A Survey of Current Evaluation and Treatment of Gout

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ABSTRACT. Objective. To record diagnostic and treatment approaches to gouty arthritis among US rheumatologists. Methods. Questionnaires were faxed to 2500 US rheumatologists. Responses were received from 518 rheumatologists. Respondents reported performing crystal analysis 80% of the time for new suspected gout; 64% use combination therapy for acute gout; nonsteroidal antiinflammatory drugs alone are used in only 27%. Urate-lowering drugs (ULD) are given to most patients. ULD treatment is given occasionally to patients with asymptomatic hyperuricemia (4%) but most frequently to patients after 2 (59%) or 3 (34%) attacks. ULD are given with the aim of achieving a serum urate (SU) level of 6 mg/dl. Conclusion. Combination antiinflammatory agents are used frequently for acute gout despite absence of evidence in the literature to support this practice. There seems to be consensus regarding the necessity of lowering SU to < 6 mg/dl. Approaches vary widely, supporting the need for longterm prospective, placebo controlled studies to provide more evidence-based guidance. (J Rheumatol 2006;33:2050–2)

Ongoing reviews of the Cochrane collaboration show that there is still very little reliable information based on randomized controlled trials on which to base treatment and diagnostic decisions in gout. Despite centuries of study of gout and the availability of effective treatment for most patients, there are still questions about optimal approaches to the diagnosis and treatment of gout. We surveyed US rheumatologists to determine current stated practices.

MATERIALS AND METHODS
Survey and participants. Two-page questionnaires were faxed to a representative sample of 2500 US rheumatologists listed in the 2004-2005 American College of Rheumatology (ACR) directory. Our original intent was also to survey internists so the questionnaires were also sent to 2500 US internists listed in the CD-ROM of the American Board of Medical Specialties (ABMS). We selected the first 2500 American rheumatologists listed alphabetically in the 2004-2005 ACR directory with fax numbers. We also selected the first 2500 internists listed in the ABMS Directory of Board Certified Medical Specialists, 2004.

Survey questions inquired about frequency of crystal identification, the use of 24-hour urine uric acid (UA) measurements, as well as the treatment of acute and chronic gout.

Key Indexing Terms:
GOUT SURVEY TREATMENT

Statistical analysis. Descriptive statistics and subgroup analyses were used extensively to summarize survey responses. We used chi-square tests for independence to compare categorical variables between groups. We used the Wilcoxon rank-sum nonparametric test to compare reported percentages between 2 groups and the Kruskal-Wallis nonparametric test when there were more than 2 groups.

RESULTS
Five hundred eighteen (21%) rheumatologists surveyed and only 22 (0.9%) internists surveyed responded. Of the respondents, 65% were private practitioners, 26% academicians, and 9% were in a combined practice. The average length of practice was 20 years. The very limited number of responses by internists were not included in the results.

Respondents reported that they perform crystal analysis 80% of the time for new patients with suspected gout and order a 24-hour UA measurement 33% of the time. Those ordering 24-hour urine UA measurements more than 50% of the time tend to have graduated on or before 1980 (chi-square test of independence, p = 0.058).

Combination therapy for acute gout is often used (64% in an otherwise healthy patient and 59% in a patient with a creatinine level of 2.2 mg/dl). The most frequently used combinations of therapies for acute gout attack in an otherwise healthy patient include nonsteroidal antiinflammatory drugs (NSAID) with intraarticular corticosteroids (IAC, 43%); NSAID with oral corticosteroids (33%); and NSAID with oral colchicine (32%). For acute gout attack in an otherwise healthy patient NSAID alone are used in 27%. For those using only one drug, NSAID were the most frequently chosen. Drugs used by rheumatologists include nonselective NSAID (77%); IAC (47%); oral prednisone (42%); oral colchicine (37%); intramuscular (IM) triamcinolone (11%); and IM ACTH (5%). Intravenous (IV) colchicine was used by 4% of rheumatologists.

The most frequently reported combination therapies for
acute gout in a patient with a creatinine of 2.2 mg/dl are IAC and oral steroids (45%). Prednisone is the most commonly used drug in patients with renal failure (71%), followed by IAC (66%). NSAID are rarely used for these patients (non-selective NSAID: 1%, COX 2 selective: 1%). Surprisingly, colchicine is commonly used (oral: 17%; IV: 4%). Dose adjustment for renal impairment was not included in the questionnaire.

For chronic gout management, xanthine oxidase inhibitors are used in 78% of patients with normal renal function and in 86% of patients with renal failure. Rheumatologists initiate urate-lowering drugs (ULD) in patients with asymptomatic hyperuricemia (4%); after first gouty attack (10%); after 2 attacks (59%); and after 3 attacks (34%). ULD treatment is initiated a mean of 20 days (range: 8–43) after resolution of an acute attack. Prophylactic treatment is given 90% of the time (colchicine: 82%; NSAID: 35%) when initiating ULD. Acute attacks are estimated to occur in 15% of patients while receiving prophylaxis compared to 42% of patients not receiving prophylaxis. Prophylaxis is given for a mean of 18 weeks (range: 2–34). Chronic prophylaxis with colchicine or NSAID is often initiated after an acute gouty attack in patients not receiving allopurinol (46% of time).

Rheumatologists prescribe lifelong ULD (91%) or for a mean of 6 years (9%). A serum urate (SU) level of 6 mg/dl is considered by 84% of rheumatologists to be the target for treatment with ULD. Once achieved, SU levels are checked every 6–12 months (mean: 8).

**DISCUSSION**

This is the largest survey of rheumatologists evaluating the treatment of gout conducted in the US to date. Any survey of this type that probes opinions of respondents with respect to management practices assumes that responses mirror actual practice. The very poor response rate by internists suggests a low level of interest and raises questions of their knowledge in diagnosing and treating gout.

The need for crystal identification in patients with gout is commonly recommended but the extent of its use is not clear. Although intuitively, crystal diagnosis is ideal, no studies have compared cost and outcome of crystal-proven diagnosis versus clinical diagnosis in determining outcome of care.

There are 3 stages in the management of gout: (1) treating the acute attack; (2) lowering excess stores of urate; and (3) providing prophylaxis to prevent acute flares. Our survey addressed questions related to these 3 stages.

We found that 64% of rheumatologists use combination therapy to treat acute gout. The use of combination antiinflammatory drugs to treat acute gouty arthritis does not follow recommendations described in most textbooks and reviews; there is little or no evidence to support such a practice and this common practice thus merits further study and evaluation.

In a French study by Rozenberg, et al\(^\text{4}\), the most widely prescribed treatment for acute gouty attack was colchicine alone (63%). In our study, NSAID were the most commonly used monotherapy in an otherwise healthy patient versus oral corticosteroids in a patient with renal failure. NSAID were the most commonly used drugs in acute gout in other survey studies as well. Among Canadian doctors, only 11% of family physicians and 6% of rheumatologists would use colchicine in an acute situation\(^\text{5}\). A similar preference for NSAID has been noted in Australia\(^\text{6}\) and New Zealand\(^\text{7}\).

In our study, colchicine is reported to be commonly used in patients with renal failure (oral: 17%; IV: 4%). Our questionnaire did not provide an opportunity to address dose adjustment for renal failure, which may be important. Many clinicians have advocated restriction or outright ban of IV colchicine therapy\(^\text{8–10}\).

There is little evidence on when to start ULD in the course of gout. Some advocate that only patients with more than 4 episodes per year should be treated\(^\text{11}\); others state that ULD treatment is cost-effective even in patients with one recurrent gouty attack per year\(^\text{12}\). Our respondents initiate ULD in patients with asymptomatic hyperuricemia (4%), a practice that has no current support in the literature; after first gouty attack (10%); after 2 attacks (59%); and after 3 attacks (34%).

Optimal treatment of chronic gout requires longstanding reduction in SU levels. Xanthine oxidase inhibitors were preferred over uricosuric drugs as ULD. It is important to note that most patients with gout are urate underexcretors and many could be treated with uricosurics rather than allopurinol. Allopurinol is the drug of choice in tophaceous disease, when creatinine clearance is less than 50 ml/min and when there is a theoretical risk of kidney stones. Once-daily dosing of allopurinol versus twice-daily dosing of probenecid may also contribute to this preference. The use of allopurinol as the main ULD is consistent with findings from other survey studies.\(^\text{5–7}\)

In a survey of prescribing practices in Ontario, Canada, 99% of rheumatologists elected to start allopurinol as the ULD of choice\(^\text{3}\). In another study, 66% of rheumatologists prescribed allopurinol as their initial ULD\(^\text{13}\), while in yet another study, 30% of French rheumatologists never use uricosurics\(^\text{14}\). No studies have evaluated the implications of these differences in approach.

It is anticipated that for most patients, ULD therapy needs to be life-long. In our study, life-long ULD was prescribed by 91% of rheumatologists, although a minority (9%) prescribed a ULD for shorter periods (mean 6 years). The reasons for this were not pursued.

Maintaining SU levels at less than 6 mg/dl has been proposed to help resolution of tophi and eventual decrease and cessation of acute gouty attacks\(^\text{15,16}\). In addition, crystals are decreased in joints. In our study, 84% of rheumatologists stated that the goal of ULD therapy was achieving SU levels below 6 mg/dl. Once this level was achieved, SU levels are supposed to be checked every 6–12 months (mean: 8).

Treatment to lower SU levels can trigger gouty attacks,
presumably because of the mobilization of urate deposits in tissues. Expert opinion suggests that ULD treatment should not be initiated during an acute attack. Our respondents felt ULD should be started at a mean of 20 days after resolution of an acute attack.

Prophylaxis with colchicine or NSAID is usually recommended until the SU level has been normalized for 3–6 months. In our study, 90% of rheumatologists give prophylactic treatment when initiating a ULD. These results are similar to those described by Rozenberg, et al. Chronic prophylaxis with colchicine or NSAID after an acute gouty attack is initiated in patients not receiving allopurinol. It is not clear if this is to get colchicine prophylaxis established before ULD or to be used apparently without using ULD.

Our study confirms the variability of reported approaches to diagnosis and treatment of gouty arthritis. Randomized longterm prospective, placebo controlled trials are needed to evaluate the therapeutic role of colchicine, perhaps in several different regimens, versus NSAID in the treatment of acute gout; and corticosteroids and ACTH and their role in the treatment of acute gout. Randomized longterm prospective, placebo controlled trials could establish when to start ULD, what the SU target level should be, which ULD should be used, whether a waiting period is necessary between an acute attack and initiation of ULD, and how long this period should be. In the absence of such trials we will continue to depend to varying degrees on expert opinions.

REFERENCES