

# Gout

## Update Pearls for Acute and Chronic Management

### October 2009

#### Recent Guidelines:

- **Diagnosis** Guidelines 2006<sup>1</sup>:  
EULAR European League Against Rheumatism  
<http://ard.bmj.com/cgi/reprint/65/10/1301>
- **Management** Guidelines 2006<sup>2</sup>:  
EULAR  
<http://ard.bmj.com/cgi/reprint/65/10/1312>
- **Management** Guidelines 2007<sup>3</sup>:  
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)<sup>4</sup>
- **JAMA** 2003:  
<http://jama.ama-assn.org/cgi/content/full/289/21/2857><sup>5</sup>
- **BMJ** 2006:  
<http://www.bmj.com/cgi/content/full/336/7639/326><sup>6</sup>

#### Patient Resources:

- [http://www.rheumatology.org/public/factsheets/diseases\\_and\\_conditions/gout.asp](http://www.rheumatology.org/public/factsheets/diseases_and_conditions/gout.asp)

#### Other Resources:

- <http://www.rheum.ca/en/>
- [Gout Risk Calculator](#)

#### 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](http://www.RxFiles.ca)

#### General Overview<sup>5,6,7,8,9,10,11,12,13</sup>

- 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 benefits<sup>2</sup>; **any NSAID could be a reasonable choice** if no contraindications<sup>14,15,16,17,18</sup>.
- 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.<sup>19,20</sup> 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 studies<sup>21</sup>: (confounding)  
Risk = naproxen < ibuprofen < indomethacin < diclofenac  
RCTs<sup>22</sup>: Risk = naproxen < ibuprofen < diclofenac ≈ Coxibs

- **Drug interactions (DIs):** NSAIDs have **MANY DIs**.
  - E.g. Lithium disrupt serum levels, ACEIs/ARBs ↑K<sub>+</sub>, 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) disturbances<sup>23</sup>
- 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.<sup>24</sup> (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 effects<sup>2</sup>
- **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**<sup>35</sup> 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 attacks<sup>25</sup>
- 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 dosing<sup>26</sup>; 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 colchicine<sup>27</sup> {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.<sup>28</sup>
- 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-term<sup>29</sup>  
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.<sup>30</sup> [A technique review]

#### Miscellaneous

- **1600kcal/day** diet for 16 weeks ↓ SUA by 100µmol/L<sup>31</sup>
- **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<sup>32,33</sup>
- **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
- **Oxyprurinol**, 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 Medicine<sup>34</sup>. 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 3<sup>rd</sup> 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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{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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