



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

ARTHRITIS SHAKES HAND WITH CHONDROITIN AND GLUCOSAMINE TO KICK OUT JOINT PAIN

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Abstract: Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. It occurs when the protective cartilage that cushions the ends of the bones wears down over time. Although osteoarthritis can damage any joint, the disorder most commonly affects joints in your hands, knees, hips and spine. Primary osteoarthritis is caused by the breakdown of cartilage, a rubbery material that eases the friction in your joints. It can happen in any joint but usually affects your fingers, thumbs, spine, hips, knees, or big toes. Osteoarthritis is more common in older people. Primary osteoarthritis is caused by the breakdown of cartilage, a rubbery material that eases the friction in your joints. It can happen in any joint but usually affects your fingers, thumbs, spine, hips, knees, or big toes. Osteoarthritis is more common in older people. Using your joints over and over damages the cartilage, leading to pain and swelling. Water builds up in the cartilage, and its proteins break down. It may start to flake or get tiny tears. In severe cases, you can lose all the cartilage between the bones of a joint so that they rub together, making it harder and more painful to use the joint. Cartilage damage can also trigger bone growths (spurs) around your joints. Osteoarthritis sometimes happens in multiple members of one family, hinting that a gene change has been handed down from parents to children. Rarely, these cases are caused by problems in collagen, a tough protein found in your connective tissue. Secondary osteoarthritis happens when your cartilage is damaged by another disease or medical condition. Things that can cause it or make it more likely include:

Obesity, which puts more stress on your joints, especially your knees. Injury or surgery to the joint. Even if a joint seems to heal the way it should, it's at higher risk for osteoarthritis later on. Unusual joints at birth (congenital abnormalities). These are more likely to wear down, especially in the hip. Body mechanics. Things that change the way your body works, such as an unusual way of walking or joints that have a wider range of motion than usual (called hypermobility), can put more stress on them. Your job or hobby. Using a joint to make the same motion over and over again -- like squatting or lifting -- may be linked to osteoarthritis.

Gout, crystal deposits in the cartilage can cause damage and osteoarthritis. Uric acid crystals cause arthritis in gout, while calcium pyrophosphate crystals cause arthritis in pseudogout. Rheumatoid arthritis and other inflammatory conditions of the joints, which lead to joint damage and cartilage breakdown. Diabetes and other hormone disorders, which can cause inflammation that leads to osteoarthritis. Menopause. Levels of estrogen, which protects your bones and cartilage, fall after menopause. The main difference between osteoarthritis and rheumatoid arthritis is the cause behind the joint symptoms. Osteoarthritis is caused by mechanical wear and tear on joints. Rheumatoid arthritis is an autoimmune disease in which the body's own immune system attacks the body's joints. It may begin any time in life.

The main symptoms of osteoarthritis are pain and stiffness in your joints, which can make it difficult to move the affected joints and do certain activities. The symptoms may come and go in episodes, which can be related to your activity levels and even the weather. In more severe cases, the symptoms can be continuous. You should see your GP if you have persistent symptoms of osteoarthritis so they can confirm the diagnosis and prescribe any necessary treatment.

Other symptoms you or your doctor may notice include:

joint tenderness: increased pain and stiffness when you have not moved your joints for a while

joints appearing slightly larger or more "knobby" than usual. a grating or crackling sound or sensation in your joints.

limited range of movement in your joints

weakness and muscle wasting (loss of muscle bulk)

Osteoarthritis can affect any joint in the body, but the most common areas affected are the knees, hips and small joints in the hands. Often, you'll only experience symptoms in 1 joint, or a few joints at any 1 time.

Osteoarthritis of the knee: If you have osteoarthritis in your knees, both your knees will usually be affected over time, unless it occurred as the result of an injury or another condition affecting only 1 knee.

Your knees may be most painful when you walk, particularly when walking up or down hills or stairs.

Sometimes, your knees may "give way" beneath you or make it difficult to straighten your legs. You may also hear a soft, grating sound when you move the affected joint.

Osteoarthritis of the hip: Osteoarthritis in your hips often causes difficulty moving your hip joints. For example, you may find it difficult to put your shoes and socks on or to get in and out of a car. You'll also usually have pain in the groin or outside the hip. This is often worse when you move the hip joints, although it can also affect you when you're resting or sleeping.

Osteoarthritis of the hand: Osteoarthritis often affects three main areas of your hand:

the base of your thumb

the joints closest to your fingertips

the middle joints of your fingers

Your fingers may become stiff, painful and swollen and you may develop bumps on your finger joints. Over time, the pain may decrease and eventually disappear altogether, although the bumps and swelling can remain. Your fingers may bend sideways slightly at your affected joints or you may develop painful cysts (fluid-filled lumps) on the backs of your fingers. In some cases, you may also develop a bump at the base of your thumb where it joins your wrist. This can be painful and you may find it difficult to perform some manual tasks, such as writing, opening jars or turning keys.

Keywords: Osteoarthritis, Bones, Cartilage, Inflammation, Chondroitin, Glucosamine, MSM

Overview: Osteoarthritis (OA) is a progressive and degenerative joint disease marked by loss of cartilage, bone changes, and synovial membrane inflammation. Treatment with chondroprotective drugs, such as glucosamine sulfate may offer additional benefits to nonsteroidal anti-inflammatory drugs [NSAID] treating the painful symptoms of OA. Glucosamine is commonly used over the counter [OTC] as a treatment for arthritic joint pain, although its acceptance as a medical therapy varies due to contradictory findings with unclear clinical significance during clinical trials. It is currently not approved as a prescription product by the FDA, but is widely available over the counter. Glucosamine, chondroitin and methylsulfonylmethane, or MSM, are supplements available together and separately for treating osteoarthritis. Methylsulfonylmethane (MSM; CAS: 67-71-0) is an organosulfur compound with the formula $(\text{CH}_3)_2\text{SO}_2$. It is also known by several other names including methyl sulfone and dimethyl sulfone (DMSO_2). This colorless solid features the sulfonyl functional group and is the simplest of the sulfones. It is considered relatively inert chemically and is able to resist decomposition at elevated temperatures. It occurs naturally in some primitive plants, is present in small amounts in many foods and beverages, and is marketed as a dietary supplement. It is sometimes used as a cutting agent for illicitly manufactured methamphetamine. It is also commonly found in the atmosphere above marine areas, where it is used as a carbon source by the airborne bacteria *Afiopia*. Oxidation of dimethyl sulfoxide produces the sulfone, both under laboratory conditions and metabolically.^[1-3]

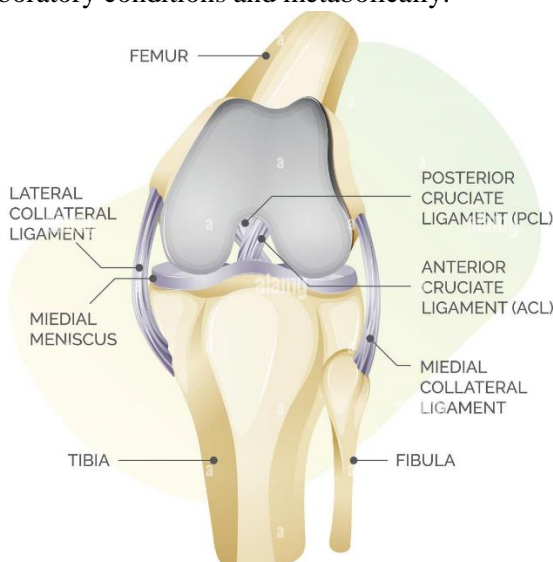


Figure-1: Knee joint cartilage cushion

Osteoarthritis, the most common form of arthritis, occurs when the cartilage that cushions joints degenerates. Glucosamine and chondroitin are substances that play a role in joint health, while MSM may offer anti-inflammatory benefits. Combination therapy may prove more beneficial than taking these substances alone, but results from studies are mixed. Glucosamine is a substance found naturally in the fluid that surrounds your joints, and chondroitin is found in the cartilage around your joints. Both substances play a role in keeping your joints cushioned and lubricated. Glucosamine is commonly taken with chondroitin to treat joint problems such as osteoarthritis. MSM is a sulfur compound found in a wide variety of foods in your diet, such as fruit, vegetables, chocolate, tea, meat and seafood. Because it may offer anti-inflammatory benefits, it's often found in joint supplements alongside glucosamine.^[4-6]

Glucosamine with Chondroitin: Researchers examined the potential benefit of glucosamine alone and in combination with chondroitin on pain in knee osteoarthritis. Patients took 1,500 milligrams of glucosamine, 1,200 milligrams of chondroitin or both daily for 24 weeks. The study concluded that the combination of glucosamine with chondroitin helps with moderate-to-severe knee pain, but is ineffective for mild pain. The study was published in the February 2006 issue of "The New England Journal of Medicine."

Glucosamine with MSM: A study published in June 2004 examined the efficacy of glucosamine alone and in combination with MSM on mild-to-moderate osteoarthritis. Patients took 500 milligrams of glucosamine, 500 MSM or both three times daily for 12 weeks. The study found that glucosamine and MSM alone and in combination improved mild-to-moderate osteoarthritis. Researchers concluded that combination therapy was more effective at reducing pain and swelling, and improving joint mobility than using either substance alone. The study was published in the journal "Clinical Drug Investigation."

Supplement Safety: Further research is needed to say whether one combination is more effective than the other at treating osteoarthritis. In addition, taking glucosamine, chondroitin and MSM alone or in combination may cause side effects, such as mild nausea, heartburn, diarrhea, constipation and stomach pain. These side effects are typically mild and may go away on their own as your body adjusts. Discontinue use and consult your health-care provider if you experience side effects that become too bothersome.^[7-9]

Glucosamine (CAS: 3416-24-8; IUPAC: (3R,4R,5S)-3-Amino-6-(hydroxymethyl)oxane-2,4,5-triol). It was discovered by Georg Ledderhose (15 December 1855, Bockenheim, Regierungsbezirk Wiesbaden, Germany – 1 February 1925, Munich, Germany) was a German surgeon. Glucosamine was first prepared in 1876 by Georg Ledderhose by the hydrolysis of chitin with concentrated hydrochloric acid which hydrolyses the amide bond to free amino group.

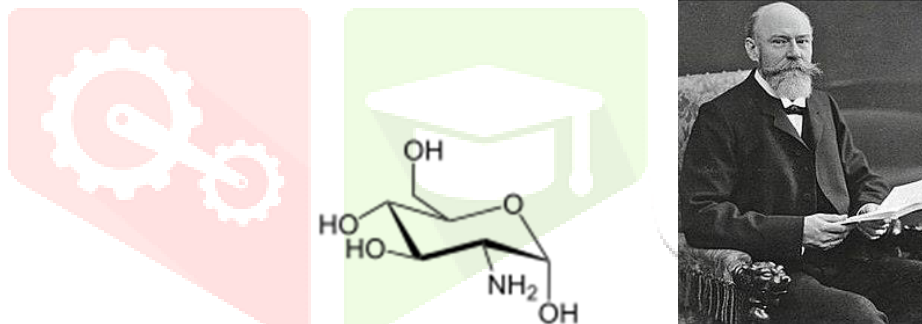


Figure-2: Glucosamine & Georg Ledderhose [Inventor]

Glucosamine is naturally present in the shells of shellfish, animal bones, bone marrow, and fungi. D-Glucosamine is made naturally in the form of glucosamine-6-phosphate, and is the biochemical precursor of all nitrogen-containing sugars. Specifically in humans, glucosamine-6-phosphate is synthesized from fructose 6-phosphate and glutamine by glutamine—fructose-6-phosphate transaminase as the first step of the hexosamine biosynthesis pathway. The end-product of this pathway is uridine diphosphate N-acetylglucosamine (UDP-GlcNAc), which is then used for making glycosaminoglycans, proteoglycans, and glycolipids. As the formation of glucosamine-6-phosphate is the first step for the synthesis of these products, glucosamine may be important in regulating their production; however, the way that the hexosamine biosynthesis pathway is actually regulated, and whether this could be involved in contributing to human disease remains unclear.^[10-12]

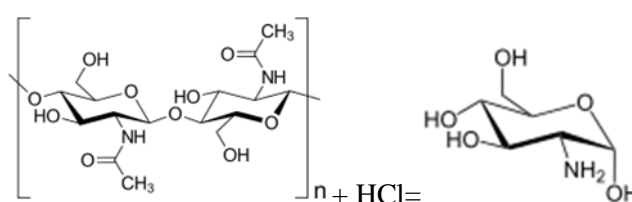


Figure-3: Production of Glucosamine by acid hydrolysis



Figure-4: Glucosamine & Chondroitin formulation

Glucosamine ($C_6H_{13}NO_5$) is an amino sugar and a prominent precursor in the biochemical synthesis of glycosylated proteins and lipids. Glucosamine is part of the structure of two polysaccharides, chitosan and chitin. Glucosamine is one of the most abundant monosaccharides. Produced commercially by the hydrolysis of shellfish exoskeletons or, less commonly, by fermentation of a grain such as corn or wheat, glucosamine has many names depending on country. Although a common dietary supplement, there is little evidence that it is effective for relief of arthritis or pain, and is not an approved prescription drug.^[13-15]



Figure-5: Osteoarthritis zones

Pharmacodynamics: The administration of glucosamine, in theory, provides a building block towards the synthesis of glycosaminoglycans, slowing the progression of osteoarthritis and relieving symptoms of joint pain. Studies to this date examining the efficacy of glucosamine sulfate have been inconclusive. Glycosaminoglycans contribute to joint cartilage elasticity, strength, and flexibility. A systematic review of various studies and guidelines determined that modest improvements were reported for joint pain and function in patients taking glucosamine. A consistent joint space narrowing was observed, but with an unclear clinical significance.^[16-18]

Mechanism of action: The mechanism of action of glucosamine in joint health is unclear, however there are several possible mechanisms that contribute to its therapeutic effects because glucosamine is a precursor for glycosaminoglycans, and glycosaminoglycans are a major component of joint cartilage, glucosamine supplements may help to rebuild cartilage and treat the symptoms of arthritis. Some *in-vitro* studies show evidence that glucosamine reduces inflammation via inhibition of interferon gamma and Nuclear factor kappa B subunit 65 (NF- κ B p65), improving the symptoms of arthritis and joint pain. Clinical relevance is unknown at this time.

Absorption: In a pharmacokinetic study, glucosamine was 88.7% absorption by the gastrointestinal tract. Absolute oral bioavailability was 44%, likely due to the hepatic first-pass effect. In a pharmacokinetic study of 12 healthy adults receiving oral crystalline glucosamine, plasma levels increased up to 30 times the baseline levels and C_{max} was 10 microM with a 1,500 mg once-daily dose. T_{max} was about 3 hours. AUC was $20,216 \pm 5021$ after a 15,000 mg dose.

Metabolism: Glucosamine undergoes metabolism in the liver. Metabolism information for glucosamine is limited in the literature.^[19-21]

Route of elimination: Faecal excretion of glucosamine in a pharmacokinetic study was 11.3% within 120 hours after administration. Urinary elimination was found to be 1.19% within the first 8 hours post-administration.

Half-life: The estimated half-life for glucosamine is 15 hours after an oral dose. After a bolus intravenous injection of 1005 mg crystalline glucosamine sulfate, the parent drug has an apparent half-life of 1.11 hours.

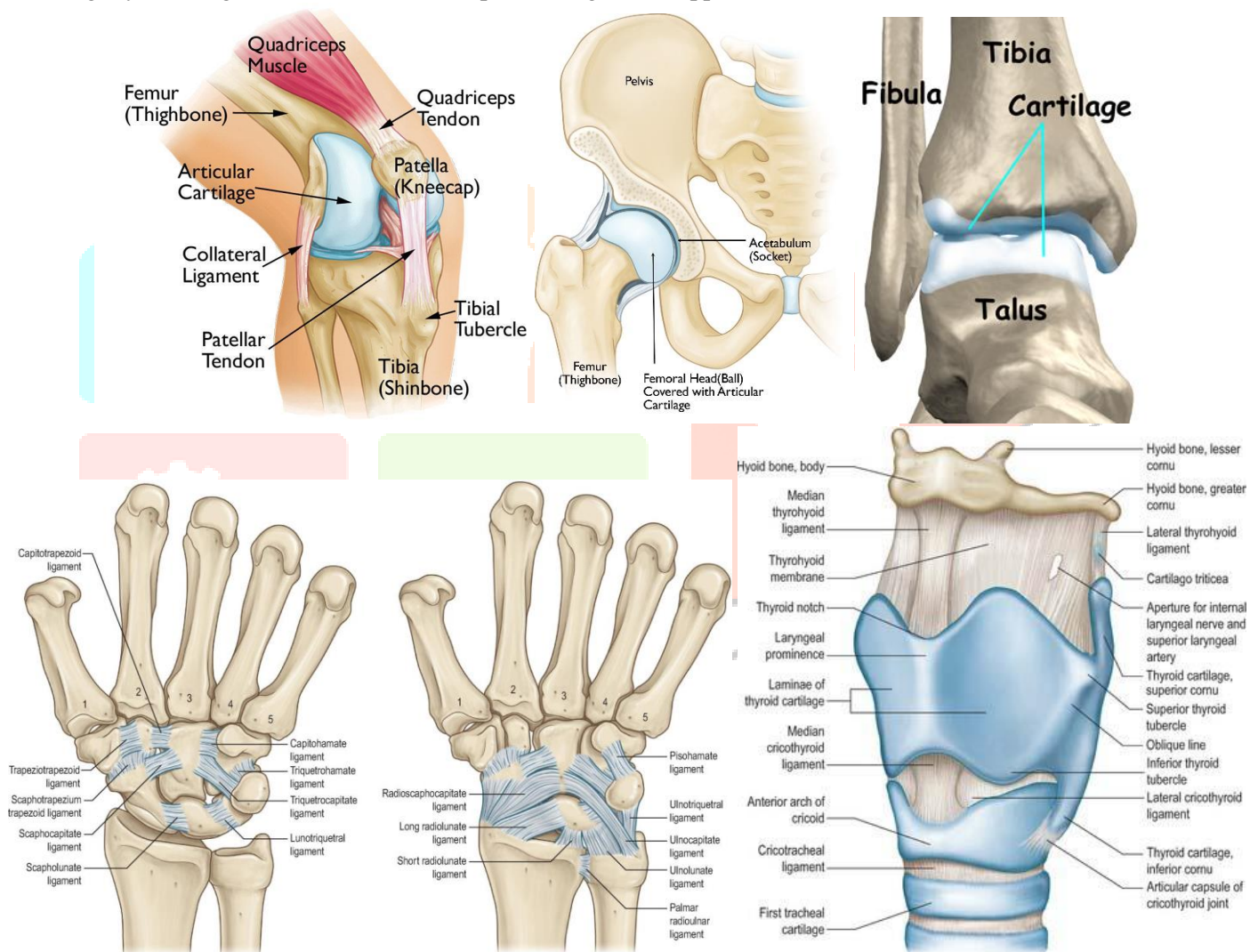


Figure-6: Cartilage cushions in various articulations

Chondroitin is a molecule that occurs naturally in the body. It is a major component of cartilage, the tough, connective tissue that cushions the joints. Commercial chondroitin comes from natural sources, such as shark and bovine cartilage, or synthetic production. Chondroitin as a supplement is now commonly used (often in combination with glucosamine) in treating the joint disease of osteoarthritis. In contrast to the symptomatic treatments, chondroitin can modify the progression of a disease process in the patient which it can be used as an alternative medicine. Chondroitin's effect toward the articular cartilage integrity as it is part of the proteoglycan molecules. The cartilage proteoglycan synthesis can speed up as chondroitin is going through the pathway of the alimentary canal. Research has been conducted to show the effectiveness of chondroitin and results indicate that it helps to manage pain in knee and hip, slow down the progression and also recovery. However, the effectiveness of the drugs is still doubtful.

Conclusion: Joints form the connections between bones. They provide support and help you move. Any damage to the joints from disease or injury can interfere with your movement and cause a lot of pain.

Cause of Joint Pain: Joint pain is extremely common, especially as you age. In one national survey, about one-third of adults reported having joint pain within the past 30 days. Knee pain was the most common complaint, followed by shoulder and hip pain. But joint pain can affect any part of your body, from your ankles and feet to your shoulders and hands. A wide range of conditions can lead to painful joints:

Osteoarthritis, a “wear and tear” disease, is the most common type of arthritis.

Rheumatoid arthritis is an autoimmune disorder that happens when your body attacks its own tissues.

Bursitis is when sacs of fluid that help cushion your joints get inflamed.

Gout is a form of arthritis that most often affects your big toe joint.

Strains, sprains, and other injuries.

Often, the pain can come with swelling and inflammation, stiffness, and loss of range of motion.

Treatments for Joint Pain: Joint pain can range from mildly irritating to debilitating. It may go away after a few weeks (acute), or last for several weeks or months (chronic). Even short-term pain and swelling in the joints can affect your quality of life. Whatever the cause of joint pain, you can usually manage it with medication, physical therapy, or alternative treatments. Your doctor will first try to diagnose and treat the condition that is causing your joint pain. The goal is to reduce pain and inflammation and preserve joint function. Treatment options include:

Medications: For moderate-to-severe joint pain with swelling, an over-the-counter or prescription nonsteroidal anti-inflammatory drug (NSAID) such as aspirin, celecoxib, ibuprofen, or naproxen can provide relief. NSAIDs can have side effects, potentially increasing your risk for gastrointestinal bleeding. If you have mild pain without any swelling, acetaminophen can be effective. Be careful when taking this medicine though, especially if you drink alcohol, because high doses may cause liver damage. Because of the risks, you should take any of these pain medications with caution. If your pain is so severe that NSAIDs aren't effective enough, your doctor may prescribe a stronger opioid medication. Because opioid drugs can cause drowsiness, you should only use them under a doctor's care. They also can cause constipation, which you can relieve by taking laxatives.

Other drugs that may help relieve pain include: Muscle relaxants to treat muscle spasms (may be used together with NSAIDs to increase the effect). Some antidepressants and antiepileptic drugs (which both interfere with pain signals)

Topical Agents: Capsaicin a substance found in chili peppers may relieve joint pain from arthritis and other conditions. Capsaicin blocks substance P, which helps transmit pain signals, and it triggers the release of chemicals in the body called endorphins, which block pain. Side effects of capsaicin cream include burning or stinging in the area where it is applied. Another topical option is an arthritis cream containing the ingredient, methyl salicylate.

Injections: For people who don't find joint pain relief from oral or topical medications, the doctor may try injections.

Steroids. Mostly commonly, they might inject a steroid medication (which may be combined with a local anesthetic) directly into the joint every 3 to 4 months. Steroid injections are most commonly used in patients with arthritis or tendinitis. If steroid injections mask an injury, you could overuse the joint and damage it even further. The procedures are effective, but in many situations the effect may be temporary.

Platelet-rich plasma therapy. Platelet-rich plasma (PRP) is made from your own blood, which is then injected into your painful joint. Your joint contains a large number of platelets and proteins that have anti-inflammatory and immune-modulating effects.

Prolotherapy. It involves a series of injections of an irritant (often a sugar solution) into joints, ligaments, and tendons. The theory is that the injections stimulate local healing of injured tissues. A treatment program may involve 15-20 shots given monthly for 3-4 months.

Other injection options include: Removing fluid from the joint (and is often done in connection with a steroid injection). Injections of hyaluronan, a synthetic version of the natural joint fluid. This is used to treat osteoarthritis.

Physical Therapy: You can work with a physical therapist to strengthen the muscles around the joint, stabilize the joint, and improve your range of motion. The therapist will use techniques such as ultrasound, heat or cold therapy, electrical nerve stimulation, and manipulation. If you are overweight, losing weight can relieve some of the pressure on your painful joints. Exercise is one effective way to lose weight (along with diet), but be careful to stick with low-impact exercises that won't further irritate the joint. Swimming and bicycling are among the best exercises because both allow you to exercise your joints without putting impact on them. Because water is buoyant, swimming also relieves some of the pressure on your joints.

Home Care: You can relieve short-term joint pain with a few simple techniques at home. One method is known by the acronym PRICE:

Protect the joint with a brace or wrap. Rest the joint, avoiding any activities that cause you pain. Ice the joint for about 15 minutes, several times each day. Compress the joint using an elastic wrap. Elevate the joint above the level of your heart. Applying ice to your painful joints can relieve the pain and inflammation. For muscle spasms around joints, try using a heating pad or wrap several times a day. Your doctor may recommend that you tape or splint the joint to minimize

movement or reduce pain, but avoid keeping the joint still for too long because it can eventually become stiff and lose function.

Alternative Treatments: Some research shows that glucosamine and chondroitin supplements can help with joint pain and improve function. Both of these substances are components of normal cartilage, which helps cushion the bones and protect joints. Glucosamine and chondroitin supplements are available in capsule, tablet, powder, or liquid form. Although these supplements don't work for everyone, they are safe to try because they don't have any significant side effects. No matter what treatment you're following, get medical help right away if the pain gets intense, your joint suddenly becomes inflamed or deformed, or you can no longer use the joint at all.

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