Inflammatory Arthritis

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Anatomy of a synovial joint

- Inner lining layer just inside the capsule is **synovium.**
- Synovium secretes **synovial fluid**
- Synovial membrane has two type of cells:
  - **Type A cells**: macrophage like cells, synthesize and release lytic enzymes, phagocytose joint debris.
  - **Type B**: **predominant** cell type. **Fibroblast like** cells, synthesize and secrete hyaluronic acid and glycoproteins of synovial fluid.
- Viscous and lubricating property of synovial fluid: **hyaluronic acid**.
- Synovial fluid has **variable viscosity**: viscosity decrease with increased rates of shear(increased speed of joint movement)

Examination of synovial fluid

	Non-inflammatory	Inflammatory	Septic	Hemorrhagic
Appearance	Yellow	Yellow	Purulent	Bloody
Clarity	Clear	Cloudy	Opaque	Opaque
Viscosity	High	Decreased	Decreased	Variable
Cell count	200-2000 (< 25 % PMN)	2000-75000 (> 50 % PMN)	80,000 (> 80 % PMN)	RBC >> WBC
Ex	Osteoarthritis Trauma Osteonecrosis	RA Reiter's syndrome SLE Gout & pseudogout Fungal / TB/ Viral	Bacterial arthritis	Trauma Fracture Ligament tear Hemophilia PVNS Charcot's

Inflammatory arthritis

- Condition of joints that involve immune system and cause inflammation.

1. Rheumatoid arthritis
2. Reiter's syndrome(conjunctivitis, urethritis and synovitis)
3. Ankylosing spondylitis
4. Psoriatic arthritis
5. Reactive arthritis
6. Gout and Pseudogout
7. Lupus arthritis

Features of inflammatory arthritis

1. **Signs of inflammation**: erythema, warmth, pain, swelling
2. **Systemic symptoms**:
   a) Prolonged morning stiffness, usually lasting several hours
   b) Fatigue, weight loss, low grade fever
3. **Laboratory evidence of inflammation**:
   a) Elevated ESR b) elevated CRP
   c) Thrombocytosis d) anaemia of chronic disease
4. **X-ray**: rarefaction,
   - In case of non-inflammatory arthritis: sclerosis.

Rheumatoid Arthritis

- **Chronic multisystem disorder**, mainly affects the joints
- **Non suppurative, proliferative and inflammatory synovitis.**
- Progress to **destruction of articular cartilage** and ankylosis of joint.
- **Women** > men, 3 times
- Older women > 60 yrs are 6 times more involved than younger women
- Usually **starts with small joints of hand** (MCP and PIP) **and feet** (MTP and IP).
- Large joints are involved later.

Articular manifestations of RA

1. **Hands**
   - Mc involves **MCP** and **PIP** jts
   - **Spares DIP** jt.
   - Produce **opera glass hand deformity**.
2. **Feet**
   - **MTP** jts are mc involved
3. **Large joints**:
   - **Knee, elbow, hips, shoulder**
   - Occurs later than small joints

4. **Wrist**: involved in most patients,

- **Intercarpal ligament disruption**, especially radioscaphocapitate ligament: **rotatory instability of the carpus.**
- **Distal radioulnar joint stabilizing ligaments are destroyed**, leading to **ulnar head dorsal dislocation** and subluxation of the extensor carpi ulnaris tendon with secondary **ulnar translocation of the carpus.**
- **Radial deviation of hand**

5. Other joints:

- **Upper cervical spine** – facet joints with **atlantoaxial subluxation**.
- **Temporomandibular joint**.

Deformities in RA

- **Hand**

1. **Boutonniere deformity**: **flexion contracture of PIP** joint and **extension at DIP jt.**
2. **Boutonniere deformity of thumb**: **flexion at MP joint** and **hyperextension at IP jt**.
3. **Swan neck deformity**: **hyperextension of PIP jt** and **flexion at DIP jt**.
4. **Ulnar drifting of fingers** at **MCP** joint.
5. **MCP** joint **palmar subluxation or dislocation.**
6. **Z- deformity**: **radial deviation of wrist with ulnar deviation of**

- **Elbow**: **flexion deformity**
- **Knee**
  - **Early- flexion deformity**
  - **Late- triple deformity**(flexion, posterior subluxation, external rotation)
- **Ankle** : **Equinus**
- **Foot**: **hallux valgus, hammer toe**.

Extraarticular manifestations of RA

- **Tendon** involvement:
  - **Flexor and extensor tendon tenosynovitis** in the digits, palm, and over the wrist flexor and extensor surfaces.
  - **Erosive and attritional changes** and **tendon ruptures**.
- **Subcutaneous nodules**
  - Seen only with **RA factor positive patients**.
  - May occur anywhere
  - Most commonly on **extensor surface of forearm, joints or over pressure points.**

- **Pulmonary**
  - Pleural effusion
  - Lung nodules
  - Diffuse interstitial fibrosis
- **CVS**
  - Pericardial effusion
  - Constrictive pericarditis
- **Eye**
  - Sjogren syndrome- keratoconjunctivitis sicca
  - Scleritis

- **Neurologic**
  - **Peripheral nerve entrapment syndrome**: carpal tunnel syndrome(median nerve), tarsal tunnel syndrome(posterior tibial nerve)
  - **Mononeuritis multiplex**
- **Systemic manifestations:**
  - Fatigue, weight loss, low grade fever
  - More common with **RA factor positive.**

2010 American College of Rheumatology/ European League Against Rheumatism classification criteria for rheumatoid arthritis

- **Target population** (Who should be tested?): Patients who

1) have **at least 1 joint with definite clinical synovitis (swelling)**

2) with the **synovitis not better explained by another disease**

- Criteria are aimed at **classification of newly presenting patients**
- Classification criteria for RA (score-based algorithm: add score of categories A–D; a **score of 6/10 is needed for classification of a patient as having definite RA)**

A. Joint involvement	
1 large joint	**0**
2-10 large joints	**1**
1-3 small joints (with or without involvement of large joints)	**2**
4-10 small joints (with or without involvement of large joints)	**3**
> 10 joints (at least 1 small joint)	**5**
B. Serology (at least 1 test result is needed for classification	
Negative RF and negative ACPA	**0**
Low-positive RF or low-positive ACPA	**2**
High-positive RF or high-positive ACPA	**3**
C. Acute-phase reactants (at least 1 test result needed)	
Normal CRP and normal ESR	**0**
Abnormal CRP or abnormal ESR	**1**
D. Duration of symptoms	
< 6 weeks	**0**
> 6 weeks	**1**

- **Large joints** refers to **shoulder, elbow, hip, knee, and ankle joints**.
- **Small joints** refers to the **metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists**.
- **Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are excluded from assessment**

Rheumatoid factor

- **Autoantibody, IgM, directed against the Fc region of IgG.**
- **Not specific** for rheumatoid arthritis
- 70 % to 90% patients of RA have positive test for RA factor.
- Can also be seen in **autoimmune disorders, inflammatory disease and chronic infections**
- Early in the disease the prevalence of positive RA factor is lower(50 %), therefore **cannot be used for screening**
- **A negative test should not rule out rheumatoid arthritis**.

- **Presence of RF is assoc. with**
  - more severe articular disease
  - Extraarticular manifestations(multisystem disease).
- **Levels of RF parallels disease activity**.

Anti-CCP: Anti-cyclic citrullinated peptide antibody

- **More specific** than RF for RA.
- **Positive very early in the disease.**

Radiological features of RA

- Reduced joint space
- Erosion of articular margins
- Subchondral cysts
- **Juxtaarticular rarefaction or osteopenia**(osteoporosis): **earliest finding.**
- Soft tissue shadows at the level of joint because of joint effusion or synovial hypertrophy.

- **Felty's syndrome**: triad of:
  - Chronic rheumatoid arthritis
  - Splenomegaly
  - Neutropenia

DMARD nomenclature

- **Synthetic DMARDs**
  - Conventional synthetic DMARDs (csDMARDs): For example, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine.
  - Targeted synthetic DMARDs (tsDMARDs): For example, tofacitinib, baricitinib.
- **Biological DMARDs**
  - Biological originator DMARDs (boDMARDs)
  - Biosimilar DMARDs (bsDMARDs)

Treatment of RA

- **Rest and activity modification**
- **NSAID**'s
- **Disease modifying agents**
- **Steroids**: in case of mononeuritis multiplex, endocarditis, pericarditis, scleritis.
- **Immunomodulators** like **anti- TNF (Etanercept, infliximab)**
- **Physiotherapy**
- **Surgery**: correction of deformities(hand and feet), synovectomy(knee jt) , arthroplasty(knee or hip jt, advanced disease)

Poor prognostic factors

- Moderate (after csDMARD therapy) to high disease activity according to composite measures
- High acute phase reactant levels
- High swollen joint counts
- Presence of RF and/or , anticitrullinated protein antibody, especially at high levels
- Combinations of the above
- Presence of early erosions
- Failure of two or more csDMARDs.

EULAR 2016 recommendation for treatment of RA

1. Therapy with DMARDs should be started as soon as the diagnosis of RA is made.
2. All DMARDs irrespective of type of drug, enable a better long-term outcome on early, compared with delayed institution.
3. Any chronic arthritis, even if undifferentiated, requires appropriate treatment, including DMARD therapy.
4. Treatment target should be rapidly attained rather than aiming to achieve it in a more distant future: most patients who do not attain significant improvement within 3 months, or do not achieve the treatment target within 6 months, will not reach the desired state subsequently.
5. Monitoring should be frequent in active disease (every 1–3 months); if there is no improvement by at most 3 months after the start of treatment or the target has not been reached by 6 months, therapy should be adjusted.

6. MTX should be part of the first treatment strategy:
   - MTX reduce comorbidities and mortality in RA.
   - Possibility to individualise dose and method of administration.
   - Not to exceed 25mg/week.
7. In patients with a contraindication to MTX (or early intolerance), leflunomide or sulfasalazine should be considered as part of the (first) treatment strategy.
8. Short-term GC should be considered when initiating or changing DMARDs, in different dose regimens and routes of administration, but should be tapered as rapidly as clinically feasible.

Seronegative spondylo-arhtropathies(SSA)

- Seronegative means **absence of rheumatoid factor**
- Include:
  1. Ankylosing spondylitis
  2. Reactive arthritis: Reiter's syndrome and enteritis associated arthritis.
  3. Psoriatic arthritis
  4. Arthritis associated with inflammatory bowel disease (Enteropathic arthritis)

Features of SSA: share common clinical and genetic features:

- Involvement of the axial skeleton (sacroiliac joints and spine) > Peripheral arthritis,
- Enthesitis and dactylitis,
- Acute anterior uveitis,
- Associated psoriasis or inflammatory bowel disease
- Presence of the HLA-B27 antigen, and
- **Absence of RF**

- Depending on the predominant clinical manifestations, SSA can be classified as

1. **Axial SSA** (characterized by predominant involvement of the spine and/or sacroiliac joints): Axial SSA is characterized by chronic inflammatory back pain and based on clinical and radiological features can be separated into two groups
   i. **Ankylosing spondylitis (AS)**: defined by the presence of definite structural changes on radiographs in the sacroiliac joints, and
   ii. **Nonradiographic axial SSA**: defined by the presence of sacroiliac inflammation as detected by MRI or the presence of HLB27 in combination with the presence of features typical of spondyloarthritis.

2. **Peripheral SSA** (peripheral arthritis, enthesitis, and/or dactylitis)

Ankylosing spondylitis (Marie- strumpell disease)

- Usually begins in **2nd to 3rd decade**
- **Male**: female = 2-3:1
- Upto **95%** cases are positive for **HLA B27.**
- Joints involved:
  - **Mc involve SI joint and axial skeleton:** Begins in SI joint, extends upwards to involve spine
  - Peripheral joints : involved in 1/3rd of patients.
  - Hips and shoulder are involved in severe cases.
  - **Hip is mc involved peripheral jt.**
  - May also involve knee and ankle joint.

Pathology of AS

- **Enthesitis**: inflammation of insertion of tendons, ligaments or joint capsule.
- **Sacroilitis is earliest manifestation**
- Involvement of **costovertebral joints**: *diminished chest expansion*
- **Extraarticular manifestations**: **anterior uveitis, aortic valve disease, carditis and pulmonary fibrosis**
- Pathological changes progress in **three stages**:
  1. Inflammation with granulation tissue formation and erosion of adjacent bone.
  2. Fibrosis of granulation tissue
  3. Ossification of fibrous tissue, leading to ankylosis of joint.

Clinical features

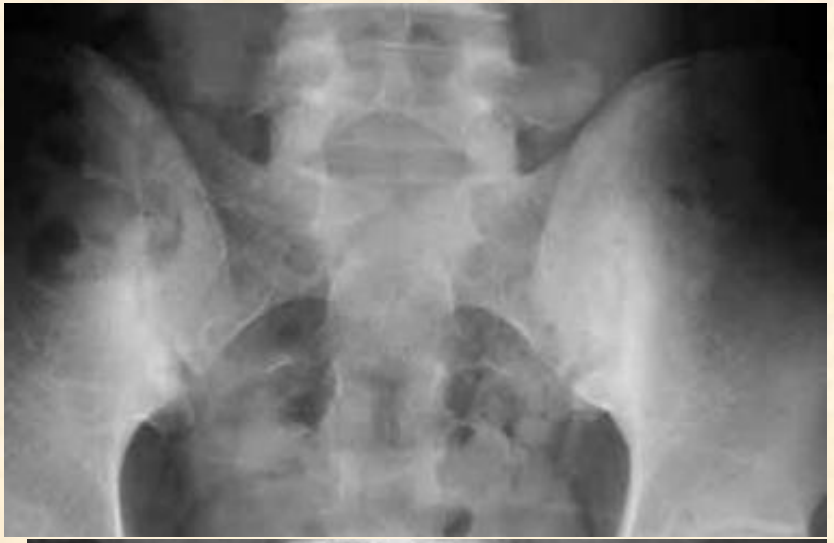
- **Low back pain** of insidious onset
- Duration **less than 3 months**
- Significant **morning stiffness** and **improvement with exercise.**
- Significant pain relief in response to NSAID's
- *Limited chest expansion*
- ***Diffuse tenderness over spine and sacroiliac joints***
- *Loss of lumbar lordosis, increased thoracic kyphosis*
- ***Decreased spine movements in all directions***

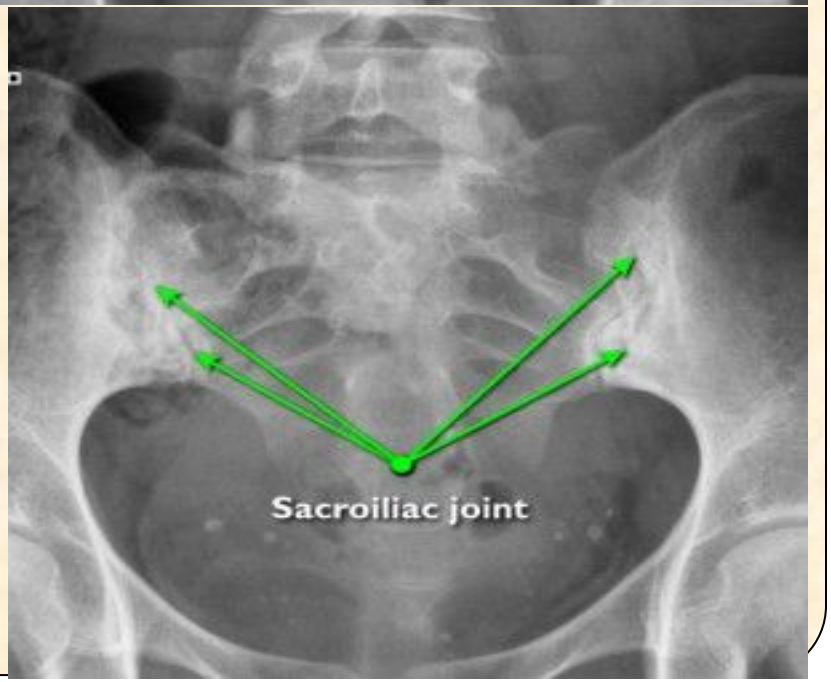
Radiological features of AS

- **Sacroilitis** is most consistent:

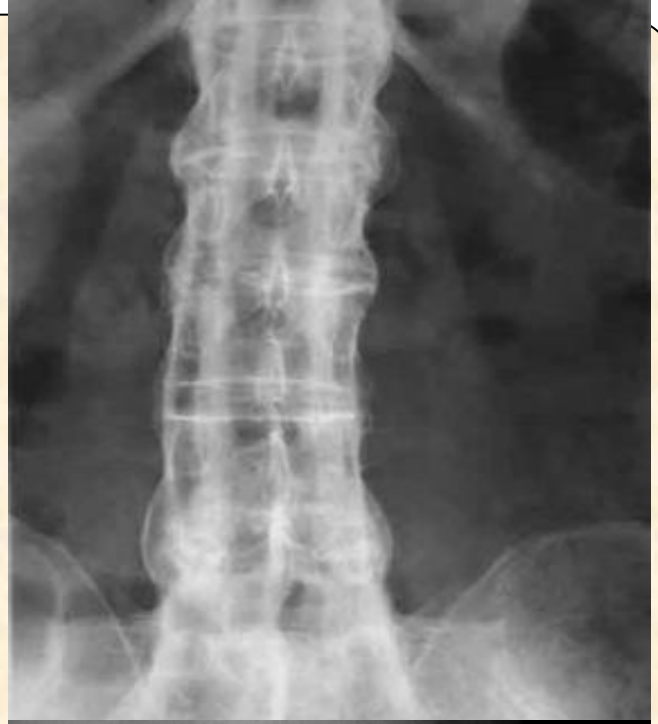
1. Sclerosis of articulating surfaces of SI joints
2. Widening of SI joint space: erosion of joint surface
3. Bony ankylosis of SI joint

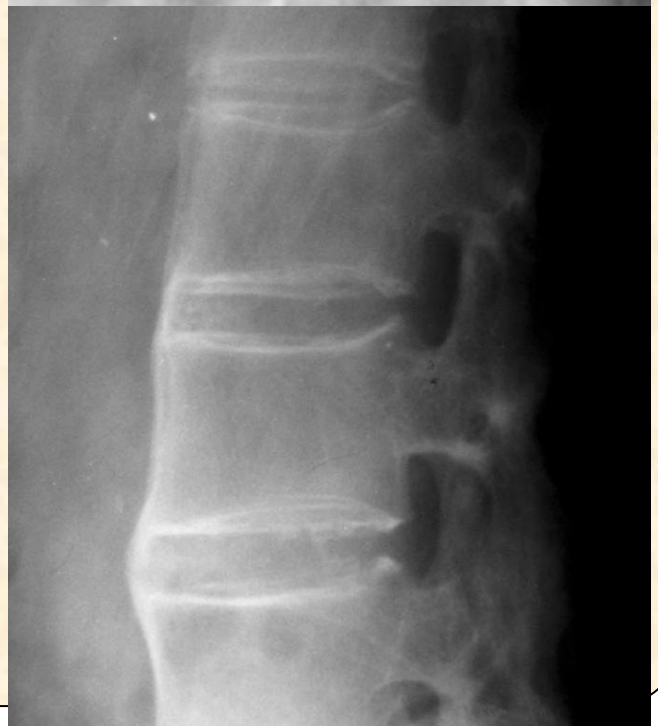
- **Calcification of sacroiliac and sacrotuberous ligament**





- **Lumbar spine**:
  - **Squaring of vertebrae**: Calcification of ligaments
  - **Loss of lumbar lordosis**
  - Bridging osteophytes (**syndesmophytes**)
  - **Bamboo spine**: ossification of outer fibres of annulus fibrosus





- **Enthesopathy:**
  - Calcification at attachment of tendons and ligaments, particularly pelvis and around heel.

- **MRI**
  - Give **early** and **more accurate** diagnosis, when x-rays are normal
  - Identify early *intraarticular inflammation*, *cartilage changes* and *bone marrow edema.*

Diagnostic Criteria:
Modified New York criteria

1. **Radiological criterion**: Bilateral sacroiliitis grade II or unilateral sacroiliitis grade III to IV.
2. **Clinical criteria**

(a) Low back pain and stiffness of at least 3 months duration improved by exercise and not relieved by rest.

(b) Limitation of motion of the lumbar spine in both the sagittal and the frontal planes.

(c) Limitation of chest expansion relative to values normal for age and sex.

Definite AS is diagnosed if the radiological criterion plus 2 of the 3 clinical criteria are present.

Complications of AS

- Spinal fractures
- Hyperkyphosis
- Spinal cord compression
- Lumbosacral nerve root compression

Treatment

- Measures to maintain satisfactory posture and preserve movement:
  - **Spine exercise**
- Drug therapy
  - **NSAID's** : mc used is **indomethacin**
  - **Phenylbutazone**: most effective but can cause **aplastic anemia**, so reserved for non-responders
  - **DMARD's**: for severe cases
  - **TNF inhibitors**: severe cases.
- **Surgery**: to correct deformity

Psoriatic Arthritis

- Occurs in **5% patients** of psoriasis.
- Usual age of onset: **30-50 yrs**
- No sex predilection
- **Patterns of joint involvement**:
  1. Arthritis of **DIP jts**
  2. **Asymmetrical oligoarthritis: mc pattern**
  3. **Symmetrical polyarthritis**: similar to RA
  4. **Axial involvement**: similar to AS
  5. **Arthritis mutilans**: severe chronic absorptive arthritis.

- **Shortening of digits** called **telescoping** bcz of **osteolysis (absorptive arthritis)** is characteristic: causes severe deformity of hand (**opera glass hand**) and feet (**opera glass foot**).
- **Greater tendency for fibrous and bony ankylosis** than RA.
- **Treatment:**

1. **Anti- TNF agents**: infliximab, etanercept. For long standing resistant cases.
2. **Methotrexate: DOC**.
3. Other drugs: sulfasalazine, cyclosporine, retinoic acid, Psoralen and UV-A.

Gout

- Endpoint of group of disorders that produce **hyperuricemia.**
- Transient attacks of acute arthritis initiated by **crystallization of monosodium urate into joints.**
- Eventually leads to chronic gouty arthritis with **deposition of masses of urates in joints and other sites**, creating **tophi.**
- Mc joint involved is **MTP joint of great toe**.
- **Males** > females.
- Usually **> 35 years** age

Clinical features of gout

A. **Acute Arthritis**:

- mainly affects **peripheral joints** like joints of toes, tarsus, ankle and small joint of hands.
- **First attack** is usually in **MTP jt of great toe**.
- Occurs in *recurrent attacks*
- Onset is **sudden**, affected joint is **swollen, red and glossy**.
- Severe pain with restriction of movement
- **Joint is normal between attacks**.

B. **Chronic gout**:

- **several joints** may be affected together
- Joints are **thickened, nodular and painful on movement**.

C. **Bursitis**

- **Olecranon bursa** is mc affected.
- ***Palpable deposits of uric acid salts***.

D. **Tophi:**

- Pathognomic.
- **Large aggregations of urate crystals surrounded by: macrophages, lymphocytes and large foreign body giant cells.**

- **Tophi are seen in**:
  - Articular cartilage of joints
  - Periarticular: ligaments
  - Tendons (Achilles tendon)
  - Soft tissues
  - Ear lobes
  - Synovial fluid
  - Skin of finger tips, palms and sole.

Diagnosis of gout

- **Definite diagnosis**: Examination of synovial fluid or tophi with **polarized light microscope** for **monosodium urate crystals**
  - These crystals are **strongly negative birefringent, bright yellow, needle shaped objects.**
- **Serum urate levels: not diagnostic**
  - can be normal at time of acute attack or in between attacks,
  - role only in monitoring effect of urate lowering drugs
- **Synovial fluid examination**:
  - Moderately elevated leucocytes: 500-80000 cells/Ul
  - Predominantly PMN

Radiological features

- Acute gout: no x-ray changes
- **Chronic gout:**
  - **Peri-articular erosion**.

Treatment of gout

- **Acute attack**:

1. **NSAID's: DOC**
2. **Colchicine**: fastest acting drug, reserved for patients in whom NSAID's are contraindicated.
   - can cause GI disturbance
3. **Prednisolone**: orally, in case of no response to NSAID's and cholchicine

- **Chronic gout:**

1. **Allopurinol: DOC**
2. Other drugs: probenacid, sulfinpyrazone, febuxostat.

Pseudogout

- **Calcium pyrophosphate dihydrate(CPPD) arthropathy**
- Involves **large joints: knee jt is mc involved**
- Other jt: wrist, elbow, shoulder, ankle
- **Small joints involvement is uncommon.**
- Age> 60 yrs
- Presents as:
  - **Asymptomatic chondrocalcinosis**
  - **Acute synovitis- Pseudogout**
  - **Chronic pyrophosphate arthropathy**.

- **Radiological feature**:
  - **Chondrocalcinosis**: seen as **puctate and/or linear radiodense** deposits in **fibrocartilagenous joint menisci or articular hyaline cartilage**.
- **Synovial fluid polarized light microscopy**: **weakly positive birefringent rhomboid crystals of CPPD.**
- **Associated with certain disease**:
  - Primary hyperparathyroidism
  - Hypomagnesemia
  - Hypothyroidism
  - Hemochromatosis
  - Hypophosphatasia

Hemophilic arthritis

- **Initial stage**: hemarthrosis produce a warm, tensely swollen and painful joint.
  - Blood in the joint is gradually resorbed and joint function return to baseline in 2-3 weeks
- **Recurrent bleeding** into joint causes **chronic arthritis**.
- **Knee** joint> ankle> elbow> shoulder> hip joint
- **Pseudotumor**: when bleeding involves **periosteum or bone**:
  - Children: distal to elbow and knee, good response to treatment
  - Adults: femur and pelvis, refractory to treatment.

- **Bleeding in muscles**: iliopsoas and gastrocnemius
- **Radiological features**

1. Osteoporosis
2. Epiphyseal overgrowth
3. Subchondral cysts
4. Patellar squaring
5. Elbow- trochlear widening
6. Knee- intercondylar notch widening
7. Ankylosis or fibrous pseudoarthrosis.
8. Degenerative joint disease(sec OA)

Thank you