Gout

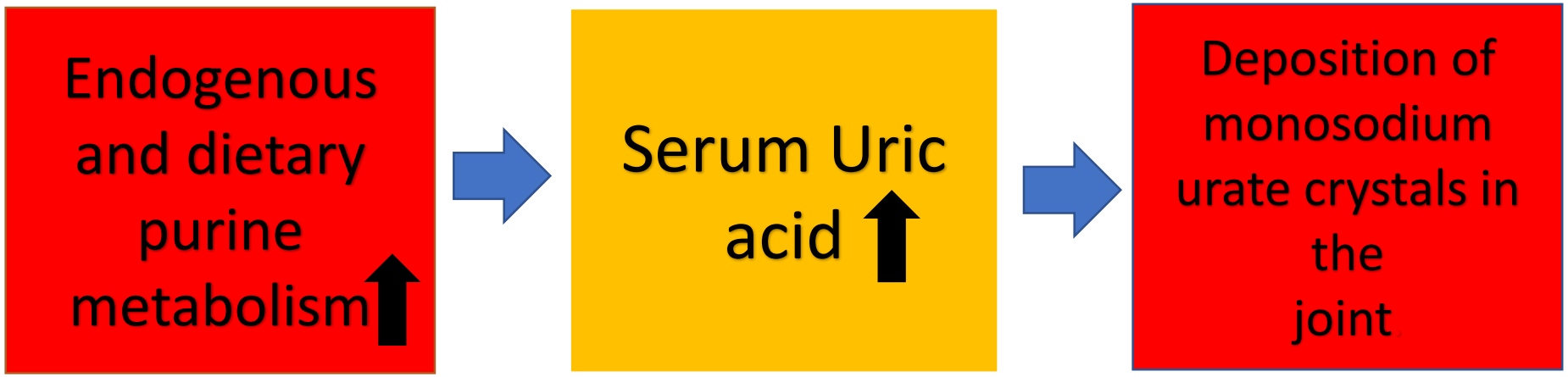
GOUT

- Gout is an inflammatory arthritis associated with **hyperuricaemia** and intra-articular **sodium urate crystals.**

EPIDEMIOLOGY

- The prevalence of gout has increased substantially in the last two decades to 2.5% in the UK and 3.9% in the USA.
- Asian populations are also increasingly at risk as their diet becomes more Western.
- This rising prevalence is due to changing diets with **purine-rich foods**, **high saturated fats** and **fructose**-containing drinks; **alcohol misuse**; increasing co-morbidities that promote **hyperuricaemia**; and suboptimal management.
- Gout is more common in **men** than women (5 : 1); it rarely occurs before young adulthood.

PATHOGENESIS



PATHOGENESIS

SERUM URIC ACID LEVEL INCREASED

Increased production of uric acid

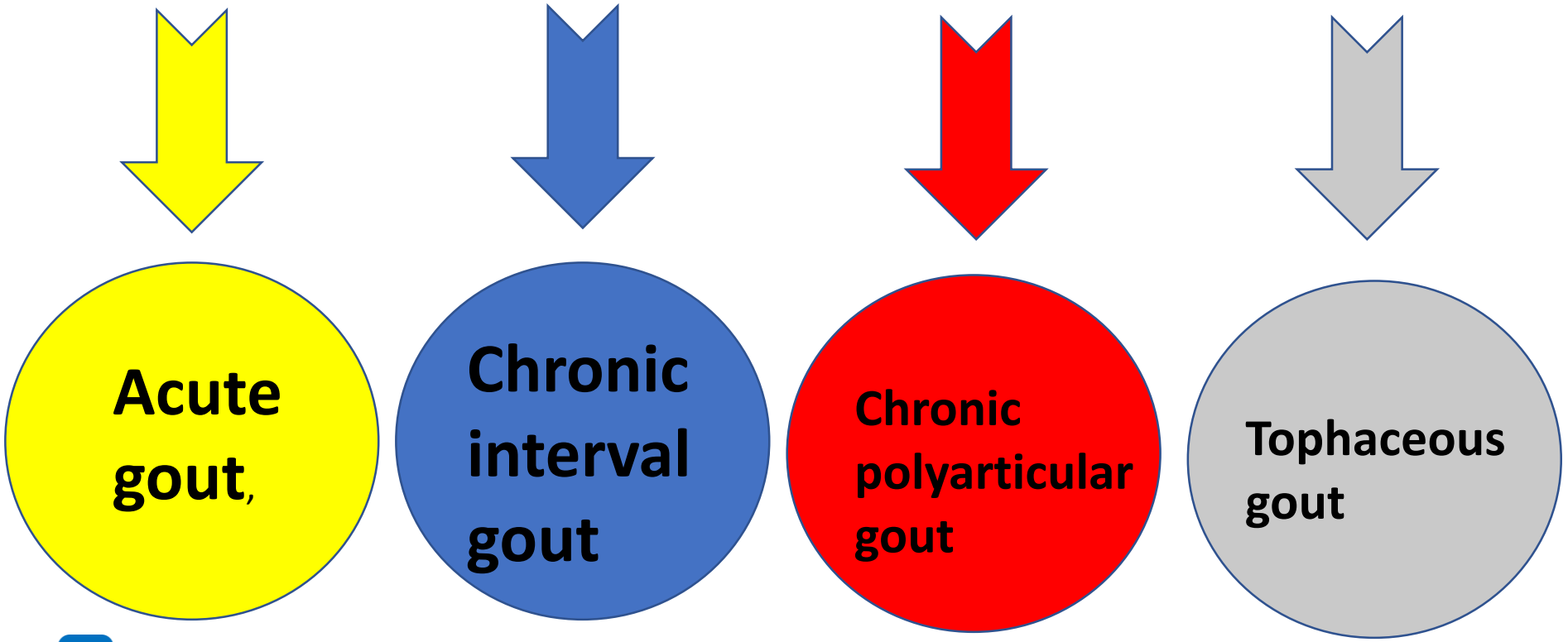
1. Myeloproliferative disorders, e.g. polycythaemia vera
2. Lymphoproliferative disorders, e.g. leukaemia
3. Others, e.g. carcinoma, severe psoriasis
4. Inborn errors

Impaired excretion of uric acid

1. CKD
2. Drug therapy,(thiazide diuretics, low-dose aspirin)
3. Hypertension
4. Lead toxicity
5. Primary hyperparathyroidism or hypothyroidism
6. Increased lactic acid production from alcohol, exercise, starvation

CLINICAL FEATURES

- Hyperuricaemia may be asymptomatic or cause:



CLINICAL FEATURES

Acute gout

Presents typically in a middle-aged male with a sudden onset of agonizing pain, swelling and redness of the first MTP joint.

The attack may be precipitated by excess food, alcohol, dehydration or diuretic therapy

CLINICAL FEATURES

Acute gout

Untreated attacks last about 7 days.
Recovery is typically associated with desquamation of the overlying skin.

In 25% of attacks, a joint other than the great toe is affected.
In severe attacks, overlying crystal cellulitis makes gout difficult to distinguish clinically from infective cellulitis.

CLINICAL FEATURES

Chronic Interval gout

with acute attacks superimposed on low-grade inflammation and potential joint damage.

Chronic Polyarticular gout

which is rare, except in elderly people on longstanding diuretic treatment, in renal failure, or when allopurinol is started too soon after an acute attack

CLINICAL FEATURES

Chronic tophaceous gout

Individuals with persistently high levels of uric acid can present with chronic tophaceous gout, as sodium urate forms smooth white deposits (tophi) in skin and around joints, on the ear, fingers or the Achilles tendon

Large deposits are unsightly and ulcerate. There is chronic joint pain and sometimes superimposed acute gouty attacks.

CLINICAL FEATURES

Chronic tophaceous gout

Tophaceous gout is often associated with renal impairment and/or the long-term use of diuretics.

Periarticular deposits lead to a halo of radio-opacity and clearly defined ('punched out') bone cysts on X-ray.
There may be acute or chronic urate nephropathy or renal stone formation

INVESTIGATIONS

- **The clinical picture is often diagnostic, as is the rapid response to NSAIDs or colchicine.**

Joint fluid microscopy is the most specific and diagnostic test but is technically difficult

Serum uric acid is usually raised (>600 µmol/L). If it is not, it should be rechecked several weeks after the attack, as levels fall immediately after an acute episode.

Serum urea, creatinine and estimated glomerular filtration rate

Management

Pharmacological management for symptoms relief

1.NSAIDs

High doses rapidly reduces the pain and swelling.

After 24–48 hours, reduced doses are given for a further week..

2. Colchicine

loading doses will cause diarrhea or colicky abdominal pain, so 500 µg 2–3 times per day is usually sufficient to terminate attacks without side-effects.

3.Corticosteroids

oral prednisolone or intramuscular or intra-articular depot methylprednisolone is used.

Management

Dietary advices

Reduce alcohol intake, especially beer, which is high in purines and fructose, and consumption of non-diet carbonated soft drinks, which are also high in fructose.

Reduce total calorie and cholesterol intake, and avoidance of purine-rich foods, such as offal, red meat, shellfish and spinach.

These modifications can reduce serum urate by 15% and delay the need for drugs that reduce serum urate levels.

Management

Treatment with agents that reduce serum uric acid levels

The aim of treatment is to reduce the uric acid level below the 360 µmol/L level; some guidelines recommend a level below 300 µmol/L.

1. Allopurinol

Allopurinol should only be used when the attacks are frequent and severe (despite dietary changes), or associated with renal impairment or tophi, or when the patient finds NSAIDs or colchicine difficult to tolerate.

Allopurinol is a xanthine oxidase inhibitor, which reduces serum uric acid levels rapidly; it is relatively non-toxic but should be used at low doses (50–100 mg) in renal impairment.

Management

Treatment with agents that reduce serum uric acid levels

1. Allopurinol

- It should never be started within a month of an acute attack and always under cover of NSAIDs or colchicine for the first 2–4 weeks before and 4 weeks after starting allopurinol, as it may induce acute gout.
- Skin rashes and gastrointestinal intolerance are the most common side-effects.
- A hypersensitivity reaction is the most serious but rare adverse event, as is bone marrow suppression.
- Allopurinol remains the drug of first choice, unless there are strong contraindications to its use.

Management

Treatment with agents that reduce serum uric acid levels

2.Febuxostat (80–120 mg)

is a non-purine analogue inhibitor of xanthine oxidase that is well tolerated and as effective as allopurinol. It is safer in renal impairment, as it undergoes hepatic metabolism rather than renal excretion,

3.Pegloticase,

a pegylated recombinant uricase given intravenously, lowers urate levels dramatically but its place in therapy is unclear.

Management

Treatment with agents that reduce serum uric acid levels

4.Losartan

Losartan is an angiotensin I receptor antagonist and is uricosuric in hypertensive patients with gout. It may reduce the risk of gout in patients with the metabolic syndrome.

4.Anakinra and canakinumb

Anakinra blocks IL-1β and canakinumab is a human monoclonal antibody with specific cross reactivity for IL-1β but not for other members of the IL-1 family.