

Enhanced Primary Care Pathway: Gout

1. Focused summary of gout relevant to primary care

Significance: Gout is a chronic, progressive, inflammatory disease requiring appropriate long-term management. Gout is increasing in incidence and prevalence and is the **most common cause of inflammatory arthritis in men over 40** years of age. It is **very rare in premenopausal women**. Gout is a **curable disease** that is vastly undertreated worldwide, mainly due to misconceptions regarding urate lowering therapy, resulting in permanent joint damage and disability. Poor adherence to therapy is common, and patients require ongoing education and monitoring. Hyperuricemia and gout are strongly associated with hypertension, the metabolic syndrome, renal impairment and cardiovascular disease.

Clinical Features: Classic acute gout typically affects one joint but several joints can also be involved. The most commonly involved areas (in decreasing frequency) are: the first MTP ("podagra"), instep, ankle, heel, knee, wrist, fingers and elbow. Gout can also affect bursae, especially over the elbows, knees or Achilles tendon. The affected joint and surrounding soft tissues are **exquisitely painful, warm, red and swollen**, and can resemble cellulitis. Patients may not be able to tolerate even a bed sheet touching the affected joint and may be unable to walk. The attacks usually last 3 to 10 days, and **peeling of the skin** over the joint may occur as the attack resolves. Without urate lowering therapy, the attacks may increase in frequency, involve multiple joints, persist longer and deposits of uric acid in the soft tissues (tophi) will occur. **Tophi are strongly associated with destructive and deforming joint disease.**

Potential Triggers of Gout Attacks:

Dietary	Excess alcohol, purines (meat, seafood), fructose (soda, juice, energy drinks)
Drugs / iatrogenic	Diuretics, low dose ASA, chemotherapy, radiation
Acute medical illness	Hemorrhage, infection, renal insufficiency, dehydration, surgery
Trauma	Injury to joint (may be minor)
Endocrine	Thyroid (hypo/hyper), hyperparathyroidism and uncontrolled diabetes

Diagnosis: Although the **gold standard test is identification of uric acid crystals in fresh synovial fluid** on polarized microscopy, this may not be feasible in some patients, or in a primary care setting. **Serum uric acid levels can be normal during an acute gout attack**, but will be elevated at some point in almost all gout patients. Although not all hyperuricemic patients have gout, the risk of gout is high with persistent serum urate levels >580 umol/L. X-rays are NOT useful for making an early diagnosis before permanent damage occurs. However, classic marginal erosions are often present on those with a long clinical history. Ultrasound can demonstrate active inflammation while Dual energy CT is an emerging technology that is very useful in demonstrating MSU crystal deposition in diagnostic dilemmas. Diagnostic dilemmas should be referred to Rheumatology.

If synovial fluid analysis is not possible, diagnostic algorithms may help to determine whether the probability of gout is low, intermediate or high. The **"Gout Diagnosis Calculator"** was developed for this purpose (see Links below for free app). If the probability is intermediate, the patient should be followed closely and synovial fluid analysis performed when possible. The ACR-EULAR Gout Classification Criteria Calculator (see Links below for URL) is another helpful diagnostic tool for gout.

2. Checklist to guide your in-clinic review of this patient with gout symptoms

- ☐ Is the history consistent with typical gout attacks? Consider using diagnostic tool (see link below)
- ☐ Are there any red flags to suggest infection?
- ☐ Does the patient have a history of kidney stones, or tophi on examination?
- ☐ Are there any potential gout triggers, including lifestyle factors?
- ☐ Review and treat modifiable cardiac risk factors.

3. Links to additional resources

For physicians:	Diagnostic rule for gout without joint fluid analysis: Download “Gout Diagnosis Calculator” free from the App Store or use the online tool at: https://www.mdcalc.com/acute-gout-diagnosis-rule
	Classification Criteria for Gout (online tool) http://goutclassificationcalculator.auckland.ac.nz/
	http://rheuminfo.com/diseases/gout (has information for physicians and patients)
	www.goutinstitute.ca
	https://www.niams.nih.gov/health_Info/Gout/default.asp
For patients:	www.rheuminfo.com/diseases/gout
	www.gouteducation.org
	http://www.albertahealthservices.ca/assets/info/nutrition/if-nfs-healthy-eating-for-managing-gout.pdf

4. Suspected Gout Pathway

This AHS Calgary Zone pathway has been developed with consideration of guidelines. **The following is a best-practice clinical pathway for management of Gout in the primary care medical home.**



GOUT PATHWAY

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Specialist LINK | Local: 403.910.2551 | Toll free: 1.844.962.5465 (LINK) | www.specialistlink.ca

REFER TO RHEUMATOLOGY

Suspected Acute Gout attack: Treat as soon as possible

Red Flags

- Fever, chills, signs of cellulitis or sepsis
- If septic arthritis is suspected it is a medical emergency

YES

REFER TO ER
Work-up for infection

NO

Comorbidities

- Organ transplant
- Stage 4 or 5 CKD (eGFR < 30 ml/min)
- Contraindications to treatment (*see expanded detail*)
- Not responding to treatment

YES

NO

Typical Clinical Features

- Onset more often at night
- Usually monoarticular, lower extremity joint
- Complete resolution of early attacks in days to weeks, even if untreated
- Pain peaks within 12 to 24 hours

Medication/Lifestyle Review

- Diet and Alcohol
- Diuretics
- Screen for comorbidities (eg., HTN, renal, diabetes, lipids)

YES

Stop or modify offending agent, if possible or appropriate

Baseline Investigations:

- CBC, Cr, urate, CRP, ALT, glucose
- If synovial fluid obtained, do cell count, culture and crystals
- Consider x-rays (typical gouty erosions?)

Therapeutic Options in Acute Attack (in order):

- 1) Colchicine (0.6 mg bid max dose); +/- steroids or NSAIDs
 - Steroids (80 mg IM or 30 mg po daily x 5 days)
- 2) NSAIDs (limited use given comorbidities)

YES

- See expanded detail for dosage and contraindications
- Follow-up in 2-4 weeks or if high clinical evidence of recurrent gout

Consider Urate Lowering Therapy (ULT)

- Allopurinol (or febuxostat)
- Can start during attack if steroids given
- Continue prophylaxis with colchicine BID for first 3-6 months
- Do not stop ULT if a gout attack occurs

YES

- Treat to target serum urate:
 - < 360 umol/L
 - < 300 umol/L (if tophi or severe gout)
- Follow-up in 2-4 weeks or if high clinical evidence of recurrent gout
- See expanded detail for dosage and contraindications

Contraindications:

Allopurinol hypersensitivity in high-risk ethnic groups including Chinese, Thai and Korean patients

YES

• See expanded detail

If no improvement refer to Rheumatology

1. GENERAL PRINCIPLES

- All patients with gout should be fully informed of the causes of gout, management principles & lifestyle modifications (including weight loss, regular exercise, alcohol use and diet)
- Screen all patients for comorbidities including renal impairment and cardiovascular risk factors
- Treat acute attacks as soon as possible; early treatment can prevent a full blown attack
- Gout generally cannot be managed with diet alone, but **can be cured with a combination of diet control and urate lowering therapy**.
- ~40% of urate is from diet; 60% is a normal waste product (blocked by allopurinol or febuxostat)

Dietary Advice for Gout

Patients should limit consumption of	<ul style="list-style-type: none"> - meats, especially organ meat (liver, kidney etc.) - seafood, especially shellfish, sardines and anchovies - alcohol, especially beer
Moderate intake of other purine-rich foods should not aggravate gout	<ul style="list-style-type: none"> - purine-rich vegetables (asparagus, cauliflower, spinach, mushrooms) - nuts - legumes (beans and peas)
Intake of the following may reduce the risk of gout attacks	<ul style="list-style-type: none"> - coffee (use decaffeinated if > 2 cups/day) - vitamin C (500 mg/day) - low fat dairy (milk, yoghurt) - tart cherries (not in pill form)

2. TREATMENT OF ACUTE GOUT ATTACKS

TREATMENT	DOSAGE	COMMENTS
Oral colchicine	<ul style="list-style-type: none"> - 0.6 mg po BID until attack subsides - 0.3 mg OD - BID if GFR 30–50 mL/min - more effective if started within the first 36 hr of an attack 	<ul style="list-style-type: none"> - contraindicated if severe renal (GFR <30 mL/min) or hepatic insufficiency - DO NOT use old regimens with frequent doses until patient has diarrhea - use caution if on immunosuppressive drugs due to potential drug interactions
Corticosteroids	<ul style="list-style-type: none"> - prednisone 30 mg PO OD x 5 days OR - Kenalog® (triamcinolone acetonide) 1 mg/kg or 80 mg IM x 1 into gluteal muscle (use a 22 G x 1.5 inch needle) 	<ul style="list-style-type: none"> - can be used safely in chronic kidney disease - safer than NSAIDs or colchicine in the elderly
NSAIDs	<ul style="list-style-type: none"> - indomethacin 25-50 mg TID, <u>OR</u> - naproxen 250-500 mg BID - then taper off after symptoms subside 	<ul style="list-style-type: none"> - often contraindicated due to comorbidities - other NSAIDs (full dose) may be as effective as indomethacin - consider gastroprotection
Intraarticular steroids	<ul style="list-style-type: none"> - 40 - 80 mg of triamcinolone (Kenalog®) for larger joints - 10 - 20 mg of methylprednisolone (DepoMedrol ®) for small joints or bursae 	<ul style="list-style-type: none"> - useful in treatment of 1 or 2 involved joints - sometimes more effective than oral corticosteroids - aspirating excess synovial fluid prior to injection of steroid has therapeutic benefit - synovial fluid aspirate should be sent to lab for cell count, culture, and crystals

3. TREATMENT OF CHRONIC GOUT

A. Indications for urate lowering therapy (Note: Treatment is usually LIFELONG!)

- More than 2 or 3 acute attacks of gout within 1 to 2 years (or unremitting gouty inflammation)
- Radiographic evidence of joint damage due to gout (x-ray, ultrasound or dual energy CT)
- Presence of tophi
- Established gout with chronic kidney disease stage 2 or worse (GFR <90 mL/min)
- Renal stones (urate)

B. Gout Flare Prophylaxis (Mandatory while initiating urate lowering therapy)

- Continue colchicine prophylaxis for:
 - 3 months after achieving the serum uric acid goal in patients without tophi, OR
 - 6 months after achieving the serum uric acid goal in patients with 1 or more tophi, OR
 - continue prophylaxis for longer if acute gout flares persist
- It is common practice to treat with BOTH corticosteroids (single IM dose or short course PO) AND colchicine when initiating urate lowering therapy.

Colchicine	0.6 mg po OD or BID, or 0.3 mg po OD or BID if elderly or GFR 30 to 50 mL/min Do not use if GFR < 30 mL/min
Corticosteroids	- Kenalog® (triamcinolone acetonide) 80 mg IM deep into gluteal muscle, <u>OR</u> - Prednisone 20 mg PO OD in patients with contraindications to NSAIDs and colchicine, taper by 5mg per week
NSAID	e.g. naproxen 250 mg to 500 mg po BID with a proton pump inhibitor Potential for significant side effects if comorbidities (renal disease, elderly) Avoid prophylaxis with combination of NSAIDs and oral prednisone

C. Initiation of Urate Lowering Therapy (Target: serum urate < 360 umol/L; <300 umol/L if tophi)

- **Allopurinol** 300 mg PO OD can be started in patients on prophylaxis with steroids and colchicine.
- Alternatively, the dose can be slowly titrated up to minimize the risk of gout attacks as follows:
 - Allopurinol 100 mg PO OD x 2 to 4 weeks →
 - Allopurinol 200 mg PO OD x 2 to 4 weeks →
 - Allopurinol 300 mg PO OD thereafter (300 mg is sufficient for most; cost ~33¢ per tablet) →
 - Allopurinol dose may be increased to 400 mg if serum urate level remains above target →
 - Refer to Rheumatology if not responding.
- CBC, CRP, Cr, ALT, albumin, uric acid monthly until urate stable, then every 6 to 12 months
- **Febuxostat** 80 mg PO OD or every other day can be used instead of allopurinol in patients with stage 4 or 5 CKD (GFR < 30 mL/min), or other contraindications to allopurinol. Blue Cross requires a special authorization form (cost ~\$1 per tablet), but most private insurers do not.

4. CONTRAINDICATIONS / REASONS TO STOP URATE LOWERING THERAPY

The vast majority will tolerate allopurinol well. The most common concern is an ↑ in gout attacks during initiation of treatment, such that gout prophylaxis is mandatory. **DO NOT stop allopurinol for a gout attack. Allopurinol and febuxostat should not be used in patients on azathioprine (Imuran®)** due to the risk of bone marrow failure (refer to rheumatology). Patients with **allopurinol hypersensitivity** (rash, fever, ↓ platelets, ↑ liver enzymes) should stop immediately and never take this drug again.

HLA-B*58:01 TESTING FOR ETHNIC GROUPS AT RISK FOR HYPERSENSITIVITY REACTIONS

Chinese, Thai and Korean patients are at risk for life-threatening allopurinol hypersensitivity reactions. HLA-B*5801 screening should be considered in these patients before starting allopurinol, and if positive allopurinol should not be used. This genetic test can be ordered through CLS. High-risk individuals should be treated with febuxostat instead.

The Gout Enhanced Primary Care Pathway was developed by the following individuals in collaboration with the Calgary Zone Primary Care Networks, the Division of Rheumatology, and Alberta Health Services:

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