; asymmetric involvement	Hands, later large joints; multiple symmetric involvement
Fingers	Herberden's nodes	Ulnar deviation, spindle swelling
Nodules	No	Rheumatoid nodules
Systemic features	None	Uveitis, pericarditis, etc.
Constitutional symptoms	None	Fever, malaise in some
Laboratory findings	None	Rheumatoid factor; ↑erythrocyte sedimentation rate; anemia, leukocytosis, hyperglobulinemia
Joint fluid	Clear, normally viscous; no inflammatory cells	Clear; low viscosity, high protein; neutrophils, some lymphocytes; immunoglobulins, complement, rheumatoid factor

OSTEOARTHRITIS = THE PAIN COMES WITH MOVEMENT
RHEUMATOID ARTHRITIS = THE PAIN STARTS IN EARLY MORNING (PAIN AT REST)

Gout

Podagra: Gout of the foot, especially the big toe

1) Pathogenesis

- Gout affects about 1% of the population, and shows a predilection for males.

- It is caused by excessive amounts of uric acid.

- **Monosodium urate crystals** precipitate from supersaturated body fluids and induce an acute inflammatory reaction.

- Gout is marked by:
  - recurrent episodes of acute arthritis
  - sometimes accompanied by the formation of large crystalline aggregates called tophi
  - eventual permanent joint deformity.

- Risk factors for the disease include obesity, excess alcohol intake, consumption of purine-rich foods, diabetes, the metabolic syndrome, and renal failure.
- **Gout is divided into :**

1. Primary 90%
2. Secondary 10 %forms

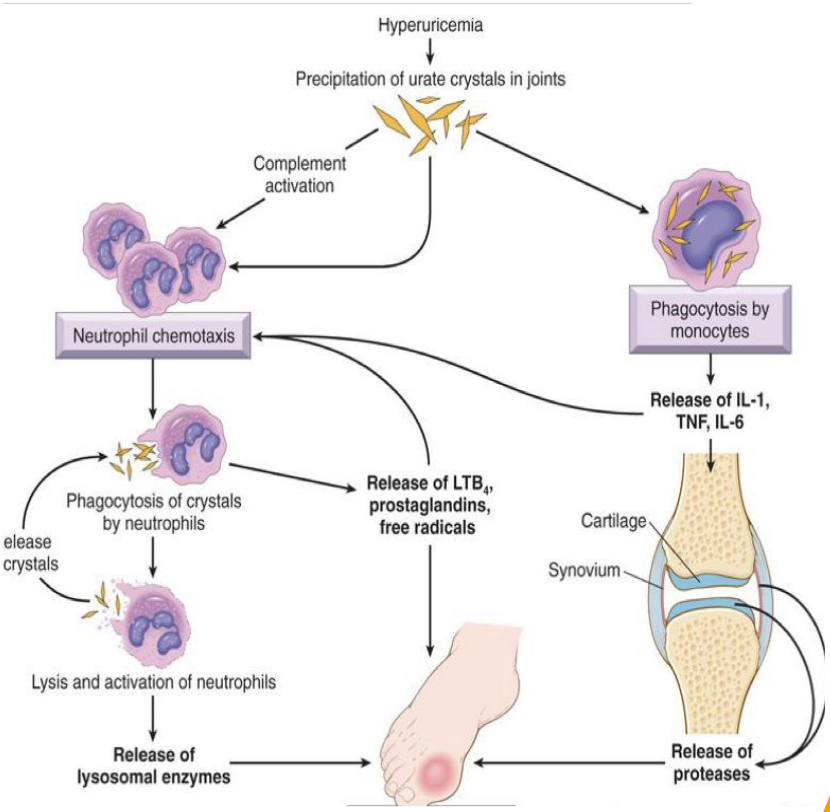
Metabolic disorder, very common, it affects the joints, caused by an error of the metabolism
of purine (contribute in the DNA Structure), there is two types of gout:
1-Primary: we do not know the cause of it (idiopathic), very high uric acid, and the uric acid is metabolite of purine.
2-Secondary: Caused by any disease characterized by the death of cells in large numbers (Cancer), for example leukemia, lymphoma, tears them with cytotoxic drugs (chemotherapy) which increase the turnover of purine, another cause of secondary Gout, which happened in people taking Thiazide (diuretics) can cause high uric acid (by decrease excretion of uric acid). Certain diets can cause high uric acid, very rich in meat and alcohol.

Gout (Cont.)

Table 20–3 Classification of Gout

Clinical Category	Metabolic Defect
Primary Gout (90% of cases)	
Enzyme defects—unknown (85% to 90% of cases)	Overproduction of uric acid Normal excretion (majority) Increased excretion (minority) Underexcretion of uric acid with normal production
Known enzyme defects—e.g., partial HGPRT deficiency (rare)	Overproduction of uric acid
Secondary Gout (10% of cases)	
Associated with increased nucleic acid turnover—e.g., leukemias	Overproduction of uric acid with increased urinary excretion
Chronic renal disease	Reduced excretion of uric acid with normal production
Inborn errors of metabolism	Overproduction of uric acid with increased urinary excretion, e.g., complete HGPRT deficiency (Lesch-Nyhan syndrome)

HGPRT, hypoxanthine guanine phosphoribosyl transferase.



Gout (Cont.)

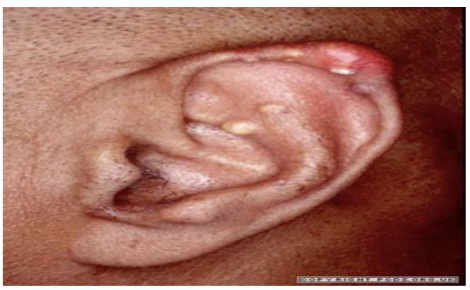
2) Morphology

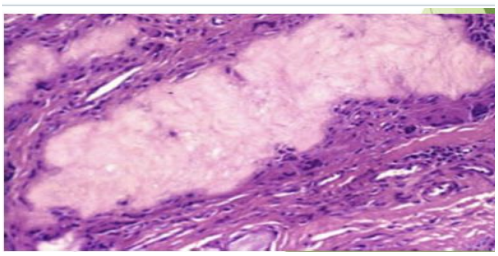
- Acute arthritis is characterized by a dense neutrophilic infiltrate permeating the synovium and synovial fluid. Long, slender, needle-shaped monosodium urate crystals frequently

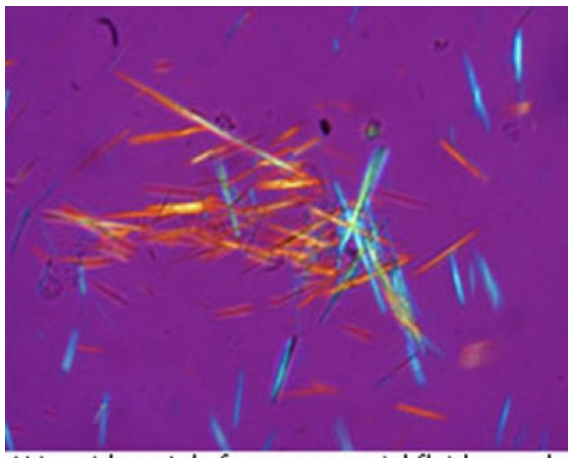
- Chronic tophaceous arthritis evolves from repetitive precipitation of urate crystals during acute attacks. The synovium becomes hyperplastic, fibrotic, and thickened by inflammatory cells

- **Tophi are pathognomonic for gout**. They are formed by large aggregations of urate crystals surrounded by an intense inflammatory reaction of lymphocytes, macrophages, and foreign-body giant cells

- Tophi can appear in the articular cartilage of joints and in the soft tissues, including the ear lobes & nasal cartilages







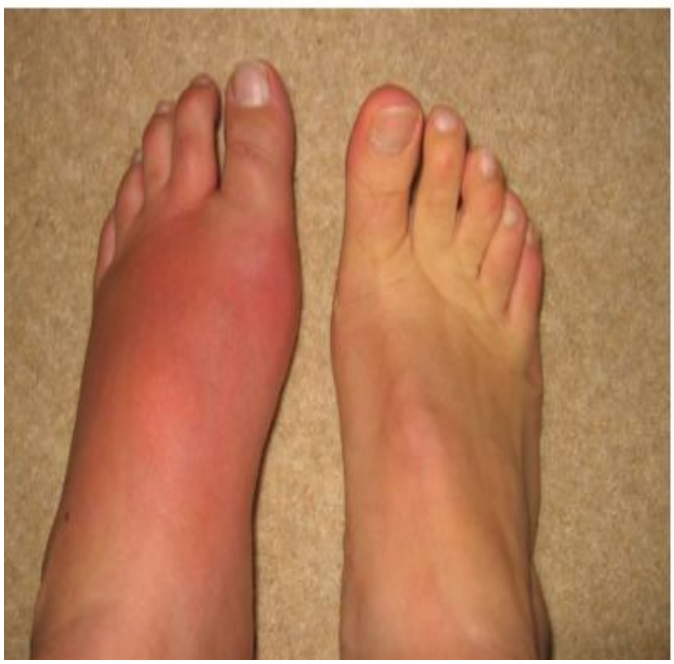
Uric acid crystals from a synovial fluid sample

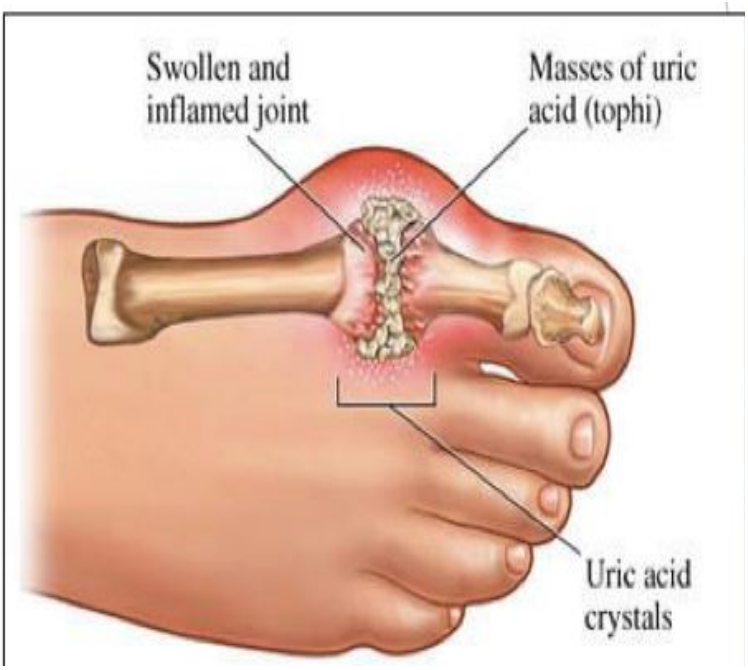
the Tophus is uric acid crystals surrounding inflammatory cells, accumulate in tendon of achilles, they produce a mass or nodules in tendons (especially tendon of Achilles) , and helix of the ear.

Gout (Cont.)

3) Clinical features

- The most commonly affected site is: **first metatarsophalangeal joint.**
- It is swollen, red, and very painful.
- Renal manifestations of gout can appear as renal colic associated with the passage of gravel and stones.





Pseudogout
Calcium pyrophosphate crystals

This condition is due to the deposition of calcium pyrophosphate crystals in the synovium (pseudogout) and articular cartilage (chondrocalcinosis). It can occur in three main settings:

- Sporadic (more common in the elderly).
- Hereditary
- Secondary to other conditions, such as previous joint damage, hyperparathyroidism, hypothyroidism, haemochromatosis and diabetes.
- The crystals first develop in the articular cartilage (chondrocalcinosis[12]), which is usually asymptomatic. From here, the crystals may shed into the joint cavity resulting in an acute arthritis, which mimics gout and is therefore called pseudogout.

Pseudogout can be differentiated from gout in three ways:

- The knee is most commonly involved.
- X-rays show the characteristic line of calcification of the articular cartilage.
- The crystals look different under polarizing microscopy, they are rhomboid in shape .

(12): calcium in the cartilage

Dr. Alrikabi's notes

★ **Non-infectious arthritis:** not caused by organisms like bacteria of viruses.

★ **These diseases are very common and important.**

★ **Structure of the joint:**
The joint usually consist of the end of two bones, and the ends of These bones are covered with articular cartilage (usually Hyaline Cartilage and its rich in collagen type ll). There is a space between the cartilage which is the synovial space which contains synovial cells. If there is an accumulation of large amount of fluid in the joint then this is what we call Articular effusion or joint effusion (increase in the amount of fluid inside the joint.), we usually aspirate this fluid to study the cells and cytology, and most important we look for crystals in the fluid.
So we have the articular cartilage (covering the end of two bones), and the synovial cavity lined by the synovial membrane, and then we have ligament around it, and then the insertion of muscles, ALL OF THESE STRUCTURES CAN BE AFFECTED IN ANY JOINT DISEASE, part of them or all of them.

★ **1-Osteoarthritis (Degenerative joint disease):** Degenerative or deterioration in the function of cells and tissues because of the aging process. Very common disease, seen in people over the age of 50, and when it occurs usually there is no cause of it because of the aging process. There are factors which make the disease more symptomatic, more common in females than males (Primary Osteoarthritis because of the aging and menopause), sometime osteoarthritis is secondary (trauma, fractures, certain metabolic disorders (Mucoploysaccharidosis), certain congenital diseases like achondroplasia). (X-ray of the pelvic osteoarthritis patient) the articular space between the pelvic bone the head of the femur almost gone, narrowed, and this will lead to irritation (friction) all the time and she will start having pain, we also have increased density of the bone because of new bone formation, and there will be or Osteophytes (the outgrowth of the bone), and sometime this osteophytes they break and go to the synovial space (cavity), this is called mice joint.

- **Gross-pathology:** a disease of cartilage, IT AFFECTS THE CARTILAGE AND START IN THE CARTILAGE (the degeneration in the cells and matrix), you can see osteophytes (pathological).

- **The joint of osteoarthritis patients:** absence and fibrillation of the articular cartilage (complete loss of the cartilage), osteophytes (outgrowth of the bone).

Dr. Alrikabi's notes (Cont.)

- **Why do we get this degeneration?**
  Because it is part of the aging process, the chondrocytes (the cell forming the cartilage) dies, and this will create inflammatory reaction (MILD INFLAMMATION), which is associated with certain cytokines especially Nitric oxide, Tumor growth Factor beta1 (TGF-B1), and Tumor necrosis factor (TNF), and this will enhance this deterioration.

- **Osteophytes** help us sometimes to diagnose, because they form the Heberden's nodes (in the distal pharyngeal areas), and Bouchard's nodes (in the proximal metacarpal/metatarsals pharyngeal.

- **A lot of joints get affected in osteoarthritis,** hips, knees, hands, feet, spine. Osteoarthritis love the weight bearing joints like the knees.

★ **2- Rheumatoid arthritis:** an autoimmune disease which is multisystemic, it affects many organs like the lung, lymph node, spleen, skin but it loves the joint, like osteoarthritis it affects females more than males between the age of 20 – 60 years old. IT IS A DISEASE OF THE SYNOVIUM, it is not a disease of the cartilage, even if the cartilage and bone is affected, BUT IT ALWAYS START FROM THE SYNOVIUM. (Unlike osteoarthritis which starts in the cartilage).
OSTEOARTHRITIS = THE PAIN COMES WITH MOVEMENT
RHEUMATOID ARTHRITIS = THE PAIN STARTS IN EARLY MORNING (PAIN AT REST)

- **The pathology of Rheumatoid arthritis:**
  Hyperplasia in the synovial, very dense inflammatory infiltrate, we see large number of lymphocytes, large number of plasma cells. With time you get a little bit of erosions in the cartilage, and then formation of special type of granulation tissue inside the joint called **Pannus**, Pannus consists of vascular granulation tissue with lot of fibrin, this will lead to adhesions and deformities (very severe).
- **What happens at the level of cells?**
  Autoimmune disease —> stimulation of the T lymphocyte CD4 —> helper T cell —> secrete cytokines which are:
  1-IL-17
  2-Tumor necrosis factor (TNF). *most of the drugs of Rheumatoid arthritis are anti-TNF
  3-Interferon Gamma

- **Synovial:** contain fat, blood vessels, and synovial cells.
  In the Rheumatoid arthritis the synovial has a lot of edema, lymphoid follicles, plasma cells, hyperplasia.

Dr. Alrikabi's notes (Cont.)

The joints affected by the Rheumatoid arthritis is almost the same as osteoarthritis, but it love the small joint.

- **How to diagnose rheumatoid arthritis:**
  1- Rheumatoid factor test: it is an IgM antibody, against Fc segment of the IgG, it is usually positive in most of these patients. This test is sensitive but it is NOT SPECIFIC.
  2- Anti-CCP (anti-Cyclic Citrullinated Proteins): when the arginine is metabolized it produces citrulline, and rheumatoid arthritis patients they develop antibodies against citrulline. THIS TEST IS VERY SPECIFIC, because it is positive in more 70% of the patients.

- **Rheumatoid Arthritis can cause a lot of deformities:**
  1-Ulnar Deviation: extreme swelling in the joint.
  2-Disused Atrophy: caused by disuse of the muscles, the muscles between the metatarsals bones or metacarpals are atrophic. يقول ممكن يسآل الجزء عن هذا
  3-Swan-neck deformity
  4-Boutonnière deformity

- **Rheumatoid nodules:**
  When the rheumatoid arthritis affects the skin it is called **Rheumatoid nodules**, it can cause vasculitis, and it can cause interstitial lung disease, it can affects also the spleen and this will cause splenomegaly (enlarged spleen), and enlarged lymph nodes. They are RARELY seen in rheumatoid arthritis, but when they are seen it means that the disease is very severe and advanced.

- **Rheumatoid episcleritis:** when rheumatoid arthritis affects the eye.

★ **3-Gouty arthritis (Gout):**
Metabolic disorder, very common, it affects the joints, there is an error of metabolism of purine (contribute in the DNA Structure), there is two types of gout: 1-Primary: we do not know the cause of it (idiopathic), very high uric acid, and the uric acid is metabolite of purine. 2-Secondary: Caused by any disease characterized by the death of cells in large numbers (Cancer), for example leukemia, lymphoma, tears them with cytotoxic drugs (chemotherapy) which increase the turnover of purine,

so that will produce more uric acid. There is another cause of secondary Gout, which happened in people taking Thiazide (diuretics) can cause high uric acid (by decrease excretion of uric acid). Certain diets can cause high uric acid, very rich in meat and alcohol.

To have Gout you need to have Monosodium Urate Crystals, then accumulation of these crystals in the joint and create an inflammatory reaction, and the inflammatory reaction will cause the symptoms of gout.

Whether it is primary or secondary we have hyperuricemia (high uric acid), gout is **usually presented with pain in the big toe**, it can affect joints in hand and knee. Sometime Gout is very severe and is associated with the formation of Tophus , the Tophus is uric acid crystals surrounding inflammatory cells, accumulate in tendon of achilles, they produce a mass or nodules in tendons (especially tendon of Achilles) , and helix of the ear.

- **Pathogenesis:**
  Accumulation of Monosodium urate crystals in the joint —> create an inflammatory reaction —> chemotaxis —> macrophages and neutrophils will engulf the crystals, but they cannot digest it —> the macrophage and neutrophils will release the crystals and will release proteolytic enzymes which are found in the lysosomes of these enzymes, and these enzyme will come to the tissue and destroy it (lyse the tissue), and there will be Also a release of certain cytokines: IL-1 , TNF.
  *what causes the pain in Gout is the migration of macrophages and neutrophils and the release of proteolytic enzymes.

★ **4-Pseudogout:** the symptoms are associated with gout, but it is not associated with uric acid increase or Monosodium urate crystals. In Pseudogout there will be accumulation of Calcium Pyrophosphate Crystals, It usually seen in older people, it affect the joint of hand and feet, they are rhomboid in shape, unlike monosodium urate crystals which are needle shaped.

Quiz

1. Which part of a joint does osteoarthritis usually affect:
A) Bone
B) Cartilage
C) Tendon
D) All of the above

2. Which one of these following antibodies are diagnostic marker for rheumatoid arthritis:
A) Anti CCP
B) Anti IgG
C) Anti IgM
D) Anti IgA

3. Osteoarthritis affecting the distal interphalangeal joints (i.e. first finger joint from the finger tip) is known as:
A) Bouchard's nodes
B) Richard's nodes
C) Heberden's nodes

4. Rheumatoid arthritis (RA) is different from some other forms of arthritis because it:
A) Is more painful than other forms
B) Occurs below the waist
C) Is symmetrical, affecting the right and left sides of the body
D) Generally, occurs above the waist

5. An otherwise healthy 44-year-old man with no prior medical history has had increasing back pain and right hip pain for the past decade. The pain is worse at the end of the day. On physical examination he has bony enlargement of the distal interphalangeal joints. A radiograph of the spine reveals the presence of prominent osteophytes involving the vertebral bodies. There is sclerosis with narrowing of the joint space at the right acetabulum seen on a radiograph of the pelvis. Which of the following diseases is he most likely to have:
A) Gout
B) Rheumatoid arthritis
C) Osteoarthritis
D) Osteomyelitis

6. 40 years-old Businessman present with severe pain and redness in his first metatarsophalangeal joint. The doctor ordered a blood test and the results show a high level of uric acid. What is the most likely diagnosis?
a- Osteoarthritis
b- Rheumatoid arthritis
c- pyogenic arthritis
d- Gouty arthritis

1- B | 2- A | 3- C | 4- C | 5- C | 6- D

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Thank you

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