LEARNING OBJECTIVES
Upon completion of this activity, participants should be better able to:
- Describe the pathophysiologic underpinnings of gout
- Differentially diagnose gout based on hyperuricemia, joint assessment, and risk factors
- Discuss current and emerging treatment strategies that reduce risks of acute gout attacks
- Tailor treatment regimens for patients with gout
- Engage patients in open dialogue about gout as a chronic disease, treatment options, and adherence

INTRODUCTION
Gout is an inflammatory arthritis caused by the formation of monosodium urate (MSU) crystals in and around joints and other tissues.¹,² Acute attacks cause severe pain and swelling, whereas poorly managed gouty arthritis can progress to a chronically painful condition with permanent damage to joint tissues.³ Approximately 8.3 million adults in the United States have gout, which is the most common inflammatory joint disease in men.¹,² However, the disparity in gout prevalence between the sexes decreases after women reach menopause due to the loss of the uricosuric effect of estrogen.¹ The incidence and prevalence of gout have grown over the last 40 years for a variety of reasons, including aging of the general population, increased use of thiazides and loop diuretics, dietary trends,
GOUT

and higher rates of comorbidities linked to hyperuricemia, such as obesity and type 2 diabetes mellitus (T2DM).1

HYPERURICEMIA AND THE PATHOPHYSIOLOGY OF GOUT

The development of gout depends on the presence of hyperuricemia—ie, abnormally high serum urate levels—although for unknown reasons most individuals with elevated serum urate levels remain asymptomatic and do not develop gout.4,5 Serum levels of urate vary in healthy individuals; a range of 3.5 to 7.0 mg/dL is often quoted as “normal” for men, whereas urate levels are usually 0.5 to 1.0 mg/dL lower in women.4,5 The upper end of this range approaches the saturation point for urate in biologic fluids, or approximately 6.8 mg/dL.6,7 When circulating urate concentrations exceed this threshold, MSU crystals can spontaneously form in tissues throughout the body. However, because urate crystallizes more readily at lower temperatures, MSU crystals most commonly accumulate in cooler areas of the body, such as the distal joints of the feet and fingers. MSU crystals induce direct, self-limiting inflammatory responses and are phagocytosed by macrophages and neutrophils to stimulate proinflammatory cytokine production.8-10

It is important to recognize that the urate burden underlying gout development begins to accumulate long before symptoms manifest. Asymptomatic hyperuricemia and silent crystal deposition may occur for 20 or 30 years prior to the first acute attack (Figure 1).3 As the disease progresses, patients experience recurrent episodes of acute gouty arthritis with intercritical periods between flares. If hyperuricemia remains uncontrolled, long-term gouty complications develop, including chronic inflammation, erosive joint damage, and ongoing pain.3 In addition, elevated serum urate levels have been identified as an independent risk factor for chronic kidney disease (CKD), cardiovascular disease, and hypertension.11-13 In fact,

![Figure 1. Gout: stages of a chronic disease.](image-url)
a recent study found that patients with gout who did not receive treatment to reduce hyperuricemia were at greater risk during the 6.5-year follow-up for cardiovascular disease and all-cause mortality compared with patients treated with urate-lowering therapy, further highlighting the negative consequences of gout undertreatment. In most countries, the merits of assessing asymptomatic adults for hyperuricemia and then providing therapy to lower abnormal values remain a matter of debate; in Japan, for example, all adults are screened for hyperuricemia, and those with serum urate levels >8 mg/dL are treated with urate-lowering regimens.

Indeed, the vast majority of patients with gout will eventually require long-term pharmacologic treatment to reduce high circulating urate concentrations and prevent the associated sequelae. Serum levels of urate—a product of purine metabolism—are determined by a number of factors, including dietary purine intake, urate excretion via the intestines and kidneys, and cellular degradation of purines to urate. The last process is targeted by the most commonly prescribed urate-lowering agents, xanthine oxidase inhibitors, which interfere with the breakdown of purines into urate. The principal pathologic cause for almost all patients with gout, however, is inadequate renal urate excretion. Like other small metabolites, uric acid is filtered out of circulating blood in the nephrons of the kidneys. Subsequently, approximately 90% of urate is reabsorbed via transporter proteins in the nephron’s proximal tubule. Some medications—the so-called uricosuric agents—seek to enhance renal excretion of uric acid, primarily by inhibiting urate reuptake in the proximal tubule, and increasing urate excretion in the urine.

OVERCOMING DIAGNOSTIC CHALLENGES IN GOUT
Prompt identification of patients with gout is hampered by a number of challenges, including the self-limiting and often infrequent symptoms of early-stage disease and potential patient embarrassment over historical depictions of gout. The differential diagnosis includes a number of other conditions, including septic arthritis, pseudogout, cellulitis, osteoarthritis in the toe and small hand joints, rheumatoid arthritis, psoriatic arthritis, spondyloarthropathy, and Lyme disease. Fortunately, most gout attacks present in a manner that allows for a straightforward clinical diagnosis. For example, when a man with obesity, diabetes, and hypertension treated with a diuretic presents with excruciating, acute-onset pain in the big toe that was not preceded by trauma, he is highly likely to have gout. Up to 80% of initial acute attacks are monoarticular, with approximately 50% of flares affecting the metatarsophalangeal (MTP) joint of the big toe. Other common sites for acute gout flares include bursae, tendons, and joints near the elbows, wrists, fingers, knees, ankles, and feet. General laboratory testing should include serum urate levels, although importantly, urate levels are often lower during an acute flare due to the uricosuric effects of interleukin-2, which is present at higher concentrations during attacks. Imaging modalities can be useful for assessing patients with suspected gout, but are often impractical and/or unnecessary. Ultrasound, computed tomography, and magnetic resonance imaging are all sufficiently sensitive to pick up signs of early disease, whereas plain x-rays are of little use unless typical bone erosion and damage have already occurred.
The gold standard for gout diagnosis remains aspiration of an affected joint, with the fluid sample sent to a laboratory that is equipped to look for MSU crystals via compensated polarized light microscopy. Urate crystals can be identified by their needle and rod shapes with strong negative birefringence. Joint aspiration can also detect infections and help rule out other causes of joint pain, such as rheumatoid arthritis and pseudogout. In practice, however, patients are often reluctant to have painful joints aspirated, and the procedure is performed on only about 1 of 10 patients who receive a diagnosis of gout in primary care or even in rheumatology practices. Clinicians can also consider the 1977 American College of Rheumatology (ACR) Criteria for Classification of Acute Gout, which require patients to meet at least 6 of the 12 possible diagnostic criteria (Table 1). Of note, the ACR criteria have been shown to have a sensitivity of 70% and a specificity of 78.8%, suggesting that strictly relying on this approach will result in misdiagnosis for 1 of 5 cases. Thus, if a presumptive gout diagnosis with the ACR criteria is unclear, an affected joint should be aspirated and fluid should be analyzed for the presence of MSU crystals.

**TREATMENT OF ACUTE GOUTY ATTACKS**

Recommended treatment strategies for acute gout flares depend on pain onset and severity, the number of involved joints, and comorbidities. If pain has developed within the last 24 hours and is mild to moderate, or symptoms manifest in 1 to 3 small joints or 1 to 2 large joints, the 2012 ACR gout guidelines recommend monotherapy with a nonsteroidal anti-inflammatory drug (NSAID), systemic corticosteroids, or colchicine. Colchicine is less likely to help if the symptom onset occurs more than a day prior to administration. If the pain is severe or symptoms are polyarticular, involving multiple large joints, the guidelines suggest a number of potential combination regimens: (1) colchicine plus an NSAID, (2) oral corticosteroids plus colchicine, or (3) intra-articular steroids plus any of the other modalities. Acute therapy should be initiated within 24 hours of flare onset and patients on urate-lowering therapy should continue to take these medications during acute attacks. Finally, certain comorbidities can affect the medication choice, such as avoiding NSAIDs or corticosteroids in patients with gastric ulcers or T2DM, respectively.

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**Table 1. 1977 ACR Criteria for the Classification of Acute Gout**

<table>
<thead>
<tr>
<th>Criteria</th>
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<tr>
<td>1. &gt;1 attack of acute arthritis</td>
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<tr>
<td>2. Maximum inflammation developed within 1 day</td>
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<tr>
<td>3. Monoarthritis attack</td>
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<td>4. Redness observed over joints</td>
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<tr>
<td>5. First MTP joint painful or swollen</td>
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<tr>
<td>6. Unilateral first MTP joint attack</td>
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<tr>
<td>7. Unilateral tarsal joint attack</td>
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<tr>
<td>8. Tophus (proven or suspected)</td>
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<tr>
<td>9. Hyperuricemia</td>
</tr>
<tr>
<td>- During acute gout flares, serum urate levels are ≤6.0 mg/dL in 14% and</td>
</tr>
<tr>
<td>&lt;8.0 mg/dL in 32% of cases</td>
</tr>
<tr>
<td>10. Asymmetric swelling within joint on x-ray</td>
</tr>
<tr>
<td>11. Subcortical cysts without erosions on x-ray</td>
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<tr>
<td>12. Joint fluid negative for infection</td>
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</table>

≥6 of the 12 criteria = Probable gout
As acute symptoms come under control, patients should be educated about gout as a chronic but curable condition that requires ongoing self-management efforts. Specific advice on general health recommendations, lifestyle modifications, and dietary guidelines should be tailored based on each individual’s sociocultural background and health literacy level (Table 2). Websites with evidence-based information—for example, www.gouteducation.org and www.jointsaflame.com—can help with patient and caregiver education. Patients should also understand that while good diet and fitness choices are important for both managing gout and improving overall health, these efforts may not produce sufficient reductions in hyperuricemia; studies suggest these modalities usually decrease serum urate concentrations by 10% to 18%, which will fail to get the vast majority of individuals to goal. The ACR also recommends screening patients for comorbidities and risk factors that can contribute to hyperuricemia, including obesity, excessive alcohol intake, chronic kidney glomerular or interstitial disease, psoriasis, T2DM, and lead exposure, among others. Finally, clinicians should evaluate the burden of gouty disease in each patient (eg, palpable tophi, frequency and severity of acute and chronic symptoms) and eliminate nonessential urate-elevating medications, if at all possible.

Urate-Lowering Therapy
Assuming an absence of contraindications, treatment intolerance, and clinically problematic drug–drug interactions, guidelines from the ACR outline 4 general scenarios in which pharmacologic urate-lowering therapy should be initiated: (1) the presence of tophus identified via clinical examination or imaging, (2) ≥2 acute gouty attacks per year, (3) comorbid CKD stages 2 to 5 or end-stage renal disease, and (4) a history of urolithiasis. The goal of urate-

<table>
<thead>
<tr>
<th>Avoid</th>
<th>Limit</th>
<th>Encourage</th>
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<tr>
<td>• Organ meats high in purine content (eg,</td>
<td><strong>Serving sizes of:</strong></td>
<td>• Low-fat or nonfat dairy</td>
</tr>
<tr>
<td>sweetbreads, liver, kidney)</td>
<td>• Beef, lamb, pork</td>
<td>products</td>
</tr>
<tr>
<td></td>
<td>• Seafood with high purines (eg,</td>
<td></td>
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<td></td>
<td>shellfish)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• High-fructose corn syrup–sweetened</td>
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<tr>
<td></td>
<td>sodas, other beverages, or foods</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Serving of naturally sweet fruit</td>
<td></td>
</tr>
<tr>
<td></td>
<td>juices</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Table sugar, sweet beverages, and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>desserts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Table salt, including in sauces</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Alcohol overuse (≥2 drinks/d for men</td>
<td></td>
</tr>
<tr>
<td></td>
<td>or &gt;1 drink/d for women)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Any alcohol use during periods of</td>
<td></td>
</tr>
<tr>
<td></td>
<td>frequent attacks or in poorly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>controlled advanced gout</td>
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<tr>
<td></td>
<td>• Alcohol (particularly beer, but also</td>
<td></td>
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<td></td>
<td>wine and spirits) in all patients</td>
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lowering therapy is to push serum urate levels below individualized target values. The most common goal is <6.0 mg/dL, although some patients—including many with tophi—may need to reduce circulating urate concentrations below 5.0 mg/dL to improve gout signs and symptoms. Currently, the initial medication is usually a xanthine oxidase inhibitor (allopurinol or febuxostat) (Figure 2). If these agents are contraindicated, not tolerated, or not sufficiently effective, probenecid can be considered an alternative first-line option or as an add-on agent. To reduce the risk of acute gout attacks when urate-lowering therapy is first prescribed, anti-inflammatory prophylactic treatment should also be initiated either concurrently or even 1 or 2 weeks in advance. Regular monitoring of urate levels can then guide drug titration and other approaches to treatment intensification until the target is achieved.

The maximum daily allopurinol dose approved by the US Food and Drug Administration (FDA) is 800 mg (or lower in the presence of CKD), although published efficacy and safety data for doses >300 mg are somewhat limited. Treatment should begin at 100 mg/d or less (50 mg/d in patients with severe CKD), with gradual dose escalation every 2 to 5 weeks until the urate target is achieved. In practice, however, allopurinol is often underdosed. One small study of patients with gout found that the mean allopurinol dose required to bring urate values below 6.0 mg/dL was 372 mg/d, whereas a review of a US managed care database showed that more than 95% of allopurinol prescriptions were for daily doses ≤300 mg. When doses >300 mg are required, a twice-daily dosing schedule can help avoid gastrointestinal side effects. Renal and liver function should also be checked before and periodically during allopurinol treatment.

Limitations of allopurinol as a urate-lowering therapy include the potential for intolerance; 5% to 10% of patients will experience an issue requiring discontinuation, such as skin reactions, liver abnormalities, or gastrointestinal symptoms. Pruritic rash occurs in about 2% of newly treated patients. The most serious adverse event is major allopurinol hypersensitivity syndrome, a potentially fatal response to allopurinol exposure characterized by devastating rash, fever, worsening renal function, acute hepatocellular injury, eosinophilia, and leukocytosis. The syndrome, which can be fatal in 25% of cases, usually occurs during the first months after initiating therapy. Several risk factors have been identified, including CKD, concomitant use of

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**Figure 2. 2012 ACR guideline recommendations for urate-lowering therapy.**

<table>
<thead>
<tr>
<th>Treat to individualized serum urate targets</th>
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</thead>
<tbody>
<tr>
<td>Select first-line agent</td>
</tr>
<tr>
<td>Xanthine oxidase inhibitor</td>
</tr>
<tr>
<td>Allopurinol OR Febuxostat</td>
</tr>
</tbody>
</table>

If ≥1 xanthine oxidase inhibitor is contraindicated or not tolerated, alternative first-line agent:

| Probenecid |

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a thiazide, and an HLA-B*5801 genotype at 1 of the genes that codes for major histocompatibility complex proteins. Pharmacogenetic screening for the HLA-B*5801 allele—particularly in Han Chinese, Thai, and Korean patients, who are more likely to be carriers—can help identify patients who should probably receive an alternative urate-lowering medication.44 If this test is unavailable, allopurinol should not be used for these patient subgroups.

The other xanthine oxidase inhibitor that is commonly prescribed for gout is febuxostat. The starting dose is 40 mg/d, with labeled use in the United States up to 80 mg/d, although ACR guidelines allow for doses up to 120 mg/d (a dosage level that is approved in Europe).4,16,45 Febuxostat does not require dose adjustments for mild to moderate renal or hepatic impairment and is more selective but more expensive than allopurinol.45 In 3 phase 3 trials, significantly higher percentages of patients treated with febuxostat 80 mg/d achieved serum urate levels <6.0 mg/dL at their final follow-up visit compared with patients treated with allopurinol 300 mg/d, although suboptimal allopurinol dosing in the study protocols should be considered when interpreting these data (Figure 3).46-48

Another class of urate-lowering agents, the uricosurics, increase renal urate excretion by inhibiting urate reabsorption from filtrate in the kidney. The uricosuric probenecid is included in the ACR gout guidelines as an alternative urate-lowering monotherapy for patients who have a contraindication or are intolerant to at least 1 xanthine oxidase inhibitor.16 It is most commonly used as an add-on agent to a xanthine oxidase inhibitor when patients do not achieve their urate target. Probenecid is not recommended if creatinine clearance is <50 mL/min or in patients with a history of urolithiasis because it increases urolithiasis risk, especially in individuals with acidic urine.16,49 Losartan, atorvastatin, and fenofibrate are less potent uricosurics that do not carry an FDA approval for the treatment of gout.16,50 Lesinurad is a new uricosuric agent in late stages of development. Results from 3

![Figure 3. Phase 3 trials comparing febuxostat and allopurinol.46-48](image)

*P <.001 vs allopurinol; *P <.05 vs placebo and vs allopurinol; †P <.05 vs placebo.

APEX = Allopurinol- and Placebo-Controlled, Efficacy Study of Febuxostat; CONFIRMS = Efficacy and Safety of Oral Febuxostat in Participants With Gout; FACT = Febuxostat vs Allopurinol Control Trial.
phase 3 trials have been reported. In Combining Lesinurad With Allopurinol in Inadequate Responders (CLEAR 1 and 2), more patients achieved serum uric acid targets (<6.0 mg/dL) after 6 months of treatment with lesinurad 200 mg or 400 mg once daily plus allopurinol than with allopurinol plus placebo (Figure 4). In the Combination Treatment Study in Subjects With Tophaceous Gout With Lesinurad and Febuxostat (CRYSTAL), compared with patients treated with febuxostat alone, more patients treated with lesinurad and febuxostat achieved the primary end point of urate levels <5.0 mg/dL, including larger reductions in overall tophus area.

In the rare situation when gout is severe and refractory to treatment, primary care clinicians should consider referring the patient to a rheumatologist. Referrals may also be appropriate when the etiology of hyperuricemia is unclear, urate targets are difficult to reach in patients with renal impairment, and individuals experience multiple or serious adverse events in response to pharmacologic urate-lowering therapy. Patients who respond poorly to commonly prescribed urate-lowering agents may benefit from pegloticase, a therapeutic pegylated version of the urate oxidase enzyme uricase. In a 6-month trial of pegloticase 8 mg infused intravenously every 2 weeks, 40% of patients showed rapid and sustained decreases in serum urate concentrations and tophi dissolution by the final follow-up visit. Of note, however, 58% of study subjects were classified as nonresponders, some of whom may have developed neutralizing antibodies. Infusion reactions and gout flares were also common in the study. Coadministration of anti-inflammatory treatment (eg, glucocorticosteroids) may be needed to prevent antipegloticase antibody formation and gout flares. Oral urate-lowering agents should be discontinued during pegloticase treatment to avoid masking any loss of pegloticase’s serum-urate lowering effect.

Figure 4. Phase 3 data examining lesinurad + allopurinol vs allopurinol alone.61

\( a \)P <.0001 vs placebo + allopurinol. N = 603 (CLEAR 1) and 610 (CLEAR 2).
Prophylaxis for Acute Gout Flares

The introduction of urate-lowering therapy can induce the dispersal of MSU crystals from internal stores, which can precipitate acute gouty flares. The risks for this outcome can be observed in data from a clinical study comparing febuxostat versus allopurinol as gout treatments. In the study protocol, prophylactic medications (colchicine or naproxen) were withdrawn after week 8, resulting in a spike in acute attack frequency during the subsequent 4-week period (Figure 5). Current ACR guidelines, therefore, recommend that all patients also receive a pharmacologic anti-inflammatory prophylactic regimen when they are initiating urate-lowering therapy. First-line prophylactic approaches include low-dose colchicine (0.5 or 0.6 mg once or twice daily). Low-dose NSAIDs (with a proton pump inhibitor when indicated) can also be used, but FDA warnings against prolonged use suggest that the agents should be used as a second-line option. Low-dose prednisone or prednisolone (≤10 mg/d) is reserved as a third-line option. Prophylaxis should be continued for a minimum of 6 months from the initiation of urate-lowering therapy, although more extended coverage may be necessary; if no tophi are identified, the anti-inflammatory agent should be provided until 3 months after circulating urate levels fall below the target threshold, whereas prophylaxis is needed for 6 months after targets are achieved in cases in which ≥1 tophus is detected.

Strategies to Improve Treatment Adherence

In real-world practice, serum urate levels in most patients who have received a gout diagnosis have not been treated to values <6.0 mg/dL, even when urate-lowering therapy has been prescribed. Barriers to better outcomes include inadequate medication dosing and especially poor adherence rates for urate-lowering agents. In 1 study comparing treatment adherence

![Figure 5. Increased risks for acute gout flares when urate-lowering therapy is initiated without prophylaxis.47](image)

N = 762 patients with gout.
across 7 medical conditions (gout, hypertension, hypercholesterolemia, T2DM, osteoporosis, hypothyroidism, and seizure disorders), medication adherence was worst for gout; only about 1 of 3 patients took >80% of their urate-lowering doses during the first year of therapy. By comparison, almost 3 of 4 patients with hypertension were categorized as adherent. Anti-inflammatory prophylaxis when initiating urate-lowering therapy can help improve adherence, because flares induced by initial changes in urate storage can cause patients to stop treatment. Studies suggest that open discussions on gout and lifestyle changes combined with monitoring of serum urate levels and appropriate drug titration can help engage patients in their plans of care, improve adherence, and enhance overall outcomes. In 1 study of a nurse-led management approach that emphasized patient education, more than 9 of 10 patients were able to achieve recommended urate targets.

SUMMARY
The increasing prevalence and potentially severe consequences of gout underscore the importance of prompt diagnosis and appropriately aggressive treatment. For most patients, management requires a combination of short-term, primarily pharmacologic interventions for painful flares together with multimodal urate-lowering regimens to reduce the risk of acute episodes, reverse MSU deposition, and prevent long-term consequences of uncontrolled hyperuricemia. Patients with gout will benefit from increased use of treat-to-target strategies and the growing number of therapies that can be used to reduce serum urate levels. Lifestyle changes and adherence to prescribed treatment—even in the absence of acute symptoms—must be emphasized at each patient interaction to maximize reductions in the chronic urate burden and optimize therapeutic outcomes.

CASE: A Thai American Man With Recent-Onset Severe Pain in the Tarsal Joint

PRESENTATION
Adam, a 52-year-old Thai American accountant, presents with recent-onset, acute pain on the top of his right foot, in the tarsal joint. The pain is severe (rated 9/10) and greatly limits his mobility. He has had 3 similar attacks in the last 5 years, although the pain has always been self-limiting and, in his words, “nothing to bother a doctor about.” Adam reports that the pain on the top of his right foot first developed 18 hours ago and has remained excruciating.

Adam's medical history includes a diagnosis of hypertension 4 years ago, for which he takes lisinopril/hydrochlorothiazide 20 mg/12.5 mg daily. One year ago, he was diagnosed with T2DM, which is well controlled with metformin 1000 mg twice daily. He is a...
nonsmoker and has never experienced urolithiasis. Looking at Adam’s family history, his father died of a myocardial infarction at age 64, whereas his mother is relatively healthy at age 88.

Physical Examination
- Height: 5 ft 8 in
- Weight: 183 lb (body mass index [BMI]: 27.8 kg/m²)
- Blood pressure: 124/82 mm Hg
- Temperature: 97.8°F
- The affected tarsal joint is red, swollen, warm, and very tender
- No tophi are evident on examination
- No other joints appear to be affected at this time

Laboratory Findings
- Glycated hemoglobin (A1C): 6.5%
- Lipid panel
  - Total cholesterol: 184 mg/dL
  - Low-density lipoprotein cholesterol: 105 mg/dL
  - High-density lipoprotein cholesterol: 45 mg/dL
  - Triglycerides: 172 mg/dL
- Estimated glomerular filtration rate: 80 mL/min/1.73 m²
- Urine albumin-creatinine ratio: 4.2 mg/mmol
- Serum urate: 8.3 mg/dL

Based on Adam’s history, monoarticular symptoms, hyperuricemia, and other examination and laboratory findings, Adam receives a diagnosis of gout. The kidney function tests also show that Adam has CKD stage 2. The clinician recommends preventing future attacks by lowering Adam’s serum urate to <6.0 mg/dL and discusses the available treatment options to get him to goal. Adam and his clinician agree on a plan to reduce the risks of flares during the initial 6 months and review what steps Adam should take if a gout attack occurs.

Clinical Decision Point
*According to ACR guidelines, which of Adam’s presenting characteristics is an absolute indication for a urate-lowering medication in a patient with gout?*
A. Comorbid T2DM
B. Comorbid CKD stage 2
C. Hyperuricemia
D. BMI ≥25 kg/m²

COMMENT
Urate may be nephrotoxic, and hyperuricemia has been linked to various forms of nephropathy. Additional studies are required to clarify the potential renal benefits of lowering serum urate levels in patients with gout and CKD. Nevertheless, ACR guidelines identify
CKD stage 2 to 5 or end-stage renal disease as an indication, by itself, for pharmacologic urate-lowering therapy in patients with prior gout attacks and current hyperuricemia.\textsuperscript{16} Correct answer: B

CASE (cont’d)
The clinician prescribes colchicine 1.2 mg initially and 0.6 mg 1 hour later for Adam’s acute attack. He is advised to rest and avoid activities that will put pressure on the affected joint. As a result, his pain is reduced to tolerable levels within 24 hours. Adam is also educated on gout as a chronic disorder, including the risks of not addressing his growing urate burden and the opportunity to “cure” his disease with lifestyle changes and medication to lower his serum urate levels. The clinician also provides Adam with recommendations and online resources (eg, www.gouteducation.org) on adjusting his diet and advises him to continue with his current weight loss program and weekly exercise regimen.

Because of his Thai ancestry, Adam is tested for the $HLA^B*5801$ allele. After the results come back negative, Adam is prescribed allopurinol 100 mg once daily, which will be titrated up in the coming weeks based on ongoing monitoring of his serum urate levels. He also receives low-dose colchicine (0.6 mg twice daily) as acute gout prophylaxis for 6 months to accompany the initiation of allopurinol.

CASE CONCLUSION
Adam was treated with colchicine for his pain and acute symptoms and 2 weeks later, with allopurinol as a urate-lowering agent. Low-dose colchicine was also provided as prophylaxis against additional acute attacks. Adam will be monitored regularly to titrate the allopurinol dose until his serum urate levels fall below 6.0 mg/dL.

REFERENCES


**CLICK HERE TO COMPLETE THE EVALUATION AND SELF-ASSESSMENT QUESTIONS.**