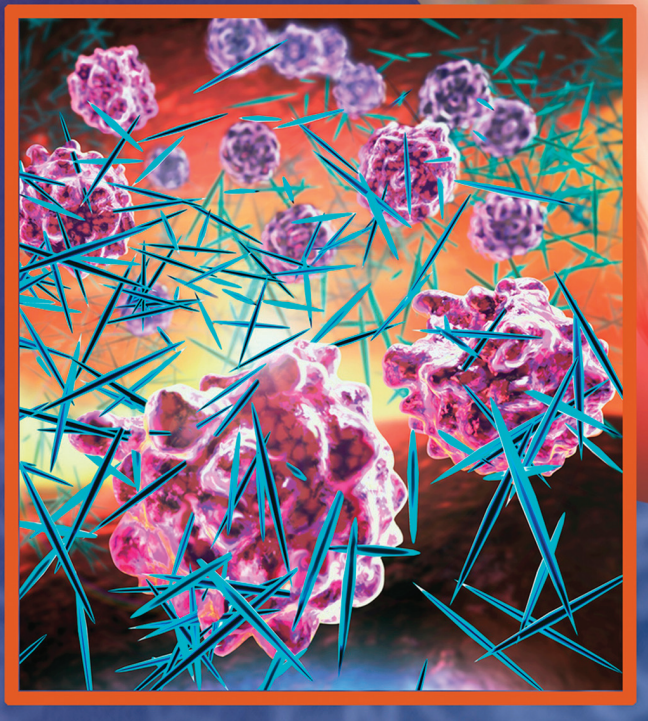
Gout



CE 2.1 CONTACT HOURS Rx 0.5 CONTACT HOURS

diagnosis & management

What NPs need to know

Abstract: Gout is the result of hyperuricemia, from either the body's overproduction or underexcretion. It can result in joint deterioration and destruction when improperly managed. Because primary care providers diagnose and treat the vast majority of patients with gout, it is important that they understand current guidelines and evidence-based practice.

By Eva Hardy, MSN, RN, APN-BC

Gout is the most easily diagnosed, yet the most undertreated of the arthropathies. It is the only chronic form of arthritis that is curable if appropriately treated.[1] Its process is well understood and has had efficacious treatment options for at least the last 50 years. However, for most primary care providers (PCPs), there are challenges to the diagnosis and management of this chronic condition. Hyperuricemia is the root cause of gout, and in recent years has become recognized as an independent risk factor for cardiovascular disease.[1] According to Chen and Schumacher, there is an increasing prevalence in several populations of significant comorbidities including cardiovascular disease, hypertension, renal insufficiency, and metabolic syndrome.[2] In the past decade, a series of educational meetings have been conducted by rheumatology experts to try to inform PCPs of the most effective ways to diagnose and manage gout. This article attempts to summarize the most important points from some of the major meetings, as well as the most current medical literature on the topic of diagnosing and managing gout. It will explore the epidemiology, pathophysiology, clinical presentation, diagnostic guidelines, standards of treatment recommended by experts, and patient education information that is needed to provide thorough and effective care of gout by PCPs.

Epidemiology

In Western populations, roughly 1% of people will develop gout at some point in their lifespan.[2] In the United States, gout affects approximately 3 to 5 million people with prevalence on the rise.[3] Between the genders, approximately 2% of men older than age 30 and women older than age 50 are afflicted.[3] Out of almost 4 million annual healthcare provider visits, more than two-thirds occur at the PCP's office.[3] Risk factors for gout have been well documented in medical literature. Nonmodifiable risk factors include being a man or postmenopausal woman, familial history, end-stage kidney disease, or being an organ transplant recipient.[3] Modifiable risk factors include excessive alcohol use (particularly beer), diuretic use, a diet high in purines, and metabolic syndrome resulting from obesity.[4] Study results have shown that although heavy alcohol use with beer increased the incidence, moderate use of red wine did not.[2] Also, although high-purine diets of red meat and seafood increased risk, consumption of high-purine legumes did not. It is interesting to note that there has been a two- to threefold increase in the incidence of gout in the last few decades paralleled with the increase in obesity and metabolic syndrome.[5]

Pathophysiology

Hyperuricemia has long been known to be the culprit for the development of gout and is defined as a serum uric acid

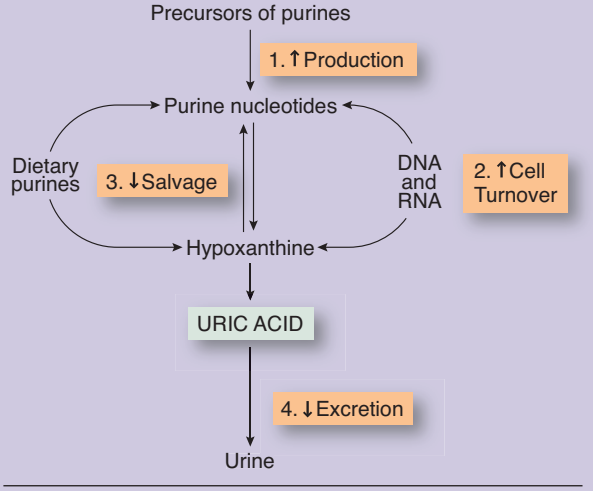
Key words: gout, gout diagnosis and management, hyperuricemia

concentration greater than 6.8 mg/dL.[3] This is the level at which urate solubility occurs at normal body temperature. Uric acid is the end product of purine metabolism (see *Pathogenesis of hyperuricemia and gout*). Hyperuricemia can result from either urate overproduction due to genetic factors or dietary intake (about 12%) or, more commonly, from urate underexcretion.[2] Urate is filtered in the glomerulus and undergoes tubular reabsorption and excretion, with about two-thirds secreted in the urine.[6]

There are four phases of gout: asymptomatic hyperuricemia, acute gouty arthritis, intercritical gout, and chronic tophaceous gout. Although hyperuricemia precedes gout, in some cases, patients may be asymptomatic without ever having a gouty attack.[3] Less than 25% of patients with urate levels greater than 9 mg/dL develop gout over 5 years.[4] Because it is impossible to predict which patients with asymptomatic hyperuricemia will develop gout, asymptomatic hyperuricemia is not usually treated.[3]

It is more probable that hyperuricemia in conjunction with local factors leads to acute gouty arthritis.[2] This occurs when the urate precipitates and deposits in joints as monosodium urate (MSU) crystals, and begins an inflammatory response.[2] Leukocytes are then attracted to the synovial space where the MSU crystals are phagocytized and destructive enzymes are released causing further inflammation and tissue damage.[6] Attacks are usually sudden in onset and nocturnal.[6] They also appear to be related to sudden increases or decreases in serum uric acid levels triggered by alcohol intake, dehydration, joint injury, recent surgery, or fever.[6]

Pathogenesis of hyperuricemia and gout



Source: Rubin R, Strayer D, eds. *Rubin's Pathology: Clinicopathologic Foundations of Medicine*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:1142

The intercritical phase is painless and can last indefinitely. Over time, attacks will occur more frequently, affect more joints, and last longer.[6] Some 60% of patients will have a second attack in the first year, and 78% will have a second attack within 2 years.[3] A study conducted in 2004 demonstrated the ongoing deposition of urate crystals in joints during intercritical periods.[4] A large number of the patients were asymptomatic at the time of arthrocentesis.[4] Dore stated that, "The results of the study demonstrated the importance of not only treating acute gout, but also of treating hyperuricemia during these intercritical periods to prevent joint damage and destruction."[4]

As the attacks become repeated and prolonged, the patient enters the chronic phase, characterized by the development of tophi (see *Gouty tophi of the hands*). After approximately 10 years of recurrent attacks, tophi will likely develop.[4] Tophi are accumulations of MSU crystals in hard, white nodules deposited in subcutaneous tissue, synovial membranes, tendons, and soft tissues.[6] They are most often found on cartilaginous surfaces (auricle and nose), the ulnar surface of the forearms, over joints, and along the Achilles tendons.[6] Deposits of the crystals in the renal tubules can also lead to renal calculi and nephropathy.[6] In recent decades, this last stage of gout has become uncommon because it can be prevented with proper medication treatment.[3]

Clinical presentation

The typical presentation of gout includes a sudden and progressively severe onset of monoarticular pain and swelling, usually in the lower extremities and most commonly in the great toe (podagra). The onset of symptoms is more often than not at night and has duration of 3 to 10 days without treatment. Montgomery described the affected joint(s) as having erythema, swelling, warmth, and tenderness. Patients might also complain of headache, fatigue, and chills.[6] After longer periods and recurrent attacks, the presentation may become polyarticular with significant joint destruction associated with insufficient treatment.

Sometimes there are atypical presentations of gout that can mimic other disorders. It is important, but can be difficult, to differentiate the symptoms of gout from rheumatoid arthritis (RA), osteoarthritis (OA), and septic arthritis.[7] In immunocompromised groups (such as patients with diabetes, dialysis, or an organ transplant), gout and infection can have similar, and even overlapping, presentations.[4] Typical inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein can be elevated in both but lack diagnostic specificity.[7] Clinical signs and symptoms may also be unreliable indicators.[7] According to Chui and Lee, approximately one-half of the patients with septic arthritis

and over one-third of those who develop overlapping septic arthritis and gout will be afebrile on clinical presentation.[7] Therefore, even if crystals have been found previously, aspiration and culture are warranted in the previously stated groups.[5] If aspiration cannot be done, it is reasonable that these patients should be immediately referred to a rheumatologist or ED for definitive evaluation and treatment.[4] Dore stated that atypical presentations of gout may involve several small joints in the upper extremity or may have symmetric or asymmetric polyarticular presentations, as with RA or OA.[4] Also, it is important to differentiate tophaceous gout from rheumatoid nodules. In the upper extremities, for example, RA nodules are typically found on the extensor surface of the forearm, and tophi are usually located in the olecranon bursa.[4] In addition, tophi are hard, painless, and irregular, and can erode and drain a chalky substance.[6]

Diagnosis

During an acute attack, aspiration and analysis of translucent synovial fluid with the presence of yellow urate crystals, a moderate amount of white blood cells, and negative cultures is the gold standard for the diagnosis of gout.[6] Additionally, it is important to assess renal function, and baseline lab testing should include a complete blood cell count, urinalysis, blood urea nitrogen, and serum creatinine.[3] According to Weaver et al., in one study conducted, only 11% of patients were diagnosed with gout by confirmation of MSU in synovial fluid.[8] Because arthrocentesis may be impractical for most PCPs, the American College of Rheumatology (ACR) has provided evidence-based criteria for diagnosing gout.[3]

For a diagnosis of gout to be made, at least six of the criteria must be present in the absence of a synovial fluid analysis. Although hyperuricemia is listed as one of the criteria and is a risk factor for developing gout, serum uric acid levels can be normal during an acute flare of gout. Therefore, it is not recommended that those levels be drawn during an acute attack, but rather about 2 weeks after it has subsided.[4]

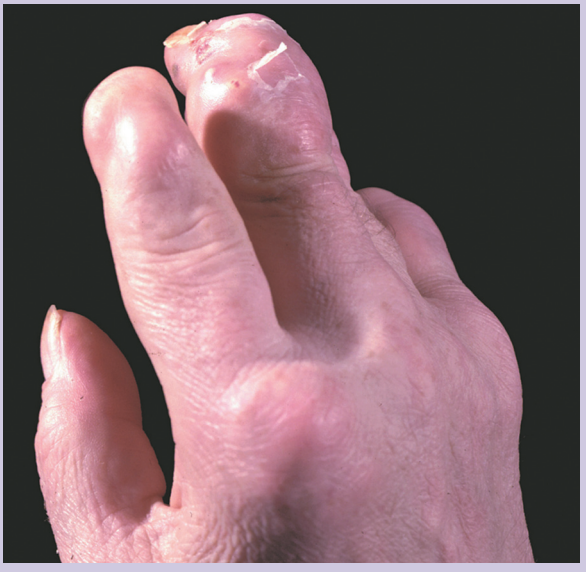
Treatment

Acute gout. There are two major phases in the management of gout. First, the PCP must treat the acute inflammatory flare and then begin chronic management to prevent further episodes by reducing serum uric acid levels. Introduction of nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine (now marketed as Colcrys), and oral and parenteral corticosteroids is the recognized standard of initial treatment.[4] To date, there is no definitive data that one NSAID is more effective than another. However, maximum prescription doses are recommended with decreases in pain reported in as little as 4 hours and gradual improvement over the preceding week. It is recommended that NSAID doses be tapered and continued for several days after the patient is asymptomatic.[2] Colchicine is highly effective when given within the first 12 to 36 hours of an attack and acts as an anti-inflammatory but not as an analgesic.[3] However, it is metabolized by the liver and excreted by the kidney, so its dosage must be lowered in older adults or in those with hepatic or renal dysfunction.[2] It also produces gastrointestinal (GI) adverse reactions in up to 80% of patients.[3] The corticosteroid, prednisone, is used successfully in patients with polyarticular episodes and if NSAIDs are contraindicated.[2] Just as with NSAIDs, the corticosteroid dose should be tapered and continued for a short time even after the attack has subsided. If a patient has not been treated with oral prednisone, adrenocorticotropic hormone given I.M. is also very useful.[3] Nevertheless, it may require multiple injections and therefore may be less appealing to most patients.

Intercritical and chronic gout. It is not clear in the evidence-based literature when urate-lowering therapy should be initiated, but it is critical to prevent further crystal accumulation and recurrent gouty flares. Therapy should be initiated 1 to 2 weeks after an acute attack has resolved.[4] It is generally accepted that it should be started

Gouty tophi of the hands

The following shows gouty tophi of the hands. There are multiple rubbery nodules, with ulceration of one of the nodules.



Source: Rubin R, Strayer D, eds. *Rubin's Pathology: Clinicopathologic Foundations of Medicine*. 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:1143.

for those patients with tophi, nephrolithiasis, and for those with hyperuricemia and two or more attacks per year.[3] The key goal in urate-lowering therapy is a reduction and maintenance of serum uric acid to less than 6 mg/dL. According to Chen and Schumacher, uric acid levels less than 6 mg/dL have been shown to decrease the number of flares, reduce MSU accumulation in the joints, and dissolve tophi.[2]

Two classes of drugs can achieve long-term reduction of serum uric acid: xanthine oxidase inhibitors and uricosurics. Allopurinol is a xanthine oxidase inhibitor and is the most commonly used drug in effectively reducing hyperuricemia regardless of its etiology when taken through the remainder of the lifespan. Dosing of allopurinol should be titrated on an individual basis until the target serum urate level is reached. Two possible problems with administration of allopurinol are hypersensitivity syndrome (which occurs in about 2% of patients and is potentially fatal) and refractoriness to the drug itself.[2,9] Hypersensitivity reaction consists of an erythematous desquamating rash, hepatitis, eosinophilia, fever, and declining renal function.[4] If allopurinol is contraindicated, febuxostat (Uloric) is a recently approved xanthine oxidase inhibitor for the chronic management of hyperuricemia associated with gout.[3] Febuxostat is not recommended for treatment of asymptomatic hyperuricemia. Liver enzymes may elevate with use of this drug, so alanine aminotransferase and aspartate aminotransferase levels will need to be closely monitored to avoid hepatic damage. In clinical trials, a higher rate of cardiovascular thromboembolic events was observed in patients treated with febuxostat than those treated with allopurinol.[3] Low-dose NSAIDs and colchicines are recommended for prophylaxis during this period with the concurrent use of a urate-lowering agent until the serum uric acid level is stable at less than 6 mg/dL and acute attacks have been absent for 3 to 6 months.[3]

For patients who cannot tolerate either of the available xanthine oxidase inhibitors, drugs in the uricosuric class should be considered. Patients must have serum creatinine levels less than 1.8 mg/dL, not fall into the class of uric acid overproducers (based on a 24-hour urine collection), and be willing to drink at least eight glasses of water per day to decrease the risk of nephrolithiasis.[2] Probenecid was the first drug of this class to be available. Avoid concurrent use of aspirin with probenecid because aspirin will block the effect of probenecid. Stamp et al. stated that probenecid can block excretion of penicillin, increase serum concentration of furosemide, and extend heparin metabolism.[1] Sulfinpyrazone is another uricosuric available. Its main adverse effect is GI disturbance and is specifically contraindicated for those patients with peptic ulcer disease.

Rheumatologic consultation

Statistics show that only about 3% of patients are referred by a PCP to a rheumatologist for management of gout, but acute gout is a common cause for inpatient rheumatology consultation.[10] Barber et al. cited a retrospective study of gout patients seen in consultation by a rheumatologist versus those who were not.[10] Patients evaluated by rheumatology were 21.9% more likely to have gout diagnosed by synovial fluid analysis, 25.7% more like to have had culture and sensitivity in the workup, and 18.3% more likely to have documented serum urate levels.[10] In the treatment of acute gout, patients with a rheumatology consult were 30.3% less likely to have NSAIDs and higher doses of colchicine ordered, but were 32.4% more likely to receive an intra-articular cortisone injection.[10] Prophylaxis with allopurinol was recommended or begun in a 31.1% more patients consulted by rheumatology, and those patients were also more likely to have the drug titrated to target serum urate concentrations.[10]

Patient education

Once the patient is asymptomatic and has begun the intercritical phase, education regarding the importance of chronic therapy and follow-up should be initiated. Approximately less than 20% of patients will actually make lifestyle changes, but education about joint destruction during the intercritical periods and requiring routine follow-up can help to achieve that objective.[4] NPs need to stress the importance of lifelong compliance with urate-lowering drugs to avoid further joint damage. Because gout and hyperuricemia have now been found to be elements of metabolic syndrome and cardiovascular disease, it is also necessary for the NP to stress the importance of weight loss and regular exercise where applicable. Treatment of comorbid conditions is also a key recommendation in the management of gout.[9] If the patient is also being treated for cardiovascular disease and hypertension, it may best to make a rheumatology referral because aspirin, niacin, and diuretics all have been found to precipitate attacks.[6] Teaching the patient about dietary modifications can also be helpful. Avoidance of alcohol, red meat, and seafood can help to lower serum urate. Increasing citrate and dairy can increase urinary pH.[6] Also, patients should be encouraged to increase water intake to at least 2 liters per day to lessen the risk of developing kidney stones.

Implications for practice

Gout is a well-documented and extensively studied disease whose prevalence is on the increase in Western societies in conjunction with the increasing prevalence of metabolic syndrome. If synovial fluid analysis is not done, then

diagnosis must meet at least six of the ACR's diagnostic criteria. It is also crucial that infection be ruled out initially because the symptoms of an acute gout attack can mimic the infectious process. The NP must have knowledge of the phases of the disease in order to effectively manage gout. In particular, the intercritical phase must be well managed to decrease the incidence of acute attacks and also to limit the risk of joint destruction.

Highly effective drugs have been available for treatment of gout for several decades and new ones continue to be developed. Treating the underlying epidemic of metabolic syndrome, however, could definitely lessen the risk of patients developing gout. Therefore, NPs must recognize the potential for certain patients to develop gout so that treatment can begin immediately and continue throughout the patient's lifespan to avoid further joint destruction. Referral to a rheumatologist should be considered for patients who require a more definitive diagnosis and treatment options.

Patient education for prevention of hyperuricemia needs to be done in those patients who have metabolic syndrome and an active diagnosis of gout. NP

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