

Gout

Update Pearls for Acute and Chronic Management

October 2009

Recent Guidelines:

- **Diagnosis** Guidelines 2006¹:
EULAR European League Against Rheumatism
<http://ard.bmj.com/cgi/reprint/65/10/1301>
- **Management** Guidelines 2006²:
EULAR
<http://ard.bmj.com/cgi/reprint/65/10/1312>
- **Management** Guidelines 2007³:
British Society for Rheumatology
<http://rheumatology.oxfordjournals.org/cgi/reprint/kem056av1>

Review Articles:

- Lancet 2009:
[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)60883-7/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60883-7/fulltext)⁴
- JAMA 2003: <http://jama.ama-assn.org/cgi/content/full/289/21/2857>⁵
- BMJ 2008:
<http://www.bmj.com/cgi/content/full/336/7639/329>⁶

Patient Resources:

- http://www.rheumatology.org/public/factsheets/diseases_and_conditions/gout.asp

Other Resources:

- <http://www.rheum.ca/en/>

Highlights: ★

- 1) Colchicine, NSAIDs or a corticosteroid may be considered for acute gout with choice depending on the patient.
- 2) Colchicine has traditionally been dosed very high causing significant GI side effects/toxicity; use BID (or TID) for acute attack. Alternately 1.2mg x1 followed by 0.6mg in ~ 1 hour may be used for initial therapy.
- 3) Why use indomethacin when you can use other NSAIDs such as naproxen or ibuprofen.
Indomethacin never shown to be better than any other NSAID.
- 4) Allopurinol dosing: Don't start, stop or change dose until an acute attack has resolved. Then *start low &/or go slow. Adjust for renal fx!*
- 5) A short course of corticosteroids can be useful in patients unsuitable for NSAIDs or colchicine.
- 6) Due to similar risk factors, consider assessing CV risk in gout patients.
- 7) Weight loss likely more beneficial than a low-purine diet.

RxFiles Related:

Gout Chart:
<http://www.rxfiles.ca/rxfiles/uploads/document/s/members/CHT-Gout.pdf>

NSAID Chart:
<http://www.rxfiles.ca/rxfiles/uploads/document/s/members/CHT-NSAID-Cox2.pdf>

References
available online at
www.RxFiles.ca

General Overview^{5,6,7,8,9,10,11,12,13}

- Gout is the most common form of inflammatory joint disease in men over the age of 40. Diagnosis is usually made on presentation of acute attack – i.e. “typical” attacks, or presence of tophi. (Definitive diagnosis requires the presence of uric acid crystals in the synovial fluid upon joint aspiration).
- Rule out: **arthritis** (septic, rheumatoid, osteo) & **pseudogout**

Which NSAID to use for gout?

- Many studies have shown that different NSAIDs provide similar benefits²; **any NSAID could be a reasonable choice** if no contraindications^{14,15,16,17,18}.
- Indomethacin commonly used historically, however other NSAIDs equally effective with less side effects.
Consider naproxen, ibuprofen or celecoxib. See chart.

When should you avoid NSAID use?

- **Contraindications (CI):**
 - Chronic kidney disease (CKD) Stage ≥IV: prostaglandins are required to maintain renal perfusion.^{19,20} Caution CrCl<40
 - Heart failure (HF): can cause exacerbations salt & H₂O retention
- **Precautions:**
 - those with a gastrointestinal (GI) history of ulcer or bleed; may consider use if also GI protection (e.g. PPI)
 - elderly & indomethacin: ↑ CNS risks e.g. headache, confusion
 - those at high cardiovascular (CV) risk

Systematic Reviews: CV Risk with NSAIDs

Observational studies²¹: (confounding)
Risk = naproxen < ibuprofen < indomethacin < diclofenac
RCTs²²: Risk = naproxen < ibuprofen < diclofenac ≈ Coxibs

- **Drug interactions (DIs):** NSAIDs have **MANY DIs**.
 - E.g. Lithium disrupt serum levels, ACEIs/ARBs ↑K₊, warfarin increased bleeding risk, ASA & ibuprofen displacement of ASA

What dose for colchicine in acute gout?

- Colchicine has traditionally been dosed high, leading to almost routine gastrointestinal (GI) disturbances²³
- 1 RCT investigated this traditional dosing: (N=43) in 1987 compared placebo vs colchicine 1mg po stat, followed by 0.5mg po q2h until attack stopped or they felt too ill to continue colchicine.²⁴ (Max 8tabs/day; 12 tabs/attack)
 - NNT to reduce clinical symptoms: pain, tenderness, redness, swelling = 2; NNT to reduce pain = 3
 - NNH to cause diarrhea/vomiting = 1
- Uncontrolled reports show that **colchicine 0.6mg BID-TID (or less)** is effective while reducing GI side effects²
- **FDA** recently updated dosing of colchicine in gout:
 - ⇒ **1.2 mg** (2 tablets) at the first sign of the flare followed by **0.6 mg** (1 tablet) one hour later. Max recommended dose for gout flares is 1.8 mg over a 1 hour period.
- Patients with **reduced renal function**³⁵ may tolerate colchicine as long as well hydrated (0.6mg BID-TID x2d, daily x7d then discontinue or ↓ to every other day). {Avoid if possible if on dialysis. Avoid if history of solid organ transplant.}

Allopurinol, etc. for Prophylaxis?

- Allopurinol can be used in both over-producers & under-excreters. Using allopurinol to maintain a serum uric acid (SUA) level of 274-393µmol/L has shown a 30% risk reduction in recurrent gout attacks²⁵
- It should not be **started, stopped or changed** in an acute attack as this can destabilize uric acid crystals.
- Consider if **≥3 attacks/year**, or ↑ risk (e.g. chemotherapy, ↑SUA levels, advanced disease)
- Doses should be individualized and titrated (range: 50mg every other day to ≤800mg daily)
 - **CKD:** as a **rule of thumb** if CrCl <50ml/min, start at 50mg, with 50mg ↑'s (MAX 300mg/d). {More complicated dosing regimens also available (see CPS)}.
 - **Elderly:** consider every other day initial dosing²⁶; Risks vs benefit becomes less clear as age increases.
- **Prophylaxis with colchicine or an NSAID** (for ~ 3-6+ months) is recommended when initiating allopurinol.
- Significant side effects include **hypersensitivity** and **Stevens Johnson syndrome**. (Also rash, diarrhea.)

What is the role of steroids in gout?

- **Short-term** corticosteroids may be an option for acute attacks when unable to use NSAIDs or colchicine²⁷ {e.g. Depot-Medrol 40-80mg x1 IM, prednisone 25-50mg PO x 3-5 days or intra-articular (IA) injection x1.}
- Short courses (≤ 2 wks) do not require tapering.²⁸
- A review of 3 trials (N=74) comparing corticosteroids to NSAIDs showed that corticosteroids to be equally effective, with fewer side effects if used short-term²⁹
If frequent or prolonged use, side effects can be minimized with local injections. Uncontrolled trial using triamcinolone intra-articularly (IA) showed pain relief within 48hrs in all 19 patients.³⁰ [A technique review]

Miscellaneous

- **1600kcal/day** diet for 16 weeks ↓ SUA by 100µmol/L³¹
- **ASA:** Low-dose (<2g/day) more greatly associated with gout attacks; >2g ASA is uricosuric; In 2° prevention, the CV benefits of low-dose ASA likely outweigh the risks of precipitating a gout attack.

Extras

- **Losartan & fenofibrate** have some uricosuric effects^{32,33}
- **Febuxostat (Uloric®):** used in Europe & recently FDA approved; a xanthine oxidase-inhibitor not chemically related to allopurinol; may be equivalent to allopurinol in preventing attacks (may be superior in decreasing uric acid levels); may be safer option in renal dysfunction; more study needed
- **Uricase** – a biotechnology drug still in testing stages; enzyme not produced by humans which helps to break down uric acid
- **Oxyipurinol**, a metabolite of allopurinol is currently in clinical trials; theoretically less side effects
- **Rilonacept (Arcalyst®)** a potential competitor for colchicine
- **Warm off the press!** Vitamin C shown to be independently associated with lower risk of gout: Published in Mar 9, 2009 edition of Archives of Internal Medicine³⁴. A 20 year observational study showed that vitamin C intake reduced risk of gout in men who took >250mg/day. The benefits were seen with ingestion of 500mg/day, furthermore, even greater reductions in risk were observed if 1000 or 1500mg/day. But caution: low urinary pH may increase kidney stone formation.

Case: Acute attack

A 46yo male presents to you, his family physician, having had excruciating pain in his big toe last night. This is the 3rd occurrence in the last 3 months. Advil has worked the last 2 times to get rid of it, but the initial pain is so bad that it keeps him up all night. His dad, who had the same problems, suggested he cut down on the amount of beer he drinks, but he doesn't think that's working and he wants something that'll be effective! You've known this patient for many years, he is obese and has slightly elevated LDL. On the bright side, the smoking cessation plan you created together was successful and he has been smoke-free for 2 years. Upon further examination of his toe you find it is warm, swollen, and he is very guarded.

Would you prescribe anything? If so, what?

Is this patient a candidate for preventative therapy? If so, which agent would you choose?

How would you initiate? What would you monitor?

How would your approach change if patient had a history of a solid organ transplant, heart failure and GI bleeds?

What if the patient were 75 years old with decreased renal function but otherwise healthy?

CI=contraindication CKD=chronic kidney disease CNS=central nervous system CV=cardiovascular d=day DI=drug interaction IA=intra-articular IM=intramuscular NNH/NNT=number needed to harm/treat PPI=proton pump inhibitor

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References – RxFiles Newsletter : Gout (2009)

{See also RxFiles Drug Comparison Charts: Gout: <http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Gout.pdf>; NSAIDs: <http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-NSAID-Cox2.pdf>}

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Gout: Overview of Causes, Risk Factors & Incidence²

- **Uric acid crystals** may deposit in joints, nephrons & tissues (needle like, negative birefringent³. {↑serum uric acid (SUA) may contribute (>405µmol/L: theoretical saturation concentration)})
- **Pathophysiology:** ↑SUA: from ↓uric acid excretion^{85%} or ↑purine breakdown; most commonly secondary^{70%} to drugs (chemox, diuretics, ASA) disease (malignancies, renal dysfx, psoriasis), & dietary causes (beer, fish, red meat).
- **Risk factors:** ♂, CKD, HTN, obesity; also hyperglycemia, hyperlipidemia {Gout should prompt search for conditions associated with CV risk!}^{4,5,6}
- **Precipitating factors:** trauma, surgery, alcohol, starvation, ↑ purine foods & certain medications^{see Drug Induced}.
- **Incidence:** <1%; mostly elderly, ♂ & postmenopausal ♀^{7,8}. Prevalence: ≤7% in ♂ >65; ≤3% in ♀ >85³.

What are the stages and diagnostic criteria for gout?³

- 1) **Asymptomatic hyperuricemia:** ♂: >360-420µmol/L; ♀: >357µmol/L? Estrogen effect
 - <25% go on to develop acute gout⁹. ↑ if SUA ≥500 µmol/L, >600µmol/L incidence ~6%¹⁰.
 - **Usually does not require drug treatment!**^{9,10,25,30}
- 2) **Acute gouty arthritis:** quick onset 6-12hrs, **intense pain**, redness, heat & swelling, usually of one joint 90% of 1st attacks (commonly the big toe “podagra” 50%, ankle/foot, knee, finger, but also the olecranon, helix of the ear, &/or nephrons – uric acid tends to crystallize in the cooler parts of the body), pain peaks at 8-12hrs; often skin desquamation over affected joint. (May self-resolve in 3-14d^{9,10}). SUA ↑ or normal!⁷ **Elderly:** less pain; ↑ polyarticular, fever & delirium.
- 3) **Intercritical gout:** disease may progress despite symptom free period(s). {symptom free periods may decrease over time; initially may be years symptom free¹⁰}.¹⁰
- 4) **Chronic tophaceous gout:** tophi^{progression to}; bony erosions^{deformations}; nephropathy^{stones}.

What is the concern of diuretics with gout?

- Loop (eg. furosemide) & thiazide diuretics ↓excretion & ↑concentration of uric acid.
- Hydrochlorothiazide induced gout: ~1%¹¹; risk ↑ when dose ≥25mg/d¹²
- Low dose thiazide (eg. HCT12.5mg) often tolerated in patients with gout hx

What non-pharmacological therapies are recommended?

- **Acute attack:** rest, elevate limb, ice¹³, avoid contact
- **Maintenance:** useful & may ↓ the need for preventative medications
- **Diet:** compliance with low purine diets is poor¹⁴, **recommend** one less portion of meat or fish each day; drink wine instead of beer; drink a glass of **skimmed** milk each day.¹⁵ Low fat dairy & whole grains associated with ↓ gout
- **Low calorie diet more beneficial/acceptable than low purine diet!**
- Avoid liver, kidney, shellfish, sugary drinks¹⁶ & yeast extracts.
- **Lifestyle: Weight loss!!!** Smoking cessation! ↓ alcohol binging (especially beer!) ⇒ drink 2L water/day (unless CI’d), mild-moderate intensity exercise.

Are there any special treatment considerations?

- Lifelong treatment may be required; however re-assess need for treatment if attack free for many years; SUA levels may be useful¹⁷.
- **Renal dysfx & very elderly:** adjust dose for allopurinol & colchicine; consider using colchicine or corticosteroids¹⁸ as alternatives to NSAIDs.
- With NSAIDs, GI prophylaxis should be considered if history of PUD/GI bleed or ↑GI risk^{ase-70} {PPI omeprazole 20mg daily \$46 or misoprostol 200mcg tid-qid \$38-49}.
- Review CV risk due to association of gout with CVD; CV protection with ASA 81mg po daily if 2° prevention; benefit supersedes the ↑risk of gout attacks.

What are the primary drug treatment options for gout?

- **Acute attack:** Rapid treatment initiation is key: <24-48hr. {Agent choice dependent on patient (severity, CI, DI, hx, SE, etc.) [e.g. consider HF, renal fx, GI ulcer hx, diabetes, transplant hx, previous tx, age, DIs]}
 - **Colchicine** (eg. 0.6mg BID x1-3 days, then daily); stop after ≥1-2wks {FDA July/09: 1.2mg po immediately, then 0.6mg once in 1hr}
 - **NSAIDs** - High doses to achieve pain relief until 48hrs after symptom resolution (or ~3 days); then stop or taper over 1-2 weeks
 - **Corticosteroid** IM (methylprednisolone, PO prednisone (or Intra-Articular Betaject, Aristopan)^{18,19,20} {May add acetaminophen to corticosteroid if NSAIDs & colchicine CI’d²¹}}
 - **NOTE:** Do not start, stop or adjust allopurinol during an acute attack!
- **Maintenance/Prophylaxis²²:**
 - **1st attack:** lifestyle changes & remove drug causes if possible
 - **Treat if:** 1) recurrent attacks (≥3/yr); 2) ↑SUA levels >800µmol/L;
 - 3) pt undergoing chemotherapy; or 4) advanced disease
 - **1st Line: allopurinol²³** (Start low, go slow, & prophylax as below!)
 - **Wait 1-2wks after inflammation settles before initiating allopurinol** (fluctuating SUA levels prolongs attacks, may destabilize crystals)
 - **Prophylax with colchicine** (low dose or an NSAID^{not ASA}²⁴ while titrating allopurinol (usually ~ 3 – 6+ months¹⁷) unless CI’d
 - **Target SUA levels:** <300 to 360µmol/L^{1,7,17} Lifelong treatment.
 - **2nd Line: colchicine** (low dose ≤ 0.6mg daily); may not prevent complications {Alternative: probenecid may rarely be an option, but pts require good renal function}

Table 1: Overview of Drugs Commonly Used in the Management of Gout

Generic/TRADE (Strength & forms) g=generic	Class / Pregnancy category ²⁵	Side effects / CI: Contraindications	√ = therapeutic use / Comments / Drug Interactions DI/ Monitor M	Dosing: (for acute tx with NSAID & colchicine, Initial x 1-3 days then ⇒ Follow-up x1-2+ wks)	S/ 30d
Naproxen NAPROSYN, g ^{ALEVE} 125,250,375,500,750mg SR tab 500mg supp, 25ml/ml suso.	NSAIDS (non-ASA) -↓pain & inflammation	Common: N/V (Indomethacin: GI upset, headache, ↑SE especially CNS, & in elderly) CI: ↓ Renal (stage ≥IV CKD), GI ulcer, HF, transplant	√ Gout – for acute attack or when initiating allopurinol GI prophylaxis (if indicated) with a PPI or misoprostol ¹⁷ DI: Li ⁺ ; ACEI/ARBs (minor DI, except ↑K ⁺ if on NSAID, spironolactone & ACEI or ARB) M: follow-up 4-6wks after acute attack to assess need of further tx; if at renal risk Na+ @ 24hr, SCr @ 72hr {Can use in CKD stage 1-2 & dialysis; avoid in stage 3 if CrCl ≤40ml/min & CKD stage 4.}	500-750mg x1; 500mg BID; ⇒ 375-500mg BID Max ≤ 1500mg/d x1day/short term. ⇒ Usual Max 1000mg/d 600-800mg po TID; ⇒ 400-600mg TID Max 2400-3200mg	16-20 18-13
Ibuprofen (MOTRIN, ADVL, g) 300,600mg tab, 200x, 400ml) ^{OTC}	For more info on NSAIDs, Acet, & Coxibs, see RxFiles PAIN charts at www.rxfiles.ca	Common: CVD, HF; (Avoid Indocid ≥65yrs) Precautions: CVD, HF; (Avoid Indocid ≥65yrs) CI: Acute: High doses for 1st 24-72hrs of attack. Then stop, or use lowest effective dose over 1-2wks.		25-50mg po TID; ⇒ 25mg BID-TID Max 200mg/d (Historically used by other NSAIDs now preferred.)	14-17
Indomethacin INDOCID, g 25,50mg cap; 50,100mg supp	COX-2 specific inhibitor -↓ pain & inflammation	Common: GI (maybe less than some other NSAIDs) CI: CVD, Renal dysfx Precautions: GI ulcer	√ Gout – acute attack or when initiating allopurinol DI: Lithium, ACEI/ARBs M: follow-up 4-6weeks after acute attack to assess need of further tx	200mg po daily; ⇒ 100-200mg daily Max 400mg/d	54
Celecoxib CELEBREX 100,200mg cap	Analgesic/ -↓ pain (minimally effective)	Common: rash Serious: hepatotoxicity Precautions: Liver dysfx &/or alcoholism	√ Mild gout associated pain &/or in combination with corticosteroids. DI: Warfarin (if ↑ dose acetaminophen M: Liver function tests if long term & ↑EtOH intake)	650-1000mg po q6h (prn; adjunct to CS) Max 4000mg/d	15-25
Acetaminophen TYLENOL, g 325,500,650mg tab ^{OTC*}	Anti-gout: ↓ pain, inflammation: ↓s urate crystal deposition by: (Leukocyte motility, phagocytosis, etc.) Famillal Mediterranean Fever ^{1,2,24mg/d}	Common: NVD 80% @ high dose: 4-25% @ low dose ⇒ *dose/stop; rash. Serious: neutropenia, myopathy, rhabdomyolysis, liver. Precautions: CVD; ↓ renal fx ↓ dose CI: blood dyscrasias, solid organ transplant; dialysis if possible.	√ Gout – acute attack or if initiating allopurinol ²⁴ ; {SE with high doses however limiting to ≤3 tabs on 1st day then 1-2 tabs/day will ↓↓↓ diarrhea/GI side effects!!!} DI: cyclosporine ↑ myopathy, P-gp & 3A4 inhibitors: clarithromycin, erythromycin, ketoconazole, verapamil M: CBC neutropenia, Creatine Kinase (rhabdomyolysis: may ↑ with statin/fibrate & renal fx q6mon)	Initial: 0.6mg po BID - TID x 1-3 days ⇒ then daily x 7-10+ days. 0.6mg OD or BID for ~ 3- 6+ months if starting allopurinol {if ↓renal fx, ↓dose to every other day if prolonged tx ^{10+ days} }	12-16 16-25
Colchicine COLCHICINE-ODAN, g 0.6, 1.5 mg tab [ColcrysUSA] IV Colchicine not recommended →toxicity ¹⁰	Corticosteroids/ -↓ inflammatory response	Common: injection site reactions Serious: edema/HF; others rare in short term Precautions: systemic & viral infections, immunosuppression (Glucocorticoid: Prednisone 5mg = Methylprednisolone 4mg)	Useful if CI/SE's to NSAIDs & colchicine (eg. for renal, transplant, warfarin patients, etc) √ IM or IA inj x1: monoarticular attack √ IM or oral: polyarticular attack DI: aprepitant ↑CS levels, vaccines DI: rare with intra-articular minimal systemic absorption M: osteoporosis risk if prolonged / frequent use; diabetes: ?? ↑BG testing (IA: suggest minimum 3 months between treatments)	IM: Methylprednisolone: 40-80mg IM x1 {Pending age / degree of inflam IA: Small joints Phalanges; IA: Large joints Methylpred 4-10mg IA; 80mg Methylpred 20-80mg IA; 200mg Triamcin 2.5-5mg IA; 10mg Triamcin 5-15mg IA; 40mg Betameth 0.5-1ml IA; 1ml Betameth 0.5-1ml IA; 2ml	5-9/vial 5/1ml vial 5/1ml vial
Methylprednisolone DEPO-MEDROL, g 20x, 40,80mg vial	Hydrocortisone	Common: insomnia, ↑BP, ↑BG, GI upset, mood ↓ Serious: most rare in short term; edema/HF	{Betamethasone [sodium phosphate & acetate] BETAJECT 3mg/1ml vial @ IM, IA \$8 / vial ; {Fast acting Long acting} Betamethasone 0.5-1mg/1ml vial @ IM, IA \$8 / vial ; {Triamcinolone hexacetone ARISTOSPAN 20mg/1ml vial @ IM, IA \$14/vial}	25-50mg po daily x 3-5 days & stop ²⁰ ; no taper! {if catch early eg. 1st sign, 10mg x1-2 may be adequate}	15
Triamcinolone KENALOG 10 & 40, g 10mg/ml 5ml, 40mg/ml 1ml, 40mg/ml 5x5ml vial	SOLU-CORTEF 100,200mg vial				
Prednisone WINPRED, g 1,5,50mg tab (Prednisolone 1mg/ml susp)	Methylprednisolone MEDROL 4, 16 mg tab				
URICOSURICS (rarely used!): Probenecid BENERYL, g 500mg tab; 1g BID ³⁴ (0.5-2g/d); SE: rash, GI upset; CI: nephrolithiasis Hx; renal: ineffective if CrCl<50ml/min; Must drink 2L H ₂ O/d DI:azathioprine. (Also Sulfinpyrazone ANTURAN g, 200mg tab; 100-200mg BID ^{37,72} ; no longer used.)					
Allopurinol ZYLOPRIM, g 100, 200, 300 mg tab	Xanthine oxidase (Xanthase) inhibitor/ -↓uric acid production -↓BP in young hypertensive pts -Adjunctive to K ⁺ citrate for uric acid stones	Common: rash, diarrhea Serious: Allopurinol Hypersensitivity Syndrome <1% (20-30% mortality) ↑risk if ↓ renal fx (eg. ACEI, NSAID), elderly, diuretic use); start low! Stevens-Johnson syndrome ²⁶ CI: Acute gout attack Precautions: renal ↓ dose or liver dysfx	√ Maintenance; adjust dose for SUA, renal fx, tolerability & response DI: rash when combined with ampicillin incidence 20% or amoxicillin; antacids; ↑ toxicity of 6-MP, azathioprine & cyclophosphamide ⁷ ; warfarin ^{INR} M: SUA & renal fx q3mon 1st year then q6mon ¹⁰ (See CPS for dosing info in ↓renal fx) Note: Allopurinol desensitization ²⁷ possible (susp ↑s from ≤50ug to 100mg over ≥28day).	Start at 100mg; ↑100mg q2-4wks ↑ risk of rash, etc. Usual dose: 300mg daily, preferably after food Usual range: 100-800mg (divide doses ≥300mg to ↓GI SE) If GFR<50ml/min, start 50mg/day; ↑ 50mg increments. MAX 300mg/d	15 10-26

• = dose for renal dysfunction S=scored tab X=Non-formulary Sask ⊖=Exception Drug Status Salk ⊗=not covered by NIHB ⊕=covered by NIHB ⊕=NIHB EDS BG=blood glucose BP=blood pressure CS=corticosteroids CI=contraindication CKD=chronic kidney disease CVD=cerebral vascular disease DI=drug interaction dx=diagnosis fx=function GI=stomach HF=heart failure HR=heart rate HTN=hypertension hx=history IA=intra-articular Li=lithium M=monitor MI=myocardial infarction n/v=nausea/vomiting OTC=over the counter pt=patient SE=side effect SUA=serum uric acid sx=symptoms tx=treatment wt=weight

Other Meds for Tx: Oxypurinol²⁸ oral allopurinol metabolite: in clinical trial; losartan & fenofibrate²⁹: modest uricosuric effect (potential losartan use if gout + hypertension); Opioids possible adjunct^{anesthetic}; ACTH¹⁰; Febuxostat^{31,32,33,34}: xanthine oxidase antagonist like allopurinol but unique structure, T.L.F.T. in UK/ USA 40-80mg po od, not CND.

Pegloticase: urate oxidase Phase III: given IV q2-4weeks; Benzbromarone³ urate excretion: orally special access Canada 35,36,37, & Ketorolac IA inj; Rasburicase IV in USA for tumor lysis syndrome in cancer pts. **HERBAL:** no documented efficacy; ?caffeine, devil's claw & garlic have been used. Anecdotal support: berry juice/ berries.

Rule out Pseudogout (calcium pyrophosphate crystals in synovial fluid, commonly the knee), "Appears like OA, but in all the wrong places" possibly treat with colchicine 0.6mg/d or CS; **Septic arthritis** aspirate the joint, WBC, temperature & vitals, do gram stain & culture; & **Rheumatoid arthritis.**

Drug induced: acetazolamide, ASA low dose, chemo, cyclosporine, diuretic, ethambutol, lead, levodopa, niacin, tacrolimus, teriparatide **Food induced:** purine rich eg. red meat, fish, beer, spirits **Diagnosis:** Diagnostic certainty → analyze synovial fluid for uric acid crystal or id'ing a tophus containing uric acid crystal under polarized light microscopy. May see "mouse bite" erosions. **Optional 24hr urine collection:** to see if ↓excretor or ↑producer^{3,10} but does not alter tx; (if uric acid excretion ≥1g with reg. diet → over-producer, if CL uric acid <6ml/min → under-excretor) since allopurinol effective for both^{1,5} **58**

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