MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437

Pathology

teamwork 437

Lecture Five (5) : Arthritis.

Color Index

- VERY IMPORTANT
- Extra explanation
- Examples
- **Diseases names: Underlined**
- Definitions

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&
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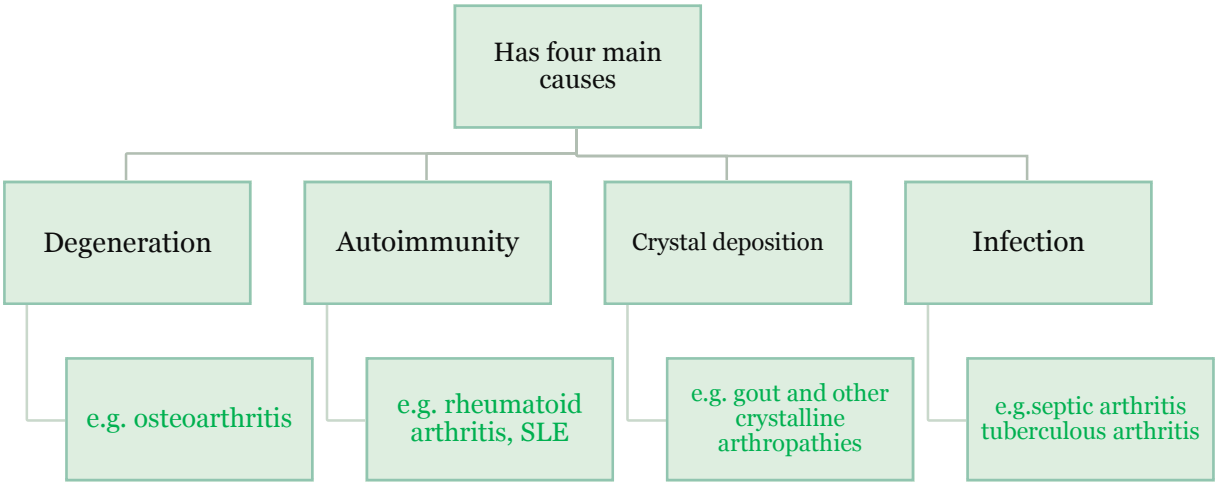
نَستَهِينُ كل غالٍ كي نُحقِقَ الحُلم . . إن سئِمنا لا نُبالي بل نسِير للأمام . . إنّ قِمةَ الجِبالِ تستَحِقُ لا جَرم

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]

INFLAMMATORY DISEASE OF JOINTS (ARTHRITIS AND SYNOVITIS)



OSTEOARTHRITIS :

Definition and incidence :

- Osteoarthritis (degenerative joint disease) is the most common

Joint disease and is characterized by the progressive degeneration of articular cartilage In weight- bearing joints.

- mostly old people (over 50)
- affects females more than males

Osteoarthritis can be : primary or secondary

Primary osteoarthritis:

- Appears insidiously with age and without apparent initiating cause
- Usually affecting only a few joints
- Cause is usually IDIOPATHIC

Secondary osteoarthritis: (Known Cause)

- Some predisposing condition, such as previous traumatic injury, developmental deformity, or underlying systemic disease such as diabetes, hemochromatosis, or marked obesity

- Secondary osteoarthritis affects young people
- often involves one or several predisposed joints
- less than 5% of cases

Pathogenesis: Articular cartilage bears the brunt of the degenerative change 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) and to have high tensile strength. These attributes are provided by proteoglycans and type II collagen, both produced by chondrocytes

Important for Cartillages

- Chondrocytes function is affected by a variety of influences:

-Mechanical stress - Aging - Genetic factor

Regardless of the inciting stimulus, there is an imbalance in the expression, activity, and signaling of cytokines and growth factors that results in degradation and loss of matrix.

Early osteoarthritis is marked by:

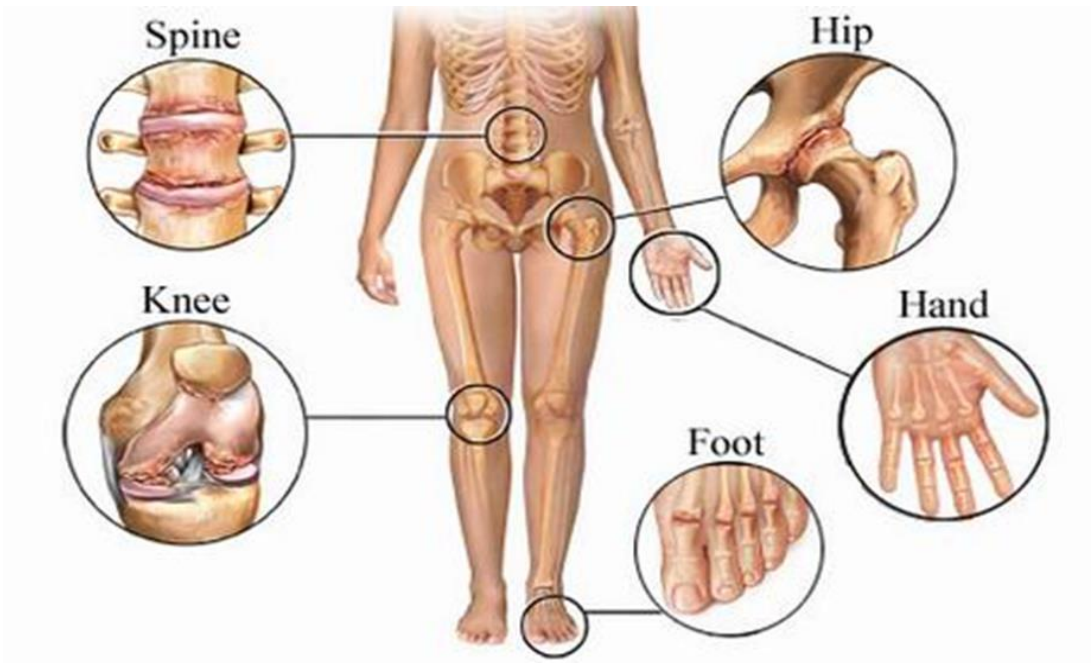
- degenerating cartilage containing: more water and less proteoglycan
- The type II collagen network also is diminished, presumably as a result of decreased local synthesis and increased breakdown

Gender has some influence:

Women : knees and hands

Men : hips

Osteoarthritis Common sites :



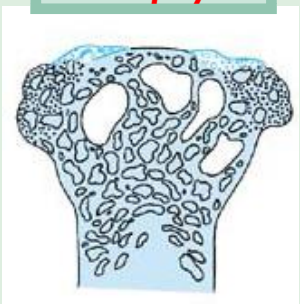
Normal articular cartilage

Fragmentation of articular surface and thinning of cartilage

Calcification of cartilage margins. Patchy loss of cartilage revealing bare bone (eburnation).

Small cysts develop in the bone ***(Due to forced leakage of synovial fluid into the subchondral region)***

Osteophytes



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)

MORPHOLOGY

- **fibrillation and cracking of the matrix** occur as the superficial layers of the cartilage are degraded

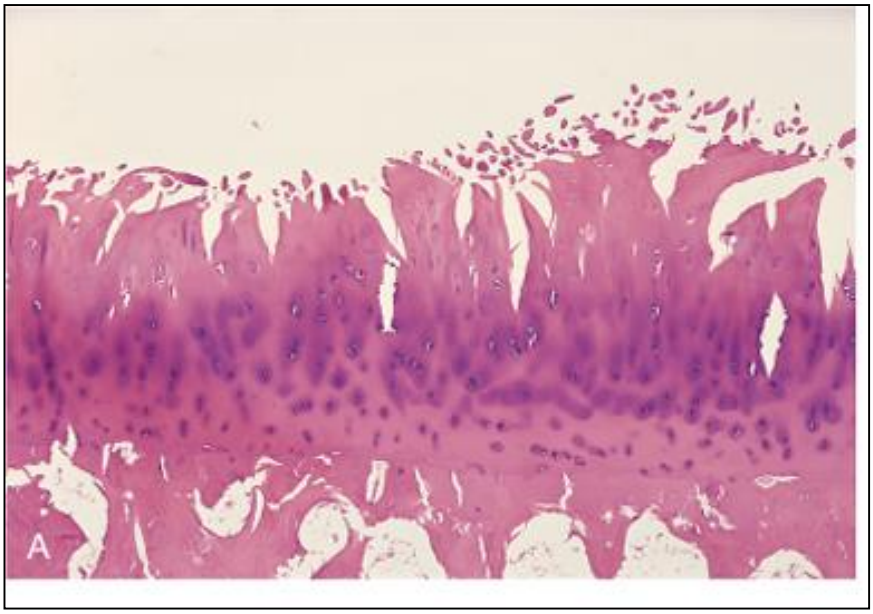
- Eventually, full-thickness portions of the cartilage are lost, and the subchondral bone plate is exposed and is smoothened by friction, giving it the appearance of polished ivory **(bone eburnation)**

الغشاء يلي مفروض يمنعها من الاحتكاك مب موجود ، فتصير العظام تحكتك مع بعض فيصير شكلها كانها مصقولة

- Small fractures can dislodge pieces of cartilage and subchondral bone into the joint, forming loose bodies **(joint mice).** (That runs in MULTIPLE Directions)

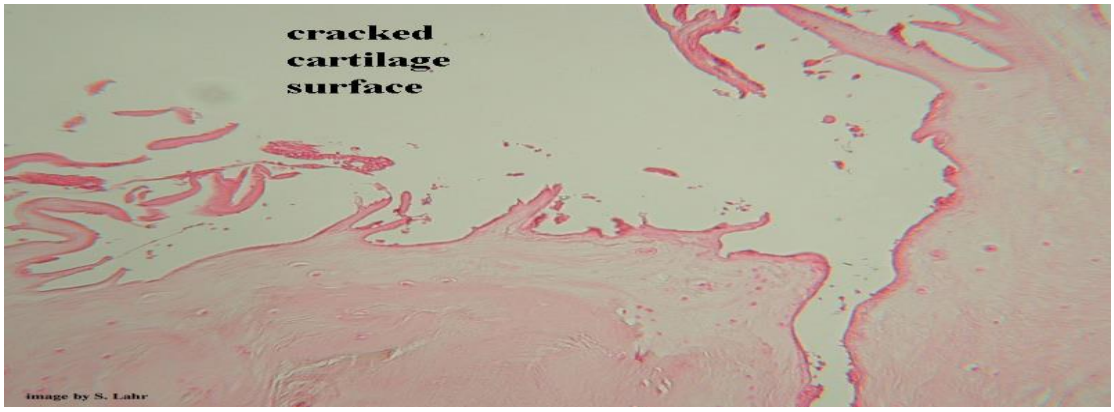
- The fracture gaps allow synovial fluid to be forced into the subchondral regions to form fibrous walled **cysts.**

- Mushroom-shaped **osteophytes** (bony outgrowths) develop at the margins of the articular surface

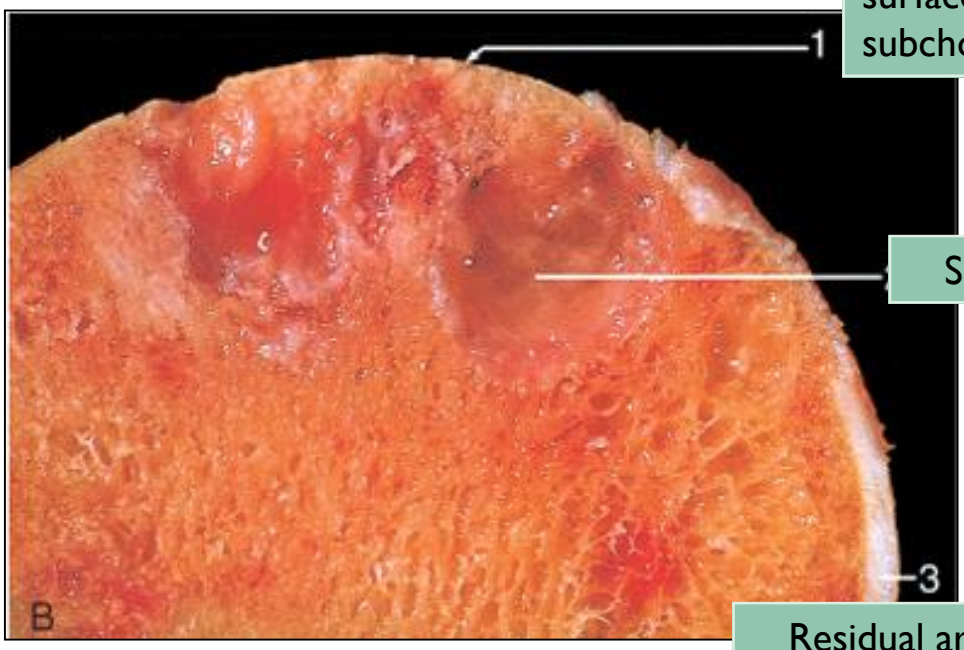


Osteoarthritis. **:** Histologic demonstration of the characteristic fibrillation of the articular cartilage.

Cracking and fibrillation of cartilage



SEVERE OSTEOARTHRITIS



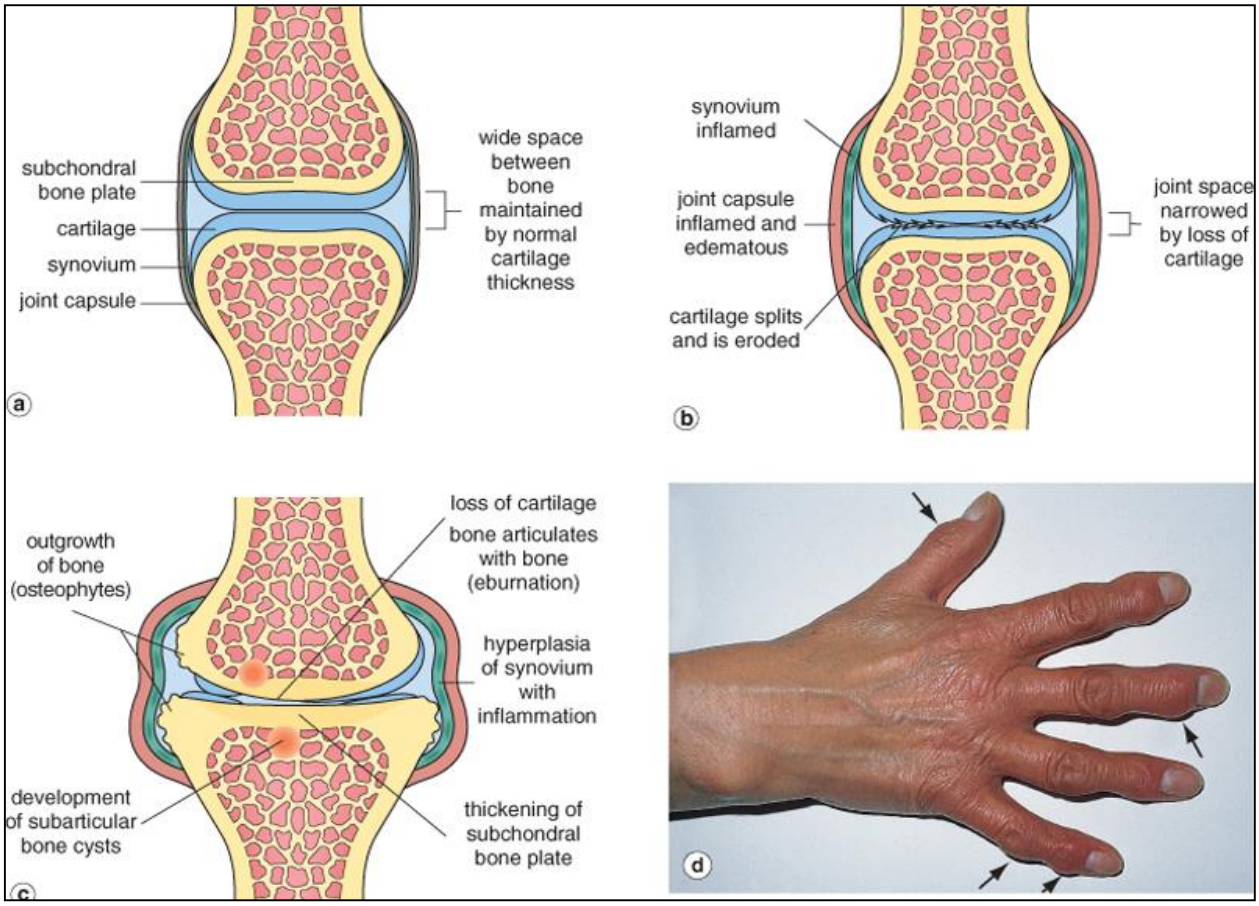
Eburnated articular surface exposing subchondral bone

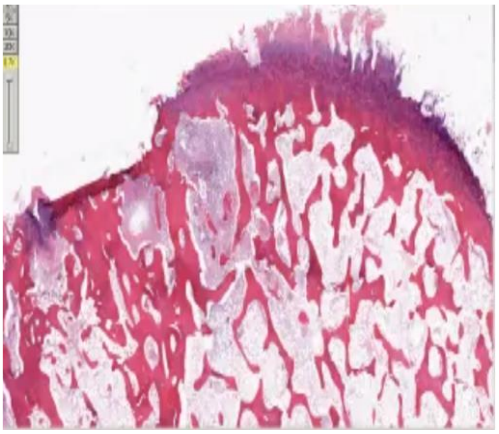
Subchondral cyst

Residual articular cartilage

PATHOLOGICAL CHANGES IN OSTEOARTHRITIS

Very good
Video ☺





Heberden's nodes (osteophytes on the distal interphalangeal joints of the fingers)

Bouchard nodes (osteophytes on the metacarpophalangeal (proximal) joints of the hand)

CLINICAL COURSE

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

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

- Hips, knees, lower lumbar and cervical vertebrae, proximal and distal interphalangeal joints of the fingers, first carpometacarpal joints, and first tarsometatarsal joints of the feet are commonly involved. **Heberden nodes** in the fingers, representing prominent osteophytes at the distal interphalangeal joints, are characteristic in women.

N.B :- Here the DIP & PIP (in Hand) are NOT spared , while in Rheumatoid arthiritis , the DIP is spared and it affects PIP.

COURSE & PROGNOSIS

- Slowly Progressive

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

RHEUMATOID ARTHRITIS

❖ **What is Rheumatoid Arthritis?**

- RA is a systemic, chronic inflammatory autoimmune disease affecting many tissues but principally attacking the joints.
- It causes a nonsuppurative proliferative synovitis that frequently progresses to destroy articular cartilage and underlying bone with resulting disabling arthritis.
- Its an Autoimmune , So of course it will be more prevalent in Women more than men
- The peak incidence is in the second to fourth decades of life, but no age is immune.

❖ **What are the pathogenesis?**

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

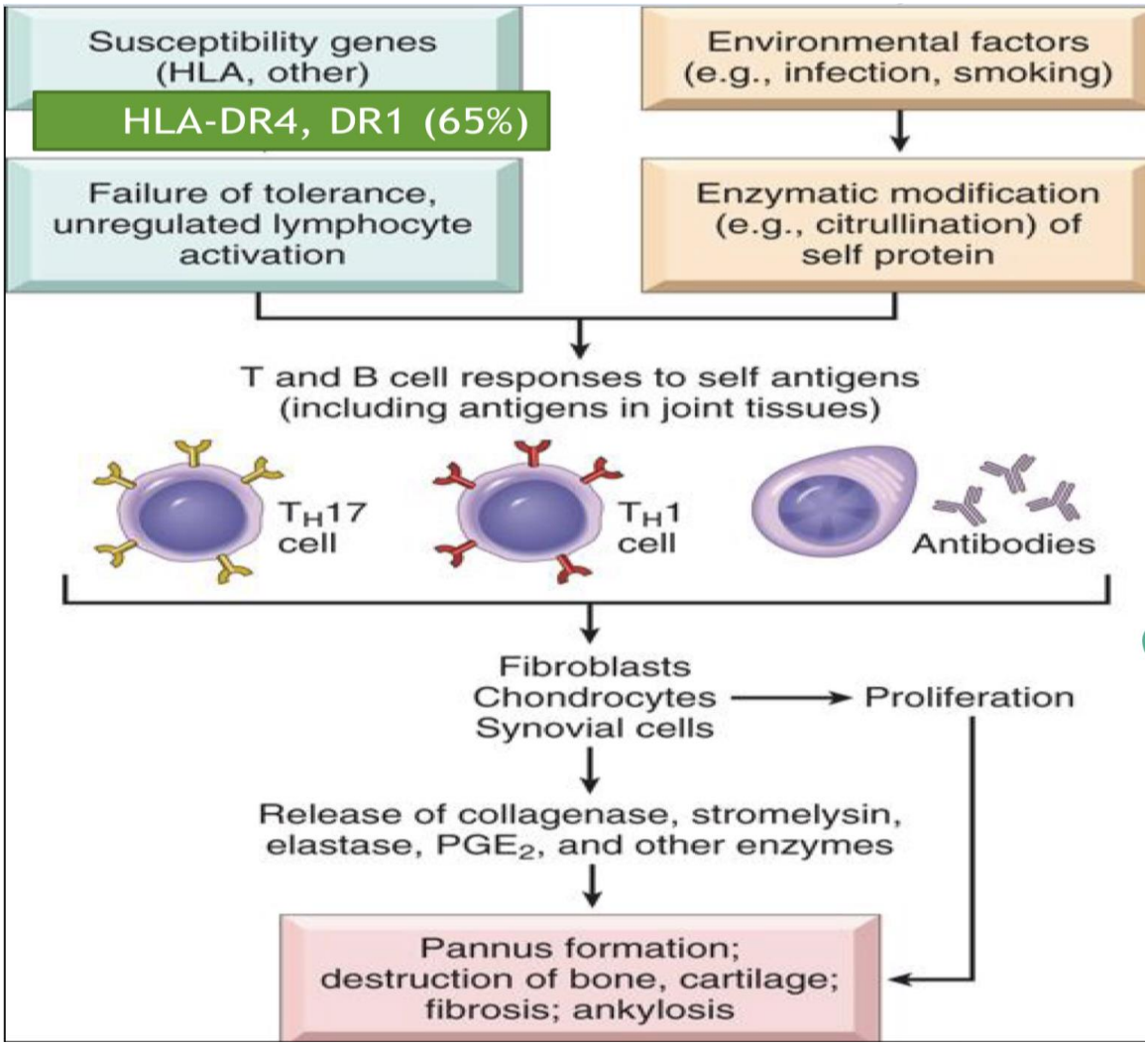
❖ **Genetic factors**: Mainly involves HLA-DRB1

❖ **Environmental factors:** Many candidate infectious agents whose antigens may activate T or B cells have even considered, but none has been conclusively implicates .

- 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. However, the role of rheumatoid factor in the pathogenesis of the joint or extraarticular lesions has not been established.

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



RHEUMATOID ARTHRITIS

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 most specific for a diagnosis of rheumatoid arthritis

- ESR and C-reactive protein. (But its not that important as Anti CCP)

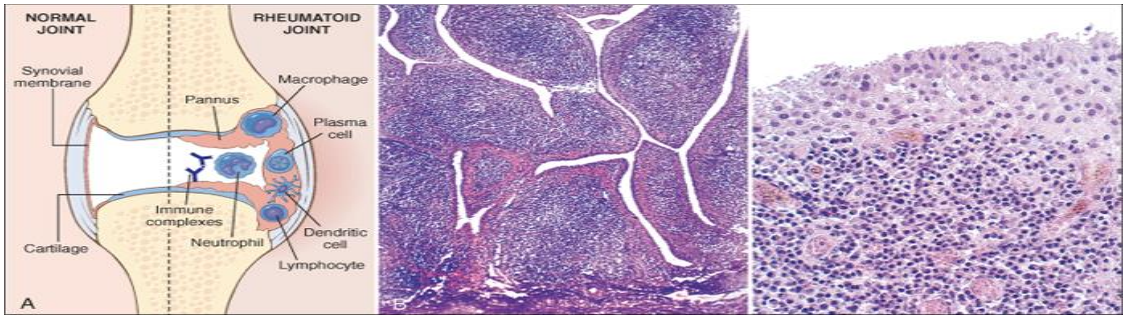
Pathologic Features:

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

Pannus (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

A

dense perivascular inflammatory cell infiltrates

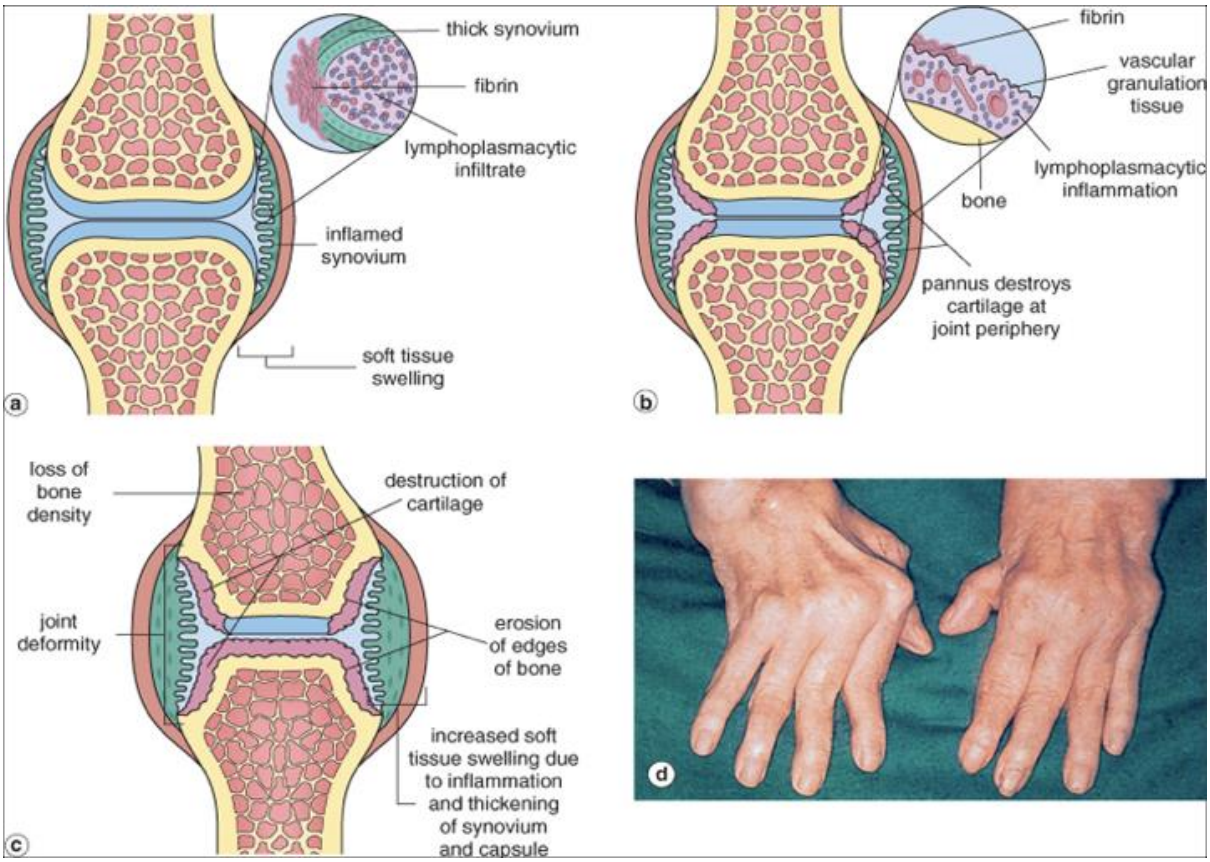
neutrophils and aggregates of organizing fibrin on the synovial surface.

synovial cell hyperplasia and proliferation

B

increased vascularity

Pannus formation



C

increased osteoclast activity in the underlying bone ➔ bone erosion

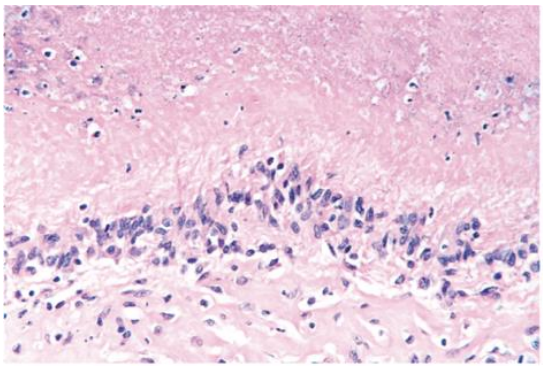
D

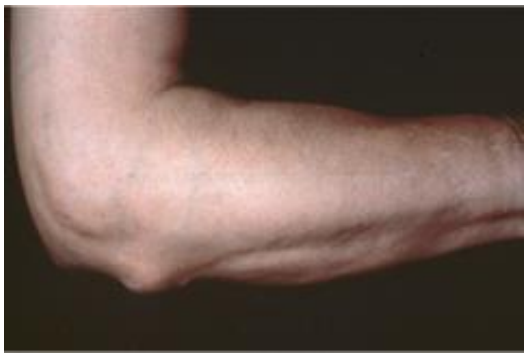
swan neck finger

RHEUMATOID ARTHRITIS

Rheumatoid Subcutaneous Nodules:

- develop in about one fourth of patients
- occurring along the extensor surface of the forearm
- 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





Clinical Features:

- symmetric arthritis, 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.

RA CLINICAL FEATURES

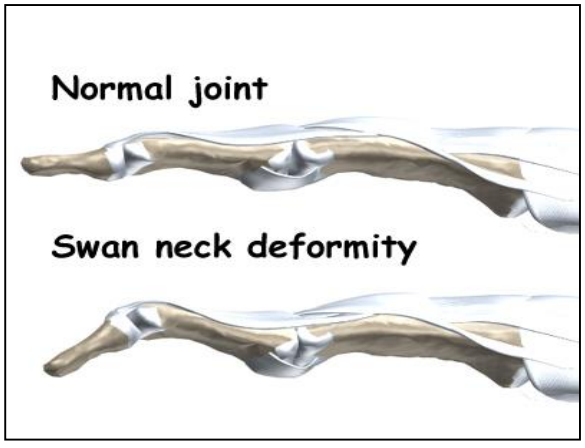
1. symmetric arthritis, principally affecting the small joints of the hands and feet, ankles, knees, wrists, elbows, and shoulders.
2. Most often, the proximal interphalangeal and metacarpophalangeal joints are affected, but distal interphalangeal joints are spared.
3. Axial involvement, when it occurs, is limited to the upper cervical spine; similarly, hip joint involvement is extremely uncommon.
4. Weakness , low grade fever
5. aching and stiffness of the joints, particularly in the morning
6. 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).**

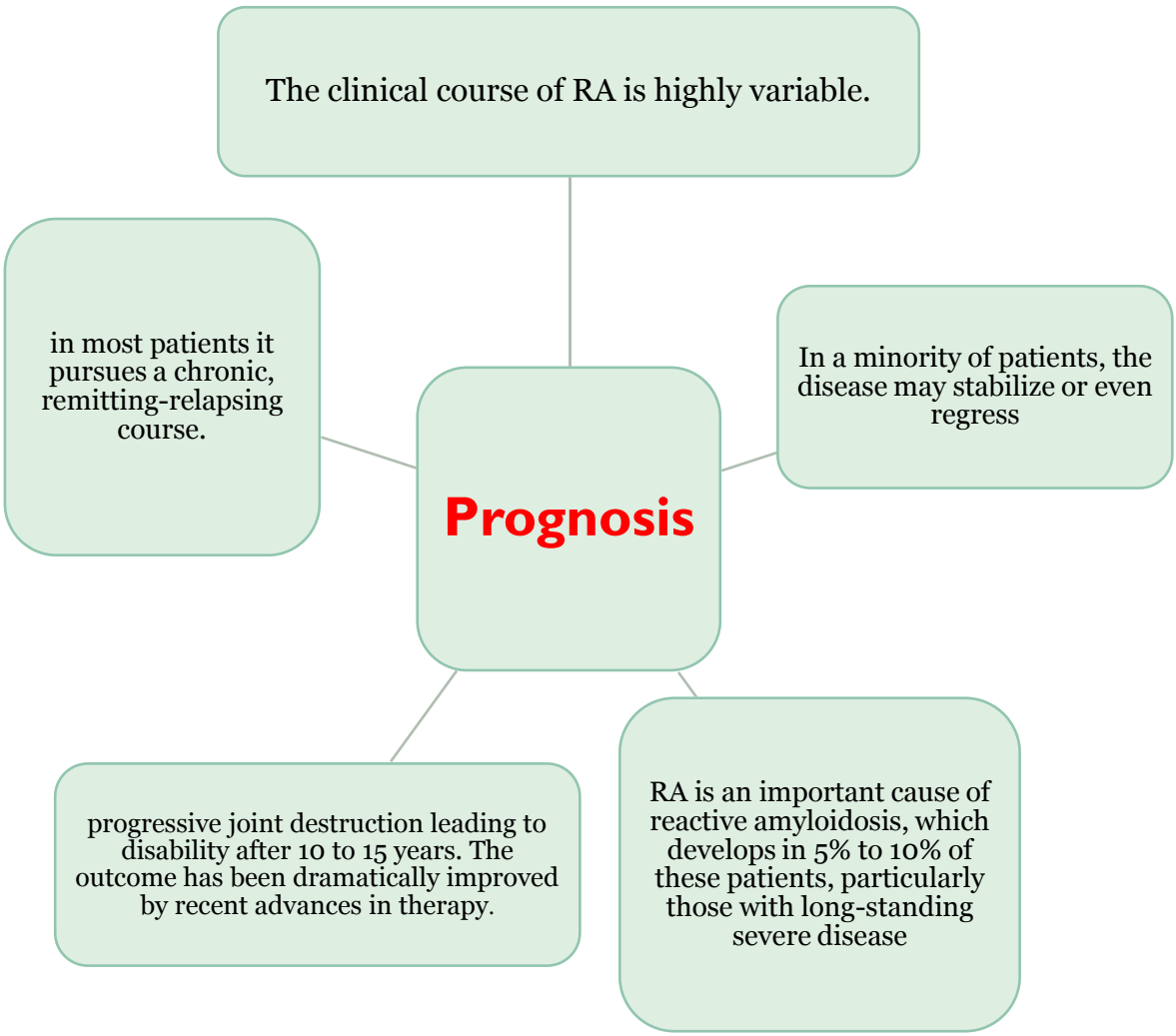


boutonniere deformity

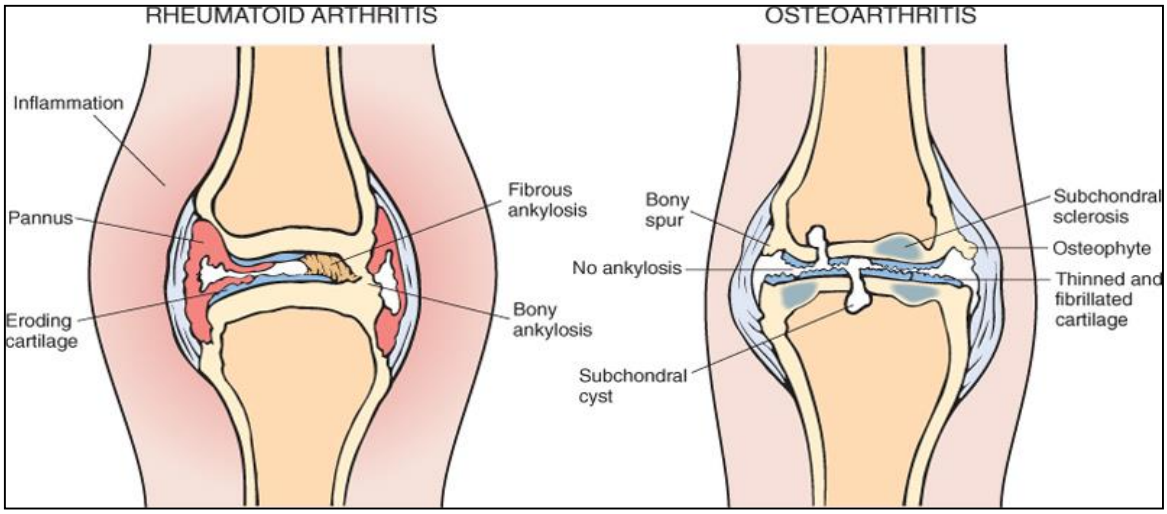
RHEUMATOID ARTHRITIS

X-ray

1. Loss of articular cartilage leading to narrowing of the joint space.
2. Joint effusions.
3. Erosions



COMPARISON OF THE MORPHOLOGIC FEATURES OF RA AND OSTEOARTHRITIS



Comparison of Osteoarthrosis & Rheumatoid Arthritis

	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

Link it with "Gout" from Biochemistry , it will be extremely easy ☺

Gout (monosodium urate crystals)

- Gout affects about 1% of the population, and shows a predeliction for males.(most common in males)
- It is caused by excessive amounts of **uric acid**
- **Monosodium urate crystals** precipitate from supersaturated body fluids and induce an acute inflammatory reaction.
- **What is Gout marked by?**
  1. recurrent episodes of acute arthritis
  2. sometimes accompanied by the formation of large crystalline aggregates called **tophi** (حصوات)
  3. eventual permanent joint deformity.
- **What are the risk factors for gout?**
  1. Obesity
  2. consumption of purine-rich foods (such as meat)
  3. excess alcohol intake
  4. Diabetes
  5. the metabolic syndrome
  6. Renal failure (because there will be underexcretion of uric acid => accumulation of uric acid => hyperuricemia which may lead to gout but not always)

Don't skip the table

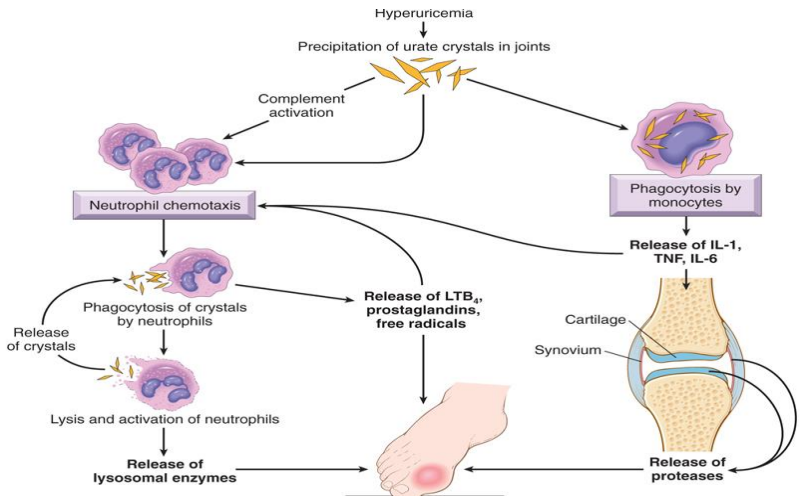
Gout

- Primary (most common) 90%
- Secondary 10%

Table 20–3 Classification of Gout

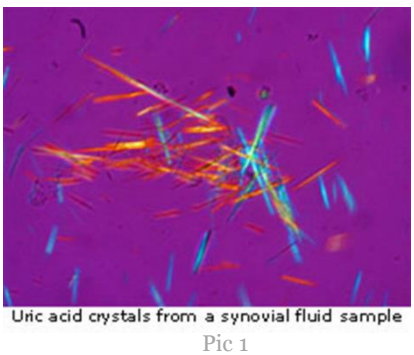
Clinical Category	Metabolic Defect
Primary Gout (90% of cases)	
Enzyme defects—unknown (85% to 90% of cases)	Overproduction of uric acid Normal excretion (majority) Increased excretion (minority) Underexcretion of uric acid with normal production
Known enzyme defects—e.g., partial HGPRT deficiency (rare)	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.

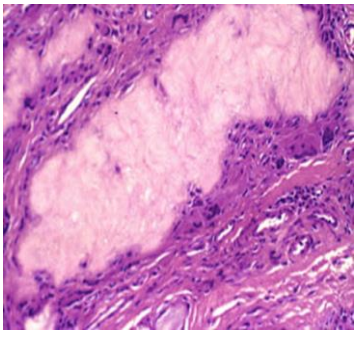


Gout Morphology:

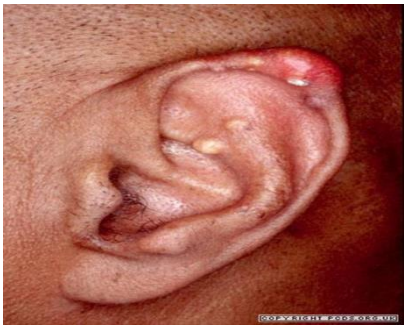
- **Acute arthritis:** is characterized by a dense neutrophilic infiltrate permeating the **synovium and synovial fluid**. **Long, slender, needle-shaped monosodium urate crystals** frequently are.(look at pic 1 **you have to now the shape**)
- **Chronic tophaceous arthritis:** evolves from **repetitive** 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. (look at pic 2)
    - Tophi can appear in the articular cartilage of joints and in the soft tissues, including the ear lobes & nasal cartilages (look at pic 3)


Uric acid crystals from a synovial fluid sample

Pic 1



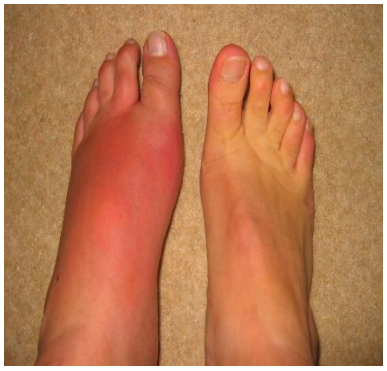
Pic 2

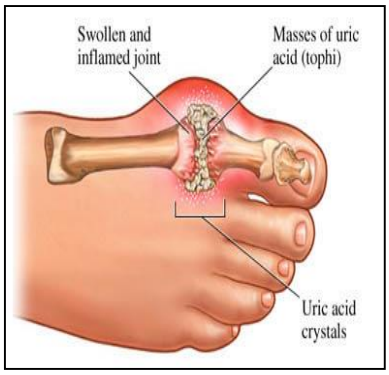


Pic 3

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

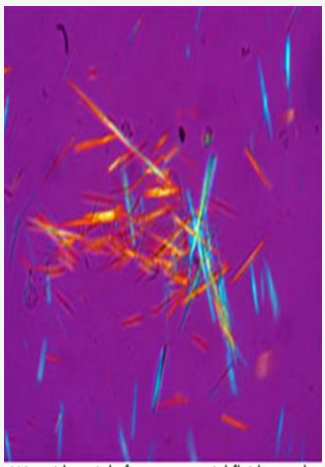
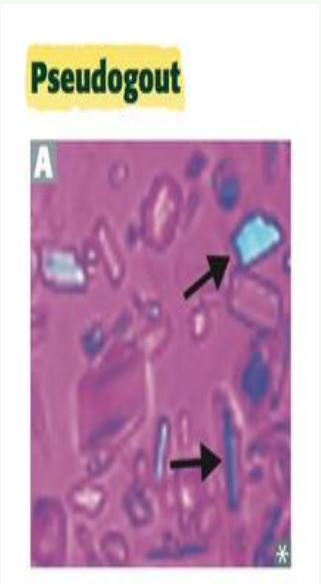




Pseudogout (Calcium pyrophosphate crystals)

- 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:
  1. Sporadic (more common in the elderly).
  2. Hereditary.
  3. Secondary to other conditions, such as previous joint damage, hyperparathyroidism, hypothyroidism, haemochromatosis and diabetes.
- The crystals first develop in the **articular cartilage (chondrocalcinosis**), 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**.*

* في البدايه يتجمع في articular cartilage وهنا ما راح يكون لها اعراض بعدين ممكن تروح joint وتسبب اعراض تشبه gout عشان كذا يكون اسمها pesodogout

Gout	Pseudogout
first metatarsophalangeal joint is most commonly involved	The knee is most commonly involved.
_	X-rays show the characteristic line of calcification of the articular cartilage.
Long, slender, needle-shaped crystals  Uric acid crystals from a synovial fluid sample	rhomboid shaped crystals 
monosodium urate crystals	calcium pyrophosphate crystals

MEMBERS :

Males:

-Leader : فيصل الطحان

عبدالجبار اليماني

محمد باحاذق

أحمد الراشد

عبدالله بالعبيد

عبدالله السرجاني

أحمد الحربي

أنس السيف

فايز الدرسوني

داود إسماعيل

فهد الفايز

محمد بن معيوف

فهد النحابي

سعد الفوزان

سيف المشاري

تميم الوهيبي

رشيد البلاع

عبدالله المعيذر

محمد الأصقه

محمد الصويغ

عبدالعزيز المهنا

نواف السبيعي

خالد العقيلي

Females:

-Leader : بثينة آل ماجد

-روان الحربي

-وفاء العتيبي

-الجوهرة الشنيفي

-رزان الزهراني

-رهف الشمري

-روان مشعل

-منيرة المسعد

-لميس السويلم

-نوف العتيبي

-رزان الزهراني

-هديل عورتاني

-فاطمة بالشرف

-ابتسام المطيري

-رناد الفرم

-غرام جليدان

-بلقيس الراجحي

-نورة القاضي

-آلاء الصويغ

-ريم القحطاني

Gently contact us if you have any questions/comments and suggestions:

* EMAIL: pathology437@gmail.com
* TWITTER : @pathology437

GOOD LUCK! ☺

Resources:-

1- Females slides
2- Robbins reference book

Pathology

teamwork 437