PRIMEVIEW

GOUT

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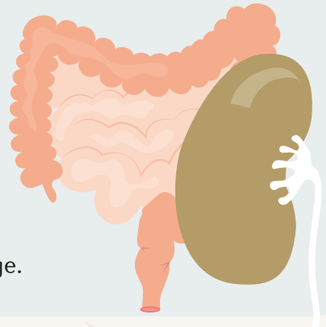
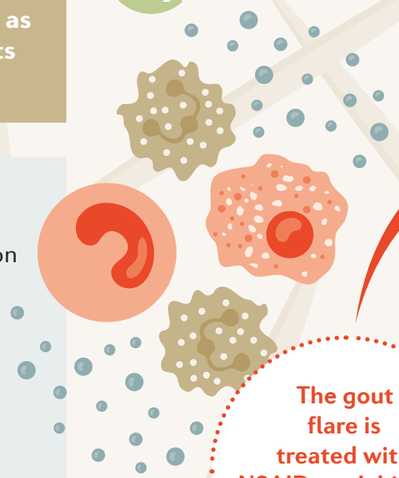
Gout is a chronic disease caused by deposition of monosodium urate (MSU) crystals, which usually manifests as acute inflammatory arthritis in the joints of the lower limbs.

MECHANISMS

The natural history of gout involves progression from hyperuricaemia (elevated blood levels of uric acid) to the deposition of MSU crystals. Hyperuricaemia can be due to the overproduction of urate (from, for example, high intake of purine-rich foods, fructose or alcohol) but the major contribution is from the under-excretion of urate by the kidneys or the gut, due to variants in genes encoding urate transporters. Although an elevated urate concentration is required for MSU crystal deposition, why this occurs only in some people with hyperuricaemia is unknown. In people with gout, an acute inflammatory response to deposited MSU crystals, termed a gout flare, involves increased production of pro-inflammatory cytokines, particularly IL-1β, by macrophages and monocytes, and the infiltration of neutrophils into affected tissues. However, neutrophils also limit inflammation by producing anti-inflammatory mediators and sequestering and degrading pro-inflammatory factors in aggregated neutrophil extracellular traps. Gout flares usually resolve spontaneously in 7–10 days. Without treatment, unresolved chronic inflammation and tissue remodelling can result in the formation of nodules called tophi, consisting of inflammatory granulomatous tissue and deposited MSU crystals, which can lead to joint damage.



MANAGEMENT



The gout flare is treated with NSAIDs, colchicine, corticosteroids or IL-1 inhibitors

Long-term management requires urate-lowering therapy (ULT) to achieve a target serum urate concentration (<0.36 mmol/l for most patients)

Anti-inflammatory prophylaxis is used to prevent a gout flare when starting ULT or when the ULT dose is increased

Screening for and management of comorbidities, such as hypertension and hyperlipidaemia, is important to improve long-term outcomes in patients with gout

Education of patients and health-care providers about gout management principles, such as the role of ULT and serum urate targets, is crucial for successful treatment

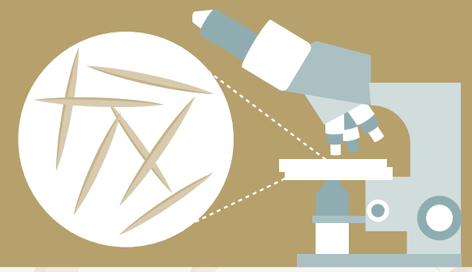
ULTs include inhibitors of urate production, drugs that increase renal urate excretion, or enzymes that metabolize urate

EPIDEMIOLOGY

Estimates of gout prevalence are in the range 2.7–6.7% in countries with a western lifestyle and incidence is rising. Gout is particularly common in indigenous Taiwanese and Polynesian peoples and is estimated at >8% of adults in these populations. Hyperuricaemia is the main risk factor for gout, so factors that increase the risk of developing hyperuricaemia, such as genetic variants, obesity and some medications and medical conditions, are also associated with increased gout risk. Sex and age are also important risk factors; twice as many men than women develop gout, and the prevalence of gout more than doubles in adults of >60 years of age.

DIAGNOSIS

Hyperuricaemia is the most common laboratory finding in people with suspected gout (based on clinical findings, such as monoarthritis). However, a definitive diagnosis requires confirmation of the presence of MSU crystals by microscopic examination of synovial fluid. Ultrasonography and dual-energy CT can be useful to evaluate disease severity in people with gout or to detect MSU crystals in people with atypical manifestations, such as arthritis in multiple joints at first presentation or tophus formation without prior gout flares.



OUTLOOK

The growing prevalence of gout requires population-level strategies to reduce environmental factors that increase gout risk. However, perceptions about gout as a self-inflicted disease of excessive consumption hamper efforts to treat the disease effectively, by causing patient embarrassment, affecting patient understanding of the disease aetiology and placing an unhelpful focus on largely ineffective dietary interventions. The intermittent nature of the disease (asymptomatic periods interspersed with gout flares) make education about the rationale for long-term ULT especially important. High-quality care involving patient education and shared decision-making represents the approach most likely to yield cost-effective, efficacious long-term treatment of gout.

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