in the clinic

Gout

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CME Objective: To review current evidence for the prevention, diagnosis, and treatment of gout.

The information contained herein should never be used as a substitute for clinical judgment.

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For several thousand years, gout has been recognized as a very painful form of acute and frequently recurrent arthritis. Gout is increasing in prevalence because of the higher prevalence of obesity, a high-caloric Western diet, diuretic use, and an aging population (1). Gout currently affects more than 5 million persons in the United States alone (2). It is the most common cause of inflammatory arthritis in men, with the highest incidence in men in their forties. Gout is caused by monosodium urate (MSU) crystals formed in joints and tissues when serum urate levels exceed 404.5 μmol/L (6.8 mg/dL), the approximate saturation point in human biological fluids. Gout causes acute mono- or polyarticular arthritis as well as chronic inflammation, which leads to joint destruction. Treatment is aimed at lowering serum urate levels and reducing the inflammatory response to the MSU crystals. After few advances in treatment for several decades, several new drugs for prevention of gout are now available.

Prevention and Screening

Risk Factors for Gout

- Hyperuricemia
- Male sex if younger than 60 years
- Obesity
- Diet high in purines (for example, red meat, shellfish)
- Consumption of alcohol (especially beer and spirits) and high-fructose drinks (for example, sodas, some juices)
- Medications (especially thiazide diuretics or cyclosporine)
- Renal insufficiency
- Lead exposure
- Organ transplantation
- Specific diseases (for example, hypertension, diabetes, hyperlipidemia, the metabolic syndrome, hematologic malignant conditions)
- Genetic risk factors

What are the risk factors for gout?

In 2280 prospectively followed healthy men in the Boston Veterans Administration Normative Aging Study, the serum urate level was the strongest predictor of gout (3). However, in that study, only 22% of the participants with serum urate levels greater than 535.4 μmol/L (9 mg/dL) developed gout over a 5-year period. Overall, about 10% of persons with hyperuricemia develop gout (4). Gout usually occurs only after many years of hyperuricemia. It is not currently recommended to treat asymptomatic hyperuricemia to prevent the disease. However, once gout develops, the urate level is predictive of flares.

Among 2237 elderly patients with known gout, those with high serum urate concentrations (356.91 to 534.8 μmol/L [6 to 8.99 mg/dL]) were 2 times more likely to have a flare in 12 months than patients with normal levels (<356.91 μmol/L [<6 mg/dL]), and those with very high serum urate concentrations (>535.4 μmol/L [>9 mg/dL]) were 3 times more likely. Moreover, the highest uric acid levels were associated with higher total and gout-related direct health care costs per episode (2)

Age and sex

Men have higher serum urate levels and a higher risk for gout than women, in part because estrogen stimulates renal excretion of uric acid. In persons younger than 30 years, the prevalence of gout is far greater in men than in women, but the gender gap narrows such that men and women older than 60 years have equal risk for gout and women in their eighties have greater risk for gout than men in their eighties. Especially among elderly persons, the prevalence of gout is increasing.

In a managed-care population of patients older than 75 years, the prevalence of gout roughly doubled from 21 to 41 cases per 1000 in 1990 to 1999 but changed little in persons younger than 65 years during that decade (1).

Weight

Obesity is also an important risk factor for gout. Observational studies suggest that weight control may be effective in reducing the risk for gout, but this has not been evaluated in a clinical trial.

In the Health Professionals Follow-up Study, which included more than 47 000 men, the risk for gout over 12 years increased linearly with increasing body mass index (BMI). Multivariate relative risks (RRs) for gout rose from 1.95 (95% CI, 1.44 to 2.65) for a BMI of 25 to 29.9 kg/m^2 to 2.97 (CI, 1.73 to 5.10) for a BMI of 35 kg/m^2 or greater versus a BMI of 21 to 22.9 kg/m^2 (P < 0.001 for trend). A loss of more than 10 lbs since study entry was associated with a 30% reduction in risk for gout (RR, 0.61 [CI, 0.40 to 0.92]) (5).

Diet

Uric acid is produced from the metabolism of purines that come

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2. Wu EQ, Patel PA, Mody RR, et al. Frequency, risk, and cost of gout-related episodes among the elderly: does serum uric acid level matter? J Rheumatol. 2009;36:1032-40. [PMID: 19369467]

exogenously from specific foods and endogenously from cellular metabolism (Box). Persons with gout may benefit from limiting dietary purines.

In an observational study of 47 150 men, the risk for gout increased by 21% for each additional portion of meat per day and by 7% for each additional portion of seafood per week. On the other hand, moderate consumption of purine-rich vegetables, such as mushrooms, was not associated with an increased risk for gout. Furthermore, the incidence of gout decreased with increasing intake of dairy products. Protein from dairy products does not seem to carry the same risk as protein from meat or fish sources (6).

Consumption of high-fructose foods and drinks has recently been recognized as a risk factor for gout.

In an observational study of 46 393 male health professionals, the adjusted RR for gout for 5 to 6 servings of sugar-sweetened soft drinks per week was 1.29 (CI, 1.00 to 1.68), for 1 serving per day was 1.45 (CI, 1.02 to 2.08), and for 2 or more servings per day was 1.85 (CI, 1.08 to 3.16) versus less than 1 serving per month (P = 0.002 for trend). Intake of fruit juice or fructose-rich fruits, such as apples and oranges, was also associated with a higher risk for gout (P < 0.05 for trend). Diet soft drinks were not associated with risk for gout (7).

Alcohol

Alcohol increases serum urate levels and even moderate levels of alcohol use can precipitate an attack in persons predisposed to gout. Alcohol may also interfere with renal excretion of uric acid. In particular, binge drinking increases urate levels. The risk differs by the type of alcohol, with beer and spirits being the more risky and wine less so.

An analysis of the National Health and Nutrition Examination Survey III revealed that serum urate level increased with consumption of beer and liquor and that persons with the highest intake (≥1 serving per day) had serum urate levels that were 58.9 µmol/L (CI, 48.8 to 69.6) higher (for beer) and 34.5 µmol/L (CI, 21.4 to 47.6) higher (for liquor) than in nondrinkers. This effect was greater for women and persons with BMIs less than 25 kg/m^2. On the other hand, wine consumption had an opposite effect: 1 or more servings per day was associated with a lower serum urate level (–13.7 µmol/L [CI, –28.6 to –1.8]) (8).

Similarly, among 47 150 men, the adjusted RR of gout was 1.32 (CI, 0.99 to 1.75) for alcohol consumption of 10.0 to 14.9 g/d (about 1 drink), 1.49 (CI, 1.14 to 1.94) for 15.0 to 29.9 g/d, 1.96 (CI, 1.48 to 2.60) for 30.0 to 49.9 g/d, and 2.53 (CI, 1.73 to 3.70) for 50 g or more per day (P <0.001 for trend) versus men who did not drink alcohol. Beer had the strongest association with gout, followed by spirits (9).

Medications

Diuretics, especially thiazides, are strongly linked to the development of gout. Diuretics increase renal resorption of uric acid, leading to hyperuricemia. Diuretic use is a common factor contributing to gout in older persons. Low-to-moderate levels of aspirin also increase the risk for gout. Other drugs that decrease renal urate clearance include pyrazinamide, ethambutol, and pyrazinoate. In addition, nicotinic acid, vitamin B_{12}, cancer chemo-therapy, and levodopa increase serum urate levels. Cyclosporine increases tubular resorption of uric acid and can cause polyarticular gout.

Lead exposure

Chronic occupational lead exposure has been associated with an increased incidence of gout because of reduced uric acid excretion, which leads to higher serum urate levels. Even low-level exposure has been reported to increase the risk for gout (10).

Organ transplantation

Persons who have received a renal transplant have an especially increased risk for gout, because of the combination of renal insufficiency and treatment with cyclosporine to prevent rejection. Other types of organ transplantation are also associated with an increased risk for gout. However, tacrolimus has less of an effect on urate levels and is now used more often.

High-Purine Animal and Fish Sources

- Red meat (beef, pork, lamb)
- Meat extracts (broth, gravy)
- Organ meats (such as sweetbreads, liver, and kidney)
- Seafood (shrimp, anchovies, mussels, scallops, sardines, herring, fish roe, canned tuna, shrimp, and lobster)
- Yeast products (beer and baked goods)

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Diseases associated with an increased risk for gout

Patients with renal insufficiency have an increased risk for gout because, as renal function decreases, so does renal clearance of uric acid (11). Hypertension, diabetes, hyperlipidemia, and the metabolic syndrome are also associated with increased risk for gout. Hematologic malignant conditions predispose to gout because of increased production of uric acid from rapid cellular turnover (12). Patients with hypothyroidism also have an increased incidence of gout due to decreased renal plasma flow and impaired glomerular filtration of uric acid (13). To a lesser extent, patients with hyperthyroidism may also have an increased risk due to increased uric acid production. Psoriasis has also been associated with an increased risk for gout, probably from increased cell turnover in plaques.

Genetic risk factors

Several genetic variants have been associated with gout. One variant reduces the efficiency of uric acid transport across the membranes of the kidney (4), whereas 2 other gene mutations are associated with high levels of uric acid (14, 15).

Inherited metabolic disorders, such as hypoxanthine-guanine phosphoribosyl transferase deficiency, phosphoribosyl pyrophosphate synthetase overactivity, and glucose-6-phosphatase deficiency, can lead to purine overproduction that predisposes a person to gout. Genetic disorders, such as the Bartter syndrome, polycystic kidney disease, and the Down syndrome, can also lead to hyperuricemia via decreased renal clearance of urate.

Are there effective strategies for preventing gout?

Primary prevention of gout involves lifestyle changes to reduce risk factors and lower serum urate levels, but prospective studies of the effectiveness of lifestyle changes are lacking. Pharmacologic therapy of asymptomatic hyperuricemia is not recommended, because of the potential toxicity of long-term prophylactic treatment.

Drugs are required to prevent gout in patients receiving chemotherapy for hematologic malignant conditions. Uric acid–lowering drugs and hydration reduce the risk for secondary gout due to tumor lysis in these persons. Without this treatment, uric acid nephropathy with tubular obstruction can develop. Allopurinol, which prevents formation of uric acid from products of purine breakdown of nuclear material, must be initiated 1 to 3 days before chemotherapy and, therefore, can delay treatment. Because of allopurinol's limitations for the prevention of the tumor lysis syndrome (16), rasburicase, a recombinant form of urate oxidase, recently approved by the U.S. Food and Drug Administration (FDA), has become a widely used alternative (17). The drug promotes conversion of uric acid to the more soluble allantoin. Table 1 shows standard dosing. Patients who are glucose-6-phosphatase deficient or allergic should not take rasburicase. There is a 10% incidence of developing antibodies to this drug.

Is gout associated with increased risk for cardiovascular disease, and can this be prevented?

High serum urate levels have been associated with serum markers of inflammation, including C-reactive protein, fibrinogen, interleukin (IL)-6, and elevated neutrophil counts (18–20). Cardiovascular disease has also been associated with markers of inflammation (21). This shared association with chronic inflammation may explain why the risk for cardiovascular disease is increased in persons with gout or hyperuricemia.

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Table 1. Drugs to Prevent or Treat Gout

Drug (Mechanism of Action)	*Dose*	*Benefits*	*Side Effects and Notes*
Prevention of Gout			
Allopurinol (Xanthine oxidase inhibitor; inhibits uric acid synthesis)	Start at 100–200 mg/d, increase by 100 mg/d every 1–4 wk to serum urate goal. Average dose 400–600 mg/d, maximum dose 800 mg/d. Modify initial dose for elevated creatinine, divide doses to reduce GI toxicity.	Most effective in long-term prevention if urate level below <365.9 mmol/L (6 mg/dL)*.	GI effects (nausea, diarrhea). Rash, headache, urticaria, interstitial nephritis. Rare but devastating hypersensitivity reactions. Do not use in acute attack; use colchicine to reduce acute flare when starting drug; not preferred for prevention of the tumor lysis syndrome†.
Febuxostat (Xanthine oxidase inhibitor; inhibits uric acid synthesis)	Start 40–80 mg/d; increase dose to 80–120 mg/d to achieve goal urate level. Steady state uric acid level after 2 wk of use.	Most effective in long-term treatment if urate level <365.9 mmol/L (6 mg/dL).	Liver function abnormalities, diarrhea, headache, nausea, rash. No dose adjustment for mild-to-moderate renal insufficiency.
Rasburicase (Recombinant form or urate oxidase; promotes conversion of uric acid to allantoin)	0.1 to 0.2 mg/kg intravenously for 1 to 7 d.	Use for prevention of the tumor lysis syndrome.	Do not use if glucose-6 phosphatase deficient. 10% incidence of autoantibodies. Start 4–24 h before chemotherapy.
Probenicid (Uricosuric)	0.5–2 g/d, divided twice per d and dose adjusted until serum urate level normalizes.	Most effective in long-term prevention if urate level <365.9 mmol/L (6 mg/dL).	Do not use with aspirin. Increases methotrexate toxicity. Rare anaphylaxis. Use only if underexcrete urate; twice-daily dosing required; not effective in patients with renal disease.
Colchicine, oral (Multiple anti-inflammatory effects‡)	0.6 mg twice per d for CrCl ≥50 mL/min per 1.73 m^2, 0.6 mg once per day for CrCl 35 to 49 mL/min per 1.73 m^2, or 0.6 mg every 2 to 3 d for CrCL 10 to 34 mL/min per 1.73 m^2. Continue for 6 mo after serum urate level <365.9 mmol/L (6 mg/dL) or until tophi disappear.	To prevent gout, combine with allopurinol or probenicid when starting therapy.	GI intolerance with nausea, vomiting, or diarrhea. Bone marrow suppression. Myopathy or neuropathy may be increased with renal disease or statin use. Dermatitis, urticaria, alopecia, purpura. CYP3A4 inhibitor, so may need dose adjustment with other inhbitors (clarithromycin cyclosporine). May need to reduce dose with calcium channel blockers. Avoid if CrCl <10 mL/min per 1.73 m^2or if severe liver disease§.
Acute Gout			
Nonsteroidal anti-inflammatory drugs (Block formation of inflammatory prostaglandins and analgesic effects)	Varies by type of NSAID (e.g., naproxen, 750 mg initial dose then 250 mg every 8 h, taper over 2–10 d to 1 wk)‖.	Effective in acute gout, within 12–24 h of onset.	GI bleeding, renal toxicity, hepatotoxicity. Risk for fluid overload especially if history of CHF. Increases blood pressure. Reversible platelet dysfunction. Do not use if anticoagulated. Avoid in elderly patients. Start quickly at high dose, then rapidly taper. Do not use aspirin, because it can increase urate levels. Use proton-pump inhibitor if history of GI bleeding¶.
Colchicine, oral (Multiple anti-inflammatory effects‡)	0.6 mg 2 or 3 times per d until symptoms subside or GI intolerance occurs. Alternatively, 1.2 mg followed 1 h later by 0.6 mg.	Relatively short time to therapeutic onset.	GI intolerance with nausea, vomiting, or diarrhea. Bone marrow suppression, myopathy, neuropathy, dermatitis, urticaria, alopecia, purpura. Note: intravenous colchicine no longer available. Start rapidly. Reduce dose for liver or renal disease and avoid if on dialysis. Avoid in elderly patients. GI toxicity dose-related. Bone marrow effects can be severe at high doses. Myopathy and neuropathy occur at any dose. CYP3A4 interactions.
Corticosteroids, oral (Multiple anti-inflammatory effects)	Prednisolone, 35 mg/d, or prednisone, 40–60 mg/d (in divided doses) until symptoms begin to subside, then rapidly taper over several d.	Useful when NSAIDs are contraindicated (e.g., renal insufficiency). Preferred for polyarticular gout.	GI bleeding, especially in elderly patients. Do not use if active peptic ulcer disease. Increases blood glucose. Fluid retention. Impaired wound healing. Optimal steroid regimen still not clear.
Corticosteroids, intra-articular (Multiple anti-inflammatory effects)	Triamcinolone hexacetonide, 40 mg for large joints, 5–20 mg for small joints. Methylprednisolone acetate, 40–80 mg for large joints, 20–40 mg for small joints. Betamethasone acetate, 3–6 mg for large joints, 0.75–1.5 mg for small joints.	Especially useful if only 1 joint is inflamed and patient has contraindications to other agents.	Risk for damage to nerve, tendon, or vascular structures if administered improperly. Risk for joint infection. Other side effects same as those with oral formulation. Must be performed by using sterile technique. Rule out infectious cause before injecting corticosteroid into joint.

CrCl = creatinine clearance; GI = gastrointestinal; NSAID = nonsteroidal anti-inflammatory drug.

** Chao J, Terkeltaub R. A critical reappraisal of allopurinol dosing, safety, and efficacy for hyperuricemia in gout. Curr Rheumatol Rep. 2009;11:135-40. [PMID: 19296886]*

† Davidson MB, Thakkar S, Hix JK, et al. Pathophysiology, clinical consequences, and treatment of tumor lysis syndrome. Am J Med. 2004;116:546-54. [PMID: 15063817]

‡ Terkeltaub RA. Colchicine udate: 2008. Semin Arthritis Rheum. 2009;38:411-9. [PMID: 18973929]

§ Terkeltab RA. Clinical practice. Gout. N Eng J Med. 2003; 349:1647–55. [PMID: 14573737]

‖ Harris MD, Siegel LB, Alloway JA. Gout and hyperuricemia. Am Fam Physician. 1999;59:925-34. [PMID: 10068714]

Wallace SL, Singer JZ. Therapy in gout. Rheum Dis Clin North Am. 1988;14:441-57. [PMID: 3051159]

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In the Multiple Risk Factor Intervention Trial, the risk for nonfatal acute myocardial infarction (MI) was increased for persons with gout (adjusted odds ratio [OR], 1.26 [CI, 1.14 to 1.40]; P < 0.001) and for persons with hyperuricemia (adjusted OR, 1.11 [CI, 1.08 to 1.15]), but fatal acute MI was not associated. In persons with incident diabetes mellitus, a history of gout was associated with a more than 2-fold increase in the adjusted OR of acute MI (2.49 [CI, 1.97 to 3.13]) (22).

Because of these associations, some have recommended identifying persons with hyperuricemia before they develop gout to avert associated diseases (23), whereas others have reported that the increased risk for cardiovascular disease and all-cause mortality associated with an elevated serum urate level is not modifiable (24). Studies to clarify this issue are underway.

Prevention and Screening..... Hyperuricemia is the most important risk factor for gout. However, other factors also affect this risk, because only 1 of 10 persons with hyperuricemia develops gout. Important predictors of gout in patients with hyperuricemia include age less than 60 years in men, diet high in nonvegetable purines, alcohol consumption (especially beer and liquor), diuretic use, and obesity. Several genetic variants place some families at increased risk for gout. Common diseases that increase risk for gout include diabetes, the metabolic syndrome, hyperlipidemia, hypothyroidism, and hypertension. Pharmacologic therapy of asymptomatic hyperuricemia is not recommended to prevent gout except when treating hematologic malignant conditions. In patients with at least 1 gout attack, risk for recurrence needs to be reduced through lifestyle modifications, such as dietary changes and gradual weight loss. In addition, patients should avoid medications that increase serum urate levels.

CLINICAL BOTTOM LINE

Diagnosis

What symptoms and physical examination findings suggest gout?

A patient report of episodic self-limited joint pain, swelling, and erythema is highly sensitive but not specific for gout. Specificity is increased to about 80% to 90% by a history of podagra (attack in the first metatarsophalangeal joint) and the finding of a possible tophus (chalky deposits of MSU in soft tissues around joints and helix of ear) (25). Patients often report recent trauma, which can trigger the release of crystals into the joint space, resulting in an attack of gout. Attacks often begin in the middle of the night or early morning.

On examination, gout is characterized by warmth, swelling, redness, and is usually accompanied by severe joint pain. An estimated 90% of first attacks are monoarticular.

Associated fever and constitutional features are sequelae of the release of cytokines. Because lower temperatures favor crystal deposition, the helix of the ear and lower extremities (that is, midfoot, first metatarsophalangeal joint, ankle, or knee) are often sites of crystal deposition and tophus development. Crystals are also more likely to form in previously diseased joints; persons with other forms of arthritis have increased risk for gout. Acute flares also occur in periarticular structures, including bursae and tendons (such as the olecranon bursa and bursae around the knee).

Gout attacks initially subside in 3 to 14 days without treatment, in part because crystals dissolve, are phagocytized, or are resequestered in the synovial tissue. Although the symptoms may resolve, crystals are still present in the joint and

attacks are likely to recur. The estimated flare recurrence rate is 60% in 1 year after the initial attack, 78% in 2 years, and 84% in 3 years (26). Crystalline deposits often grow if untreated, resulting in chronically stiff and swollen joints. Subsequent attacks tend to last longer and may involve more joints or tendons. Chronic gout can involve multiple joints and mimic rheumatoid arthritis.

Tophi are collections of MSU crystals that incite a chronic granulomatous inflammatory response, forming cool lumps in the tissues around affected joints and the helix of the ear. Some patients have tophi as the presenting physical finding. Tophi involving Heberden nodes (osteoarthritis of distal interphalangeal joint) or the finger pads are particularly characteristic of gout in elderly women taking diuretics.

What tests can diagnose gout?

Many patients do not have a sufficiently high probability of gout to diagnose the first attack definitely by clinical and laboratory tests alone. Serum urate levels are helpful but may be normal during an acute flare (Box). Conversely, hyperuricemia can occur in asymptomatic persons (27). The diagnosis is best established by documenting the presence of MSU crystals obtained by aspirating the fluid from an inflamed joint or a suspected tophus. Crystals of needle or rod-shaped MSU in polymorphonuclear leukocytes are seen in the synovial fluid and confirmed by using polarized microscopy. In material aspirated from a tophus, the crystals tend to be seen alone, because the material is usually acellular. Birefringent crystals are also typical of pseudogout, which is caused by calcium pyrophosphate dihydrate crystals (Table 2) but can be distinguished from MSU crystals because they diffract polarized light more weakly and more often have a rhomboid or shorter rod shape.

When gout is suspected, order a cell count with differential and culture as part of the synovial fluid examination to help define the diagnosis. Accumulations of joint fluid due to acute or chronic gout are almost always inflammatory in nature, with leukocyte counts between 2 to 75 × 10^9 cells/L. If the leukocyte count is very high (>75 × 10^9 cells/L), septic arthritis should be considered, even in the presence of MSU crystals. Be aware of substantial overlap between the leukocyte cell counts in gout and septic arthritis. For example, most episodes of joint sepsis occur in joints that are already diseased, including joints that have been affected by gout. An adequate examination of synovial fluid can avert unnecessary joint lavage, arthroscopy, or arthrotomy.

Joint aspiration sometimes fails to establish the diagnosis, such as when no crystals are seen or no fluid is obtained. Patients may decline the procedure or have contraindications. The preliminary American College of Rheumatology criteria for the definition of gout offers alternatives to establish the diagnosis (Box) (28). However, the purely clinical aspects of these criteria without examination of joint fluid may not have adequate accuracy for distinguishing gout from rheumatoid arthritis or other inflammatory joint diseases (25).

What is the value of radiography or ultrasonography in the diagnosis of gout?

In acute gout attacks early in the course of disease, radiography may occasionally help rule out other causes of joint pain and swelling, such as fractures or calcium pyrophosphate deposition disease (pseudogout). Later in the course of disease, radiography can show more long-term changes due to gout. However, gout is less likely to cause joint space–narrowing than is either psoriatic arthritis or rheumatoid arthritis

Tests Useful in Gout Diagnosis

- Serum urate level
- Complete blood count with differential (if considering septic arthritis)
- Serum creatinine
- Examination of synovial fluid or tophus aspirate (polarized microscopy, cell count, culture)
- Radiography (especially rule out other causes)

American College of Rheumatology Preliminary Criteria for Diagnosis of Gout

The presence of characteristic urate crystals in the joint fluid during attack, or

A tophus proved to contain urate crystals by chemical or polarized light microscopic means, or

6 of the following criteria:

- More than 1 attack of acute arthritis
- Maximum joint inflammation developed within 1 day
- Monoarticular arthritis (although gout can be polyarticular)
- Redness of joint
- First metatarsophalangeal joint pain or swelling
- Unilateral first metatarsophalangeal joint attack
- Unilateral tarsal joint attack
- Suspected tophus
- Hyperuricemia
- Asymmetrical swelling within the joint on radiography
- Subcortical cysts without erosions on radiography
- Joint fluid culture negative during attack

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Table 2. Differential Diagnosis of Gout

Disease	*Characteristics*	*Notes*
Rheumatoid arthritis	Symmetrical polyarthritis preferentially in small joints of hands and feet. Affects about 1% of the population. Subcutaneous rheumatoid nodules in about 20% of patients with rheumatoid arthritis. Radiographic changes include soft-tissue swelling, diffuse joint-space narrowing (within a joint), marginal erosions of small joints, and symmetrical multiple joint involvement. Usually osteopenic and without signs of repair (osteophytes).	Acute rheumatoid arthritis synovitis sometimes mimics gout. Involvement of many joints makes rheumatoid arthritis the more likely diagnosis. Hands more likely to be involved in rheumatoid arthritis than in gout.
Calcium pyrophosphate deposition disease (pseudogout)	Can mimic osteoarthritis or gout. Resembles osteoarthritis or rheumatoid arthritis on radiography, but some evidence of bony repair (osteophytes or lack of osteopenia) is usually present. Cartilage calcification, especially in fibrocartilage of knee meniscus, symphysis pubis, glenoid and acetabular labrum, and triangular cartilage of wrist, is pathognomonic for CPPD. Osteoarthritis in unusual places (wrist, elbow, metacarpophalangeal joints, or shoulder) without a history of trauma should suggest CPPD. Affects 10% to 15% of persons older than 65 years.	Diagnosed by CPPD crystals in synovial fluid and by chondrocalcinosis on radiography (most commonly in fibrocartilage) Concomitant crystal disease (calcium pyrophosphate dihydrate deposition, hydroxyapatite) is increasingly common with age in a hallux valgus (bunion), causing potential confusion with gout.
Septic arthritis	Fever, arthritis, great tenderness. Joint sepsis may occur in previously abnormal joints, and up to one half have concomitant rheumatoid arthritis. The source (skin, lungs) is often evident. Radiography generally shows swelling and effusion. If not treated promptly, damage occurs, with diffuse joint-space narrowing.	Must be diagnosed early to avoid joint destruction.
Cellulitis	Patient has erythema and swelling of extremity that is very tender and is often febrile. Soft-tissue lymphatic drainage often abnormal because of peripheral venous insufficiency, previous surgery, or previous infection in the area. Radiography shows soft-tissue swelling but no joint changes.	Infection often due to *Staphylococcus* or *Streptococcus* infection. Joint examination may be difficult, but if painful to move joint, aspiration is recommended.
Reactive arthritis	Inflammatory oligoarthritis, weight-bearing joints often affected and may have tendon insertion inflammation. Fingers and toes may resemble sausages (dactylitis). Extraarticular manifestations include conjunctivitis, urethritis, stomatitis, and psoriaform skin changes. Soft-tissue swelling on radiography. The only acute bony change is dactylitis.	Patient usually has had infection with an appropriate organism (*Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, or *Chlamydia* species or intravesicular bacilli Calmette–Guérin) within 3 weeks before onset of initial attack.
Fracture or trauma	Tenderness along the affected bony surface. History of trauma, except stress fractures. Radiography should show disruption of the cortex related to the fracture.	Radiography should show fracture (more than 1 view may be required).
Osteoarthritis	Bony enlargement, no acute signs of inflammation (erosive changes can be seen in Heberden nodes and confused with gout) but acute exacerbations of joint symptoms, especially after use. Radiography may show focal joint-space loss, bony repair with osteophytes, subchondral sclerosis. Central erosions sometimes in finger joints.	Hallux valgus (bunion) is very common and is the most commonly affected joint (as in gout).
Psoriatic arthritis	Joint distribution and appearance similar to reactive arthritis. Predilection for distal interphalangeal joints of fingers, often with concomitant nail changes. Radiography similar to reactive arthritis, with soft-tissue swelling and possible dactylitis. If long-standing, the patient may have diffuse joint-space narrowing. Small joints of hands may also have central erosions. Some tendency to have subchondral sclerosis and other signs of bony repair.	Patients with psoriasis may have elevated uric acid levels proportional to proliferative state of skin.
Sarcoidosis	Acute disease (the Lofgren syndrome) generally involves ankles, sometimes with erythema nodosum or subcutaneous nodules. Radiography may show subcutaneous nodules and soft-tissue swelling.	Parotitis, uveitis, hilar adenopathy, or lung involvement are features of sarcoidosis but not of gout.

CPPD = calcium pyrophosphate dihydrate.

(Table 2). Unlike radiographic findings in rheumatoid arthritis, chronic gout shows a prominent, proliferative bony reaction, and tophi can cause bone destruction away from the joint.

What conditions are in the differential diagnosis of gout?

Gout is commonly confused with other conditions. Key features of diseases that can be confused with gout are shown in Table 2.

Diagnosis..... Misdiagnosis of gout is common, and joint pain and hyperuricemia alone will not establish the diagnosis. It is established by documenting the presence of MSU crystals or is strongly suggested by fulfilling the clinical criteria from the American College of Rheumatology preliminary definition. In patients not known to have gout, clinicians should order tests to measure serum urate and serum creatinine levels and aspirate synovial fluid from an involved joint or a suspected tophus. Joint fluid from gout can resemble fluid obtained from a joint with pseudogout or septic arthritis, but the former can be distinguished by a skilled examination of the type of crystals, and the latter can be distinguished by constitutional symptoms and cultures. Radiography and ultrasonography may also be useful in distinguishing other forms of inflammatory joint disease from gout.

CLINICAL BOTTOM LINE

Treatment

When should clinicians consider hospitalizing a patient with gout?

Because acute gout can be difficult to distinguish from septic arthritis without careful joint fluid analysis, it may be necessary to hospitalize the patient and administer empirical antibiotics until a definite diagnosis can be established. Prompt antibiotic treatment for septic arthritis is needed to prevent severe joint destruction and disability. Repeated synovial fluid analysis may be warranted for cell count, bacterial culture, and the presence or absence of MSU crystals to establish a definitive diagnosis.

Gout is one of the most painful conditions known. Effective pain management is essential. Patients whose pain cannot be controlled by outpatient analgesics, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or oral narcotics, may also need to be hospitalized. Aspiration of the joint may improve pain if sufficient fluid is removed to decrease intra-articular pressure.

What is the role of nondrug therapy in managing patients who already have gout?

Long-term management of gout can be improved by lifestyle changes, such as reducing consumption of foods high in purines, alcohol, and high-fructose and sugary drinks. Weight loss may decrease serum urate levels. Staying hydrated by drinking plenty of water may reduce the risk for recurrence.

Diets high in fiber, vitamin C, folate (for example, fruits and vegetables), and dairy products seem to be protective.

Clinicians should review the medications that their patients are taking and identify any that may impair uric acid secretion. Thiazide diuretics and low-dose aspirin are the most common drugs to interfere with handling of uric acid by the kidney. When possible, substitute another drug that does not adversely affect uric acid excretion.

What is the role of drug therapy in the acute treatment of gout?

Acute attacks of gout often have a rapid onset and last 1 week without treatment. Optimum management of acute gout requires pain relief and control of inflammation. The choice of agents depends largely on patient characteristics and especially on comorbid conditions (Table 1).

NSAIDs

For mild-to-moderate pain, NSAIDs are usually the first-line therapy because of combined analgesic and anti-inflammatory effects. Two to 10 days of NSAIDS is usually enough to treat a gout attack. Ibuprofen and naproxen seem to be as effective as indomethacin but better tolerated.

Long-Term Treatment of Hyperuricemia Is Recommended After Discussion With the Patient Who Has:

- At least 2 or 3 acute attacks of gout
- Tophaceous gout
- Severe attacks or polyarticular attacks
- Radiographic evidence of joint damage from gout
- Identifiable inborn metabolic deficiency causing hyperuricemia
- Nephrolithiasis

Aspirin should not be used, because low-to-moderate doses increase the risk for gout and high doses are too toxic. Initiating treatment quickly is essential. To hasten the anti-inflammatory action, start the NSAID at a higher dose and taper over about 1 week (29, 30). Gastrointestinal toxicity from NSAIDs is an important concern. Proton-pump inhibitors can reduce NSAID ulcers by more than 50% versus no treatment (31).

Colchicine

Colchicine has long been a mainstay for the treatment of acute gout because it has many anti-inflammatory effects (32). However, colchicine has a narrow therapeutic window due to common side effects. Doses should be reduced for renal or hepatic dysfunction. It should be avoided in elderly persons, and should not be administered with other strong CYP3A4 inhibitors.

The FDA recently withdrew approval for all intravenous preparations of colchicine. Oral colchicine treatment is most effective when initiated 12 to 36 hours after the start of an acute gouty attack. Only 1 small randomized trial has been conducted of a higher-dose regimen (that is, oral colchicine, 1 mg, and then 0.5 mg every 2 hours until a complete response or toxicity developed) (33). Although colchicine reduced pain by 50% in nearly three quarters of treated patients, all treated patients developed diarrhea or vomiting after a median of 24 hours of treatment or a mean dose of 6.7 mg. Currently, experts recommend treating with lower doses of oral colchicine (0.6 mg 2 to 3 times per day), but the efficacy of this regimen has not been evaluated in randomized, controlled trials (34). A recent presentation reported that colchicine, 1.2 mg, followed 1 hour later with 0.6 mg, was effective in treating acute gout (35). Myopathic effects and myelosuppression are rare with short-term treatment.

Corticosteroids

Corticosteroids are the preferred treatment for acute gout in patients with renal insufficiency or other contraindications to NSAIDs. For monoarticular gout, an intra-articular corticosteroid injection can be very effective. Oral corticosteroids are preferred for polyarticular gout. In a randomized trial, prednisolone, 35 mg/d, was similar in effectiveness to naproxen, 500 mg twice per day (36). Patients with diabetes may develop increasing hyperglycemia while taking corticosteroids.

Narcotics

When pain is severe, narcotic analgesics can be used on a short-term basis until the inflammatory process starts to resolve, but this has not been rigorously studied. Combinations of oxycodone, hydrocodone, or codeine may be given orally. In severe cases, morphine may be given intravenously or subcutaneously, or meperidine may be given intravenously or intramuscularly.

What is the role of drug therapy to prevent gout and complications of hyperuricemia?

For patients who have had several gout attacks, long-term pharmacotherapy should be started during an intercritical period when the disease is quiescent, with the goal of decreasing and maintaining serum urate levels in the normal range (Box). Treatment is also warranted for patients with tophi or joint damage seen on radiography (37). Patients who have had just 1 attack or an unusually high serum urate level may prefer to be treated after discussing the pros and cons of mediations. In addition, it is also important to prevent nephrolithiasis due to uric acid stones, which occur in 10% to 40% of patients with gout.

Tophi can be dissolved by decreasing the serum urate level to low levels, such as 237.9 to 297.4 μmol/L (4 to 5 mg/dL), that seem to promote more-rapid dissolution of crystals and

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tophi (38). Patients with tophi almost always require lifelong therapy.

In a trial of stopping of urate-lowering medications in patients treated for 5 years who had no palpable tophi and mean uric acid levels during that time of less than 416.4 μmol/L (<7 mg/dL), nearly half had a recurrence of gout attacks from 6 to 60 months after therapy had been discontinued (39). Uric acid levels returned to the level before urate-lowering therapy was used (mean of 535.4 μmol/L [9 mg/dL]).

Hyperuricemia is related to diminished renal function. A systematic review of 9 prospective cohort studies reported that 8 identified an independent association between hyperuricemia and development of renal insufficiency (40). Research is currently being conducted to evaluate whether treating hyperuricemia can prevent or reduce a decline in renal function.

Uricosurics

Tissue MSU deposits can be eliminated only if the concentration gradient between the tissues and serum is adequate. Hyperuricemia results from either overproduction/overconsumption or low renal excretion. To distinguish these when uricosuric therapy is being considered, a 24-hour urine collection for uric acid and creatinine should be performed. The urine is collected during an intercritical period. Renal excretion is low if the level of uric acid in the urine collection is less than 600 to 700 mg/d while consuming a low-purine diet. Treatment with a uricosuric drug is warranted for underexcretion of uric acid. Probenecid is the only uricosuric available in the United States. A uricosuric drug should not be used in patients with nephrolithiasis because it can promote the formation of stones.

Xanthine oxidase inhibitors

Allopurinol and a recently FDA-approved drug, febuxostat, are xanthine oxidase inhibitors that inhibit the activity of an enzyme involved in purine metabolism, thus decreasing uric acid production and lowering serum urate levels. When starting treatment with these drugs, it is important to wait until an acute attack of gout has resolved, because these drugs mobilize uric acid from tissue deposits, prolonging attacks. To decrease the likelihood of a gout flare while starting treatment, allopurinol should be started at the minimal effective dose and the dose increased until the goal of a serum urate level less than 356.9 μmol/L (6 mg/dL) has been achieved (41) (Table 1). Concurrent colchicine prophylaxis may help decrease flares. Gastrointestinal side effects of allopurinol are dose-dependent but generally mild with doses under 300 mg/d. At higher doses, side effects may be reduced by giving the drug in divided doses. Allopurinol may be combined with uricosurics, such as probenecid, if allopurinol is ineffective; however, this may compromise the uric acid–lowering effect of allopurinol by promoting excretion of this drug and its major active metabolite, oxypurinol.

While patients are taking allopurinol, it is important to monitor the liver panel, chemistry profile, and complete blood count regularly in conjunction with the serum urate level before and after starting allopurinol treatment. Asymptomatic increases in liver enzymes can occur in up to 5% of patients, and serious hepatotoxicity can occasionally occur (41).

It is recommended to reduce the dose of allopurinol in patients with renal insufficiency and to warn patients to immediately report side effects, such as a rash. The rash is typically maculopapular with pruritus and occurs in about 2% of patients. A rash is more common when the patient is also treated with ampicillin or amoxicillin. The allopurinol hypersensitivity syndrome is a serious complication, occurring in 1 to 4 patients per 1000, with death occurring in up to one quarter of cases (42). This hypersensitivity syndrome has multiple manifestations, including a severe cutaneous reactions, such as the Stevens–Johnson syndrome, eosinophilia, leukocytosis, fever, hepatitis, or renal failure. It is probably due to cell-mediated immunity to allopurinol and oxypurinol (43).

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43. Braden GL, Warzynski MJ, Golightly M, et al. Cell-mediated immunity in allopurinol-induced hypersensitivity. Clin Immunol Immunopathol. 1994;70:145-51. [PMID: 8299230]

Febuxostat has recently been approved by the FDA for treatment of hyperuricemia and gout. In a randomized trial, febuxostat was more effective (at a dose of either 80 or 120 mg/d) than lower-dose allopurinol (300 mg/d) in reducing uric acid to less than 356.9 μmol/L (6 mg/dL) (44). A 5-year study of using febuxostat showed that it nearly eliminated gout flares (45). Febuxostat does not require dose adjustment for mild-to-moderate renal impairment. A recent review reported that allopurinol and febuxostat had a similar incidence of minor side effects, but it is not clear whether febuxostat was associated with greater cardiovascular side effects (46).

Colchicine

To prevent gout flares, colchicine can be combined with allopurinol or probenecid. Dosing of colchicine is based on renal function. It should not be used in patients with severe renal insufficiency or hepatobiliary dysfunction (47) (Table 1).

A small randomized trial in patients starting allopurinol found that low-dose colchicine (0.6 mg twice per day) significantly reduced the frequency and severity of gout flares (47). If diarrhea developed, it was generally managed by reducing the dose to 0.6 mg once per day.

Colchicine treatment is generally continued for 6 months after the serum urate level is less than 356.9 μmol/L (6 mg/dL) or until tophi disappear. Emerging research indicates that the dose of colchicine should be reduced in patients receiving calcium-channel blockers to reduce adverse effects (37). Caution when used with other strong CYP3A4 inhibitors. Long-term colchicine in patients with renal disease or statin use can cause neuromyopathy (48).

NSAIDs

NSAIDs have not been specifically studied as anti-inflammatory prophylactic agents, but they may be preferable when there is pain from joint damage, such as from osteoarthritis.

New medications under investigation

Research has indicated that IL-1 inhibition might be effective in relieving inflammation associated with acute gout, because via activation of the inflammasome, MSU crystals stimulate monocytes and macrophages to release IL-1 β. An IL-1 inhibitor called anakinra is being investigated off-label to treat gout flares not responsive to usual treatment. Other IL-1 antagonists are also under study.

In a small, open-label trial of 10 patients with gout who were intolerant of or did not respond to standard anti-inflammatory therapies, anakinra (100 mg/d subcutaneous for 3 d) resulted in 100% response rate in 48 hours or less and 79% mean pain improvement with no adverse effects (49).

In addition, pegloticase is a recombinant, pegylated formulation of a modified mammalian urate oxidase in late-stage development for treatment-failure gout to control hyperuricemia as well as treat gout.

When should clinicians consider specialty consultation for patients with gout?

Misdiagnosis of gout is common (50). Consultation with a rheumatologist or orthopedist should be considered for suspicion of joint sepsis, poorly controlled gout, unusual features of possible gout, or gout along with other forms of arthritis. A specialist in rheumatology or inherited metabolic diseases should be asked to consult for young patients with gout (for example, younger than 20 years)

Recent evidence suggests that many primary-care physicians do not manage gout well.

In an analysis of 10 British primary-care practices, 60% of patients with acute gout took high-dose regimens of colchicine that are not recommended. Only 23% of patients had treatment for hyperuricemia within 1 year after a gout attack (51).

In a retrospective, case–control study of 138 consecutive in-patients with gout, 57% had a rheumatology consultation.

44. Becker MA, Schumacher HR Jr, Wortmann RL, et al. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. N Engl J Med. 2005;353:2450-61. [PMID: 16339094]
45. Schumacher HR Jr, Becker MA, Lloyd E, et al. Febuxostat in the treatment of gout: 5-yr findings of the FOCUS efficacy and safety study. Rheumatology (Oxford). 2009;48:188-94. [PMID: 19141576]
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Patients with a consultation were more likely to have had a synovial fluid analysis (P < 0.001) and to have fulfilled preliminary American College of Rheumatology criteria for gout than those without a consultation (65% vs. 37%; P = 0.002). Rheumatology care was associated with more treatment with intra-articular corticosteroids (44% vs. 12%; P < 0.001) and more care consistent with European League Against Rheumatism (EULAR) recommendations (52).

In addition, consultation with a nephrologist can help in managing patients with renal insufficiency or urate nephropathy and its implications for drug therapy. A consultant may aid in investigation of drug interactions, timing of uric acid–lowering therapies, and assessment for underlying causes of gout.

Treatment..... Differentiating acute gout from other forms of inflammatory arthritis, especially septic arthritis and pseudogout, is challenging. When septic arthritis is a possibility, aspirate and analyze joint fluid promptly. If infection is a concern, hospitalize patients and administer empirical antibiotics until a definite diagnosis is established. Patients whose gout-related pain cannot be controlled with outpatient analgesics may need to be hospitalized. Optimum management of acute gout requires control of inflammation as well as pain relief, usually with NSAIDs, colchicine, or corticosteroids. For patients with chronic gout, long-term pharmacotherapy is advised to reduce and maintain serum uric acid levels at less than 356.9 µmol/L (6 mg/dL). Medication and lifestyle changes, including dietary modifications, weight loss, and reducing alcohol consumption, may reduce recurrence. Consultation with a rheumatologist is warranted for guidance in diagnosis and management of unusual or complex cases.

CLINICAL BOTTOM LINE

Practice Improvement

Are there practice guidelines relevant to gout prevention and management?

In 2007, the British Society for Rheumatology/British Health Professionals in Rheumatology released a guideline on management of gout (www.rheumatology.oxfordjournals.org/cgi/content/full/kem056av1). The recommendations on acute gout attack management with the strongest evidence base include starting analgesic, anti-inflammatory drug therapy immediately and continuing it for 1 to 2 weeks; treating with fast-acting oral NSAIDs at maximum doses when patients have no contraindications; prescribing concurrent gastroprotective agents when patients have an increased risk for peptic ulcers, bleeding, or perforation; continuing allopurinol during an attack in patients already taking this drug; and using corticosteroids in patients who cannot tolerate NSAIDs or who are refractory to other treatments. Colchicine offers an effective alternative but may be slower to work than NSAIDs. In regard to prevention, the guideline with the strongest evidence was to co-administer colchicine with allopurinol or a uricosuric drug for up to 6 months.

The European League Against Rheumatism (EULAR) issued a guideline regarding evidence-based recommendations for the diagnosis of gout (www.ard.bmj.com/cgi/content/abstract/65/10/1301?siteid=bmjjournals&ijkey=7jOEXurujRa0k&keytype=ref). They developed 10 key recommendations, with the primary points being: MSU crystals are very likely to be identified from joint fluid during acute gout; classic podagra and presence of tophi have the highest clinical diagnostic value for gout; hyperuricemia may be a useful diagnostic marker; radiography has little role in diagnosis except in late

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52. Barber C, Thompson K, Hanly JG. Impact of a rheumatology consultation service on the diagnostic accuracy and management of gout in hospitalized patients. J Rheumatol. 2009;36:1699-704. [PMID: 19567626]

or severe gout; and risk factors (for example, diet or diuretics) and comorbid conditions (for example, chronic renal failure or diabetes) are associated with gout (37).

The EULAR also issued a guideline regarding management of gouts (ww.ard.bmj.com/cgi/content/abstract/65/10/1312?siteid=bmjjournals&ijkey=uZK1Nk6Uq8MCs&keytype=ref). Recommendations address patient education about modifying lifestyle risk factors and appropriate treatment of associated comorbid conditions and other risk factors (for example, stopping diuretics). They also recommended managing acute attacks with NSAIDs, intra-articular corticosteroids, or colchicine. Urate-lowering therapy was recommended for patients with recurrent attacks, tophi, arthropathy, or radiographic changes of gout. Allopurinol was preferred for attack prevention. Alternatives included a uricosuric, allopurinol desensitization for those with an allergy, or other xanthine oxidase inhibitors. For prophylaxis against acute attacks, either colchicine or an NSAID are recommended.

Are there quality measures relevant to the prevention and management of gout?

The National Quality Measures Clearinghouse lists 4 measures related to gout (www.qualitymeasures.ahrq.gov/search/searchresults.aspx?Type=3&txtSearch=gout&num=20): 1) the proportion of patients with hyperuricemia and gouty arthritis who were offered treatment with a urate-lowering drug; 2) the proportion of patients with tophaceous gout who were given an initial prescription for urate-lowering medication and who concurrently received a prophylactic anti-inflammatory agent (excluding those with renal impairment or peptic ulcer disease); 3) the percentage of patients with renal impairment and gout who are prescribed allopurinol at a dose less than 300 mg/d; and 4) the percentage of patients with history of nephrolithiasis or significant renal insufficiency and gout who were started on urate-lowering therapy and prescribed a xanthine oxidase inhibitor rather than a uricosuric.

in the clinic

Tool Kit

Gout

PIER Module

http://pier.acponline.org

Access the PIER modules on gout and arthrocentesis. PIER modules provide evidence-based, updated information on current diagnosis and treatment in an electronic format designed for rapid access at the point of care.

Patient Information

www.rheumatology.org/public/factsheets/diseases_and_conditions/gout.asp?aud=pat
www.rheumatology.org/publications/classification/gout.asp

Patient-oriented information about gout from the American College of Rheumatology.

http://pier.acponline.org/physicians/public/d160/pt.educ/d160-s8.html

Information for patients from the ACPs PIER module on gout.

www.arthritis.org/foods-for-gout.php

Information about safe foods for persons with gout.

www.niams.nih.gov/Health_Info/Gout/gout_ff.asp (English)
www.niams.nih.gov/Portal_en_espanol/Informacion_de_salud/Gota/default.asp (Spanish)

Information about gout in English and Spanish for patients by the National Institute of Allergy and Infectious Diseases.

www.niams.nih.gov/Health_Info/Gout/default.asp

Answers to questions about gout from the National Institutes of Health.

www.nlm.nih.gov/medlineplus/gout.html

Access MEDLINE Plus information about gout for patients, including an interactive tutorial available in both English and Spanish.

http://pier.acponline.org/physicians/public/d160/figures/d160-figures.html

Access figures showing tophaceous material viewed under light microscopy and polarized microscopy and gout-related photos and information on joint aspiration.

THINGS YOU SHOULD KNOW ABOUT GOUT

What is gout?

- Gout is a very painful type of arthritis caused when crystals form in joints or soft tissues.
- Gout causes sudden joint swelling, redness, heat, and pain, often in the big toe.
- Acute attacks often start at night and last about 1 week.
- A build-up of uric acid known as tophi can form lumps around joints and tissues and damage joints.

Who is most likely to develop gout?

- Middle-aged men
- Women after menopause
- People with high uric acid levels
- Overweight people
- Certain foods increase the risk for gout (red meats, organ meats [liver], shellfish, some fish [anchovies], alcohol, and sugary soft drinks).
- Some medications, such as diuretics (water pills), and some diseases, such as diabetes and kidney problems, increase the risk for gout.

How is gout diagnosed?

- The best way to diagnose gout is to have the doctor draw some fluid from the joint with a needle and have it examined under a microscope for urate crystals.

What should I do if I think I have gout?

- Contact your doctor to treat the pain and shorten the attack.
- The pain and inflammation can be treated by nonsteroidal anti-inflammatory drugs (such as naproxen or ibuprofen), colchicine, or corticosteroids (either by mouth or as an injection into the joint).
- After more than 1 gout attack, you need to take medicine long-term to lower the uric acid level and to prevent gout and other complications. You need to take the medicine just as the doctor prescribed it in order for it to work.
- Lifestyle changes and switching some medications that can raise the level of uric acid can also help.

For More Information

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Web Sites With Good Information About Gout

www.rheumatology.org/public/factsheets/diseases_and_conditions/gout.asp?aud=pat
American College of Rheumatology: Gout

www.arthritis.org/disease-center.php?disease_id=42
Arthritis Foundation: Gout

www.niams.nih.gov/Health_Info/Gout/default.asp
National Institute of Arthritis and Musculoskeletal and Skin Diseases: Questions and Answers About Gout

www.gouteducation.org/
Gout and Uric Acid Education Society

Patient Information

CME Questions

MKSAP
MEDICAL KNOWLEDGE Self-Assessment Program

1. A 68-year-old woman has had 4 or 5 episodes of joint pain and swelling, lasting 3 to 8 days, that involved the right knee and left elbow. She is asymptomatic between attacks, and sulindac, 200 mg twice per day, has usually relieved the symptoms. Her most recent episode was 4 months ago.

   On physical examination, none of her joints is swollen or tender, but there is marked crepitus on extension of the knee. She also has a positive bulge sign over the left knee and pain on full extension of the left elbow.

   Which of the following tests would confirm the diagnosis?

   A. Arthrocentesis of the knee and laboratory analysis of the synovial fluid by an expert in crystal identification
   B. Measurement of serum uric acid
   C. Measurement of serum rheumatoid factor
   D. Radiography of the knee
   E. MRI of the knee with gadolinium contrast

2. A 62-year-old man is evaluated for left anterior hip pain that started 3 days earlier. He was recently hospitalized for kidney stone extraction and was discharged 4 days ago. The pain is worse with activity and disturbs his sleep. He has chills but no rash, palpitations, or back pain. He has history of degenerative joint disease in his hips and knees and has gout attacks in his first metatarsophalangeal joints about 3 times per year. There is no history of tick exposure.

   On physical examination, temperature is 38.7°C (101.7°F), pulse rate is 110/min, and blood pressure is 142/72 mm Hg. The patient has markedly decreased range of motion and pain in his left hip and some warmth over the anterior and lateral aspect. All other joints are normal on palpation.

   Which of the following tests is most appropriate?

   A. Serology for *Borrelia burgdorferi*
   B. Urethral swab for *Neisseria gonorrhoeae*
   C. Antinuclear antibody and rheumatoid factor titers
   D. Hip joint aspiration
   E. Bone scan

3. A 55-year-old woman who has had rheumatoid arthritis for 10 years is evaluated because of severe pain in the left shoulder that developed during the previous day. In recent months, her disease has been poorly controlled on a regimen of methotrexate, hydroxychloroquine, and low-dose prednisone. She has approximately 90 minutes of morning stiffness.

   On physical examination, her temperature is 36.8°C (98.2°F), her pulse rate is 82/min, and her blood pressure is 110/70 mm Hg. She has moderate tenderness of the small joints of her hands and of both wrists. Her left shoulder is warm and very tender; she can move it only slightly before being limited by pain.

   What is the best next step in this patient's management?

   A. Orthopedic consultation for possible shoulder arthroplasty
   B. Aspiration of the shoulder
   C. Radiography of the shoulder
   D. MRI contrast arthrography of the shoulder
   E. Physical therapy for the shoulder

4. A 38-year-old man with a history of idiopathic focal and segmental glomerulosclerosis developed end-stage renal disease and subsequently underwent a cadaveric renal transplantation 28 months ago. He presents to your office for a routine follow-up visit. His transplantation was uncomplicated, without delayed graft function or clinically apparent acute rejection episodes. His immunosuppression regimen consisted of prednisone, cyclosporine, and azathioprine. His serum creatinine concentration on discharge was 123.76 µmol/L (1.4 mg/dL). He was given colchicine for a suspected gouty attack 4 months ago and continues to take the drug once a day.

   At a follow-up clinic appointment 3 months ago, his blood pressure was elevated and his serum creatinine concentration was 150.28 µmol/L (1.7 mg/dL). The urinary protein-to-creatinine ratio was less than 0.3. He was given diltiazem for better control of blood pressure. His immunosuppressive regimen remained unchanged.

   At the current visit, physical examination reveals a mild tremor and blood pressure of 150/90 mm Hg. Cardiac, pulmonary, and abdominal examinations are unremarkable. There is no tenderness at the transplant site, and the patient has trace bilateral edema.

   Laboratory studies found the following results: Serum creatinine level, 194.48 µmol/L (2.2 mg/dL); serum uric acid level, 713.82 µmol/L; urinalysis, specific gravity of 1.010, trace proteinuria, and no glucosuria, hematuria, or ketonuria; urine microscopy, few broad casts, scattered renal epithelial cells; urine protein-to-creatinine ratio, 0.4; and urine uric acid–to-creatinine ratio of 0.6.

   What is the most likely cause of this patient's current renal dysfunction?

   A. Transplantation renal artery stenosis
   B. Recurrent focal and segmental glomerulosclerosis
   C. Cyclosporine toxicity
   D. Uric acid nephropathy
   E. Polyoma virus nephropathy

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP, accessed at http://www.acponline.org/products_services/mksap/15/?pr31). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.