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Gout: can we create an evidence-based systematic approach to diagnosis and management?

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The management of gout can be subdivided into four phases. Asymptomatic hyperuricaemia represents the basic underlying metabolic abnormality that can lead to gout. Studies are evaluating whether interventions may be indicated in some cases. Diagnostic criteria for gout and acute flares are still not well defined unless urate crystals are found. Acute attacks of gout are treated with anti-inflammatory measures and the agent of choice is often determined by attack stage, severity and comorbidities that may contra-indicate one or more agents. After attacks subside, there are asymptomatic periods during which decisions must be made about when and how to start urate-lowering measures. If hyperuricaemia persists, there is generally persistence of urate crystals in the joint. Anti-inflammatory prophylaxis is needed when urate-lowering therapy is started. Lifestyle measures should be addressed. If chronic tophaceous gout is diagnosed, urate lowering should be started without delay. New agents are under development that may help with difficult cases.

Key words: gout; uric acid; allopurinol; uricosurics; xanthine oxidase; colchicines.

Gout is probably as well understood as any disease we are asked to manage. We understand much about how monosodium urate (MSU) crystals induce inflammation[1], and about the underlying epidemiology, importance of and causes of hyperuricaemia.[2] Nevertheless, surveys have documented that management often falls short and we

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continue to see preventable tophaceous gout. How might we improve diagnosis and management, and is there evidence to support such proposals?

DIAGNOSIS

Accurate clinical diagnosis is essential before therapy, and even more so before embarking on lifelong chronic treatment. Assuring the accuracy of diagnosis is also critical in assessing results of clinical trials. Despite this, there has been little evaluation of diagnostic accuracy in the clinical setting. Algorithms for therapy often begin with an assumed diagnosis.

Is there a gold standard for diagnosis of either gout or acute gouty arthritis? Most accept that the documented presence of MSU crystals establishes the diagnosis of gout.[2] However, crystal documentation is often not attempted by primary care providers for various reasons. Microscopic crystal identification is observer and equipment dependent, and studies have shown inconsistencies among laboratories on examination of wet drop preparations.[3] It is well documented that errors are made leading to both over- and underdiagnosis. There is no simple automated method to be certain about crystal presence. An aggressive 'hands on' education has been shown to produce reasonable but not perfectly consistent results.[4] Examination of air-dried smears stained with Wright's and Gram stains can also detect crystals. Examination of Gram stains has been shown to be comparable with wet drop preparations.[5] Adequate numbers of leukocytes are needed to make satisfactory smears.

By definition, MSU crystal identification (if accurate) establishes the presence of gout, but it does not prove that an individual symptomatic episode is due to gout. MSU crystal presence and septic arthritis can occur in the same joint more often than many recognize. Might there be some other definitive test such as with imaging? A recent review noted that imaging with ultrasound or magnetic resonance imaging has potential value in the identification of tophi and large crystal deposits, but does not promise specificity or sensitivity.[6]

How can we define clinical flares? In a large prospective study of urate-lowering therapy, investigators were asked to report flares of acute gouty arthritis. Detailed features were not required. Between 43% and 53% of subjects reported 'flares' after withdrawal of colchicine or naproxen prophylaxis. Not all flares were actually treated with analgesics or anti-inflammatories.[7] How many of these 'attacks' were due to associated osteoarthritis, muscle strains etc.? A recent Delphi exercise is beginning to collect expert opinion on features thought to define flares.[8]

Thus, clinical criteria for acute gouty arthritis are important. Clinical criteria were proposed by the former American Rheumatism Association in 1977.[9] Experts compared clinically diagnosed cases of gout, rheumatoid arthritis, septic arthritis and pseudogout. A recent analysis showed that the six proposed clinical criteria were 87.6% sensitive, but 19.5% of the other diseases would be misdiagnosed as gout.[10] Ongoing studies are attempting to improve clinical criteria. Meanwhile, crystal diagnosis seems to be the most reliable method for definitive diagnosis.

What about the diagnosis of hyperuricaemia? Most hospitals and clinical laboratories report a range of normal serum uric acid levels based on population means $\pm$ two standard deviations. This may lead to normal values of 4–8 mg/dL (240–480 μmol/L). However, it may be more relevant to define hyperuricaemia in a biological context, as a level at which urate crystals may precipitate in joints and other tissues. Based on a few studies, it has been proposed to be 6.8–7.0 mg/dL.[102]