Glucosamine and chondroitin sulfate for the treatment of osteoarthritis: Comment on the article by Akama and Saito

To the Editor:

Drs. Akama and Saito mentioned our meta-analysis of chondroitin sulfate (CS) in the treatment of osteoarthritis in a recent issue of *Arthritis Care and Research* (1,2). Their positive criticism of our paper is very much appreciated.

They also, however, mentioned some skepticism concerning the efficacy of glucosamine and/or chondroitin sulfate treatment, which we were aware of when performing our meta-analysis. One of our major caveats with respect to the methodologic quality of the publications included in the meta-analysis was that none of the trials were analyzed on an intent-to-treat (ITT) basis. A recent publication by Mazieres and colleagues (3) showed a positive trend but no significant changes in Lequesne's algofunctional index and in pain at rest in patients with knee osteoarthritis treated with CS compared with placebo, when analyzed on an ITT basis. The completer analysis, however, revealed statistically significant superior efficacy of CS—results that are very similar to those reported in our paper.

With respect to the efficacy of glucosamine sulfate (GS), the most recent publication by Reginster and associates (4) has to be noticed: A significant decrease in joint space narrowing in patients treated with GS compared with placebo has been shown during a 3-year period, indicating a disease-modifying capacity of GS for the first time. Moreover, symptomatic efficacy was revealed using the WOMAC index as an outcome measure. All meta-analyses (2,5) as well as the controlled trials mentioned above prove the overall excellent tolerability of CS and GS, even when compared with treatment with nonsteroidal antiinflammatory drugs (2).

In contrast to the United States and apparently Japan, Austria (and most European countries) handles CS as a drug that is available only by prescription; it is currently not fully reimbursible by the insurance companies, however. With respect to the symptomatic efficacy, excellent tolerability, and the perspective of a disease-modifying capacity (especially for GS), which is indeed of increasing evidence in light of the Reginster trial (4) (trials investigating the same issue for CS are currently underway), one should keep this therapeutic option in mind when creating a therapeutic strategy for osteoarthritis patients. In the recently published European League Against Rheumatism recommendations for the treatment of knee osteoarthritis, the current position of GS, CS, and other slow-acting symptomatic drugs in osteoarthritis in the treatment concepts seems to be accurately defined (6).

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Reply

To the Editor:

As we mentioned previously (1), many Japanese orthopedists, rheumatologists, and physicians have been skeptical that glucosamine sulfate (GS) and/or chondroitin sulfate (CS) are truly effective in osteoarthritis (OA). However, we agree that the efficacy of GS and/or CS in knee OA cannot be denied. To our knowledge, there have been few studies by Japanese doctors actively investigating the usefulness of GS and CS in OA, and there are few reports on this subject in the Japanese literature. However, several orthopedists have recently been interested in the efficacy of glucosamine hydrochloride (although not GS exactly) and CS in knee OA (2). Moreover, they attempted to analyze a combination therapy of glucosamine hydrochloride and CS in knee OA patients (3). Although the efficacy of glucosamine hydrochloride and CS was uncertain in their study (2), they speculated that the proportion of glucosamine hydrochloride to CS might be important in the treatment of knee OA (3). The outcome of their further research is awaited with interest.

Currently in Japan, most of the CS used in the treatment of OA is purchased by the patient as a commercially available health food rather than as a "drug." It is of concern that apart from the as yet unproven clinical effectiveness, these health foods may contain impurities, and might cause serious adverse events.

In addition to symptomatic efficacy and excellent tolerability, GS and CS may possess structure modification properties, as Dr. Leeb notes. More studies using standardized methodology, such as an intention-to-treat analysis, are required to determine which patients with knee OA are suitable for treatment and also the pharmacoeconomic aspects of these "drugs." We should also consider whether

GS and CS might be useful in the treatment of patients with OA in hip, elbow, ankle, or finger joints.

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Rheumatoid arthritis: an ancient disease or a new one?

To the Editor:

My curiosity was aroused by the text accompanying the cover illustration of the June 2001 issue of *Arthritis Care & Research*. We are told that: "The study of Egyptian mummies has revealed a number of illness that would have occupied the ancient physicians including osteoarthritis, tuberculosis of the bones, gout, and **rheumatoid arthritis** . . ."

During the last decades it has regularly been debated whether rheumatoid arthritis is an ancient disease or a new one (1–5). The author of the cover text does not seem to be in doubt. I would very much appreciate learning the sources that support this statement.

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Editor's Reply

Dr. Leden's point is well taken. As he notes, recent studies suggest that what we call rheumatoid arthritis today may not have been seen in Europe in pre-Columbian days (1). Many recognize Landre-Beauvais' description in 1800 as the first clinical report on rheumatoid arthritis (2). Further investigations on this topic may provide a definite answer on this question and may also provide information about the possible causes of this devastating disease.

Gene G. Hunder, MD
Editor

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