Medicine TEAM 437

MED437 KING SAUD UNIVERSITY

Osteoarthritis & Gout

Objectives :

Osteoarthritis:

- no objectives were found.

Gout

- Describe clinical presentation of gout
- Identify drug & non-drug risk factors for gout
- Compare treatment options for acute gout attacks
- Describe options for control of hyperuricemia / prophylaxis of gout attacks

Done by :

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Resources :

Doctors slides + notes: Rizwan Mansoor M.D.

Books: Kumar, Step up, MKSAP

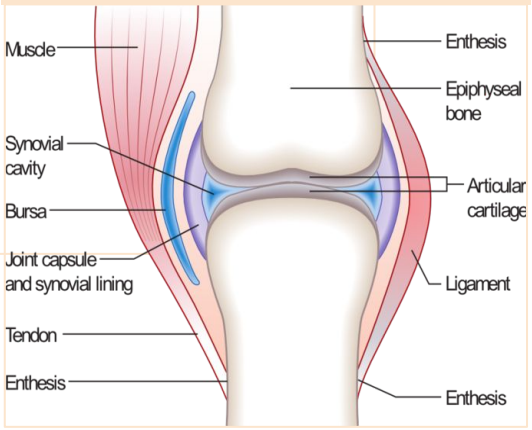
Normal Synovial Joint structure:

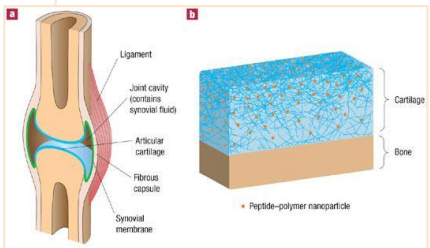
The type of joint that gets affected by OA

Consist of:

- Articular cartilage
- Subchondral bone
- Synovial membrane
- Synovial fluid
- Joint capsule

Synovial joint anatomy





Synovial Cartilage

The Articular surface of synovial joints:

- Articular cartilage (**chondrocytes**) surrounded by extracellular matrix includes proteoglycans and collagen.

The cartilage facilitates joint function and protects the underlying subchondral bone by:

- distributing large loads
- maintaining low contact stresses
- reducing friction at the joint.

It's avascular/no blood supply that's why it gets damage

Synovial Fluid:

- Formed by **synoviocytes**.
  - Synovial cells also manufacture hyaluronic acid (HA, also known as hyaluronate)
    - A glycosaminoglycan that is the major noncellular component of synovial fluid.
- It function:
  - Synovial fluid supplies nutrients to the avascular articular cartilage.
  - provides the viscosity needed to absorb shock from slow movements
  - provides elasticity required to absorb shock from rapid movements

Osteoarthritis

Definition:

Heterogeneous group of conditions resulting in common histopathologic and radiologic changes involving **Entire** joint structures, including:

- the articular cartilage
- the subchondral bone and
- the synovium

Gradual destruction of the joint through the loss of articular cartilage usually seen with periarticular bone response

Epidemiology:

- Internationally, osteoarthritis is the most common articular disease. Estimates of its frequency vary across different populations.
- 80-90% of individuals older than 65 years have evidence of radiographic osteoarthritis.
- The prevalence of osteoarthritis is higher among women than among men.
- Interethnic differences in the prevalence of osteoarthritis have been noted.

Involved joints:

Weight-bearing joints

- The knee
- The hips
- Cervical and lumbosacral spine
- Feet

The wrist, elbows, ankles are usually spared in OA

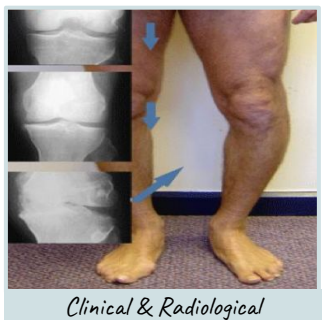
Non weight bearing joints

- The distal interphalangeal (DIP) joints.
- The proximal interphalangeal (PIP) joints.
- The carpometacarpal (CMC) joints.

Pathogenesis:

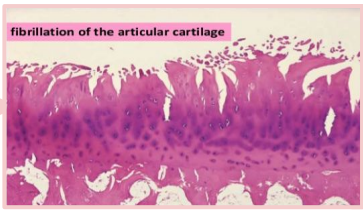
Swelling of the cartilage usually occurs → The level of proteoglycans eventually drops very low, the cartilage softens and lose elasticity and compromising joint surface integrity. → Flaking and fibrillations (vertical clefts) develop along on the surface of an osteoarthritic joint. → Over time, the loss of cartilage results in loss of joint space.

A greater loss of joint space occurs at those areas experiencing the highest loads.



Typically it affects the medial compartment

Clinical & Radiological



Cartilage morphological changes

Bone changes

Bone denuded of its protective cartilage continues to articulate with the opposing surface.

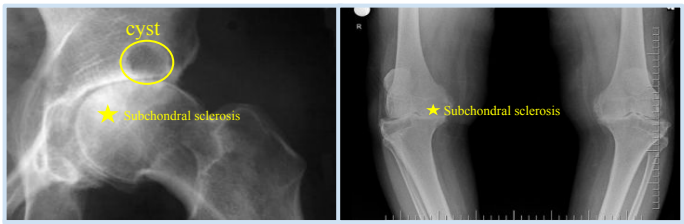
Eventually, the increasing stresses exceed the biomechanical yield strength of the bone.

The subchondral bone responds with vascular invasion and increased cellularity, becoming thickened and dense (a process known as **eburnation**) at areas of pressure.

Subchondral bone undergo cystic degeneration.

Osteoarthritic cysts are also referred to as subchondral cysts, pseudocysts, or geodes and may range from 2 to 20 mm in diameter.

Osteoarthritic cysts in the acetabulum are termed Egger cysts.



Radiographic changes

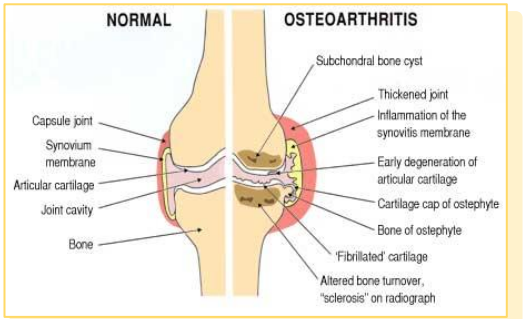
Joint changes

vascularization of subchondral marrow

Osseous metaplasia of synovial connective tissue

Ossifying cartilaginous protrusions lead to irregular outgrowth of new bone (osteophytes).

Fragmentation of these osteophytes or of the articular cartilage itself results in the presence of intra-articular loose bodies (joint mice).



Osteoarthritis Progression:

Stage 1

breakdown of the cartilage matrix occurs.

Stage 2

involves the fibrillation and erosion of the cartilage surface

Stage 3

A chronic inflammatory response in the synovium.

Further progression

The above events alter the joint architecture, compensatory bone overgrowth occurs. joint architecture is changed mechanical and inflammatory stress occurs on the articular surfaces, the disease progresses unchecked.

Etiology:

- **Risk factors:**
  - Age, obesity, trauma, genetics, hypogonadism, muscle weakness, repetitive use, Infection, crystal deposition, acromegaly, previous inflammatory arthritis (burnt-out rheumatoid arthritis)
- **Heritable metabolic causes:**
  - alkaptonuria, hemochromatosis, Wilson disease
- **Hemoglobinopathies :** sickle cell disease, thalassemia
- **Neuropathic disorders leading to a Charcot joint:**
  - syringomyelia, tabes dorsalis, and diabetes.
- **Underlying morphologic risk factors:**
  - Congenital hip dislocation and slipped femoral capital epiphysis
- **Disorders of bone:**
  - Paget disease, avascular necrosis
- **Previous surgical procedures:**
  - meniscectomy
- **Diabetes mellitus**

Case by Dr:
If you see somebody who is 35 years old he has arthritis which come out quick on both knees in some pain and swelling (MC joints) and you do CBC and you find hemoglobin is 19 and hematocrit is like 57 so what's your differential you start thinking of 2ndry causes and you look at LFTs and find liver enzymes are elevated. Why liver enzymes are elevated? you do US to the liver and you find abnormality then you do MRI and you find deposition on the liver whats you diagnose?
Hemochromatosis

Clinical Presentation:

Typical patients present with:

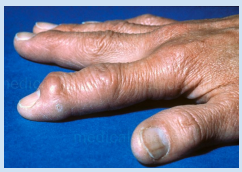
- Mechanical Joint pain which is:
  - Exacerbated by movement
  - Relieved by rest
  - Morning stiffness less than 30 minutes
  - Gelling (Stiffening of joints after a period of rest)
- Deformity in severe cases (mentioned below)

Clinical signs:

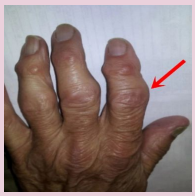
- **Crepitus**
- Limited movement of the joint
- Mild synovitis
- Periarticular tenderness
- Muscle wasting of muscles around the joint

Common bone deformities:

Heberden's nodes
are bony swellings at the DIPJs



Bouchard's nodes
are bony swellings at the IPJs



Valgus deformity
Less commonly (bone twist is away from the center of the body)

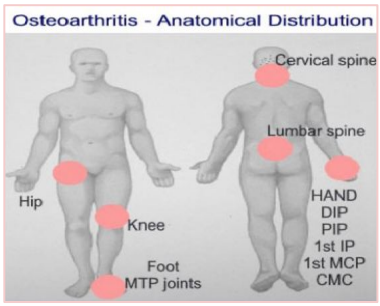
Varus deformity
resulting from marked medial tibiofemoral osteoarthritis (bone twist is toward the center of the body)

Subtypes of OA

Primary generalized OA

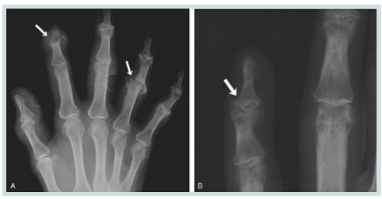
- Common form of OA
- This is usually seen in combination with nodal OA(Generalized nodal osteoarthritis)
- Onset is often sudden and severe.

Knee joint is the most common affected



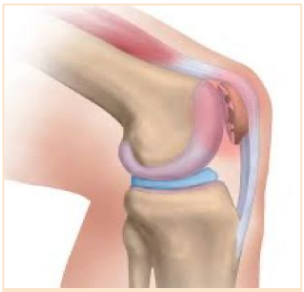
Erosive osteoarthritis

- Rare.
- The DIPs and PIPs are inflamed, and equally affected and the functional outcome is poor.
- Radiologically, there is marked osteolysis.
- Destructive phases are followed by phases of remodelling.



Chondromalacia Patellae

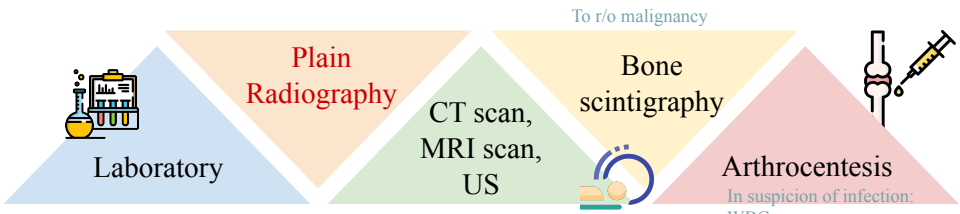
Also known as "runner's knee" condition where the cartilage on the undersurface of the patella deteriorates and softens due to overuse of the joint.
Most commonly among young athletes.



Chondromalacia Patellae
More common in young

Case by Dr:
Soccer player was playing in hilal for 20 years and he has bent knee joint he is only 45 years old "you see this kind of change for people who is 65 years old" could this be OA ? Hx was soccer player, so most likely yes. Do you need to do work up for him ? No

Work Up:



In suspicion of infection:
WBC :
>100 OA
> 1000 Inflammatory

- X-ray is the most accurate diagnostic test. Significant findings are found in advanced disease and show:
  - **narrowed joint space** (due to cartilage loss), **Osteophytes**, **Subchondral sclerosis,** and **Cyst formation**
- MRI Will show early changes (not usually necessary for patients with typical X-ray features)
- Labs are usually normal

Differential Diagnosis:

- ➔ Crystalline arthropathies (ie, gout and pseudogout)
- ➔ Inflammatory arthritis (eg, rheumatoid arthritis)
- ➔ Seronegative spondyloarthropathies (eg, psoriatic arthritis and reactive arthritis)
- ➔ Septic arthritis or post infectious arthropathy
- ➔ Fibromyalgia
- ➔ Tendonitis

  =>knee pain could lead to 2ndry OA

Treatment:

Non-pharmacological

- ❑ Lifestyle modification

  Obese patients are encouraged to lose weight as Physical measurements are the cornerstone for OA treatment
- ❑ Physical and rehab therapy

Pharmacotherapy

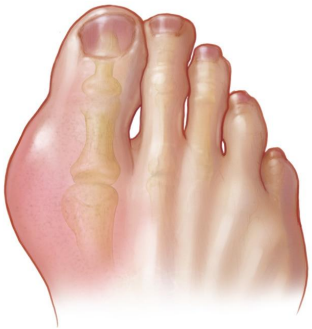
- ❑ Arthroscopy
- ❑ Osteotomy
- ❑ Arthroplasty
- ❑ Fusion and joint Lavage
- ❑ Stem cell therapy

★ Medication:

1. Paracetamol is the initial drug of choice.
2. NSAIDs are used in patients who do not respond to simple analgesics (used in short courses)
3. Intraarticular corticosteroid injections produce short-term improvement when there is a painful joint effusion; systemic corticosteroids are not used.

GOUT

Definition:



- Gout is an inflammatory reaction to monosodium urate crystals and associated with hyperuricemia.

Introduction:

- Most common inflammatory arthritis in elderly
  - Increasing prevalence
  - Highest 75-85 y.o.
  - Men > women, (< 65 y.o.)
- Deposition of urate crystals in tissue
- Gout in women:
  - Usually > 65 y.o.After menopause
  - Because of Loss of estrogen induced uricosuric (Excretion of uric acid) effect

Pathophysiology:

- **Precipitation** of monosodium urate crystals in avascular tissues
  - (cartilage, epiphyseal bone, periarticular bone)
  - Hyperuricemia likely asymptomatic for years
- The acute attack - crystals activate plasma proteases
  - Can activate factor XII & C5
  - Can adsorb opsonins in area, attracting phagocytes!

Crystals collect in the synovial fluid > phagocytized by PMNs > release of inflammatory mediators and proteolytic enzymes from the PMNs> Inflammation.

Uric Acid Homeostasis:

Urate is constantly near its limit of solubility, in a flux balance between production and elimination.

- **PRODUCTION**: Breakdown of purines from nucleic acids, Hypoxanthine converts to Xanthine which gets turned into uric acid by Xanthine oxidase.
- **ELIMINATION**: kidney- 10% of filtered load is excreted
  - Simultaneous reabsorption and secretion processes.
  - Proximal tubule, reabsorb filtered urate anions in exchange for intracellular organic anions such as lactate or ketone bodies.

Hyperuricemia:

- Hyperuricemia in **90% caused by inadequate renal elimination.**
- Above Serum levels of 6.8 mg/dl (MSU) crystals are forming somewhere in the body. The higher the serum levels over time, the higher the probability of an eventual attack of gout.
- **CRYSTALLIZATION**: dependent on pH, nucleating partners and temperature.
    - Low PH, Low Temp lead to crystal formation.
- Urate is less soluble in synovial fluid and articular cartilage, especially in peripheral joints, is colder than adjacent tissue for lack of blood supply. Therefore, crystallization is likely to initiate in **small peripheral joints.**

Clinical Features (four stages)

- **Asymptomatic hyperuricemia**:
    - Increased serum uric acid level in the absence of clinical findings.
    - may be Asymptomatic for 10 to 20 years or longer.
    - Should not be treated because over 95% of patients remain asymptomatic.

- **Acute gouty arthritis.** **(the typical attack)**
    - Sudden onset of exquisite pain.
    - Wakes the patient from sleep.
    - Classically affects the **big toe**—the first metatarsophalangeal joint which is then called **(podagra)**.
        - Other common joints affected are ankles and knees.
    - Pain and cellulitic changes
        - Erythema, swelling, tenderness, and warmth.
    - As it resolves, the patient may have **desquamation** of overlying skin.

- **Intercritical gout.**
    - Asymptomatic period between attacks.
        - High likelihood of recurrence:
        - 62% within 1st year
        - 78% within 2 years
        - 90% within 5 years
    - Attacks tend to become polyarticular with increased severity over time.

- **Chronic tophaceous gout.**
    - In people who have had poorly controlled gout for more than 10 to 20 years.
    - **Tophi** : Large, smooth, white deposits in the skin and around the joint
        - They cause deformity and destruction of hard (joints) and soft tissues.
        - Commonly in:
            - Extensor surface of forearms, elbows, knees,
            - Achilles tendons
            - External ear.

Risk Factors:

- Purine rich foods & nutritional supplements
- Drugs
  - **Thiazides**
  - **Low dose ASA** (< 1g/day?)
  - Niacin
  - Cyclosporin
  - Pyrazinamide & ethambutol
- Obesity & excessive weight gain, (especially in youth)
- Moderate to heavy alcohol intake
- High blood pressure
- Abnormal kidney function
- Leukemias, lymphomas, and hemoglobin disorders
- Trauma & Surgery somebody who has already hyperuricemia trauma/surgery could trigger acute attack
- Fructose

Diagnosis:

- Diagnosi is mainly **clinical**
  - Characteristic finding of acute onset of pain at night at first MTP joint (podagra) is enough for diagnosis.
- **Joint fluid polarized microscopy:**
  - Long, needle shaped crystals which are negatively birefringent under polarized light
    - Most specific & Diagnostic "Not always done because clinical picture is enough"
- **Serum Uric acid:**
  - Usually not helpful. Might be normal even in acute attack.
- Radiographs:
  - In chronic gout:
    - Bone erosion, overhanging edges.

Principles of Management:

Don't memorize doses..

1 Terminate acute attacks

- NSAIDs - Colchicine - Corticosteroids

2 Prevent recurrence & reverse complications

- Eliminate urate crystals from joints & tissues

3 Address co-morbid conditions

- Obesity
- Hypertriglyceridemia
- Hypertension
- Diabetes mellitus
- Excessive alcohol

1 Terminate acute attacks

Directed at WBC inflammatory response

Options:
- **NSAIDs**
- **Colchicine**
- **Corticosteroids**

- Choice depends on **co-morbidities & history**
- **More importantly** – rapidity of treatment selection!
  - Keep agent close at all times; start as soon as possible as needed
    - Especially with poor renal function, slower response = increased drug exposure over course of a flare

NSAIDS

Treatment of choice in acute gout

Choose based on: Toxicity, Cost, Convenience

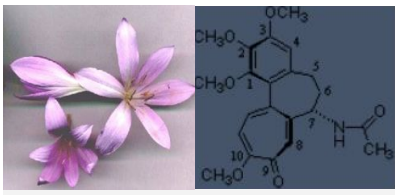
- CrCL "Creatinine Clearance" GFR =30 or less
  - Avoid in **CKD**
- Risk of ADRs
  - (Nausea, Vomiting, Diarrhea, GI Bleed, fluid retention, Acute renal failure, etc)
- Cost & availability
  - Rx vs Over the counter
- For elderly: Choose shorter half-life ($t_{1/2}$)
  - Ibuprofen (2-4hrs); diclofenac (2hrs); indomethacin (4.5hrs);
  - **Avoid in CHF, CKD, peripheral edema, PUD/GERD** +diabetes.
  - N.B. increased risk of GI bleed with concurrent ASA, even 81mg!
    - Consider adding a PPI Always give PPI when:
      1. Patient on NSAIDs+ASA
      2. Patient has history of peptic ulcer.

Colchicine

- Don't give with dialysis. CKD modify the dose
- Used for centuries
- Most specific agent in use
- **OVERALL EFFECT:**
  - **Decreases leukocyte motility**
    - Binds to tubulin and inhibits microtubule formation, arresting neutrophil motility
  - Decreases phagocytosis in joints
    - Decreases lactic acid production
  - Interruption of inflammatory process
  - PO or IV
    - Avoid IV - Potentially fatal if mis-dosed!
      - Risk of arrhythmia
  - 1 mg & 0.6 mg tablets - scored
  - **Alternative regimens**
  - 1mg loading dose, then 0.5mg q2-6hrs

  OR 0.5 - 1 mg TID

  OR 1.2 mg initially, then 0.6mg BID
- Most effective w/i first 12hrs of attack
- Dose low! Try TID dosing first
- **D/C if GI distress develops** (N/V, abdominal pain, severe diarrhea)



Colchicum autumnale
(autumn crocus), (meadow saffron)

Corticosteroids

Oral prednisone if patient does not respond to or cannot tolerate NSAIDs and colchicine.

- Reserved for:
  - Intolerant of NSAIDs or colchicine
  - Comorbidities that prohibit use of other meds
- Good alternative for elderly w/ poor renal function
  - Few trials – choice is empiric
  - Eg. Prednisone 20-60 mg /day PO
    - Are lower doses less effective?
      - Noted flares in transplant patients on 7.5-15 mg/day
- Methylprednisolone 125 mg/day IV or IM q1-4 days prn
  - Can give intra-articular – avoid if joint is septic!
  - Use smallest gauge needle (esp if on Warfarin)

If you do arthrocentesis and you see it turbid and not sure if it's septic or not you wait for the gram stain if it's negative then you can give steroids injection

- Never give intra-articular steroids unless you ruled out septic arthritis first!

Treatment of Acute Attacks:

Summary

- ➔ Start treatment A.S.A.P.!
- ➔ Avoid **NSAIDs** in CKD, CHF
- ➔ Consider a PPI for **NSAIDs** + **ASA** or Hx of PUD
- ➔ Avoid / Reduce **colchicine** dose in **CKD**, liver dz, neutropenia, on diuretics, statins, or cyclosporin
- ➔ Do not change doses of any med that can alter urate levels when treating acute attacks
- ➔ Consider **NSAIDs**, **colchicine**, **steroids** at low doses and in combination (different MOA's)

2 Prevent recurrence & reverse complications

- Must eliminate excess body urate
  - Else tophi may continue to enlarge
  - Destructive, chronic mononuclear cell inflammatory response that destroys cartilage and bone, resulting in chronic arthritis
- High likelihood of recurrence if not controlled urate levels
  - 62% w/i 1 yr
  - 78% w/i 2 yrs
  - 90% w/i 5 yrs

Hoskison, KT and Wortmann, RL

Ref: Drugs & Aging 2007;24(1):21-36

Recommend urate levels < 360 umol/L

Normal range 140- 340 (Dynacare)

- At > 360 umol/L, fluids are supersaturated and crystal can **precipitate**
- At < 360 umol/L, deposits dissolve, mobilize and are **eliminated**

Recommendations: Urate Lowering Therapy

- *EULAR:*
  - "with recurrent attacks, arthropathy, tophi or radiographic changes"
- *US Panel:*
  - "if tophaceous deposits, erosive changes on X-ray, or > 2 attacks per year"
- *Others:*
  - "After first attack" => Disease declared, high rate of recurrence
  - "Based on frequency of attacks" => Since second attack may not occur for years

Prevent recurrence & reverse complications

- *Recall*: Lowering urate can precipitate a flare!
  - Increased risk w/ more rapid & severe changes
  - ~ 25% of patients
- **Start 2-3 weeks after flare resolved**
  - Uricosuric agents - increase excretion not 1st line therapy
    - Probenecid
    - Sulfinpyrazone
  - Xanthine Oxidase Inh. – decrease production 1st line therapy
    - Allopurinol – agent of choice
    - Febuxostat – new agent (ULORIC™)

Avoiding Flares

Allopurinol

Start Allopurinol at low dose and titrate up to avoid precipitating event

- Eg. 100mg, increasing by 100 mg q2-4 weeks to target dose
- With renal dysfunction:
  - 50mg initiation, incr by 50mg + monitoring with KF tests
- If not working we add uricosuric agent

Dosing:

- 50mg to 800mg qd (usually 300mg)
- N.B. Only 21-55% attain urate < 360 umol/L on "standard" dose
  - Most insufficient doses – main barrier to control

N.B. Dose adjust for renal function

- Dosing according to CrCL may not attain control

GOAL: lowest dose to target urate < 360 umol/L

ADRs: (well tolerated)

- Common:
  - GI upset,
  - Rash
    - (esp if on Amox/Amp or Cyclophosphamide)
- Rare:
  - Blood dyscrasias
  - Jaundice
  - TEN
  - Hypersensitivity Syndrome (including rash)
- If mild rash occurs, hold and re-challenge

Febuxostat (ULORIC™)

- A non-purine, selective xanthine oxidase inh.
- More potent than Allopurinol
- **Efficacy vs Allopurinol:**
  - Lower frequency of gout flares
    - N.B. Higher frequency of flare with initiation at higher doses!
  - Improved serum urate lowering effect
  - Limited RCTs - need more evidence in:
  - Renal dysfunction, concomitant use of urate raising drugs (eg. ASA, thiazides), comparison against non-fixed doses of Allopurinol
- Start 40 mg daily (+/- food)
  - Up to 80 mg or 120 mg qd
    - after 2 weeks if UA > 360 umol/L
  - CrCL > 30mL/min – no dose adjustment
  - CrCL < 30 mL/min – unstudied – avoid
- **Side effects:**
  - Rash (1% to 2%)
  - Liver function abnormalities (5% to 7%)
    - F/U LFTs in 2 & 4 months after starting tx
  - Arthralgia (1%)
- **Cost**: 80mg tabs ~ $65/ month;
  - (no ODB coverage)

Treat the same as allopurinol

Avoiding Flares

- Start **prophylaxis** before urate lowering therapy
  - Eg. Daily, low dose NSAID or colchicine 2-3 weeks before allopurinol
    - Eg. Colchicine 0.5mg or 0.6mg qd or tid
    - Eg. Indomethacin 25 mg bid
  - Continue 3-6 months and/or [urate] < 360 umol/L

Note Bene (N.B.)

- No prophylaxis without urate lowering tx!
  - Acute flare prevented but crystal deposition in tissue continues!
  - Hence no warning signs of continued cartilage and bone damage and deposition in organs, especially kidneys!
  - *Remember*: Colchicine is NOT uricosuric

Very rarely used:

Sulfinpyrazone:

- Up to 800 mg /day divided bid
- Start: 100mg BID
  - Increase q1wk
- May decrease to 200mg/d once urate controlled
- ADRs: GI upset, rash

Probenecid:

- 500mg to 3g /day divided bid-tid
- Start: 250mg BID
  - Increase by 500mg q4wk
- May decrease by 500mg q6mo if stable > 6 mo till urate starts to rise
- ADRs: GI upset, rash

Summary of Gout Prevention

- High likelihood of recurrence
- Eliminate excess body urate to prevent chronic destructive changes
  - Colchicine is **not** uricosuric!
  - No prophylaxis without urate lowering therapy!
- Manage risk factors
  - Drugs, diet, comorbidities
- Allopurinol – drug of choice
  - Start low, go slow high risk of acute attack with high doses
  - May have to push dose to attain control

Extra:

The choice of whether to use uricosuric drugs or allopurinol depends on how much uric acid is excreted in the urine:

- **24-hour urine uric acid is <800 mg/day = underexcretion of urate**
  - Uricosuric drugs (probenecid, sulfinpyrazone)> Increases renal excretion
- **24-hour urine uric acid is >800 mg/day = overproduction**
  - Xanthine oxidase inhibitors (allopurinol, febuxostat)> decrease uric acid synthesis.

Address co-morbid conditions

- ❑ Obesity
- ❑ Hypertriglyceridemia
- ❑ Hypertension & Diabetes mellitus
- ❑ Excessive alcohol

Obesity & Hypertriglyceridemia:

- Weight loss independently lowers urate levels
- Decreased alcohol consumption, regular exercise and weight reduction will lower TGs
  - Fibrates
    - Especially fenofibrate – mild uricosuric effect

Diet Restriction:

- Total diet restriction only lowers urate levels by ~ 52.9 umol/L (1 mg/dL)
  - Very unpalatable
  - Poor compliance
- Purine sources matter
  - Increase with meat & seafood
  - Decrease with dairy
    - Daily consumption lowers urate levels
  - Oatmeal and purine rich vegetables do not increase risk of gout
    - Peas, mushrooms, lentils, spinach, cauliflower

Dietary sources

High-Purine Content

Anchovies,Beer, Bouillon (meat based), Brains, Broth (meat based), Clams, Consommé, Goose, Grain alcohol, Gravy, Heart, Herring, Kidney, Lobster, Mackerel, Meat extracts, Mincemeat , Mussels, Oysters, Partridge, Roe (fish eggs), Sardines, Scallops, Shrimp, Sweetbreads, Yeast (baker's and brewer's) taken as a supplement.

Moderate-Purine Content

Beans, dried, Fish (except those in the high-purine content list), Lentils, Meat (except those in the high-purine content list), Mushrooms.

Treatment Explanation: Extra slide

Patient comes with acute attack what to do?

- ★ **NSAIDs** are usually the treatment of choice unless the patient has:
  - Renal Impairment
  - History of peptic ulcer (you might give PPI here but better to avoid completely)
  - Heart failure
- ★ **Colchicine** comes second when NSAIDs are contraindicated. Not prefered due its sever side effect (nausea/vomiting, abdominal pain, severe diarrhea)
- ★ **Steroids**

The acute attack now passed what to do then?

- ★ All patients must do **lifestyle changes** now:
  - Avoid Thiazide + Aspirin
  - Avoid purine rich food
  - Treat obesity
  - Avoid alcohol and Fructose
    etc...

What about the next attack??

Urate lowering therapy as a prophylaxis:

- ★ You give ULT if:
  - ≥ 2 attacks per year
  - Presence of Tophi
  - Patient has renal Impairment
- ★ What to give?
  - **Mainly Allopurinol**
    - Never !! ever !! give ULT in an acute gout it might induce other attack!
    - Wait for a month after the attack before starting ULT
    - You always give (NSAIDs or colchicine) for 4 weeks before and after starting allopurinol

To sum up:

Patients comes with acute attack give NSAIDs (or any) now he's better. After awhile you decided to give him ULT (because he fits the criteria) you make sure that the last attack was at least 1 month ago then start him on (NSAIDs or Colchicine) for 4 weeks before adding allopurinol (or any ULT). Continue the NSAIDs/Colchicine for additional 4 weeks (some sources says 3-6 months) after the allopurinol. Now the patient can remain on the ULT (allopurinol) alone indefinitely.

Osteoarthritis

Gradual destruction of the joint through the loss of articular cartilage

Risk factors:

Age, obesity, trauma, genetics, hypogonadism, muscle weakness, repetitive use, Infection, crystal deposition, acromegaly, previous inflammatory arthritis (burnt-out rheumatoid arthritis)

Heritable metabolic causes
(alkaptonuria, hemochromatosis, Wilson disease)

Hemoglobinopathies
(sickle cell disease and thalassemia)

Neuropathic disorders leading to a Charcot joint
(syringomyelia, tabes dorsalis, and diabetes)

Underlying morphologic risk factors
(congenital hip dislocation and slipped femoral capital epiphysis)

Disorders of bone
(Paget disease and avascular necrosis)

Previous surgical procedures
(meniscectomy)

Diabetes mellitus

Typical presentation:

- Pain increased by movement
- Relieved by rest
-Gelling
-Morning stiffness <30 min

deformities:

Heberden's nodes
Bouchard's nodes
Valgus deformity
Varus deformity

Signes :

Crepitus
Limited movement of the joint
Mild synovitis
Periarticular tenderness
Muscle wasting around the joint

Subtypes of OA

Primary generalized OA
(F>M, with Nodal OA, most is sudden+severe, Knee joint mostly)

Erosive OA
(Rare, DIP+PIP are equally affected, Osteiolysis on imaging, Destr than Remodel)

Chondromalacia Patellae
(Cartilage under patella, Common in young)

Invest:

- Most accurate diagnostic = Xray
(Narrowed joint pain, osteophytes, subchondral sclerosis, and cyst formation)

- MRI Will show early changes
(not usually necessary for patients with typical X-ray features)

- All Labs are NORMAL

Tx:

Non pharm : Lifestyle mod (Weight loss) + Rehab and physiotherapy

Pharm : Paracetamol > NSAIDs .. ~in special cases>Intraarticular corticosteroid
Arthroscopy, Osteotomy, Arthroplasty, Fusion and joint Lavage, Stem cell therapy

Gout

an inflammatory reaction to monosodium urate crystals.

Most common inflammatory arthritis in elderly

Less Renal Elimination > Hyperuricemia ~*when Low PH, Low Temp*> CRYSTALLIZATION in small peripheral joints

Risk Factors:

- Purine rich foods & nutritional supplements
- Drugs (Thiazides, Low dose ASA, Niacin, Cyclosporin, Pyrazinamide & ethambutol)
- Obesity
- Alcohol intake (Moderate-heavy)
- HTN
- Abnormal kidney function
- Leukemias, lymphomas, and hemoglobin disorders
- Trauma & Surgery

1 Terminate acute attacks

- NSAIDs

- Choose based on: Toxicity, Cost, Convenience.
- But traditionally in non-diabetic use

indomethacin

- Avoid in CKD, CHF
- Consider a PPI for NSAIDs+ASA or Hx of PUD

- Colchicine PO (Avoid IV)

- Dont give if in dialysis.
- Avoid / Reduce dose in:

CKD, liver dz, neutropenia, on diuretics, statins, or cyclosporin

- **Not** uricosuric!

if Intolerant of NSAIDs or colchicine (ex: elderly w/ poor renal function)

- Corticosteroids

- Do not change doses of any med that can alter urate levels when treating acute attacks
- Consider NSAIDs, colchicine, steroids at low doses and in combination (different MOA's)

2 Prevent recurrence & reverse complications

(rapid & severe Lowering urate can precipitate a flare)
Recommend urate levels < 360 umol/L (if higher crystals precipitate)
Start 2-3 weeks after flare resolved

Xanthine Oxidase Inh - decrease production

1st line therapy

♦**Allopurinol** – agent of choice
1ST LOW DOSE then titer up
ADRs:GI&Rash - low dose for Renal Dysfun

♦**Febuxostat** – new agent

Uricosuric agents - increase excretion

♦**Probenecid**

♦**Sulfinpyrazone**

<u>if there is multiple attacks use prophylaxis (NSAID or colchicine) before urate lowering therapy</u>

3 Address co-morbid conditions

Test yourself:

1/ A 50 yo male came with a swollen tender red big toe and he cant move it. Which of the following exclude Gout?

A- Normal Blood uric acid level

B- Normal X-ray

C- Normal Arthrocentesis

D- Normal CBC

1: C: Normal blood uric acid level does not exclude Gout

2/ a 70 yo diabetic female came to the ER with pain on her right ankle and she is on low dose aspirin for 1 year, after investigation she was diagnosed with Gout. what's the best first line to treat this patient?

A- indomethacin

B- Ibuprofen and lower the dose aspirin more

C- indomethacin with omeprazole

D- Ibuprofen with omeprazole

2: D: indomethacin is contraindicated with DM and the patient is on Low dose aspirin so we add omeprazole

Never change the dose a drug that affect the uric acid level.

3/Which of the following sentences is true ?

A-Acute gout affect more than one joints not erosive

B- Acute gout affect one joint and is not erosive

C- Acute gout affect one joint and is erosive

D-Acute gout affect more than one joints erosive

3: B :)

4/ Hard, bony outgrowths or gelatinous cysts on the proximal interphalangeal joints Is which of the following ?
A-Heberden's nodes
B-Bouchard's nodes
C-Valgus deformity
D-Varus deformity

B: - Heberden's nodes : are bony swellings of the DIP joint
- Valgus deformity: segment distal to a joint is angled outward, that is, angled laterally, away from the body's midline
- A varus deformity: excessive inward angulation (medial angulation) of the distal segment of a bone or joint.

5/ a 70 yo female known to have HF, DM, HTN. came to the rheumatology clinic complaining of left knee morning stiffness and pain of her right knee for 2 months, the pain gets worse with climbing the stairs and Praying and relieved by setting on the couch. What is the most likely diagnosis ?
A- osteoarthritis
B- rheumatoid arthritis
C- septic arthritis
D- Gout

6/ What expected to be normal ?
A- Xray
B- CT
C- Uric acid level
D- CBC

5:A: asymmetric monoarthritis (is start as mono and progress to poly) aggravated by movement and relieved by rest)
6:D

7/ a 70 yo male known to have gout and HTN came to the ER with 1 metatarsal joint pain. He was diagnosed with gout flare. Which of the following should be given two weeks after treatment ?
A- Allopurinol
B- Febuxostat
C- Probenecid
D- Sulfinpyrazone

7:none of them: Allopurinol two weeks after it resolved not after treatment