

# 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/abstract/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** 2008:  
<http://www.bmj.com/cgi/content/full/336/7639/326><sup>6</sup>

#### Patient Resources:

- [http://www.rheumatology.org/publicfactsheets/diseases\\_and\\_conditions/gout.asp](http://www.rheumatology.org/publicfactsheets/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/documents/members/CHT-Gout.pdf>

**NSAID Chart:**  
<http://www.rxfiles.ca/rxfiles/uploads/documents/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**.<sup>See chart.</sup>

#### 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> Cautious CrCl<40
  - Heart failure (HF): can cause exacerbations salt & H<sub>2</sub>O 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<sup>e.g. headache, confusion</sup>
  - 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>s</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 100umol/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

**Acknowledgements:** We would like to thank those who contributed to the development, review and training days for this newsletter & chart topic. Dr. W. Olszynski (Rheumatology, Saskatoon). Dr. J. Kappel (Nephrology, SHR, Dr. T. Laubscher (Family Medicine, U of S, Saskatoon), Dr. A. Milne (Rheumatology, Regina), Dr. B. Nair (Rheumatology, Saskatoon), D Lamb (SHR-Pharmacy) & the RxFiles Advisory Committee. Prepared by Zack Dumont BSP, Loren Regier BSP BA, Brent Jensen BSP

**DISCLAIMER:** The content of this newsletter represents the research, experience and opinions of the authors and not those of the Board or Administration of Saskatoon Health Region (SHR). Neither the authors nor any other party who has been involved in the preparation or publication of this work warrants or represents that the information contained herein is accurate or complete, and they are not responsible for any errors or omissions or for the result obtained from the use of such information. Any use of the newsletter will imply acknowledgment of this disclaimer and release any responsibility of SHR, its employees, servants or agents. Readers are encouraged to confirm the information contained herein with other sources. Additional information and references online at [www.RxFiles.ca](http://www.RxFiles.ca)

Copyright 2009 – RxFiles, Saskatoon Health Region (SHR) [www.RxFiles.ca](http://www.RxFiles.ca)

## 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>}

- Zhang W, Doherty M, Bardin T, et al. EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the EULAR Standing Committee for International.
- Zhang W, Doherty M, Bardin T, et al. EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International.
- Jordan KM, Cameron JS, Snaith M, et al; British Society for Rheumatology and British Health Professionals in Rheumatology Standards Guideline for the Management of Gout. Rheumatology (Oxford). 2007 Aug;46(8):1372-4. Epub 2007 May 23.
- Pascal Richette, Thomas Bardin, Gout, The Lancet, In Press, Corrected Proof, Available online 17 August 2009, ISSN 0140-6736, DOI: 10.1016/S0140-6736(09)60883-7. (<http://www.sciencedirect.com/science/article/B6T1B-4X1CBNX-1/2/7350566a4f9de1ea767dcdab1b35ad1>)
- Rott KT, Agudelo CA. Gout. JAMA. 2003;289:2857-2860.
- Fox R. Management of recurrent gout. BMJ 2008;336:329, doi: 10.1136/bmj.39273.712674.94.
- Choi HK, Mount DB, Reginato AM; American College of Physicians; American Physiological Society. Pathogenesis of gout. Ann Intern Med. 2005 Oct 4;143(7):499-516.
- Teng GG, Nair R, Saag KG. Pathophysiology, Clinical Presentation and Treatment of Gout. Drugs 2006; 66(12):1547-63.
- EGgebeen AT. Gout: an update. Am Fam Physician. 2007 Sep 15;76(6):801-8. Review. Summary for patients in: Am Fam Physician. 2007 Sep 15;76(6):811-2.
- Canadian Rheumatology Association Handbook "Gout".
- Underwood M. Diagnosis and management of Gout. Clinical Review. BMJ. 2006 June 5;332:1315-9.
- Willacy H; Gout; Clinical Knowledge Summary, 5 Jan 2008
- Sutaria S, Katbamna R, Underwood M. Effectiveness of interventions for the treatment of acute and prevention of recurrent gout—a systematic review. Rheumatology (Oxford). 2006 Nov;45(11):1422-31.
- Altman RD, Honig S, Levin JM, Lightfoot RW. Ketoprofen versus indomethacin in patients with acute gouty arthritis: a multicenter, double blind comparative study. J Rheumatol. 1988 Sep;15(9):1422-6.
- Cheng TT, Lai HM, et al. A single-blind, randomized, controlled trial to assess the efficacy and tolerability of rofecoxib, diclofenac sodium, and meloxicam in patients with acute gouty arthritis. Clin Ther. 2004 Mar;26(3):399-406.
- Rubin BR, Burton R, et al.. Efficacy and safety profile of treatment with etoricoxib 120 mg once daily compared with indomethacin 50 mg three times daily in acute gout: a randomized controlled trial. Arthritis Rheum. 2004 Feb;50(2):598-606.
- Willburger RE, Mysler E, Derbot J, et al. Lumiracoxib 400 mg once daily is comparable to indomethacin 50 mg three times daily for the treatment of acute flares of gout. Rheumatology (Oxford). 2007 Jul;46(7):1126-32. Epub 2007 May 3.
- Shrestha M, Morgan DL, Moreden JM, et al. Randomized double-blind comparison of the analgesic efficacy of intramuscular ketorolac and oral indomethacin in the treatment of acute gouty arthritis. Ann Emerg Med. 1995 Dec;26(6):682-6.
- Gooch K, Culleton BF, Manns BJ, Zhang J, Alfonso H, Tonelli M, Frank C, Klarenbach S, Hemmelgarn BR. NSAID use and progression of chronic kidney disease. Am J Med. 2007 Mar;120(3):280.e1-7.
- Gaffo AL, Saag KG. Management of hyperuricemia and gout in CKD. Am J Kidney Dis. 2008 Nov;52(5):994-1009.
- McGettigan et al. Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective Inhibitors of Cyclooxygenase 2. JAMA 2006;296:1633-1644.
- Keamey et al. Do Selective cyclooxygenase-2 inhibitors and traditional NSAIDs increase risk of atherothrombosis. Meta-analysis of randomized trials. BMJ 2006;332:1302-1308.
- Schlesinger N, Schumacher R, Catton M, et al. Colchicine for Acute Gout. Cochrane Database of Systematic Reviews 2006, Issue 4.
- Ahern MJ, Reid C, Gordon TP, et al. Does Colchicine work? The results of the first controlled study in acute gout. Aust NZ J Med 1987;17:301-4.
- Yamanaka H, Togashi R, Hakoda M, et al. Optimal range of serum urate concentrations to minimize risk of gouty attacks during anti-hyperuricemic treatment. Adv Exp Med Biol 1998;431:13-18.
- Fam AG. Gout in the elderly. Clinical presentation and treatment. Drugs Aging 1998;13(3):229-243.
- Corticosteroids for the management of gout. Pharmacist's Letter/Prescriber's Letter 2008;24(9):240905.
- Boehringer S. Tapering After Short Courses of Corticosteroids: Is It Necessary? Detail-Document; Canadian Pharmacist's Letter 2003; 19(12):191210
- Janssens HJ, Lucassen PLBJ, Van de Laar DF et al. Systemic Corticosteroids for Acute Gout. Cochrane Database of Systematic Reviews 2008, Issue 2. Janssens HJ, Janssens M, van de Lisdonk EH, et al. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomised equivalence trial. Lancet. 2008 May 31;371(9627):1854-60
- Man CY, Cheung IT, Cameron PA, Rainer TH. Comparison of oral prednisolone/paracetamol and oral indomethacin/paracetamol combination therapy in the treatment of acute goutlike arthritis: a double-blind, randomized, controlled trial. Ann Emerg Med. 2007 May;49(5):670-7.
- Tallia AF, Cadone DA. Diagnostic and Therapeutic Injection of the Ankle and Foot. Am Fam Physician 2003 Oct. 68(7):1356-62.
- Desseinh PH, Shipton EA, Stanwix AE, et al. Beneficial effects of weight loss associated with moderate calorie/carbohydrate restriction, and increased proportional intake of protein and unsaturated fat on serum urate and lipoprotein levels in gout: a pilot study. Ann Rheu Dis 2000;59:539-43.
- Wortmann RL. Recent advances in the management of gout and hyper-uricemia. Curr Opin Rheumatol. 2005;17:319-324.
- Würzner G, Gerster JC, Chioloro A, Maillard M, et al. Comparative effects of losartan and irbesartan on serum uric acid in hypertensive patients with hyperuricaemia and gout. J Hypertens. 2001 Oct;19(10):1855-60.
- Choi HK, Gao X, Curhan G. Vitamin C Intake and the Risk of Gout in Men. Arch Intern Med. Vol 169(5) Mar 9, 2009; 502-7 19.Zhang W, Doherty M, Pascual E, Bardin T, et al.; EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the Standing Committee for International Clinical Studies Including Therapeutics (ESCSIT). Ann Rheum Dis. 2006 Oct;65(10):1301-11. Epub 2006 May 17.
- Gaffo AL, Saag KG. Management of hyperuricemia and gout in CKD. Am J Kidney Dis. 2008 Nov;52(5):994-1009.

## Other References :

- Choi HK, Atkinson K, Karlson EW, et al. Alcohol intake and risk of incident gout in men: a prospective study. Lancet. 2004 Apr 17;363(9417):1251-2.
- Schlesinger N, Baker DG, Beutler AM, et al. Local ice therapy during bouts of acute gouty arthritis. Journal of Rheumatology 2002;29(2):331-4.
- Gurwitz JH, Kalish SC, Bohn RL et al. Thiazide Diuretics and the Initiation of Anti-Gout Therapy. Journal of Clinical Epidemiology. 1997 Aug;50(8):953-9.
- e-CPS [database on the Internet]. Ottawa (ON): Canadian Pharmacists Association. c2008; cited 2009 Mar 9]. Available from: <https://www.e-therapeutics.ca/wps/portal/!ut/p/scr/Login>
- Clinical Studies Including Therapeutics (ESCSIT). Ann Rheum Dis. 2006 Oct;65(10):1312-24. Epub 2006 May 17.

