Case presentation

نحوه اپروچ به آقای 55 ساله با درد و تورم انگشت پای راست در درمانگاه پزشکی خانواده

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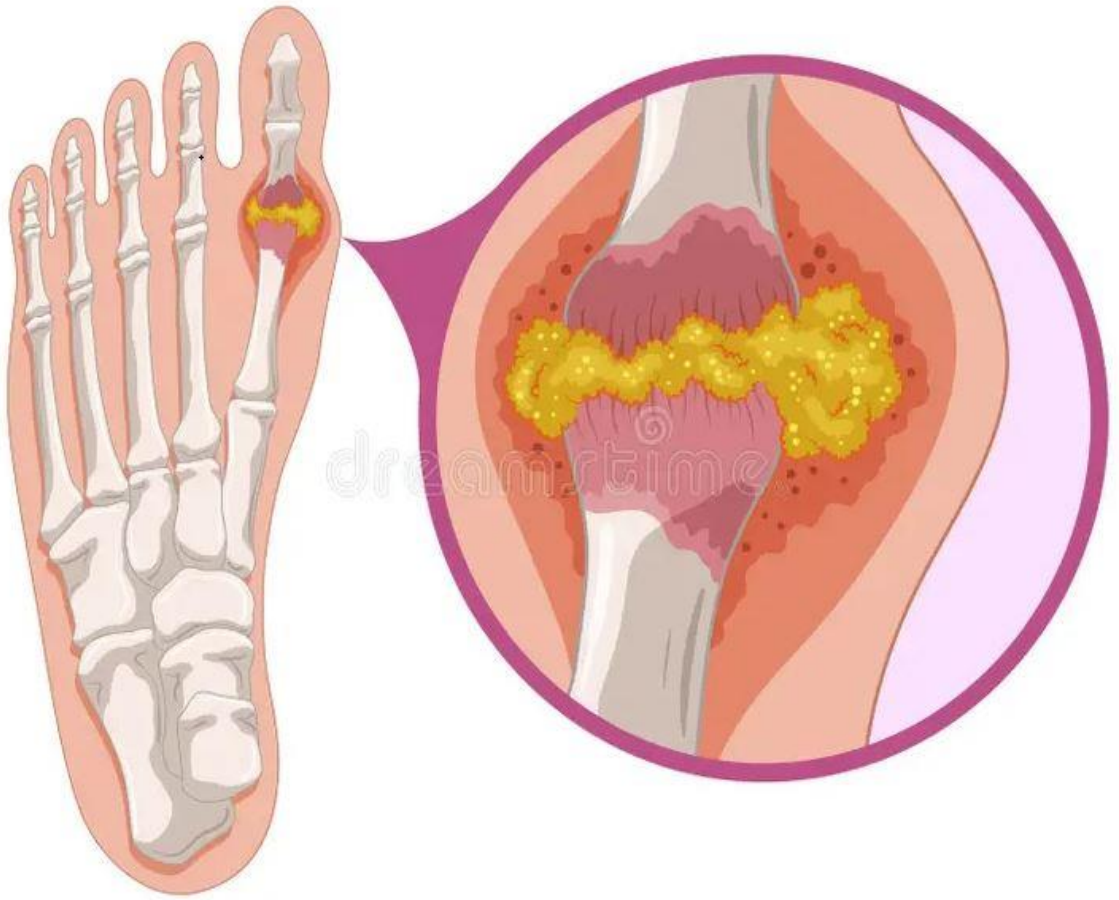


Medical history

- 55 y/o male
- Red, painful toe for a week
- So tender he doesn’t wear shoes
- No trauma Hx
- Had same symptoms months ago that resolved by itself
- No alcohol use
- No medications
- No constitutional symptom

Examination

- Redness, swelling, and tenderness at the base of the great toe (arthritis of first MTP joint)
- No warmth
- Minimally reduced active ad passive ROM

Implication: acute monoarthritis

Differential diagnosis

Important historical points:

- Hot or swollen joints may suggest infection.
- Constitutional symptoms (high-grade fever, weight loss, malaise) also raise the suspicion of infection or sepsis.
- Weakness may be a symptom of a compartment syndrome or an acute myelopathy. However, lack of strength can also be due to pain in the joint or periarticular tissues or myopathy.
- Burning pain, numbness, or paresthesia may suggest an acute myelopathy, radiculopathy, or neuropathy.

Important Ph/E points:

- Effusion? Synovitis?
- توجه به وجود گرما، افیوژن و تورم بفت نرم در معاینه
- کاهش دامنه حرکات فعال و منفعل
- وجود شواهد دیگری که به نفع یکی از تشخیص های افتراقی باشد مانند ندول های روماتوئیدی یا اختلالات بینایی

Diagnosis establishment

Differential diagnosis of acute monoarthritis

Infection
Bacterial
Fungal
Mycobacterial
Viral
Spirochete
Crystal induced
Monosodium urate
Calcium pyrophosphate dihydrate
Hydroxyapatite
Calcium oxalate
Lipid
Hemarthrosis
Trauma
Anticoagulation
Clotting disorders
Fracture
Pigmented villonodular synovitis

Tumor
Tenosynovial giant cell tumor (formerly pigmented villonodular synovitis)
Chondrosarcoma
Osteoid osteoma
Metastatic disease
Systemic rheumatic disease
Rheumatoid arthritis
Spondyloarthritis
Systemic lupus erythematosus
Sarcoidosis
Osteoarthritis
Erosive variant
Intraarticular derangement
Meniscal tear
Osteonecrosis
Fracture
Other
Plant thorn synovitis

- The differential diagnosis of an acute monoarthritis can also overlap with that of polyarthritis since virtually any polyarthritis disorder can initially present as a monoarthritis.

- ***Gout flare***
- ***Septic arthritis***

توسط آرتریوسنتز و لکوسیتوز با تعداد بالا تشیص داده میشود. پاسخ بالینی به دارودرمانی نقرس، جهت افتراق قابل اعتماد نیست.

- ***Cellulitis***

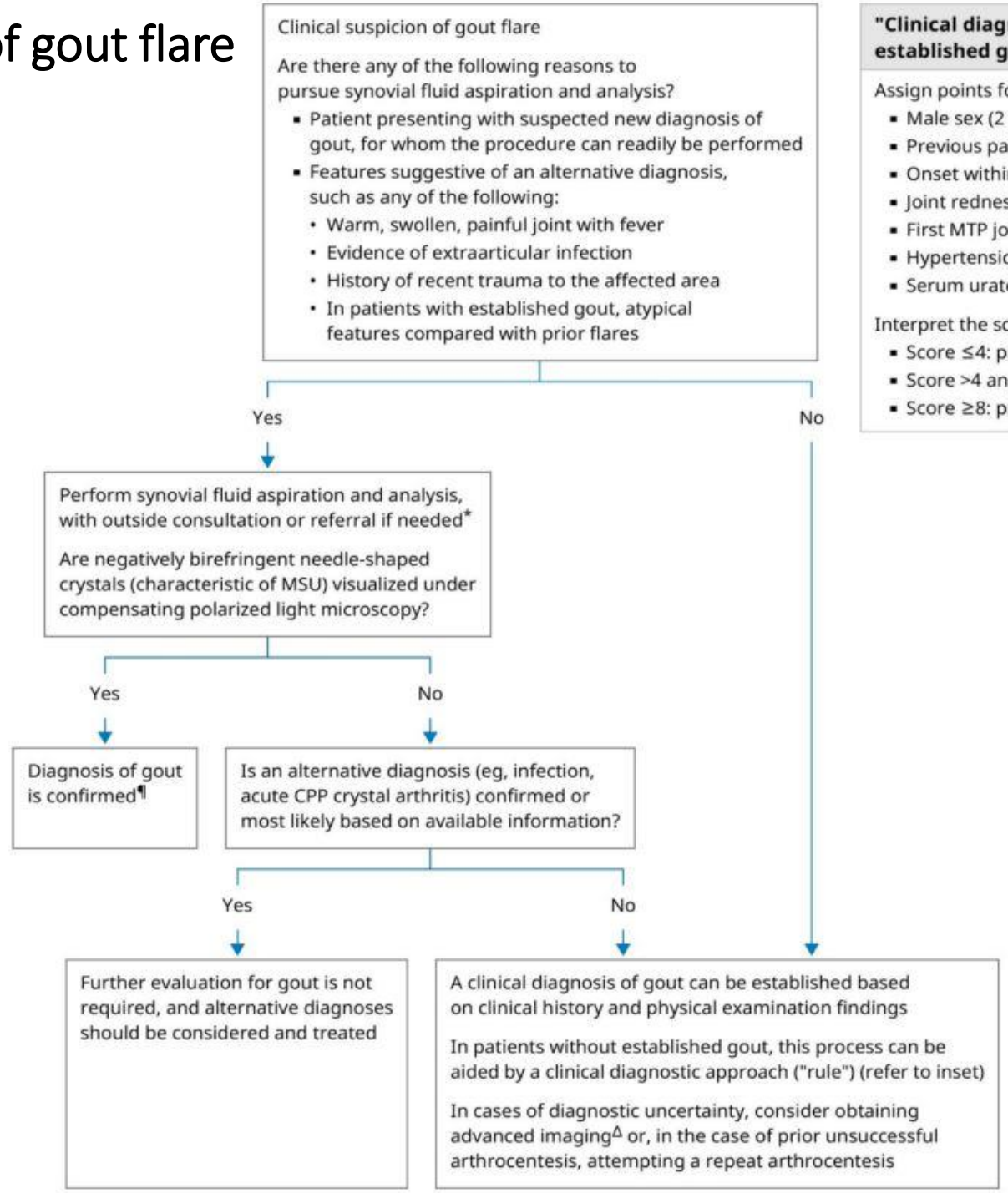
در صورت شک به سلولیت عدم انجام آرتریوسنتز از طریق پوست درگیر ارجح است. گسترش ناحیه درگیر فراتر از مفصل کمک کننده است.

- ***Pseudogout***
- ***Trauma***

شکستگی استرسی میتواند حملات خفیف نقرس را تقلید کند.

- ***Osteoarthritis***

Diagnosis of gout flare



"Clinical diagnostic rule" for patients without established gout presenting with acute monoarthritis

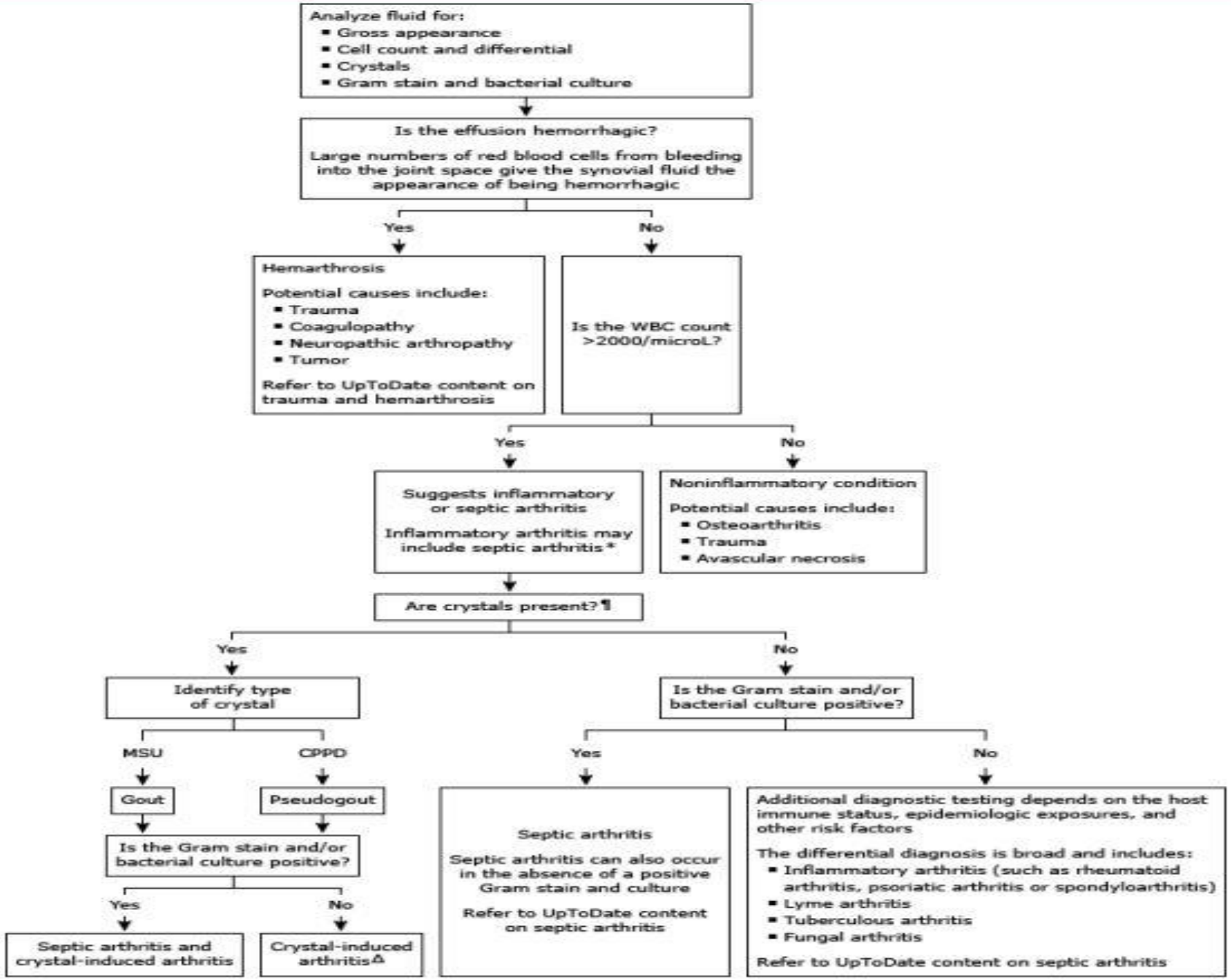
Assign points for each of the following element(s) present:

- Male sex (2 points)
- Previous patient-reported arthritis attack (2 points)
- Onset within 1 day (0.5 points)
- Joint redness (1 point)
- First MTP joint involvement (2.5 points)
- Hypertension or at least one cardiovascular disease (1.5 points)
- Serum urate level >5.88 mg/dL (3.5 points)

Interpret the score as follows:

- Score ≤4: probability of gout is low, consider alternative diagnoses
- Score >4 and <8: probability of gout is intermediate◇
- Score ≥8: probability of gout is high

Guide to interpretation of synovial fluid analysis



When to suspect?

- out flare should be suspected in patients presenting with a monoarthritis of the lower extremities, especially when there is involvement of the first metatarsophalangeal (MTP) joint
- Suspicion is further increased in the presence of hyperuricemia, recognized risk factors, and/or known triggers

Gout

- Gout is a chronic disease of monosodium urate (MSU) crystal deposition. Gout flares occur due to the innate immune response to deposited crystals.

Nonmodifiable risk factors	Modifiable risk factors
▪ Age ▪ Sex ▪ Ethnicity ▪ Genetic variants	▪ Obesity ▪ Hypertension ▪ Hyperlipidemia ▪ Metabolic syndrome ▪ Diabetes mellitus ▪ Chronic kidney disease ▪ Dietary factors ▪ Alcohol ▪ Medications altering urate balance

Gout Flare

- A typical gout flare is typically intensely inflammatory, with severe pain, redness, swelling, and disability
- At least 80 percent of initial flares involve a single joint
  - most commonly the base of the great toe or the knee
  - Other common sites are the ankle, instep, wrist, finger, and elbow.
- Maximal severity of the flare is usually reached within 12 to 24 hours.
- Gout flares almost always resolve within a few days to several weeks, even without treatment.

Type of provocation	Specific examples
Physiologic alterations	▪ Joint trauma ▪ Surgery ▪ Dehydration ▪ Starvation (eg, ketoacidosis)
Environmental alterations	▪ High ambient temperature ▪ Extremes of humidity
Changes in medications affecting urate balance	▪ Initiation and intensification of urate-lowering therapy* ▪ Withdrawal of colchicine prophylaxis ▪ Vaccination ▪ Diuretics ▪ Low-dose aspirin
Intake of alcohol or other triggering foods	▪ Alcohol (eg, beer, spirits, wine) ▪ Purine-rich foods (eg, red meat, shellfish)
Hospitalization¶	

Laboratory findings

- Synovial fluid from an affected joint should be inflammatory (ie, a white blood cell count of 10,000 to 100,000 cells/m3 with a neutrophilic predominance)
- polarized light microscopy may reveal needle-shaped, strongly negatively birefringent MSU crystals that appear bright yellow when they are parallel to the red compensator axis.
- Serum urate is elevated in almost all people with gout. However, the serum urate can drop into the normal range during a gout flare.

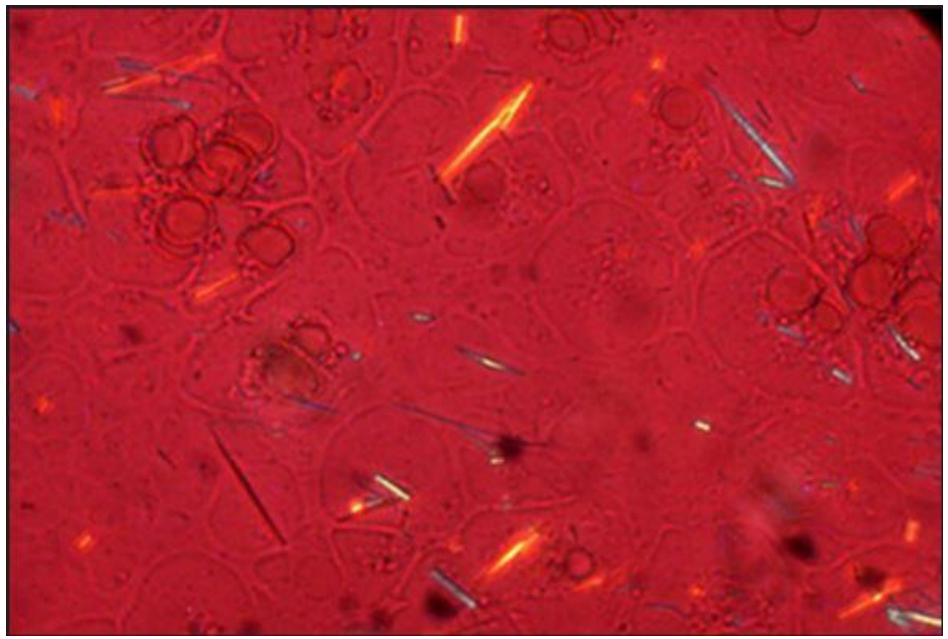
Comparison of gout and CPPD disease

Characteristic	Gout	CPPD disease
Prevalence	17 to 20 per 1000 individuals, largely adult men and postmenopausal women	<1 per 1000 individuals experience acute CPP crystal arthritis (pseudogout); CPPD disease is common in osteoarthritis and increases with age
Crystal chemistry	Monosodium urate	CPP dehydrate
Crystal appearance	Negatively birefringent; needle-shaped or rods	Weakly positively birefringent; rods or rhomboidal
Articular involvement	Monoarticular > oligoarticular; polyarticular <30%	Monoarticular > oligoarticular
Most frequently affected joints	First MTP joint	Knee, wrist, other
	Initially 50%	
	Eventually 90%	
	Ankle, knees, other	
Predisposing conditions/risk factors	Hyperuricemia*, obesity, hypertension, hyperlipidemia, alcohol ingestion, lead ingestion, hereditary enzyme defect	Hemochromatosis, osteoarthritis, hypomagnesemia, hyperparathyroidism, hereditary (rare), and increased age
Therapeutic options	Acute gout attacks	Acute CPP crystal arthritis (pseudogout)
	NSAIDs, glucocorticoids, colchicine	NSAIDs, glucocorticoids, colchicine
	Chronic gout management	Chronic CPPD disease management
	Urate-lowering agents, colchicine	NSAIDs, colchicine
		DMARDs: hydroxychloroquine, methotrexate (no randomized trials showing clinical benefit)

Work up

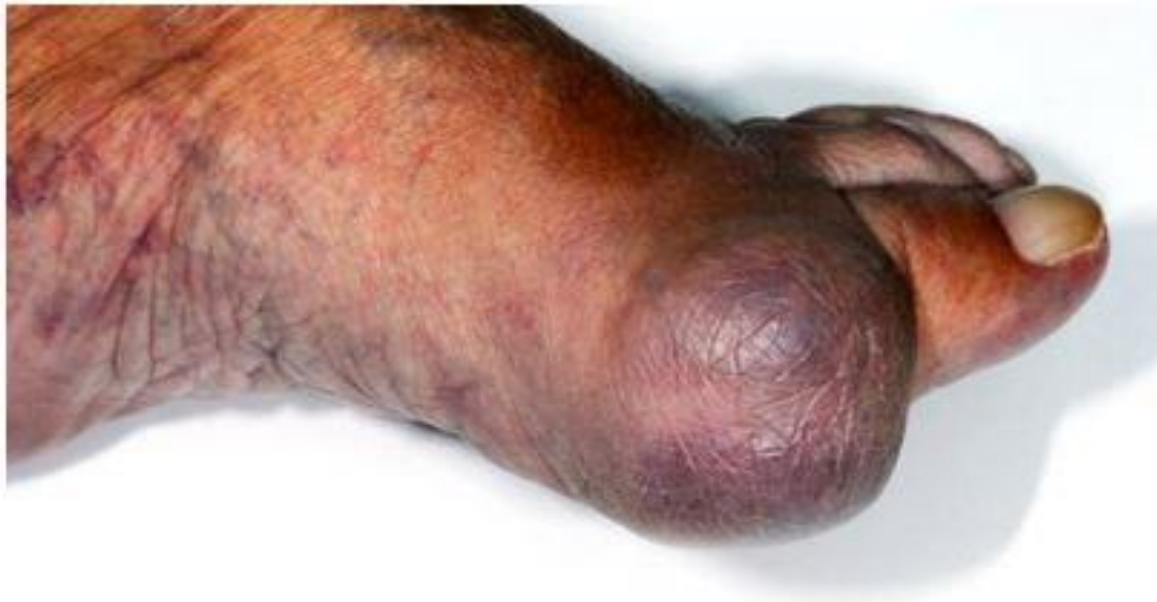
در صورت تندرنس استخوانی واضح یا سابقه تروما، رادیوگرافی از مفصل درگیر اندیکاسیون دارد.

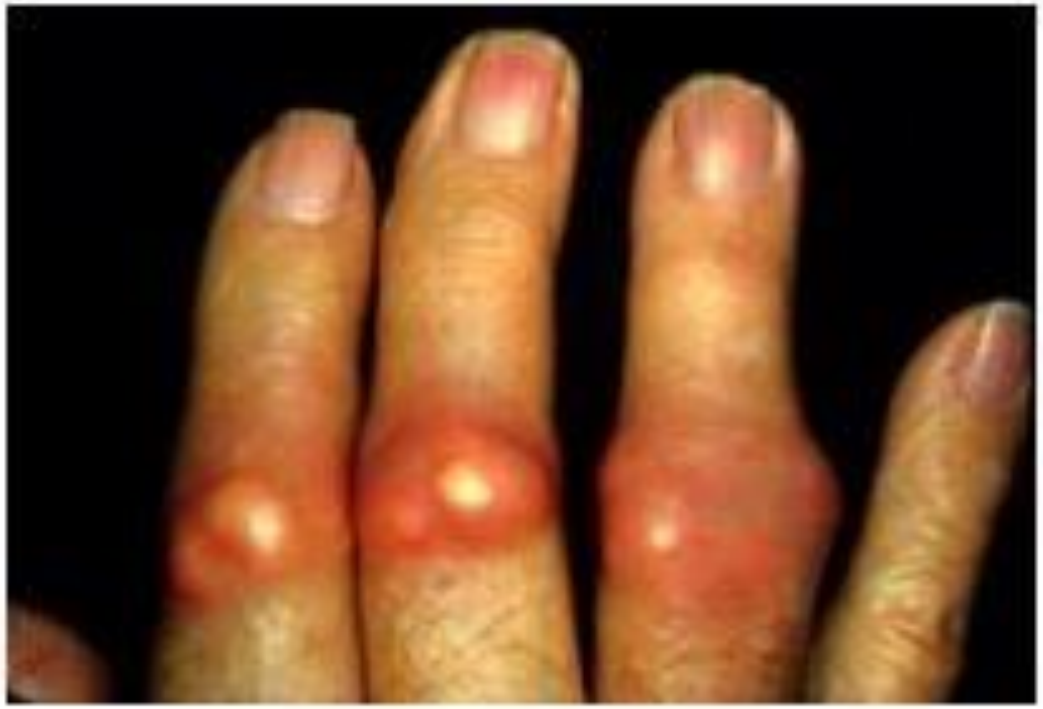
- Synovial fluid

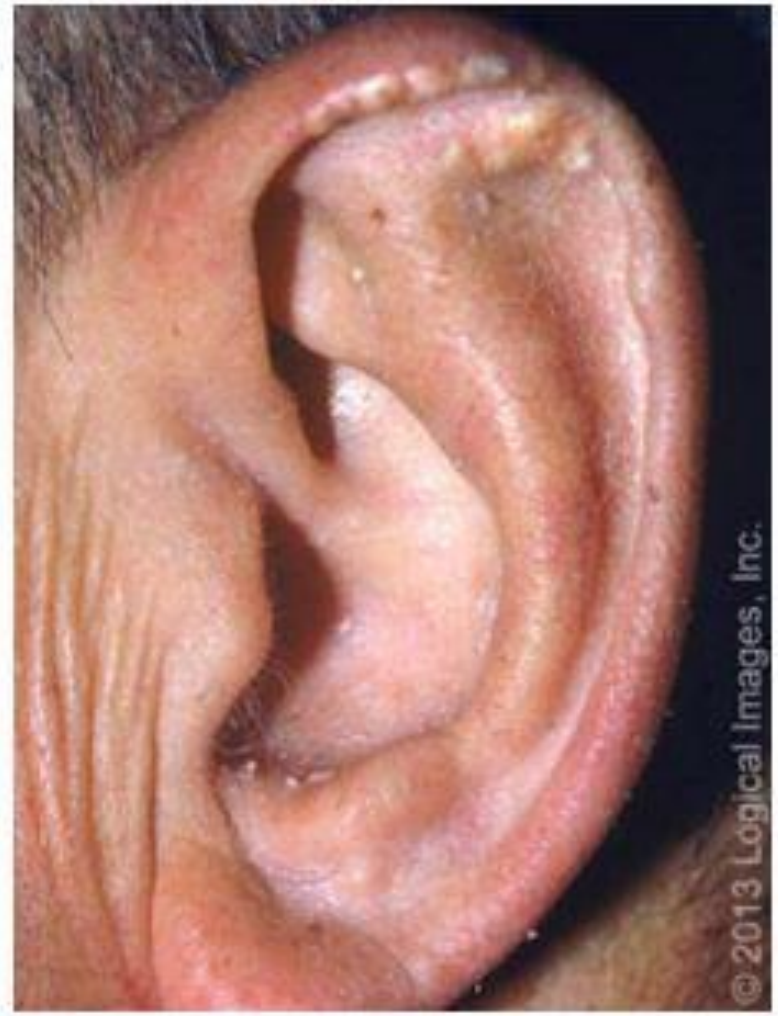


Tophaceous gout

- Tophi are collections of densely packed MSU crystals in connective tissues accompanied by chronic inflammation and often by destructive changes.
- can be visible and/or palpable but are usually not painful or tender
- may affect the ears or soft tissues (eg, articular structures, tendons, bursas, or bone)



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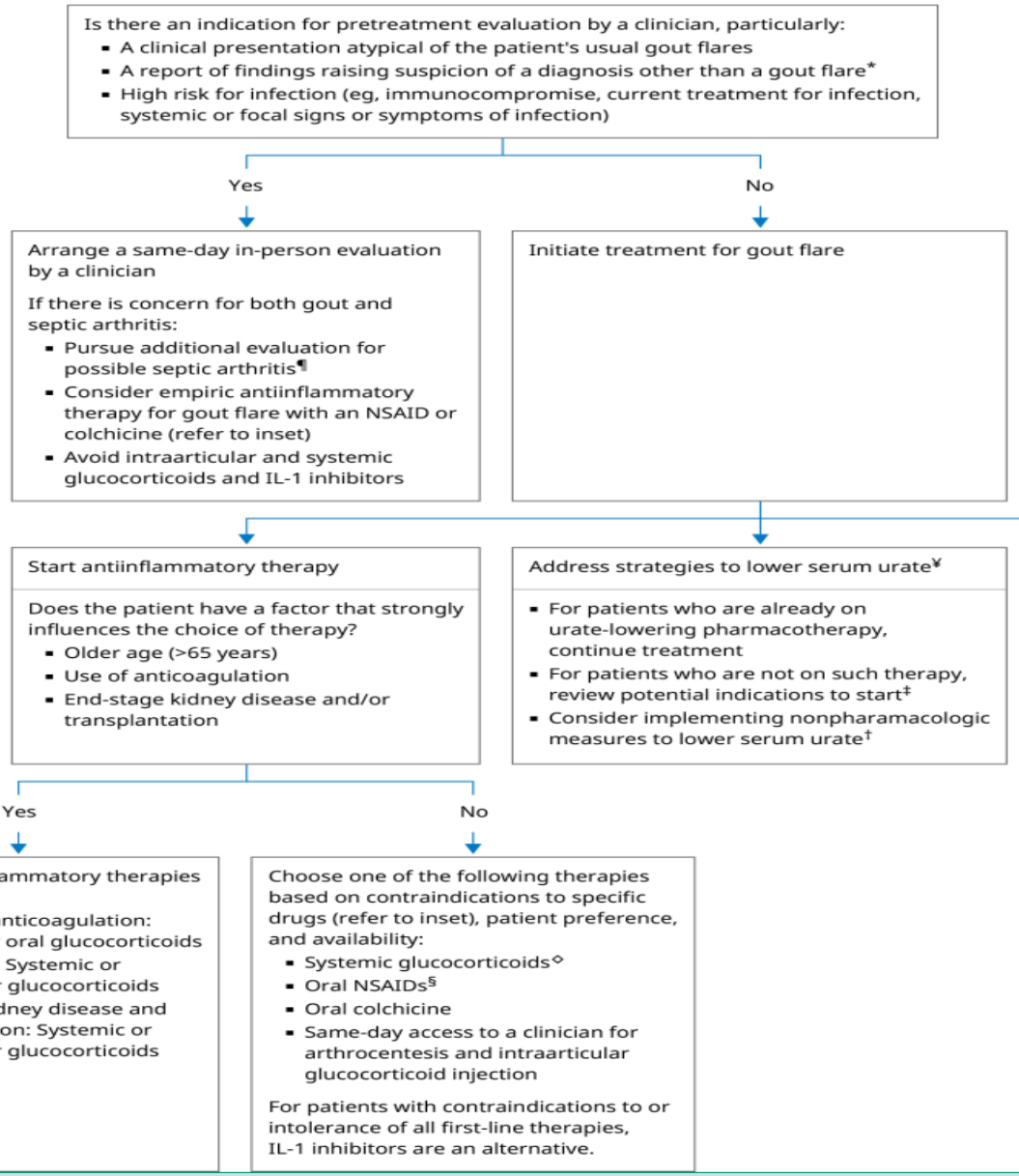
Management



Relative and absolute contraindications to antiinflammatory therapies

Systemic glucocorticoids

Reasons to avoid oral glucocorticoids or that convey increased risk with a short course of therapy include brittle diabetes mellitus, history of glucocorticoid intolerance, recent surgery with a wound that has not yet healed, and suspected concurrent infection.

NSAIDs

Reasons to avoid NSAIDs include eGFR <60, hyperkalemia, duodenal or gastric ulcer, poorly controlled hypertension, moderate to severe or uncompensated heart failure, cirrhosis, unmodifiable drug interaction (eg, anticoagulation), known NSAID allergy or intolerance.

Colchicine

Reasons to avoid colchicine include history of allergy or severe adverse reaction to colchicine; combined kidney function and hepatic impairment; and/or kidney function or hepatic impairment plus concurrent or very recent use of a drug that is a strong inhibitor of cytochrome P450 3A4 or an inhibitor of the P-glycoprotein multidrug resistance transporter (refer to the UpToDate topic on treatment of gout flares for examples of such medications). Colchicine may be less effective when used after an attack has been ongoing for greater than 24 to 36 hours.

Intraarticular glucocorticoids

Reasons to avoid intraarticular injection include more than 2 affected joints, affected joints that are not amenable to injection (eg, small joints in the hands and feet), lack of timely access (ie, within 24 hours) to a provider with sufficient expertise, and suspected joint infection.

- **NSAID**
  - NOT ASA
  - Use cautiously in elderly
  - Don’t use in CKD
  - For 7-10 days (few days after resolving of symptoms)
  - Naproxen (500 mg twice daily)

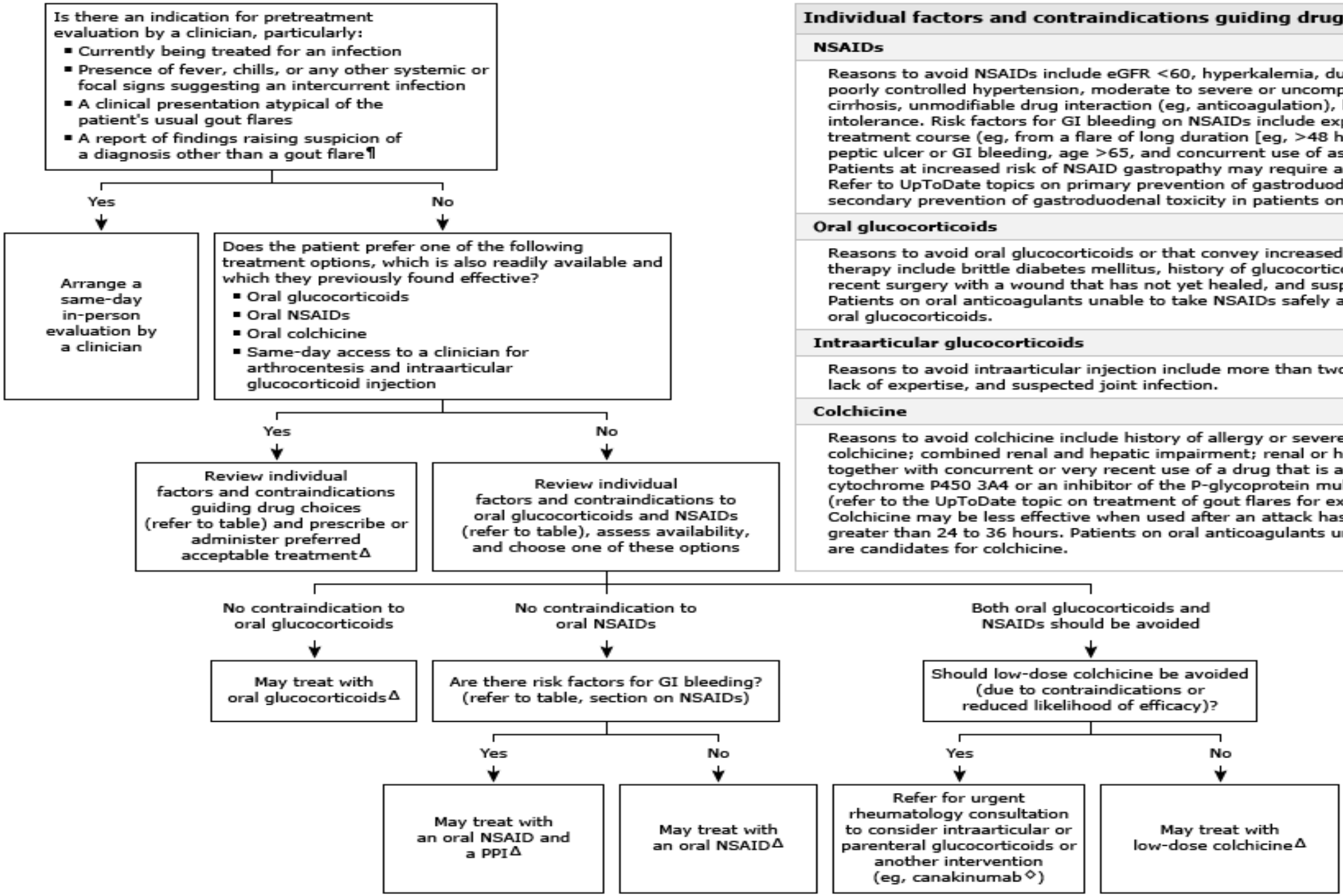
    or Indomethacin (50 mg three times daily)
  - Add PPI if high risk of NSAID gastropathy

- **Colchicine**
  - Don’t use in CKD, hepatic impairment if patient takes any drug that inhibits P-gp or reduces CYP3A4 (can cause myelosuppression and even fatal pancytopenia.
  - Depending on the size of colchicine tablet available, we use an initial dose of 1 to 1.2 mg, followed one hour later by another 0.5 to 0.6 mg, for a total dose on the first day of therapy of 1.5 to 1.8 mg.
  - Followed by 0.5 to 0.6 mg twice daily until 48 hours after resolution of the flare.
  - Attention to drug interactions and dose adjustment is necessary.

در ایران قرص 1 میلی گرمی موجود است که در روز اول 1.5 قرص با فاصله 1 ساعت شروع و در روزهای بعدی با نصف قرص هر 12 ساعت ادامه داده میشود.

- **Corticosteroids (systemic/ local)**
  - Avoid using systemic glucocorticoids in patients with concurrent infection, brittle diabetes, recent surgery with an unhealed wound, and/or history of glucocorticoid allergy or intolerance.
  - Oral prednisone 40 mg daily (or its equivalent) until the flare resolves, followed by a taper
  - IM and IV can be used if NPO
  - Longer tapering in patients with a Hx of relapsing or refractory disease
  - Better be avoided if septic arthritis is not ruled out completely

We chose naproxen and colchicine, since there was no contraindication for either and the regimen was convenient (no need for tapering).



Individual factors and contraindications guiding drug choicesΔ

NSAIDs

Reasons to avoid NSAIDs include eGFR <60, hyperkalemia, duodenal or gastric ulcer, poorly controlled hypertension, moderate to severe or uncompensated heart failure, cirrhosis, unmodifiable drug interaction (eg, anticoagulation), known NSAID allergy or intolerance. Risk factors for GI bleeding on NSAIDs include expectation of a prolonged treatment course (eg, from a flare of long duration [eg, >48 hours]), history of peptic ulcer or GI bleeding, age >65, and concurrent use of aspirin or glucocorticoids. Patients at increased risk of NSAID gastropathy may require a concurrent PPI. Refer to UpToDate topics on primary prevention of gastroduodenal toxicity and secondary prevention of gastroduodenal toxicity in patients on NSAIDs.

Oral glucocorticoids

Reasons to avoid oral glucocorticoids or that convey increased risk with a short course of therapy include brittle diabetes mellitus, history of glucocorticoid intolerance, recent surgery with a wound that has not yet healed, and suspected concurrent infection. Patients on oral anticoagulants unable to take NSAIDs safely are candidates for oral glucocorticoids.

Intraarticular glucocorticoids

Reasons to avoid intraarticular injection include more than two affected joints, lack of expertise, and suspected joint infection.

Colchicine

Reasons to avoid colchicine include history of allergy or severe adverse reaction to colchicine; combined renal and hepatic impairment; renal or hepatic impairment, together with concurrent or very recent use of a drug that is a strong inhibitor of cytochrome P450 3A4 or an inhibitor of the P-glycoprotein multidrug resistance transporter (refer to the UpToDate topic on treatment of gout flares for examples of such medications). Colchicine may be less effective when used after an attack has been ongoing for greater than 24 to 36 hours. Patients on oral anticoagulants unable to take NSAIDs safely are candidates for colchicine.

Chronic management

- Patient education on modifying diet:
  - Reduce high-purine foods (eg, red meat, shellfish) with attention to protein intake (alternative protein sources)
  - Avoid alcoholic beverages of all types
  - Avoid high-fructose corn syrup and sugar-sweetened beverages
  - Consider whole-diet approaches like DASH
- Treatment of comorbid conditions (obesity, HTN, DM, CKD)

- Addressing medications that affect urate balance:
  - Thiazide (eg, hydrochlorothiazide) and loop (eg, furosemide) diuretics are independent risk factors for hyperuricemia, incident gout, and gout flares while potassium-sparing diuretics (eg , spironolactone) are not
  - Beta blockers have been reported to increase serum urate and the risk of incident gout
  - CCBs and losartan (not other ARBs or ACEIs) have been found to decrease both urate levels and incident gout risk
  - Aspirin in higher doses (above 3 g/day) can decrease serum urate, whereas low to moderate doses (up to 3 g/day) can increase serum urate and the risk of flare for patient with gout.

- Urate-lowering therapy if indicated:
  - Two flares or more annually is often describes as an indication for urate-lowering treatment
  - Clinical or radiographic signs of severe gout, including structural joint damage (eg, gouty bone erosion), polyarticular disease, and tophaceous deposits in soft tissues or subchondral bone.
- High risk of severe gout:
  - High baseline serum urate levels
  - Early onset of symptoms
  - Genetically determined disease
  - Intolerance of medications used to manage acute gout
  - Ultrasound evidence of monosodium urate (MSU) deposits or inflamation

On follow-up:

- Symptoms resolved and did not recur
- No side effect was seen

Prevention

1. ***Primordial prevention (prevent the emergence of risk factors before they occur)***
    a) Promote healthy lifestyle from an early age:
        i. Balanced diet low in purines
        ii. Regular physical activity
        iii. Healthy weight maintenance
        iv. Avoid excessive alcohol and sugary drinks
    b) Public health policies targeting obesity, hypertension, and metabolic syndrome
2. ***Primary prevention (prevent the onset of disease)***
    a) Identify and manage risk factors in at-risk individuals:
        i. Screen and treat hyperuricemia (if asymptomatic with high risk)
        ii. Advise on diet/ lifestyle changes
        iii. Educate on avoiding known triggers (eg, alcohol, red meat, sugary drinks)
        iv. Manage conditions like hypertension, diabetes, and renal disease

3. Secondary prevention (detect and treat disease early to prevent progression or recurrence)

a) Manage early gout:

i. Treat acute gout flares promptly (NSAIDs, colchicine, steroids)

ii. Start urate-lowering therapy (ULT) if indicated

iii. Educate on adherence to therapy and lifestyle modification

4. Tertiary prevention (reduce complications and improve quality of life in established disease)

a) Prevent joint destruction, chronic gouty arthritis, tophi:

i. Long term ULT (e.g., allopurinol, febuxostat)

ii. Monitor and adjust uric acid levels

iii. Manage joint damage, kidney function

iv. Physical therapy or surgical intervention if severe damage

5. Quaternary prevention (Prevent over medicalization and protect the patient from unnecessary or harmful interventions)

a) Avoid prescribing urate-lowering therapy during an acute flare(wait until it's resolved)

b) Prevent polypharmacy, especially in elderly patients with comorbidities.

c) Educate patients about realistic expectations of treatment

d) Avoid unnecessary imaging or lab tests unless indicated.

e) Focus on shared decision-making to avoid overtreatment and patient harm.

Source: UpToDate

Monoarthritis in adults: Etiology and evaluation

Gout: Clinical manifestations and diagnosis

Gout: Treatment of flares

Gout: Nonpharmacologic strategies for prevention and treatment

Gout: Pharmacologic urate-lowering therapy and treatment of tophi