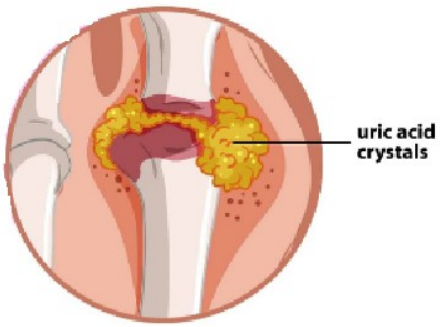
Pharmacy Department of Hospital Kuala Penyu

GOUT



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WHAT IS GOUT ?

- A disease caused by monosodium urate (MSU) crystal deposition with any of the following clinical presentations (current or prior): gout flare, chronic gouty arthritis, or subcutaneous tophus.
- A consequence of persistent hyperuricaemia.
- Consensus labels and the definitions of the basic elements of gout has been published by Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN).

No.	Consensus Label	Consensus Definition
1.	MSU crystals	The pathogenic crystals in gout (chemical formula: $C_5H_4N_4NaO_3$)
2.	Urate	The circulating form of the final enzymatic product generated by xanthine oxidase in purine metabolism in humans (chemical formula: $C_5H_3N_4O_3^-$)
3.	Hyeruric(a)emia	Elevated blood urate concentration over the saturation threshold
4.	Gout flare	A clinically evident episode of acute inflammation induced by MSU crystals
5.	Intercritical gout	The asymptomatic period after or between gout flares, despite the persistence of MSU crystals
6.	Chronic gouty arthritis	Persistent joint inflammation induced by MSU crystals
	6a. G-CAN recommendation	The label 'chronic gout' should be avoided
7.	Tophus	An ordered structure of MSU crystals and the associated host tissue response
8.	Subcutaneous tophus	A tophus that is detectable by physical examination
9.	Imaging evidence of MSU crystal deposition	Findings that are highly suggestive of MSU crystals on an imaging test
10.	Gouty bone erosion	Evidence of a cortical break in bone suggestive of gout (overhanging edge with sclerotic margin)
11.	Podagra	A gout flare at the first metatarsophalangeal (MTP) joint

EPIDEMIOLOGY

Global

- Prevalance: 0.1 - 6.8%
- Incidence: 0.58 - 2.89 per 1000 person-years
- Unusual before the age of 45 years in men / among premenopausal women

Malaysia

- No local population-based epidemiologic studies .
- Report of Hospital-based studies from a few tertiary centres in Malaysia:

- Peak age of onset: 30 - 60 years
- Gender: Predominantly males
- Multi-ethnic in origin and ethnicity distribution was dependent on the studies' region conducted, with majority were Malays and one study showed a preponderance towards the Ibans.

RISK FACTORS

NON-MODIFIABLE

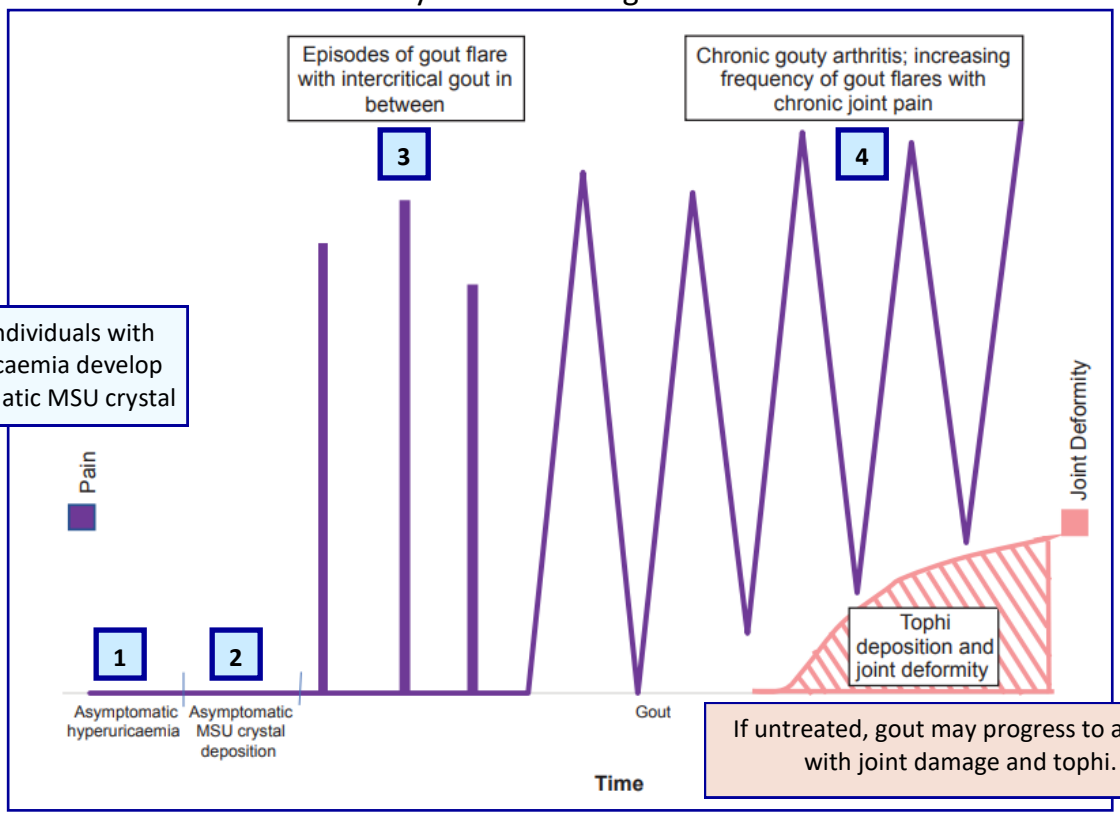
- Obesity/overweight
- Diet: Alcohol, High-fructose corn syrup, Sugar-sweetened soft drinks/ beverages , Red meat, & Seafood
- Medications: Diuretics , Non-losartan angiotensin II receptor blockers, Angiotensin-converting enzyme inhibitors, β-blockers & Cyclosporine
- Others:
  - CKD
  - Hypertension
  - Psoriasis

MODIFIABLE

- Increasing age
- Male gender
- Menopause
- Ethnicity
- Genetic : Single nucleotide polymorphism - ABCG2 gene; Enzymatic defect in purine metabolism - hypoxanthine-guanine phosphoribosyl transferase deficiency

CLINICAL PRESENTATION

The natural history of untreated gout evolves over time.



GOUT FLARE

Clinically evident episode of acute inflammation induced by MSU crystals

Symptoms of acute arthritis such as joint pain, swelling, warmth, redness and movement difficulty

Occurs abruptly with joint pain peaking in intensity within 24 hours

Prodromal symptoms of tingling, mild discomfort or itching

Throbbing or burning pain in nature with extreme joint tenderness

Excruciating pain with VAS score >7

Common affected sites are first MTP join, midfoot and ankle

Usually occurs at night, with patient's sleep interrupted due to severe joint pain

INTERCRITICAL GOUT

Asymptomatic period after or between gout flares, despite the persistence of MSU crystals.

CHRONIC GOUTY ARTHRITIS

Persistent joint inflammation induced by MSU crystals

- Chronic arthritis, with or without tophi
- Chronic joint pain
- Functional disability
- Structural joint destruction, deformity and repeated flares

Physical examination during a flare:

- Swelling, redness, warmth, profound tenderness with markedly reduced movement of the affected joint
- Desquamation of overlying skin in superficial joints as flare resolves
- Swelling, redness, warmth and tenderness of periarticular structures due to involvement of bursa or tendon
- Fever

In chronic gouty arthritis, the following signs may be present:

- Joint deformity
- Subcutaneous tophi

TREATMENT

AIM

1. To provide rapid and effective pain relief during gout flares
2. To achieve a sustained reduction in SU level --> reduction in gout flares

NON-PHARMACOLOGICAL

1. Health Education

2. Lifestyle Modification

- Reduce weight if obese/ overweight
- Limit intake of
  - Purine-rich food especially of animal origin
  - All types of alcohol
  - High-fructose corn syrup
- Encourages vegetables, fruits, whole grains, fat-free or low fat dairy products, fish, poultry, beans, nuts and vegetable oil
- Stay well dehydrated
- Smoking cessation
- Exercise

3. Concomitant medications

Medications that increase risk of gout should be discontinued or replaced with alternatives if possible.

4. Topical ice

May be used during gout flare

Ice packs should always be applied over a cloth and not directly onto the skin.

PHARMACOLOGICAL

1. Urate-Lowering Therapy

- e.g. xanthine oxidase inhibitors (allopurinol and febuxostat), uricosuric agents (benzbromarone and probenecid) and recombinant uricases (pegloticase)
- Established indications to initiate ULT for gout patients are:

  I. Recurrent gout flares (≥2 flares in 12 months) OR

  II. Presence of ≥ 1 tophi OR

  III. Presence of radiographic damage attributable to gout
- American College of Rheumatology (ACR) conditionally recommends ULT initiation for:
  - Gout patients who previously experienced >1 flare but have infrequent flares
  - Gout patients with their first gout flare based on the following indications:

    I. Moderate to severe CKD (stage ≥3) OR

    II. SU concentration >9 mg/dL (540 µmol/L) OR

    III. Urolithiasis

ULT should be continued long-term in gout patients to prevent recurrence of gout.

2. Treatment of Gout Flares

- Monotherapy: Colchicines, NSAIDS, COX-2 inhibitors, Corticosteroids
- Combination can be used if response to monotherapy is insufficient.

3. Flare Prophylaxis

- Initiation of ULT leads to dissolution of MSU deposits which causes dispersion of crystals resulting in increased gout flares.
- Should be used for at least three to six months when initiating urate-lowering therapy.
- The preferred choices are stepwise dose increase of urate lowering therapy and/or concomitant colchicine.

PHARMACOLOGICAL TREATMENT AVAILABLE IN HKP

ALLOPURINOL

Class: Xanthine oxidase inhibitors

Mechanism of Action:

- Inhibits xanthine oxidase, the enzyme that converts hypoxanthine to xanthine and xanthine to uric acid
- Increases reutilization of hypoxanthine and xanthine for nucleotide and nucleic acid synthesis -> increase in nucleotide concentration leads to feedback inhibition of de novo purine synthesis.

Dose:

- Initial: 50-100 mg daily.
- Maintenance: 300-900mg daily

Side effects:

- GI: nausea, vomiting
- Dermatologic: maculopapular rash, pruritus, **severe cutaneous adverse reaction including Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS)**
- Hepatic: Transaminitis, cholestasis
- Hematologic: Bone marrow suppression

NOT indicated for asymptomatic hyperuricemia.

STOP immediately if a skin rash/ sensitivity occurs.

NSAIDS / COX-2 INHIBITORS

Ibuprofen : 400—800mg TDS
Diclofenac: 50mg BD or TDS
Celecoxib: 400mg STAT, then 200mg BD

COLCHICINE

Class: Anti-inflammatory agent

Mechanism of Action:

- Interfere the migration of neutrophils to sites of inflammation that have been induced by deposits of monosodium urate crystals in synovial fluid

Dose:

- Gout flare: Initial dose, 1 mg, then 0.5 mg after 1 hour. No further tablets should be taken for 12 hours. After 12 hours, treatment can resume if necessary 0.5mg every 8 hours until symptoms are relieved. The course of treatment should end when symptoms are relieved or when a total of 6 mg (12 tablets) has been taken. After completion of a course, **another course should not be started for at least 3 days (72 hours).**
- Flare Prophylaxis: 0.5mg OD or BD.

Side effects:

- GI: Nause, vomiting, diarrhoea
- Haematologic: myelosuppression
- Neuromuscular & Skeletal: Neuromuscular disease, neuromyotoxicity

CORTICOSTEROIDS– PREDNISOLONE

- Flare treatment: 30—40mg OD or in 2 divided doses for 5 days.
- More severe flare: longer duration, a gradual taper over 7 to 10 days is an option.
- Multiple recent flares: slower taper over 14—21 days

REFERENCES

1. Clinical Practice Guideline Management of Gout 2nd Edition (2021). Ministry of Health Malaysia.
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