OSTEOARTHRITIS IS THE most common form of joint disease, affecting about 15% of the U.S. population and accounting for up to 30% of all primary-care patient visits. Common predisposing factors such as obesity, occupational loading, and participation in athletics have been associated with an increased risk of osteoarthritis. In addition, both meniscal and ligamentous injuries of the knee correlate with increased incidence of osteoarthritic changes in the knee and hip joints. In order to minimize the occurrence of osteoarthritis and its debilitating effects, physicians have explored a variety of avenues including nonsteroidal anti-inflammatory drugs (NSAIDs) and exercise. Recently, researchers have been exploring the efficacy of the supplement glucosamine and its effect on slowing osteoarthritic changes. The purpose of this column is to discuss glucosamine and its role in the physically active population.

Osteoarthritis

The American Academy of Orthopedic Surgeons describes osteoarthritis as the result of both mechanical and biological occurrences that disrupt the natural metabolic function of the articular-cartilage chondrocytes, the extracellular matrix, and the subchondral bone. These changes lead to softening and loss of articular cartilage, osteophyte formation, subchondral cysts, and sclerosis of subchondral bone.

Articular Cartilage

Articular cartilage serves two biomechanical functions: absorbing stress from mechanical loads and providing a smooth load-bearing surface allowing for low-friction joint movement. The functional properties of articular cartilage are attributed to the unique structure of its matrix, a mixture of chondrocyte cells and fibrous collagen in a concentrated water-proteoglycan gel. The integrity of this matrix is crucial for articular cartilage’s function and relies on three factors: water for lubrication and nourishment, proteoglycans (protein polysaccharides composed of glycosaminoglycans) to attract and hold water, and collagen fibers to hold proteoglycans in place.

With aging and the onset of osteoarthritis, the proteoglycans begin to break down. This polymerization impairs the degree and rate of diffusion in the matrix. To synthesize new cartilage at a rate greater than or equal to the rate of degradation, the matrix must be supplied with the needed raw materials. Proteoglycan polymerization in the matrix also impairs the ability of the matrix to repeatedly absorb mechanical loading without being damaged. In osteoarthritis, the rate of cartilage degradation exceeds the rate of synthesis, resulting in loss of articular cartilage, narrowing of joint spaces, decreased joint mobility, and pain.

Glucosamine

Glucosamine, formed in the body as glucosamine 6-phosphate, is an endogenous aminomonosaccharide synthesized from glucose. It is used in the formation of proteoglycans and glycosaminoglycans as a proposed substrate for their biosynthesis and perhaps as a direct stimulator of their production. Glucosamine’s primary role in halting or reversing joint degeneration appears to be a direct result of its ability to act as a building block that helps restore the proteoglycan-rich matrix.
and thus balance cartilage catabolism and anabolism. It is also proposed to inhibit the enzymes that destroy cartilage (collagenase and phospholipase) and decrease the production of superoxide free radicals that also damage tissue.\(^1,5,7,8\) The sidebar lists tissues and body systems affected by glucosamine.

Because of glucosamine’s low molecular weight and high solubility in water, it is readily absorbed in the gastrointestinal tract.\(^5,7\) In humans, approximately 87% of an oral dose of glucosamine enters the bloodstream.\(^5\) Once absorbed through the gastrointestinal tract, glucosamine concentrates in the liver, where it is incorporated into plasma proteins, degraded into smaller molecules, or used for other biosynthetic processes.\(^7\) Although absorption is very high, a substantial quantity of the absorbed glucosamine is modified or degraded to smaller compounds such as \(\text{H}_2\text{O}\) and \(\text{CO}_2\) as it makes the “first pass” through the liver. Glucosamine is rapidly integrated into articular cartilage after oral administration.\(^7\) It has also been stated that articular cartilage converts glucosamine to a greater extent than any other structural tissue does.\(^7\)

Glucosamine appears to be ineffective at inhibiting cyclo-oxygenase or the proteolytic enzymes involved in inflammation. Unlike NSAIDs, its mechanism appears to be linked to its ability to stimulate biosynthesis of proteoglycans needed to stabilize cell membranes and increase intracellular ground substance. Because the anti-inflammatory ability of glucosamine is different than that of NSAIDs, it is possible the two might work in cooperation to alleviate some types of inflammation.\(^5,7\)

**Clinical Trials**

Results of recent clinical trials suggest that glucosamine sulfate is safe and might have some efficacy in treating osteoarthritis symptoms.\(^5,10\) In a randomized placebo-controlled trial, 202 patients with knee osteoarthritis were examined to determine the long-term effect of oral glucosamine-sulfate supplementation. Patients were given either placebo or 1,500 mg of glucosamine sulfate once a day for 3 years. The authors found that joint pain and limitation of function significantly improved in the glucosamine-sulfate group compared with the placebo group, and patients receiving glucosamine sulfate did not undergo, on average, the progressive joint-structure changes radiologically observed in those taking placebo.\(^11\)

A placebo-controlled, double-blind study demonstrating the efficacy of intramuscular injections of glucosamine sulfate was conducted with 155 outpatients diagnosed with knee osteoarthritis. Intramuscular injections were given twice a week for 6 weeks. A favorable response rate to therapy was reported in 55% of patients given glucosamine sulfate intramuscularly and 33% of those given placebo.\(^7\)

One study, conducted by 252 doctors on 1,183 patients, examined the effectiveness of glucosamine sulfate for treating arthritis. Patients were given 500 mg of glucosamine sulfate orally three times a day for an average of 50 days. The treatment was judged effective by doctors in 58.7% of the patients and sufficient in another 36%. Results indicate that pain with active and passive movement was reduced, and symptoms of pain at rest, standing, and during exercise improved steadily throughout the treatment period.\(^7\)

Another recent study provided strong additional evidence that glucosamine sulfate protects joints from damage. In this double-blind placebo-controlled trial, 212 individuals were followed for 3 years. X-rays showed that joint damage was less likely to progress among those taking glucosamine sulfate. Furthermore,

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**Tissues and Body Systems Affected by Glucosamine\(^7\)**

- Articular surfaces
- Tendons
- Ligaments
- Synovial fluid
- Skin
- Bone
- Nails
- Heart valves
- Blood vessels
- Mucus secretions of the digestive system, respiratory system, and urinary tract