

Taking the stress out of managing gout

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Case 1

Mr J.P., a 43-year-old chemical engineer, is a relatively new patient in your practice. He is concerned about increasingly frequent episodes of "gout" over the past 6 months. He describes acute onset of red, swollen, painful joints in his big toes, ankles, and rarely his knees. He reports that he was diagnosed with gout 3 years ago, but cannot recall specific laboratory tests; he takes 50 mg of indomethacin 3 times daily, which is effective for each acute episode. He is now wondering about dietary and medical management to prevent gout, as the acute arthritis is interfering with his work (which involves frequent overseas travel) and his exercise (long-distance running). Mr J.P. has no other medical history of note; takes no other medications or supplements; and is a nonsmoker and has an alcohol intake of 1 to 2 glasses of wine per week. Results of his physical examination are unremarkable, with a body mass index of 25.9 kg/m², blood pressure of 126/80 mm Hg, no acute arthritis, and no tophi. You provide Mr J.P. with a handout on a low-purine diet for gout and a requisition for laboratory tests.

Bringing evidence to practice

- Consider nonsteroidal anti-inflammatory drugs (NSAIDs) other than indomethacin. Traditionally, indomethacin has been the NSAID of choice for acute attacks of gout; however, other NSAIDs have been shown to be effective in gout,¹⁻⁸ and indomethacin has never been proven to be any more efficacious.⁹ Additionally, indomethacin might be associated with more adverse effects, including central nervous system disturbances in the elderly (eg, headaches, confusion).^{3,8} Suitable alternatives would include naproxen, ibuprofen, or celecoxib, depending on cardiovascular risk, gastrointestinal risk, or desire for availability without prescription.
- **Table 1**¹⁰⁻¹⁶ provides an overview of the management of acute gouty arthritis; the full version of the RxFiles gout treatment chart is available on-line from CFPlus.*
- Compliance with low-purine diets can be challenging and acceptance rates might be low. A low-calorie diet (1600 kcal/d) was shown to decrease serum uric acid (SUA) levels by almost 100 µmol/L in obese men.¹⁷ As many of the risk factors for gout (eg, hypertension, dyslipidemia, diabetes mellitus) are also risk factors for cardiovascular disease,¹⁸ the additional benefits of weight loss and healthy eating should not be overlooked.¹⁹⁻²⁷

The recurrent attacks over the past 6 months suggest this patient might have progressed to intercritical

gout (ie, symptomatic gout with increasingly frequent attacks of acute gouty arthritis).²⁸⁻³⁵ Checking SUA levels would assist in deciding whether to begin preventive treatment.^{31,32} If SUA levels are elevated, the patient could either overproduce or underexcrete uric acid; SUA-lowering therapy with allopurinol might be beneficial in either situation.^{31,32}

Mr J.P. returns 3 weeks later. His SUA level is elevated at 614 µmol/L (normal 150 to 480 µmol/L), despite his following a low-purine diet. Other test results were normal—serum creatinine was 74 µmol/L; fasting glucose was 5.4 mmol/L. Given that weight loss is not likely to provide the same benefits for this patient as would be seen in an obese individual, the final-year medical student working with you today suggests starting treatment with allopurinol. He is uncertain how to do this, as he recalls that the drug might precipitate an acute attack of gout.

Bringing evidence to practice

- Allopurinol, a xanthine-oxidase inhibitor, impedes the production of uric acid and can be used to prevent further attacks of acute gouty arthritis.³⁶⁻³⁹ As any sudden change in SUA levels can precipitate an attack, preventive therapy with low-dose colchicine or NSAIDs during titration of allopurinol is recommended.^{18,31,32,40}
- **Table 2**^{14,31,32,40} provides an overview of the considerations for when and how to initiate allopurinol; the full version of the RxFiles gout chart is available from **CFPlus**.*

Mr J.P. was started on 100 mg of allopurinol and 0.6 mg of colchicine daily. He had no acute attacks and no medication side effects. After 4 weeks of therapy his SUA level was 443 µmol/L, so the dose of allopurinol was titrated to ideally achieve an SUA level below 360 µmol/L. After 6 months of taking 300 mg of allopurinol daily, the patient had no further episodes of arthritis and was back running in half marathons; his SUA was 335 µmol/L. Colchicine prophylaxis had been stopped after 3 months.



*The full version of the RxFiles gout treatment chart and gout newsletter are available at www.cfp.ca. Go to the full text of the article on-line, then click on CFPlus in the menu at the top right of the page.

Table 1. Managing acute gouty arthritis: *The full version of the RxFiles gout treatment chart¹⁰ is available on-line from CFPlus.*

TREATMENT	SAMPLE DOSE	COMMENTS
Colchicine, oral	0.6 mg 2-3 times daily for 1-3 d	<ul style="list-style-type: none"> Well tolerated in lower-dose regimens (eg, 0.6 mg 2-3 times daily or 1.2 mg in 1 dose and 0.6 mg 1 h later on first day, then stop¹¹) Traditional high doses lead to considerable GI adverse effects (77%-100%)^{11,12}; low doses shown to be much better tolerated (adverse effects 26%) and equally effective¹¹ Avoid in patients with solid organ transplant and, if possible, in patients on dialysis. Can be used acutely in patients with reduced renal function; however, if use is prolonged (eg, beyond 10 d), reduce dose
NSAIDs		
Naproxen, oral	500 mg twice daily for 1-3 d	<ul style="list-style-type: none"> Generally tolerated well; option if patient had previous colchicine intolerance Following 1-3 d, can reduce dose and continue for 1-2 wk Indomethacin is not more effective, and the potential for adverse CNS effects (eg, headache, confusion) is greater Which NSAID has the lowest CV risk is uncertain, but current evidence suggests naproxen < ibuprofen < celecoxib.^{13,14} Avoid ibuprofen or separate time of administration if patient is taking ASA (owing to drug interaction¹⁵) Avoid in more severe CKD (CrCl < 40 mL/min), heart failure, or history of NSAID-associated PUD
Ibuprofen, oral	800 mg 3 times daily for 1-3 d	
Celecoxib, oral	200 mg daily for 1-3 d	
Corticosteroids		
Methylprednisolone, intramuscular	40-80 mg once intramuscularly (consider age and weight)	<ul style="list-style-type: none"> Alternative in patients with contraindications to NSAIDs or colchicine (eg, patients with history of solid organ transplant or who are taking warfarin) Lower risk of side effects if used short-term Short courses (ie, ≤ 1-2 wk) do not require tapering of dose With some corticosteroids, intra-articular injection is an option if gout is monoarticular or there is a contraindication to systemic corticosteroids¹⁶ Avoid in brittle diabetic control, infection
Prednisone, oral	25-50 mg once daily for 3-5 d	

ASA—acetylsalicylic acid, CKD—chronic kidney disease, CNS—central nervous system, CrCl—creatinine clearance, CV—cardiovascular, GI—gastrointestinal, NSAIDs—nonsteroidal anti-inflammatory drugs, PUD—peptic ulcer disease.

Table 2. Starting preventive therapy for gout with allopurinol: *When and how.*

WHAT	WHEN AND HOW
When to start	Consider allopurinol if patient has 3 or more gout attacks per year, if unexplained or unavoidable. ^{31,32} Dose range 100-800 mg/d; commonly 300 mg/d
When not to start	Do not start allopurinol during an attack of gout; wait 1-2 wk after resolution of the acute episode. Additionally, allopurinol should not be stopped nor should the dose be adjusted during an acute attack of gout, as this can precipitate or worsen symptoms
How to start	<p>Start low and go slow</p> <ul style="list-style-type: none"> Start with 100 mg daily (50 mg daily if estimated GFR ≤ 50 mL/min) and increase every 2-4 wk by 100 mg (or 50 mg if initial dose is 50 mg daily). This will reduce the risk of adverse effects (eg, rash) Protect against allopurinol-induced gout attacks with low-dose colchicine⁴⁰ (0.6 mg daily or every other day if patient has reduced renal function) or an NSAID (eg, naproxen 375 mg twice daily or ibuprofen 400 mg 3 times daily for 3-6 mo); those with severe gout might benefit from more prolonged prophylaxis. If patient is on ASA for CV risk reduction, naproxen, unlike ibuprofen, does not interact with ASA-platelet adhesion¹⁴
How to maintain	<p>For maintenance therapy consider both</p> <ul style="list-style-type: none"> a target of normal serum uric acid (300-360 µmol/L)^{31,32}, and patient response or tolerance to the drug <p>Doses exceeding 300 mg daily might be required to reach target serum uric acid in some patients. To improve tolerance divide doses > 300 mg to 2-3 times daily</p>

ASA—acetylsalicylic acid, CV—cardiovascular, GFR—glomerular filtration rate.

Case 2

Mr V.S., aged 76, is in your clinic complaining of 2 days of a red, swollen, and very painful right wrist and third proximal interphalangeal joint. He denies any trauma and states that this is similar to previous gout attacks. He was diagnosed with gouty arthritis about 10 years ago and has not had an attack for 3 years. He went to a medical clinic yesterday and was prescribed colchicine, 0.6 mg 3 times daily. Today he has severe nausea, mild diarrhea, and his hand does not feel much better. Examination confirms severe acute inflammatory arthritis.

Mr V.S. has long-standing hypertension, chronic atrial fibrillation, chronic kidney disease (estimated glomerular filtration rate of 35 mL/min), and obesity (body mass index of 32 kg/m²). Current medications include amlodipine 10 mg daily, perindopril 4 mg daily, hydrochlorothiazide 25 mg daily (dose increased from 12.5 mg daily about 6 months ago), metoprolol 25 mg twice daily, and warfarin 5 mg daily. He is an ex-smoker and abstains from alcohol. What are your therapeutic options for this acute episode of gouty arthritis?

Bringing evidence to practice

- Colchicine or NSAIDs would be initial options for management of the acute attack.^{18,31,32} However, in a patient with contraindications or intolerance to these agents, a short course of corticosteroids might be a reasonable option.^{1-3,18,31,32,41}
- Systemic steroids, oral or intramuscular, are suitable for polyarticular attacks.^{1-3,18,41} When attacks are monoarticular, intra-articular injections of corticosteroids provide comparable pain relief^{16,31}; this treatment is generally reserved for use by physicians with experience in this technique.
- Diuretics have been associated with precipitating acute attacks of gout. However, a retrospective review showed that hydrochlorothiazide (12.5 mg daily) was not associated with an increased incidence of gout attacks.⁴² Hydrochlorothiazide, a first-line option for the treatment of hypertension,⁴³ is an effective, low-cost medication, and in appropriate doses it can be used safely in many patients with gout.

In a patient like Mr V.S., who has a history of hypertension and chronic kidney disease, NSAIDs are best avoided.⁴⁴ Furthermore, he has had an adverse reaction to low-dose colchicine (gastrointestinal upset), which also did not provide adequate pain relief. Because the attack appears to be polyarticular, a short course of oral prednisone is reasonable⁴¹ (See **Table 1**¹⁰⁻¹⁶ for dosage suggestions). It is possible that the recent attacks are drug-induced; therefore, consider stopping the hydrochlorothiazide and restarting the patient at 12.5 mg daily after the attack has resolved.

Mr V.S. returns to you 8 months later, having had 3 more episodes of acute arthritis involving his foot and hand, including 2 attacks after he self-terminated his hydrochlorothiazide therapy. He wants preventive therapy. His SUA level is 418 µmol/L, and his renal function remains stable.

Bringing evidence to practice

- The risk of allopurinol rash, hypersensitivity syndrome, and Stevens-Johnson syndrome is increased in patients with chronic kidney disease.⁴⁵⁻⁴⁷ Cautious initiation and dosage adjustments can reduce the risk⁴⁷ (**Table 2**^{14,31,32,40}).
- Adverse effects of colchicine appear to be dose-related and can be minimized with lower-dosage regimens that are often effective¹¹ (**Table 1**¹⁰⁻¹⁶). Additionally, to prevent attacks during initiation of SUA-altering therapy, a reduced dose of colchicine can be used safely in most patients with chronic kidney disease. 🌿

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