Glucosamine and chondroitin dietary supplements have sufficiently positive outcomes in controlled clinical trials to warrant their use in osteoarthritis. With few adverse effects compared to the conventionally prescribed nonsteroidal anti-inflammatory drugs (NSAIDs), such as acetaminophen or ibuprofen - which can cause ulcers and other serious gastrointestinal disruptions, especially in the elderly - glucosamine and chondroitin are the only treatments that have been shown to retard progression of the disease, as opposed to merely alleviating its symptoms. This is the latest news according to the *Journal of the American Medical Association* (JAMA). And it is very good news, but it is not really new.

For those who haven't followed the growing body of scientific literature that supports the therapeutic use of nutrients, it may come as a surprise that research on glucosamine and chondroitin (G&C) has been compiling for more than 30 years. Positive results and unobjectionable side effects have been the rule with glucosamine. They are becoming the rule for chondroitin as well, although the results have shown wider fluctuations, because some forms of chondroitin work much better than others.

The result of all this G&C research has been the wide availability of nutrient forms of these compounds that possess anti-inflammatory, antiarthritic, analgesic, and anabolic (molecule production) behavior in chondrocytes (cartilage cells). The abundance, high quality, and low prices of these nutrients have encouraged individuals to experiment and assess their usefulness for themselves. Anecdotal data have been overwhelmingly favorable, and best-selling books about G&C have made knowledge of these supplements even more common. So the *JAMA* article is long overdue.

*The human knee (minus the kneecap), shown somewhat separated for clarity.*
THE SOURCE OF OSTEOARTHRITIS

At the ends of your bones, where they meet other bones at the joints, lies the extraordinary and valuable biomaterial called cartilage. This elastic tissue cushions your joints and, together with synovial fluid (found in the joint spaces), reduces and ideally minimizes the friction caused by the pivoting, rotating, and inevitable rubbing of your bones where they come together. Indeed, cartilage acts as a shock absorber that helps reduce the wear and tear that come with functional stress and aging.

When healthy cartilage serves its proper function, your joints work well. When it is unduly stressed by high levels of activity, however, or is diminished in quantity by age or physical condition, degradation may result, causing inflammation, pain, loss of movement, and loss of a key element of youthfulness. This may occur in any of your joints, but especially the hands, neck, feet, knees, elbows, and hips. The spine may also be affected. Conceivably, degradation could occur anywhere in the body where bones rub together - meaning any joint.

The condition described is the most common form of arthritis, osteoarthritis. As the name implies, osteoarthritis affects bones, or more specifically, the joints of bones. If not treated, it can eventually lead to joint deformities and severe loss of mobility. Although osteoarthritis (OA) is generally age-related and doesn't normally manifest itself until the 40s, undue stress or injury or a number of other conditions can bring it on much earlier: it can affect individuals as young as 25. No less than 21 million Americans are reported to suffer from OA, and their collective loss of freedom of movement, not to mention the associated pain and impaired quality of life, is enormous.

GLUCOSAMINE AND CHONDROITIN BUILD NEW CARTILAGE AND MORE

Glucosamine is a complex sugar that the body uses as a chemical building block in the biosynthesis of some of the important constituents of cartilage. Chondroitin is one of these constituents. In the manufacture of G&C supplements, both compounds are extracted from animal products. While the mechanisms of action of glucosamine and chondroitin in the treatment of osteoarthritis are not fully understood, both compounds demonstrate anti-inflammatory action and are thought to help build new cartilage as well as dismantle old cartilage. Osteoarthritis results from the progressive breakdown of cartilage owing to an imbalance between synthesis and degradation.

GLUCOSAMINE AND CHONDROITIN PREVENT PAIN AND LOSS OF JOINT FUNCTION

Europeans have been using G&C in various forms for osteoarthritis more avidly than Americans for the last decade, and press coverage of their benefits has increased their popularity. The JAMA study on G&C was conducted in response to this phenomenon. It was a meta-analysis - a rigorous review of previously published, double-blind, placebo-controlled studies selected on the basis of their meeting certain methodological criteria. Three classes of values were assigned to the outcomes of the studies reviewed: 0.8 for a large treatment effect, 0.5 for a moderate effect, and 0.2 for a small effect. Actual values would, of course, be different. Glucosamine was found to possess moderate
benefits (a weighted average of 0.44), while chondroitin appeared to be more than twice as effective in reducing pain and improving mobility (0.96). However, the results varied widely, with the smallest range for glucosamine (0.23 to 1.28) and the largest range for chondroitin (0.53 to 4.56).

The JAMA study was not the first to look at the evidence that the benefits of G&C go beyond those of the conventional NSAID treatments. Another meta-analysis, encompassing seven trials in which 372 patients were followed for 120 days or more, was published about two months earlier. It reached many of the same conclusions about chondroitin, which was found to be at least 50% better than placebo in lessening and preventing pain and loss of joint function.4

Yet another review of the literature found 13 studies (six with glucosamine, seven with chondroitin) showing that the eligibility criteria for using these nutrient compounds in treating osteoarthritis of the hip or knee had been met.5 All of these studies were judged to have demonstrated significantly reduced pain, as well as increased freedom of movement by about 40%, compared with placebo. The results were similar for both of the nutrients.

GLUCOSAMINE AND CHONDROITIN - A SAFE ALTERNATIVE

In an editorial related to the JAMA review, concern is expressed not only regarding the use of NSAIDs (until recently the only recognized treatment), but also for the use of COX-2 inhibitors (a new class of nonsteroidal anti-inflammatory drugs), which, like the NSAIDs they are attempting to replace, have their own collection of serious side effects that pose a significant risk of gastrointestinal complications. Thus the editorialists conclude that there is a great need for alternatives for treating osteoarthritis safely and effectively. And they are right. The use of NSAIDs by elderly patients, e.g., doubles the risk of being hospitalized for congestive heart failure, and for those with a history of heart disease, it increases the risk by more than 10 times, researchers reported in the March 27 issue of Archives of Internal Medicine.6

Currently underway is a large-scale study by the National Institutes of Health evaluating glucosamine and chondroitin in patients with osteoarthritis of the knee. Scheduled to run for 16 weeks, this parallel-group, double-blind study includes four treatment "arms," in which patients will ingest orally one of the following combinations: placebo, 500 mg of glucosamine sulfate three times per day, 400 mg of chondroitin sulfate three times per day, or a combination of glucosamine and chondroitin.

As with many nutraceuticals that are currently widely regarded as beneficial for everyday, garden-variety, or difficult-to-treat disorders, it may be that the hype about G&C exceeds the benefits of any possible outcome. But once large-scale, high-quality studies such as that of the National Institutes of Health are published and critiqued, the word will assuredly go far and wide, and even traditional physicians will get information necessary to advise their patients about the benefits of these alternative therapies. If only they were reading the alternative, complementary publications now.
JAMA STUDY DID NOT DISTINGUISH AMONG CHONDROITINS

Returning to what's really new in this area . . . . Only a few analyses or commentaries have attempted to distinguish between the different varieties of chondroitins that comprise the test material of the studies. This is surprising, given that the range of positive effects from taking chondroitin was much wider than that from taking glucosamine, as reported in the JAMA review. The positive effects from taking chondroitin were also much larger. What was the type of chondroitin used in the nine studies selected for inclusion in the review? Overwhelmingly, it was mixed chondroitin 4-sulfate and chondroitin 6-sulfate (called chondroitin 4,6-sulfate for short), as mentioned explicitly in the research reports.

All the different varieties of chondroitin and glucosamine may leave people confused. Studies have shown that the biological activity of chondroitin sulfate depends on its molecular structure, and it is quite clear that there are different and complementary roles for the two forms. While chondroitin 6-sulfate is better than chondroitin 4-sulfate for inhibiting the enzymatic degradation of cartilage, the 4-sulfate is more effective for the synthesis of new cartilage.

THE POWER IN CHONDROITIN RATIOS

Other studies strongly suggest that the ratio of the two forms of chondroitin sulfate in synovial fluid is important and reflects the degree of joint health. When the 6-sulfate is too prevalent, it can interfere with the metabolism of joint tissue. As humans age, the ratio between the two forms of chondroitin eventually shifts almost entirely toward the 6-sulfate. With the summary analysis provided by the JAMA study, there can be little doubt that a 60%-40% blend of the 4-sulfate and the 6-sulfate - the same ratio that prevailed in our youth - works better than glucosamine, albeit somewhat differently.

In the research literature, it is not always clear what other forms of chondroitin are used, but the fact remains that there have been few studies with promising results that don't employ the 4,6-sulfate mixture. It seems likely that chondroitin 4,6-sulfate is vastly superior to other chondroitin formulations in providing long-range benefits for the joints.

WHICH GLUCOSAMINE

Glucosamine and its derivatives, such as glucosamine sulfate and acetylglucosamine, have been shown to be effective in supporting proper joint function. Unfortunately, though, both of the most widely used derivatives of glucosamine, the sulfate form and the hydrochloride form, have relatively short half-lives in the bloodstream, meaning they don't stay there very long. Acetylg glucosamine, however, has a longer half-life, ensuring more continuous utilization and better joint protection. Unlike other derivatives of glucosamine, it is converted to glucosamine in the body on an as-needed basis, and the levels can more easily be increased and maintained by supplementation. Acetylg glucosamine has other unique benefits, and, like chondroitin, it can inhibit the release of cartilage-degrading enzymes. Hyaluronic acid, an all-important component of synovial fluid, is readily formed from acetylg glucosamine. All in all, acetylg glucosamine is the best choice as a source of glucosamine.
When you consider the importance of your joints, a formulation combining acetylglucosamine and appropriately balanced chondroitin 4-sulfate and chondroitin 6-sulfate is worthy of both your attention and an ongoing effort to read and examine the evidence presented in the studies and reviews, such as the *JAMA* article. The more immediate impact of the glucosamine, as well as the building benefits of the chondroitin, may offer what you have been yearning for - more youthful joint functioning.

References