CRYSTAL ARTHROPATHIES

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Crystal arthropathies are joint disieses caused by deposition of crystals in the joints or periarticular tissues , leading to inflammation.

These include:

1.Gout

2.Calcium pyrophosphate deposition disease

3.Basic calcium phosphate deposition disease

Crystal	Disease
Common	
Monosodium urate monohydrate	Acute gout
	Chronic tophaceous gout
Calcium pyrophosphate (CPP)	Acute CPP crystal arthritis
	Chronic CPP crystal arthritis
	Chondrocalcinosis
	Axial disease (e.g. crowned dens syndrome)
Basic calcium phosphate (BCP)	Calcific periarthritis
	Calcinosis
Uncommon	
Cholesterol	Chronic effusions in rheumatoid arthritis
Calcium oxalate	Acute arthritis in dialysis patients
Extrinsic crystals/semi-crystalline particles:	
Synthetic crystals	Acute synovitis
Plant thorns/sea urchin spines	Chronic monoarthritis, tenosynovitis

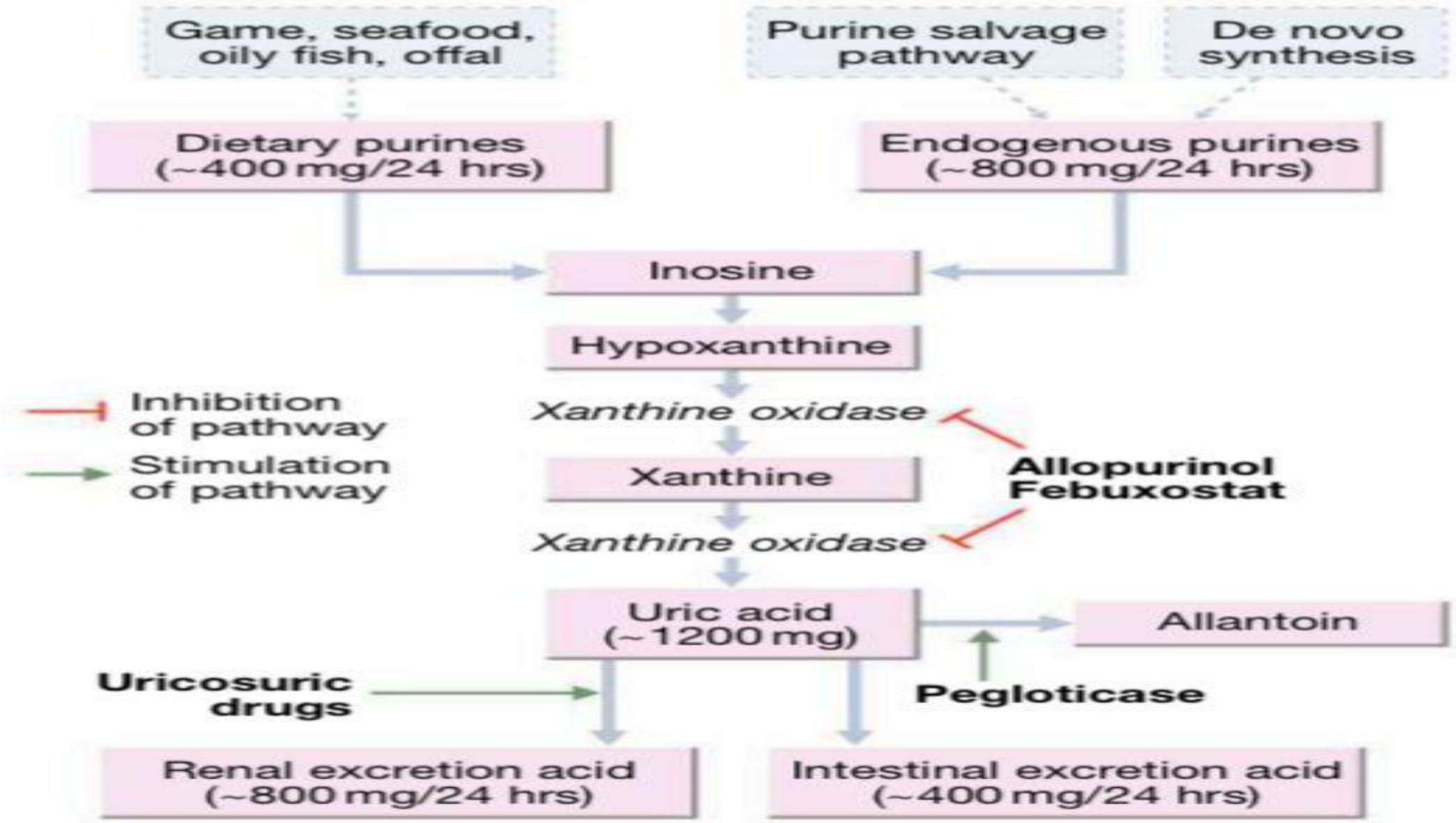
GOUT

CRYSTAL induced inflammatory arthritis caused by deposition of monosodium urate crystals in joints due to hyperuricemia.

ETIOLOGY

Due to hyperuricemia(normal = 7mg /dl)

URIC ACID METABOLISM



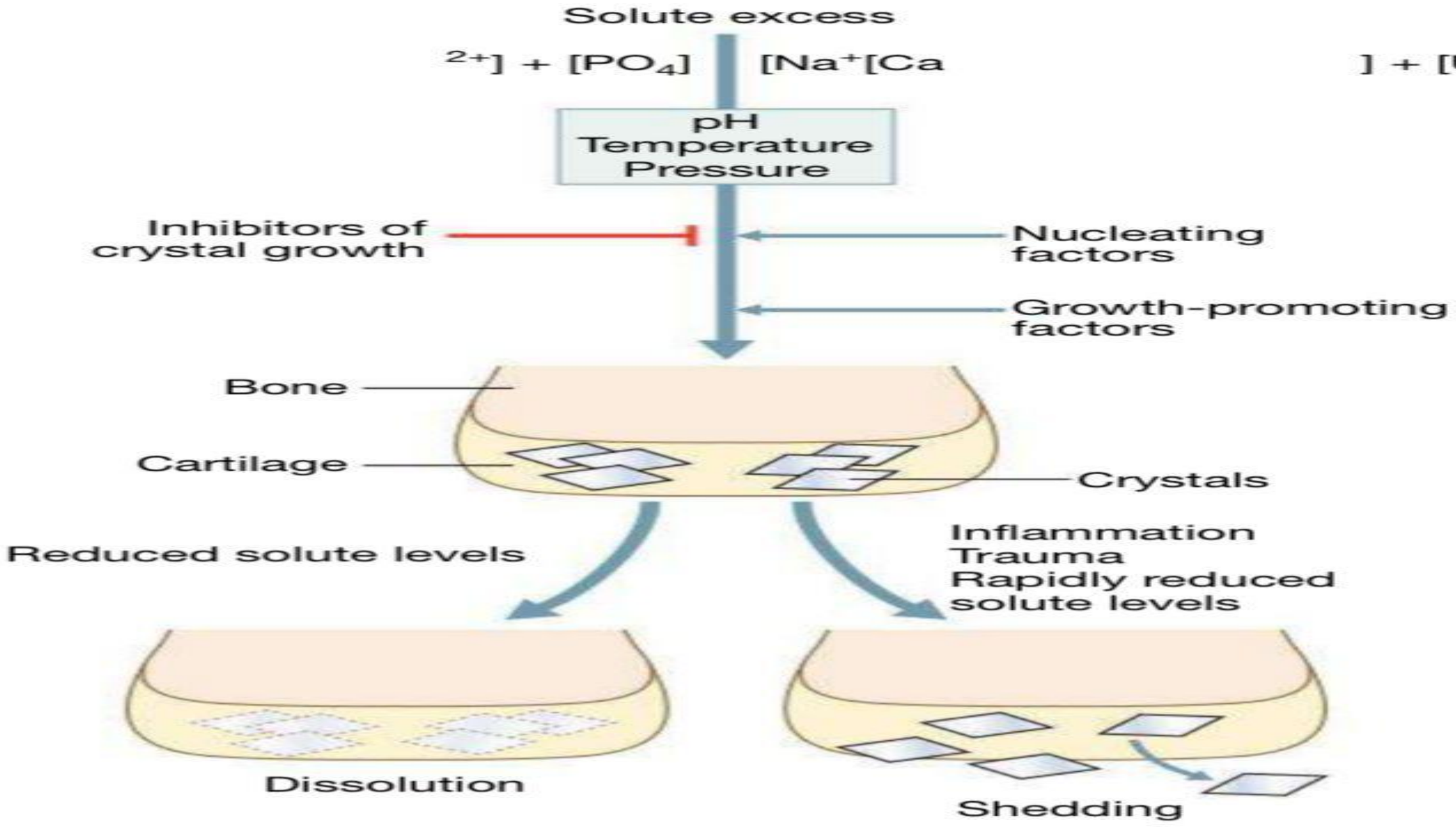


Fig. 26.23 **Mechanisms of crystal formation.**

CAUSES OF HYPERURICEMIA:

Increased Intake

- Intake of purine-rich foods (e.g. liver, kidney, meat, mushrooms)
- Beer is particularly rich in guanosine, a purine nucleoside.

Increased production

- Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) deficiency
- Phosphoribosy|pyrophosphate (PRPP) synthetase overactivity
- Glucose-6-phosphatase deficiency (glycogen storage disease, type I)
- Increased nucleoprotein turnover in hematologic conditions: Lymphoma, leukemia, hemolytic anemia
- Increased rates of cellular proliferation and cell death: Psoriasis, cancer chemotherapy, radiation therapy, malignancies
- Obesity

Decreased renal excretion (most common cause of hyperuricemia)

- Inherited isolated renal tubular defect ('under-excretors')
- Renal failure
- Lead poisoning
- Diabetic ketoacidosis
- Lactic acidosis
- Hypothyroidism
- Drugs (thiazides, pyrazinamide, cyclosporine)

EPIDEMIOLOGY

More in male(male:female ratio is >10:1)

Prevelance increases with age and increasing uric acid concentration.

CLINICAL FEATUES

GOUT can present in following ways:

1. Acute gouty arthritis
2. Chronic tophaceous gout

ACUTE GOUTY ARTHRITIS

Think: “SUDDEN RED HOT BIG TOE”

📍 Joint Involvement

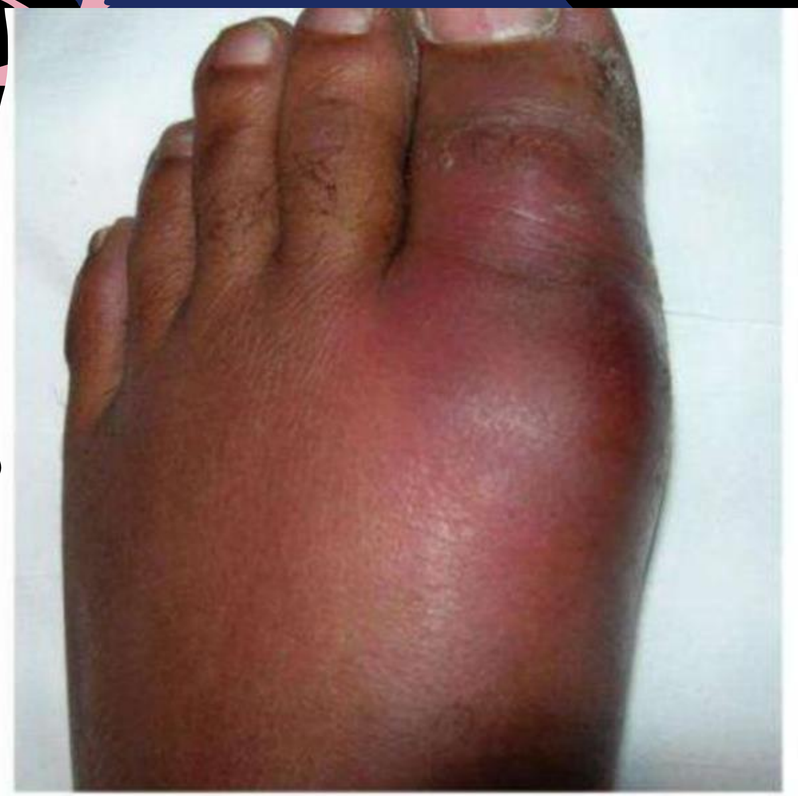
Usually monoarticular (one joint)

Most common: 1st MTP joint (Podagra) 🦶

Others (↓ frequency):

Ankle,Midfoot,Knee,Small joints of hand,Wrist,Elbow

❌ Spine & large proximal joints rarely first site



⚡ Onset

Sudden ,Often at night

Severe pain (patient can’t tolerate even bedsheet touch)

🔥 Local Signs

Redness,Swelling,Warmth,Marked tenderness,Periarticular edema

🌡️ Systemic Features (especially large joint like knee)

Fever,Malaise,Sometimes confusion

⏳ Course

Self-limited

Resolves in days to weeks ,After subsiding →

Itching (pruritus)

Peeling skin (desquamation)

🧠 Other Presentations

Bursitis,Tenosynovitis ,Can mimic cellulitis

CHRONIC TOPHACEOUS GOUT

Chronic Tophaceous Gout

🧱 Think: “TOPHI = Lumps of Uric Acid”

---Painless, firm nodules (tophi)

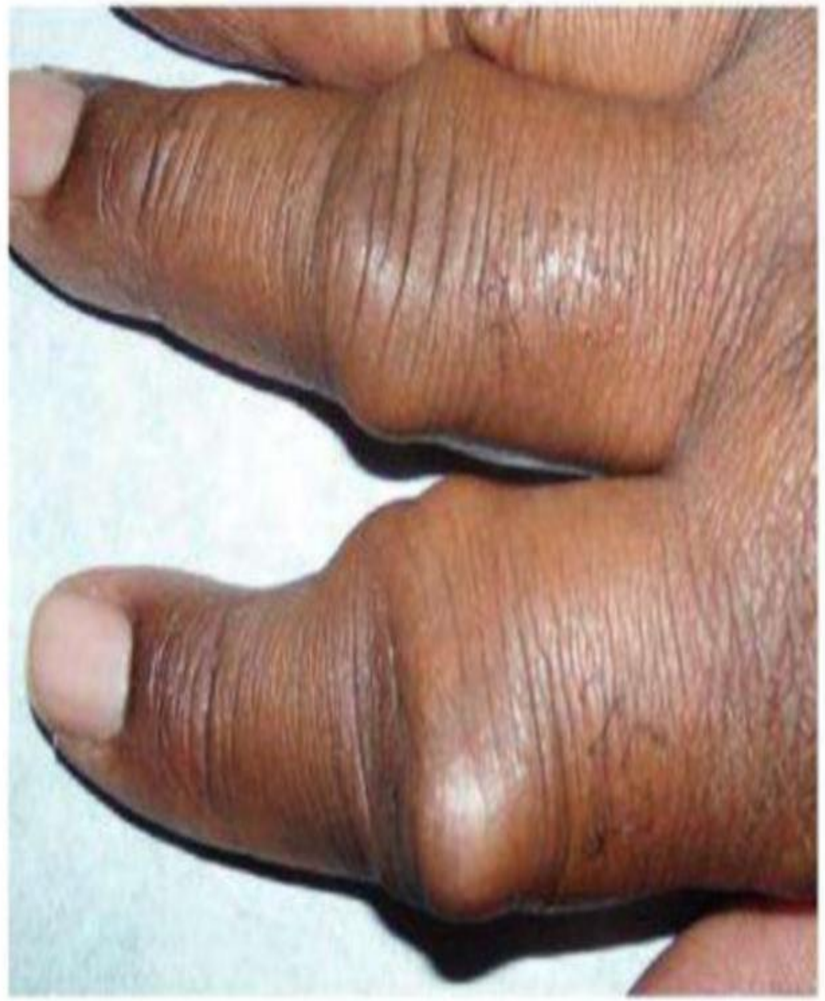
Common sites:

Ear helix,Olecranon,Achilles tendon,Fingers & toes

---Chronic joint deformity

---Recurrent attack

Large tophi may ulcerate and discharges white gritty material



Renal and urinary tract manifestations

Uric acid stones may form and cause renal colic

Urate crystal deposition in the interstitium and medulla causes chronic inflammation,fibrosis,glomerulosclerosis and secondary pyelonephritis.

Investigations

1.Polarising microscopy : definitive diagnosis

Identifies needle shaped ,negatively birefringent monosodium urate crystals in aspirate from a joint,bursa or tophus.

2.Histologic examination : birefringent urate crystals in biopsy specimen.

3.Uric acid level in blood

Elevated = >7mg /dl

4.24 hr urinary uric acid excretion

5.Urea and creatine levels to rule out renal dysfunctions.

6.Complete blood picture,ESR,and peripheral blood smear should be done to rule out any myeloproliferative disorders

7.X-ray access degree of joint damage

In early disease it appear normal but in advanced stage narrowing of joint spaces,sclerosis,custs and osteophyte may develop

Calcified tophi are visible in xray

Management
1.acute gout

1. Oral colchicine given in doses of 0.5 mg 2–4 times daily is the treatment of first choice in acute gout. It works by inhibiting the inflammation ,which reduces IL-1β production.

The most common adverse effects are nausea, vomiting and diarrhoea.

2 .Oral NSAIDs are also effective, but are used less commonly since many patients affected by acute gout have coexisting cardiovascular, cerebrovascular or chronic kidney disease.

3. Oral prednisolone (15–20 mg daily for 2–3 days) or intramuscular methylprednisolone (80–120 mg daily) are highly effective and are a good choice in older patients where there is an increased risk of toxicity with colchicine and NSAID

4. Local ice packs can also be used for symptomatic relief. Patients with recurrent episodes can keep a supply of an NSAID, colchicine or prednisolone and take it as soon as the symptoms occur, continuing until the attack resolves.

5.Joint aspiration can give pain relief, particularly if a large joint is affected, and may be combined with an intra-articular glucocorticoid injection if the diagnosis is clear and infection can be excluded.

prophylaxis

The long-term therapeutic aim is to prevent attacks occurring by bringing SUA below the level at which monosodium urate monohydrate crystals form.

A therapeutic target of < 300 µmol/L (5 mg/dL) is recommended in the British Society of Rheumatology guidelines.

Allopurinol is the drug of first choice.

It inhibits xanthine oxidase, which reduces the conversion of hypoxanthine and xanthine to uric acid. The recommended starting dose is 100 mg daily, or 50 mg in older patients and in renal impairment.

The dose of allopurinol should be increased by 100 mg every 4 weeks (50 mg in older patients and those with renal impairment) until the target uric acid level is achieved.

Acute flares of gout often follow initiation of urate-lowering therapy. The patient should be warned about this and told to continue therapy, even if an attack occurs.

The risk of fares can be reduced by prophylaxis with oral colchicine (0.5–1 mg daily) or an NSAID for the first few months.

Febuxostat

also inhibits xanthine oxidase. It is typically used in patients with an inadequate response to allopurinol and when allopurinol is contraindicated or causes adverse effects. Febuxostat undergoes hepatic metabolism and no dose adjustment is required for renal impairment.

It is more effective than allopurinol, but commonly provokes acute attacks when therapy is initiated.

The usual starting dose is 40–80 mg daily, increasing to 120 mg daily in patients with an inadequate response.

---Uricosuric drugs, such as probenecid, sulfinpyrazone and benzbromarone, lower urate levels but are seldom used in routine clinical practice.

They are contraindicated in urate over-producers and those with renal impairment or urolithiasis and require patients to maintain a high fluid intake to avoid uric acid crystallisation in the renal tubules.

---Pegloticase is a biologic treatment comprised of the enzyme uricase conjugated to monomethoxypolyethylene glycol. It breaks down uric acid and is indicated for the treatment of tophaceous gout resistant to standard therapy and is administered as an intravenous infusion every 2 weeks for up to 6 months

Life style measures

Patients should be advised to lose weight if appropriate and reduce excessive alcohol intake, especially beer.

Several antihypertensive drugs, including thiazides, β-blockers and ACE inhibitors, increase uric acid levels, whereas losartan has a uricosuric effect and should be substituted for other drugs if possible.

Patients should avoid large amounts of seafood and offal, which have a high purine content, but a highly restrictive diet is not necessary.

2. Calcium pyrophosphate deposition disease

The acute form of CPPD disease is acute calcium pyro phosphate (CPP) crystal arthritis (‘pseudogout’).

It typically involves the knee, wrist, ankle, shoulder and hip.

26.45 The main risk factors for calcium pyrophosphate deposition disease

Common

- Older age
- Osteoarthritis*
- Hyperparathyroidism (both primary and secondary)
- Hypovitaminosis-D (by causing secondary hyperparathyroidism)

Rare

- Familial factors*
- Haemochromatosis*
- Hypophosphatasia
- Hypomagnesaemia
- Hypoparathyroidism
- Wilson's disease

*May be associated with structural damage to affected joints.

Clinical features

Acute CPP crystal arthritis (pseudogout):

Sudden onset of swollen, tender joint

Joint warm, erythematous, large effusion

Fever common; patient may appear confused/unwell (especially elderly)

Knee most commonly affected

Other joints: wrist, shoulder, ankle, elbow

Triggers: trauma, intercurrent illness, dehydration, surgery

Differentials: septic arthritis, gout

Chronic CPP crystal arthritis:

May mimic rheumatoid arthritis

Typical joints: wrists, MCP 2 & 3, ankles, shoulders

Often associated with osteoarthritic changes

Variable synovitis

Effusion and synovial thickening (especially knees & wrists)

Wrist involvement may cause carpal tunnel syndrome

Intermittent inflammatory flares may occur

Investigations (CPPD)

--Joint aspiration (key test)

Synovial fluid analysis with compensated polarized microscopy → CPP crystals

Fluid often turbid ± blood-stained

Gram stain & culture to exclude septic arthritis (even if crystals present)

---X-ray of affected joints

Chondrocalcinosis (calcification of hyaline cartilage/fibrocartilage)

Peri-articular calcification

---CT scan (if needed)

Helpful for axial disease, pelvis, spine

---Screen for secondary/metabolic causes

Check and treat underlying abnormalities

Management (CPPD)

----Acute CPP crystal arthritis

Rest, ice packs, joint elevation

Joint aspiration (symptomatic relief)

Intra-articular glucocorticoid (after excluding infection)

NSAIDs (caution in elderly)

Colchicine 0.5–2 mg/day

---Chronic CPP crystal arthritis

Low-dose oral glucocorticoids

Methotrexate

Hydroxychloroquine

Long-term low-dose colchicine (0.5–1 mg/day) to prevent flares

Limited evidence for optimal treatment of axial CPPD disease.

Basic calcium phosphate deposition disease

--is caused by the deposition of hydroxyapatite or apatite crystals and other basic calcium phosphate salts (octacalcium phosphate, tricalcium phosphate) in soft tissues.

The main affected sites are tendons, ligaments and hyaline cartilage in patients with degenerative disease, and skeletal muscle and subcutaneous tissues in connective tissue diseases.

Calcific periarthritis

Due to deposition of basic calcium phosphate (BCP) crystals in tendons

Causes acute inflammatory response

-----Common sites

Most commonly supraspinatus tendon (shoulder)

Also tendons around hip, feet, and hands

-----Clinical features

Sudden onset acute pain

Rapidly developing swelling and local tenderness (over 4–6 hours)

Overlying skin may be hot and red (may mimic infection)

May occur spontaneously or be triggered by trauma

Mild fever and systemic upset common

Investigations

-X-ray: tendon calcification visible

---If aspirated: inflammatory fluid with calcium-staining (alizarin red S) aggregates

During acute attack:

-Neutrophilia

-↑ ESR and CRP

-Routine biochemistry usually normal

Treatment

- Analgesics
- Intra-articular glucocorticoid injection
- Local physical measures and physiotherapy
- Outcome / Pathogenesis
- Clinical outcome may be poor; some patients require joint replacement
- BCP crystals may activate collagenase and other proteases, leading to tissue damage

Acute Inflammatory Arthritis (BCP crystal related)

- Caused by deposition of basic calcium phosphate (BCP) crystals.
- Commonly occurs in osteoarthritis (OA).
- May occur alone or with CPP crystals (mixed crystal disease).

Can present as acute crystal-induced arthritis (similar to acute CPP crystal arthritis).

- Sudden onset joint inflammation.

Milwaukee Shoulder Syndrome

- Rare condition with extensive BCP crystal deposition.
- Affects large joints, especially the shoulder.
- More common in elderly women.
- Gradual onset with pain, often after minor trauma/overuse.
- Progressive joint destruction over months.
- X-ray: joint space narrowing, osteophytes, calcification.
- Synovial fluid: large volume, non-inflammatory, BCP crystals present.
- No acute phase response; cultures negative.
- DDx: end-stage OA, osteonecrosis, neuropathic joint.

Autoimmune Connective Tissue Disease (BCP related)

- BCP deposition may occur in:

Subcutaneous tissues

Muscles

- Seen in systemic sclerosis and other autoimmune connective tissue diseases.

Usually asymptomatic.

- May cause pain and local ulceration.

Mechanism unclear.

No specific treatment.

Thank you