



Gout is more prevalent in older adults than middle-age adults, and it affects women almost as commonly as men. An important clinical consideration regarding gout is that while hyperuricemia is commonly associated with gouty arthritis, a diagnosis of asymptomatic hyperuricemia does not generally require treatment. In addition, the clinical presentation and course of gout in older patients differ from the typical cases of middle-aged patients. Moreover, older gout patients present a challenge for physicians who manage them because of the high incidence of comorbid conditions and the likely occurrence of reduced renal function among this age group. This article reviews the diagnosis and management of asymptomatic hyperuricemia and gout in the older adult.

Key words: gout, hyperuricemia, NSAID, allopurinol, arthritis.

Diagnosis and Management of Asymptomatic Hyperuricemia and Gout in Older Adults

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Introduction

Gout is a clinical syndrome caused by an inflammatory response to deposition of monosodium urate crystals in the synovial or periarticular soft tissues. Gout is widely considered to be a disease of middle-aged men, but in fact it has an increasing frequency in men and women in older age groups. The overall prevalence of gout in the general population is 1.36% in males and 0.64% in females; however, the prevalence approaches 3.99% in people over age 65.¹

Hyperuricemia is defined as a serum urate level higher than 7.57mg/dl for men and 6.03mg/dl for women. Serum urate concentration correlates strongly with serum creatinine, body weight, height, and blood pressure.² Asymptomatic hyperuricemia has been reported in 25.8% in men and 15% in women in North America. While gout is a common complication of hyperuricemia, it is not an inevitable outcome of the condition, and many patients with hyperuricemia never develop gout-like symptoms.

Typically, gout progresses through four clinical stages: asymptomatic hyperuricemia, acute gouty arthritis attacks, intercritical gout (with variable intervals between recurrent acute attacks), and chronic tophaceous gout. This article will discuss the clinical manifestations of the various stages of this syndrome and its management.

Clinical Features

Asymptomatic Hyperuricemia

Hyperuricemia may result from increased urate production, decreased

urate elimination or a combination of both (Tables 1 and 2).

Hyperuricemia has been associated with cardiovascular disease, though it is debatable whether or not serum uric acid is an independent cardiovascular risk factor.⁴

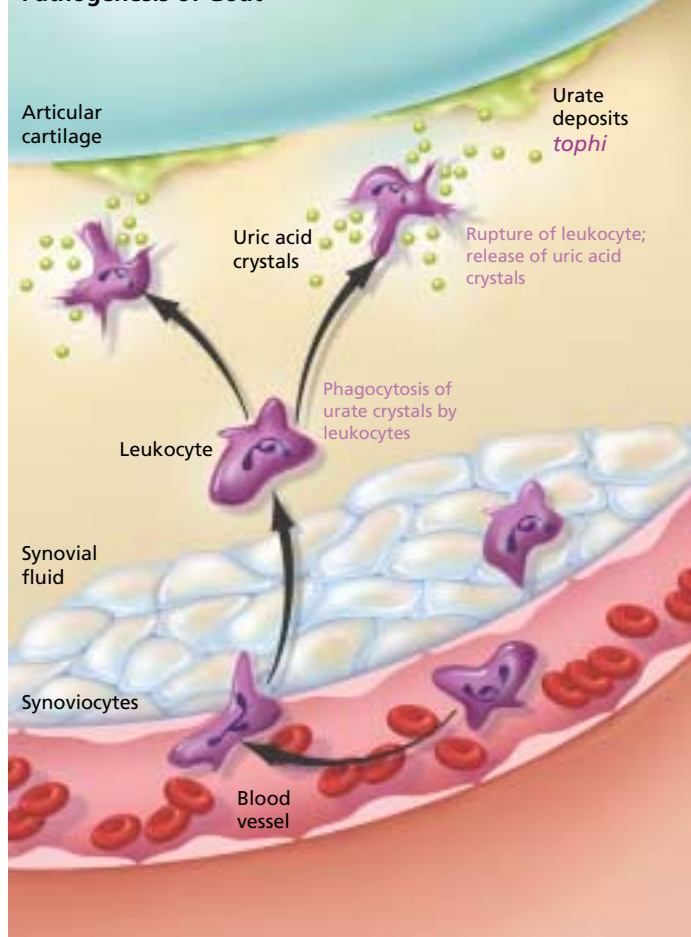
The risk of gout and tophaceous gout increases with both the degree and duration of hyperuricemia. The higher the serum urate level, however, the higher the risk factor for development of gout. A serum urate level of 9mg/dl has been associated with an annual incidence of gouty arthritis of 4.9%, while the incidence rate drops to 0.5% among those with a serum urate level of 7 to 8.9mg/dl, and 0.1% among those with urate levels below 7mg/dl.³

Because most patients with hyperuricemia do not develop gout, it is unnecessary to treat patients presenting with asymptomatic hyperuricemia with urate-lowering agents. Rather, the identification of asymptomatic hyperuricemia should alert the physician to look for and treat underlying causes of hyperuricemia and associated medical conditions (Tables 1 and 2).

Acute Gouty Arthritis

A typical acute gout attack in a middle-aged person occurs after years of sustained hyperuricemia and deposition of monosodium urate in the synovial tissue (Figure 1). The initial attack is monoarthral in about 80% of patients.⁶ Patients experience sudden, excruciating pain associated with redness and swelling of the affected joint. Lower

Figure 1:
Pathogenesis of Gout



extremity joints are usually affected, with about 60% of first attacks involving the first metatarsophalangeal joints. Acute gouty attacks may last from a few days to two to three weeks, with a gradual resolution of all inflammatory signs and a return to normal appearance.

Acute gout in older adults differs from the acute gout observed in middle-aged adults in the following respects: there is a higher frequency of polyarticular involvement; acute gout occurs in a higher frequency of older, postmenopausal female patients; there is a tendency for involvement of the small joints of the fingers; the development of tophaceous deposits appears earlier in the course of illness, often in atypical locations; and, finally, there is a greater association with diuretic use and renal disease.⁷

A diagnosis in older adults can be made readily when gout presents in a classic way. However, the presence of atypical symptoms in older patients, such as a history of prior acute arthritis, can confound physicians.

In older patients, gout should be suspected when attacks of acute pain and swelling are seen in osteoarthritic IP joints of the fingers, especially in patients with renal disease or chronic diuretic use. Gout should also be suspected when enlargement of these joints seems out of proportion with what is seen in typ-

ical Heberden's or Bouchard's nodes.

Alternative diagnoses should be considered in all patients suspected of gout. Acute arthritis may be a result of infection, secondary inflammation caused by other crystal-induced arthropathies, or other inflammatory joint diseases such as rheumatoid arthritis. In addition, gout and infection can coexist in the same joint.

Since the clinical presentations of gout in older patients are usually atypical, and the clinical elements we often rely upon for diagnosis are often not present, examination of joint fluid for the presence of urate crystals becomes very important in ruling out different forms of inflammatory arthritis in the presence of hyperuricemia and for making the correct management decision in gout cases.

Management of Acute Attacks

It is recommended that physicians begin treatment as early as possible when symptoms of an acute attack appear. Agents available for treatment include non-steroidal anti-inflammatory drugs, and corticosteroids.

Colchicine has been used in the past to treat acute attacks of gout (Table 3). Its anti-inflammatory action is thought to be mediated by alteration of the neutrophil leukocyte population; it has no effect on the serum urate level, however. Most patients experience nausea, vomiting, abdominal cramps, and diarrhea when given therapeutic doses needed to control severe attacks. Colchicine should thus be prescribed with caution in older patients and avoided in those with renal or hepatic insufficiency, or in patients already on chronic maintenance colchicine. In fact, colchicine is now rarely used in the treatment of acute gout in older patients.

Non-steroidal anti-inflammatory drugs (NSAIDs) are the drugs of choice for acute attacks. Their anti-inflammatory action is mediated by suppressing the production of prostaglandin. NSAIDs carry risks of gastritis, gastric hemorrhage, fluid retention, and interference with antihypertensive and anticoagulant therapy, particularly in older patients. In addition, mentation problems may occur with the use of these agents. Thus, in older patients, NSAIDs should be used only in low doses for short periods. Careful monitoring of renal function is particularly important in patients with impaired renal function prior to starting the treatment. In patients with increased risk of stomach bleeding, selective COX-inhibitor NSAIDs or a diclofenac-misoprostol combined preparation may have advantages over regular NSAIDs.

Corticosteroids are being used with increasing frequency in recent years for treating acute gout in the older patient. Intra-articular steroids after arthrocentesis are extremely useful. The dosage of steroid depends on the size of the joint, ranging from 5–10mg of depromedrol for small joints such as the IP joints of the extremities, to 40–60mg for larger joints such as the knee. Systemic corticosteroids could be used for patients when the use of NSAIDs is not advisable (i.e., patients with peptic ulcer disease or liver disease). Tapered doses of prednisone, starting

at 10mg tid for three days then decrease by 5mg a day every three days until it is discontinued, are often effective.

Immobilization of the affected joint over the acute stage will also help to eliminate some of the patient's discomfort.

Intercritical Gout

There is risk of repeated gouty attacks at varying intervals in those patients who have just recovered from an acute attack. It is good practice to maintain the patient on a small dose of NSAID for a period of four to six weeks. It is also recommended to do so when a urate-lowering drug is initiated (Table 3).

In patients with frequent, recurrent attacks, treatment with urate-lowering agents may be necessary. However, treatment with urate-lowering agents should only be considered in patients who have had proven urate crystal-induced gout with recurrent attacks and persistent hyperuricemia. It is not advisable to institute urate-lowering therapy in older patients because of the high frequency of the likelihood of comorbid conditions and decreased life expectancy. A strategy of observation and prompt treatment of acute attacks with NSAIDs or corticosteroids is the preferred course of action in these patients.

Chronic Tophaceous Gout

Acute gout in older patients runs a different course than in younger individuals, with a tendency for chronic, indolent progression rather than the intermittent attacks with complete resolution between attacks. Tophi develop commonly and can occur early in the course of the disease in older patients. Once the diagnosis of gout is ascertained by identification of urate crystals and x-ray evidence of joint damage from urate deposit, these patients should be treated with urate-lowering agents. Prophylactic use small doses of NSAIDs are useful for preventing attacks that may occur after initiating this treatment (Table 3).

As mentioned, urate-lowering agents should be used with care in older patients. The decision to introduce a drug to lower the serum urate level depends,

in part, on the number of previous attacks of acute gout (e.g., more than four times a year), and on the presence of tophi.

A commonly used urate-lowering agent allopurinol is a structural analogue of hypoxanthine. Allopurinol reduces uric acid synthesis by competitive inhibition of the enzyme xanthine oxidase, which catalyses the conversion of hypoxanthine to xanthine, and xanthine to uric acid.

In later life, renal clearance rates of allopurinol and oxipurinol, an allopurinol metabolite, are decreased compared with that of younger individuals, due to an age-related reduction in renal function. There is a linear relationship between renal oxipurinol clearance and creatinine clearance. An increase in oxipurinol levels in the blood may be responsible for higher allopurinol toxicity in older patients. It has been reported that thiazides increase the patient's hypersensitivity to allopurinol, and so concomitant administration should be avoided. Adverse events include hypersensitivity reactions (maculopapular rash to exfoliative dermatitis, malaise, fever, eosinophilia, liver function abnormalities, renal impairment), gastrointestinal problems (nausea, diarrhea), and neurological symptoms (headache, drowsiness).

In older patients, the dosage of allopurinol should be altered according to the creatinine clearance. One should periodically review all drugs and dosages and check the serum urate and creatinine levels to adjust the dose of allopurinol. When initiating the treatment, it is wise to increase the dose slowly, so that the proposed full dosage is reached only after two to four weeks. This will minimize the risk of an acute attack.

Uricosuric agents such as probenecid are seldom used in older patients due to the high frequency of renal insufficiency in this population and the frequency of gastrointestinal side effects. However, its use may be considered in patients whose renal clearance is normal or who are allergic to allopurinol. As for allopurinol, increase the dose of probenecid slowly when initiating the treatment. Use of uricosuric agents car-

Table 1: Common Causes of Increased Urate Production:

Idiopathic
Excessive dietary purine, alcohol intake
Myelo- and lymphoproliferation
Obesity
Hypertriglyceridemia
Psoriasis

ries a risk of precipitating renal stones. An increase in urine volume and alkalinization of urine could reduce this risk.³

Diet could also play role in lowering the serum uric acid levels. A reduction in red meat intake and an increase low-fat dairy product intake is purportedly beneficial for lowering uric acid levels.⁵

Summary

Though gout is inevitably associated with hyperuricemia, asymptomatic hyperuricemia alone does not typically require treatment, and the physician would be advised to look for and treat underlying causes and associated medical conditions (Tables 1 and 2).

The incidence of gout is higher in older adults than in middle-aged adults, and it affects women almost as commonly as men. In addition, the clinical presentation and course of gout in older patients differs from the typical pictures of the middle-aged patients. It commonly affects the small joints of the hands and

Table 2: Common Causes of Reduced Urate Excretion

Idiopathic
Renal diseases and insufficiency
Drugs, such as alcohol, diuretics, aspirin
Ketoacidosis (as in diabetes), dehydration
Hypothyroidism
Hyperparathyroidism
Sarcoidosis

Table 3: Comparison of Treatments for Gout

Drug Category	Contraindications	Dosage
Non-Steroidal Anti-Inflammatory Drugs:		
Non-selective Cox inhibitors	Avoid in patients with renal or hepatic failure and patients at risk for clinically significant gastrointestinal adverse effects, hemorrhage, congestive heart failure, or asthma.	<i>Indomethacin</i> : 50mg tid orally for three days then 50mg bid for 4–7 days <i>Naproxen</i> : 500mg bid for 7–10 days <i>Diclofenec sodium</i> : 50mg tid for 7–10 days
Selective COX inhibitors	Avoid in patients with renal or hepatic failure and patients at risk for congestive heart failure. Use with caution in patients at risk for clinically significant gastrointestinal adverse effects, including active peptic ulcer. May increase risk for cardiovascular events.	<i>Celecoxib</i> : 200mg bid for 7–10 days <i>Rofecoxib</i> : 25mg od for 7–10 days
Systemic Corticosteroids	Avoid use if joint sepsis not excluded. Use with caution in patients subject to hyperglycemia.	<i>Prednisone</i> : 10mg tid for three days, then decrease by 5mg per day every three days until discontinuation
Colchicine	Potentially severe side effects of colchicines and the efficacy and safety of other options render unnecessary the use of more extended dosing regimens of oral colchicines as a primary therapy. Patients receiving long-term low-dose oral colchicines should be regularly monitored for weakness, potential elevation in creatine phosphokinase, and bone marrow suppression. Potential drug interactions with erythromycin, simvastatin, and cyclosporine can increase risk of colchine-induced toxic effects.	0.6mg once an hour for up to three hours
Allopurinol	Caution needed in patients with renal failure, those taking azathioprine or mercaptopurine, and those taking warfarin.	50–300mg daily, dosage should be adjusted according to the creatinine clearance as follows: 300mg daily with normal creatinine clearance; 200mg daily with 50% of the normal creatinine clearance; 100mg daily with 30% of the normal clearance and <100mg daily with 30% or less of normal clearance

is usually polyarticular, and it tends to run a chronic course. Tophi formation tends to appear earlier in the disease than in middle-aged patients.

Older gout patients present a challenge for physicians who manage them because of the high incidence of comorbid conditions and the likely occurrence of reduced renal function among this age group. For these reasons, NSAIDs must be used with great caution. If allopurinol

is indicated, its dose should be calculated in portion to the creatinine clearance.◆

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