Focus on Canine Sports Medicine

Joint Protective Agents for Performance Dogs

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Degenerative joint disease (DJD) also known as osteoarthritis (OA), or simply arthritis is a debilitating disorder affecting a wide range of animal species and humans. Canine OA is a common cause of joint failure with stiffness, loss of mobility, and varying degrees of inflammation and pain. DJD is commonly caused by joint instability due to slack/lax ligaments; it can also result from strains, direct or indirect injury, and from faulty bone and cartilage development. Less efficient repair processes in the older animal make age a contributing factor, and the condition may be exacerbated by obesity and/or overexertion.

Once joint cells are stressed or damaged, enzymes are released which fray and ulcerate joint cartilage and which attack the lubricants of the joint fluid. As a result of the damage, the joint lining and capsule become inflamed and the bone underlying the cartilage less resilient. Only when these sensitive tissues (both capsule and bone) are affected, often after significant articular cartilage damage, can we then see the clinical signs of pain, swelling, and stiffness.

Articular cartilage is found in all moving joints in the dog's body (synovial joints) and its role is to protect the bones by keeping the surfaces of the bones apart from each other, to absorb shock, and to help make movement smooth. Articular cartilage does this by providing a protective, wear-resistant surface to the end of the moving bones.

Normal articular cartilage, by its rubber-like resiliency, functions to reduce pressure, and where it covers the end of a bone, its smooth surface minimizes the friction effect of shearing forces.

Cartilage of our joints derives its nutrition from the movement and contact pressure of the joint. This movement and pressure helps transmit nourishment from the joint fluid to the cellular matrix of the cartilage. This process is promoted and strengthened when there is slight incongruity of the opposing joint surfaces.

Articular cartilage is composed of chondrocytes and extracellular matrix. Chondrocytes are a cell type found in articular cartilage. Chondrocytres take an active part in the synthesis of and turnover of the extracellular matrix and the replacement of degraded matrix and its components. Extracellular matrix has two main components, tissue fluids and proteoglycans. Tissue fluids are mostly composed of water but also contain gases, small proteins, metabolites, and a high concentration of cations to balance the negatively charged proteoglycans (the second component of the extracellular matrix).

Chondrocytes and the matrix are interdependent on each other for maintenance. Chondrocytes secrete the macromolecules that make up the matrix and the matrix in turn protects the chondrocytes from mechanical damage, helping them to maintain their shape. Synthesis and degradation of matrix molecules by chondrocytes is a continuous process throughout life. The precursor lesion of osteoarthritis, namely chondromalacia, or softening of the cartilage, is observed to occur first in non-loadbearing areas of the joint.

Articular cartilage injuries are common. The normal structure and function of articular cartilage can be upset relatively easily and damage to the articular cartilage often results. There are several ways in which your or your dog's articular cartilage can be damaged.

- A sudden direct blow to the cartilage (traumatic), namely a high-energy injury, such as a bad fall on directly onto your knee or during sporting activities
- Slow damage to the cartilage following a knee injury (post-traumatic)
- Wear and tear over time (degenerative joint disease or DJD) especially when there is malalignment or instability in the joint and/or if the dog is overweight

> Diagnosis

The beginning stages of OA are not readily apparent, but, once the deterioration has reached the synovial membrane and/or the bone beneath joint cartilage, painful inflammation begins. The first visible sign of osteoarthritis pain may come in the form of a limp, sensitivity to touch in a certain area (for example, along the spine), a decrease in activity, stiffness (especially after rest), difficulty getting up, lying down, or climbing stairs, or an inability to jump.

Evidence of OA has been found in the fossils of prehistoric dinosaurs as well as in the joints of ancient mummies. It is unfortunate, however, that despite the long existence of this disease, the facts concerning specifically how OA is formed and the factors triggering its development are still incompletely known.

It has been reported that OA may affect up to 20% of the canine population over one year of age. Studies have shown that nearly 50% of musculoskeletal disorders identified over the last 10 years in 16 veterinary hospitals were due to joint disease. To date there have been no studies specifically looking at the rate of osteoarthritis found

in performance dogs. Theoretically we would expect an increased incidence of osteoarthritis in our performance dogs due to the increased impact and wear on their joints. Unfortunately, therapy for joint disease has found limited success once the cartilage changes associated with degeneration have developed.

> Traditional and Alternative Forms of Treatment

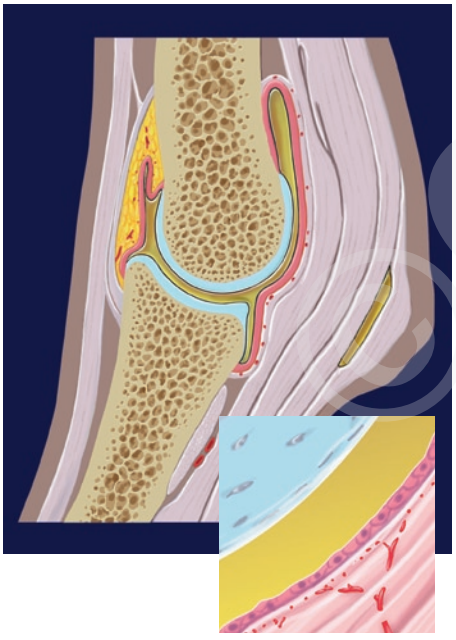
Traditional therapies such as steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for the treatment of OA. Unfortunately, many of these drugs may produce undesirable side effects with long-term use, including gastrointestinal, liver, and kidney damage.

There is increased interest among our performance dog owners for alternative modes of therapy for the medical management of OA with research focusing on slowing the process of cartilage breakdown and promoting cartilage turnover. This research has led to the development of a new class of products termed "slow-acting, disease-modifying osteoarthritis agents" (SADMOA agents). These products can be further divided into injectable products such as the polysulfated glycosaminoglycan (PSGAG) Adequan® (Luitpold Pharmaceuticals, Shirley, New York); hyaluronic acid, Legend® (Bayer Corporation, Shawnee, Kansas); and orally administered products such as glucosamine hydrochloride and chondroitin sulfate (Cosequin®/Dasuquin™, Nutramax Laboratories, Edgewood, Maryland). SADMOA agents are often individual components of healthy cartilage and joint fluid. Studies on how these products actually work are inconclusive but generally include one or more of the following: enhancement of cartilage matrix synthesis, inhibition of enzymes that degrade cartilage, and reduction of joint pain and joint inflammation. Chondroitin sulfate and glucosamine alone (and more effectively together) have been shown to have a biological effect on cartilage. There is a growing body of literature on glucosamine and chondroitin sulfate symptomatic efficacy in clinical trials and in animal models.

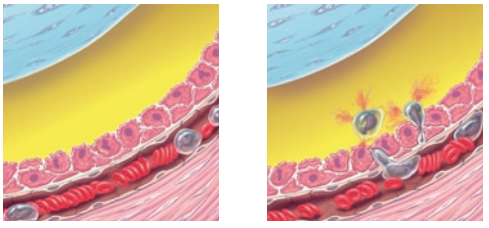
The use of joint health supplements, such as Cosequin or Dasuquin, is recommended for performance dogs in general due to the stress they place on their joints during competition and training. Repeated stress on the joints can cause excessive wear and tear on the joint cartilage or can lead to ligament or tendon injuries, further destabilizing the joint. Both can then progress to OA.

When a performance dog has DJD or OA, the protective cartilage on the surface of the joint gets worn away, and the resultant bone-to-bone contact creates pain. Glucosamine and chondroitin give the cartilage-forming cells (chondrocytes), the building blocks they need to turnover cartilage and to repair the existing damaged cartilage. These nutraceuticals are not painkillers; they actually work by healing the damage that has been done to the existing cartilage. These products generally take at least four to six weeks at a higher loading dose to begin to heal the cartilage and most dogs will need to be maintained on these products the rest of their lives to prevent further cartilage breakdown. Administering joint health supplements to all performance dogs, not just to those who already have OA, provides protection and helps slow down damage to the joint cartilage. Several studies have shown that giving Cosequin prior to joint trauma protected the joints and lessened the severity of cartilage damage. Supplements should be started when dogs begin training and should be continued long-term.

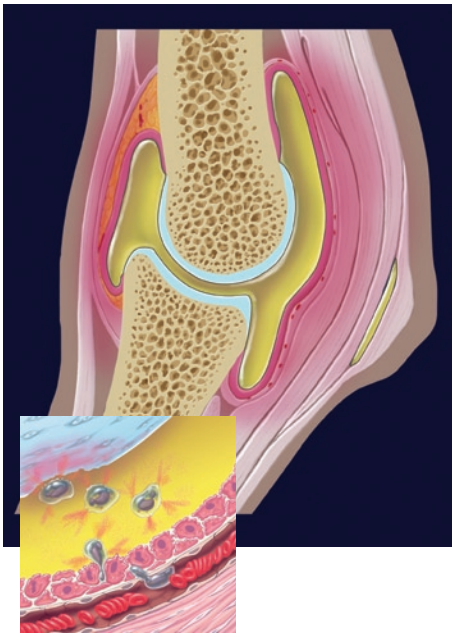
Other supplements known as omega-3 fatty acid products such as Welactin®, can also be considered to provide additional benefits to performance dogs. Certain omega-3 fatty acids support joint function as well as overall wellness.



Images of a normal joint made up of articular cartilage, subchondral bone (bone beneath the cartilage), joint capsule (surrounding joint tissue which has a significant amount of blood supply and nerve endings), and synovial fluid (joint fluid).



Injury or excessive trauma to a joint results in joint inflammation (synovitis). This allows white blood cells to invade the joint. These cells then release destructive enzymes, free radicals, cytokines, and prostaglandins, which cause further inflammation within the joint and a breakdown in the viscosity of the joint fluid.



As the negative cascade of osteoarthritis continues the degradative enzymes released by the white blood cells continue to cause further joint inflammation, decrease in viscosity, and begin to cause destruction to the articular cartilage.

This pathologic process is noted clinically in the dog by signs of lameness, joint pain, and joint inflammation (swelling and heat).

Illustrations courtesy of Bayer HealthCare Animal Health Division, Shawnee Mission, Kansas.

> Joint Supplements and How They Work

Glucosamine

Glucosamine is an amino monosaccharide unit of glycosaminoglycan, which is the building block of the cartilage matrix seen within joints. Glucosamine has been proposed in the Congress of Rheumatology as a slow-acting agent in OA based on its pharmacologic and clinical profile. Its mechanism of action may involve inhibition of inflammatory enzyme activity and stimulation of glycosaminoglycans (GAG) synthesis. The actual chemical makeup of glucosamine accounts for its favorable absorption through the gastrointestinal tract and favorable cartilage reaction. However, there are limited studies within living organisms or whole dogs, thereby also limiting documentation of its disease modification effects.

Chondroitin sulfate

Chondroitin sulfate is a long-chain polymer of repeating disaccharide units containing galactosamine sulfate and glucuronic acid and constitutes the majority of glycosaminoglycans in cartilage found on the moving surfaces of joints, or articular cartilage. Its bioavailibility is well documented with up to 70% absorption after oral administration in animals and humans. Published data indicate that chondroitin sulfate has variable effects including contributing to a pool of substrate available for cartilage matrix deposition, inhibition of proteases, stimulation of glycosaminoglycan, and collagen synthesis.

The efficacy of chondroitin sulfate in protecting articular cartilage has been documented in many animal models. For example, Uebelhart et al examined oral and intramuscular delivered agents in an inflammatory model of OA in the rabbit. Ingestion of the chondroitin sulfate resulted in lowered cartilage degeneration.

Glucosamine/Chondroitin Combination

When given in combination, glucosamine and chondroitin sulfate reportedly support cartilage production and protect existing cartilage by inhibiting enzymes in the joints that break down cartilage.

In addition to the multiple in vitro, or cellular studies, many in vivo studies have been performed evaluating the efficacy of the glucosamine chondroitin sulfate combination. Hanson et al treated equine OA with a combination of glucosamine and low molecular weight chondroitin sulfate with substantial improvement in clinical symptoms, and Canapp et al reported the same combination has a significant anti-inflammatory effect against chemically-induced inflammatory synovitis in dogs. Clinical trials in humans are numerous, more so in Europe than in the United States. The remarkable acceptance of these agents and recent positive clinical trials in the United States attest to their efficacy in treatment of OA. Recent reviews suggest that they potentially may become a basic drug for OA therapy. However, because these compounds are dietary supplements, purity is dependent on the manufacturer and varies greatly.

Cosequin contains glucosamine hydrochloride and chondroitin sulfate, long used in animals and humans to support and maintain cartilage health. In addition to the glucosamine and chondroitin sulfate that are found in Cosequin, the new product

Dasuquin contains the ingredient avocado/soybean unsaponifiables, known as ASU. ASU works along with the glucosamine and chondroitin sulfate to support the joints.

Differences do exist between various joint health supplements in terms of the quality and purity of the raw materials, so it is important to choose a supplement carefully. Because these products are naturally occurring compounds, they are very safe to use and show very few side effects. There are many different glucosamine/chondroitin products on the market, but they are not all created equal. We have seen the best results and fewest side effects from products that are formulated especially for dogs and which contain pure ingredients that are human grade in quality. Both Cosequin and Dasuquin are superior choices. Cosequin is the original glucosamine/chondroitin sulfate brand and the brand shown effective, safe, and absorbable in dogs in published, controlled U.S. studies. And now recent research using cartilage cells has shown that glucosamine and chondroitin sulfate plus ASU work even better than the combination of glucosamine and chondroitin sulfate alone at lowering expression of inflammatory mediators, compounds in the joint that are involved in cartilage breakdown, making Dasuquin an excellent option, too.

Polysulfated glycosaminoglycan

Adequan is an injectable polysulfated glycosaminoglycan (PSGAG) available in veterinary medicine. Polysulfated glycosaminoglycan is made from an extract from bovine lung and trachea. The principle GAG present in PSGAG is chondroitin sulfate. Adequan stimulates cartilage repair processes, binds to damaged cartilage, and suppresses the enzymes that eat away at joints. It helps keep joints lubricated, making movement easier and increases your dog's comfort by reducing inflammation and relieving pain. Adequan® Canine is the only FDA-approved product of its type in the arthritis treatment market and is a prescription-only injection administered by licensed veterinarians.

The use of Adequan has been evaluated for the treatment of OA. In a study performed by Lust, the effects of intramuscular (IM) administration of Adequan were evaluated in growing pups with hip dysplasia. Lust found that IM administration of Adequan from 6 weeks to 8 months of age in growing pups that were susceptible to hip dysplasia resulted in less subluxation (incomplete or partial dislocation of a bone in a joint) as determined through radiography. Treated pups also had closer coxofemoral congruity at 8 months of age; the head of the femur was found to have a better fit within the socket of the hip joint. DeHann also evaluated the effects of IM Adequan for the treatment of hip dysplasia in 84 dogs. In his study response to treatment was analyzed based on changes in lameness, range of motion (ROM), and pain on manipulation of the hip joints. DeHann found that dogs administered Adequan showed the greatest improvement in orthopedic scores compared to placebo; however, the differences in clinical improvement were not statistically significant. In his study, no local or systemic adverse reactions related to the drug were observed.

Hyaluronic acid

Another option for the treatment of OA is an injectable medication called hyaluronic acid (HA). Hyaluronan is secreted by cells in the cartilage of joints. Hyaluronan is one of the major molecular components of joint fluid, and it gives the joint fluid, also called synovial fluid, its viscous, slippery quality. The high viscosity of synovial fluid allows for the cartilage surfaces of joints to glide upon each other in a smooth fashion. By injecting HA in a joint, some people consider this a so-called joint lubrication. This is why you may hear of HA as a "motor oil" for the joint.

Numerous studies have been performed in the past decade to assess the effectiveness of HA as a treatment for OA. However, no clear understanding of how well HA injections perform has emerged. Early studies of HA were performed on too few patients and the follow-up period was limited to a short time. Some studies showed a benefit of HA injections, primarily in reduction of pain as assessed by patients, when compared to patients getting a placebo—a saline injection.

HA as a therapeutic modality for the treatment of OA is based on the physiologic importance of HA in joints. Its therapeutic goal is to restore the viscosity, lubrication and elasticity of joint hyaluronan, thereby decreasing pain, improving mobility and restoring the natural protective functions of hyaluronan in the joint.

Hyaluronic acid has been widely used intra-articularly (via direct injection into the affected joint space) in the treatment of OA in animals and humans. Intravenous HA has shown significant results for the treatment of OA in horses. The mechanism by which HA produces beneficial effects remains controversial. Possible mechanisms by which HA may act therapeutically include 1) providing additional lubrication of the joint membrane 2) controlling permeability of the joint membrane, thereby controlling effusions (seeping of fluid into surrounding tissue); and 3) directly blocking inflammation by scavenging free radicals. Other possible mechanisms include renewal of the cartilage in the joint by promotion of cartilage matrix synthesis and reaggregation of proteoglycans. HA is well tolerated with no demonstrable toxicity and few side effects. Because it is injected directly into the joint, its onset of action is rapid. Administration of intra-articular injections range from a series of 5 weekly injections to three to five week intervals.

To date, there is limited information in the literature regarding the use of intra-articular or intravenous HA for the treatment of OA in dogs. It is well established that in dogs, like horses and humans, HA concentrations and viscosity are altered in OA. It has been reported that dogs with OA, rheumatoid arthritis, and rupture of the cranial cruciate ligament have decreased joint fluid HA levels compared to normal dogs. It has also been reported that friction in canine joints was increased in the disease state, but was significantly decreased after the addition of HA. Most studies in dogs have evaluated the use of intra-articular injections of HA following transection of the cranial cruciate ligament. Dogs in these studies responded favorably to intra-articular HA administration and showed no systemic side effects from HA administration. Results showed decreased severity of OA (gross and microscopic degenerative changes), restoration of viscocity and elastic properties of joint fluid, and a direct cartilage protective effect.

HA is also currently available in an oral form. Unfortunately there are no studies supporting the efficacy of HA in an oral form as compared to the numerous studies showing positive affects on joints with the injectable form. At this time, due to the lack of data on oral HA, it is not recommended as a top joint protective supplement.

> Omega-3 Fatty Acids

Specific omega-3 fatty acids, known as "long-chain" omega-3 fatty acids (docosahexaenoic acid, or DHA, and eicosapentaenoic acid, or EPA, both found in fatty fish, such as salmon), are often recommended in pets and in people because they have far-reaching benefits in the body. (Note: if you live on the West Coast, particularly in Washington state, please be careful of feeding your dog *raw* salmon since raw salmon can carry a parasite that can fatally infect dogs; see www.vetmed.wsu.edu/ClientED/salmon.asp.)

These fatty acids are very well known for protecting heart health but also support the brain/nervous system, the kidneys, skin health, the immune system, and the joints, especially beneficial in performance dogs. A recent study performed by Hill's Science Diet Company fed one group of arthritic dogs a regular diet and a second arthritic group were fed a diet with a large increase in omega-3 fatty acids. At the end of the six-month trial, the dogs fed the omega-3 fatty acid supplemented food showed improvement in their ability to rise from lying down and a decrease in overall lameness. The omega-3 fatty acid diet appeared to decrease the inflammation in arthritic joints and decreased the amount of damaging enzymes in an arthritic joint. Foods supplemented with omega-3 fatty acids are just one of many products containing omega-3 fatty acids. They are also available in capsule and liquid form to be added to the regular diet.

DHA (an omega-3 fatty acid) supplementation has also recently been shown to improve learning ability in puppies, so administration of a long-chain omega-3 fatty acid product, such as the high-potency natural salmon oil supplement Welactin, may prove helpful both during training and in maintaining good joint function.

It has been well established in the literature that SADMOA agents are safe, able to cross into the joint, and modify the painful clinical signs associated with human and animal OA. Unfortunately, the majority of reports regarding these agents for the treatment of OA are still anecdotal. Since these agents are widely available and of very low toxicity, a trial use of them in a performance dog with OA to improve quality of life, or to perhaps prevent future problems, is a safe course to take. To substantiate the efficacy of SADMOA agents under various conditions and in varied dog populations, more formal veterinary studies are greatly needed.

References *The authors submitted nearly three pages of scientific references to accompany this article, but we were unable to publish them because of space constraints. If you would like a copy of these references, please write to editors@cleanrun.com and we will be happy to send you a file.*

Dr. Canapp, a Diplomate of the American College of Veterinary Surgeons, completed a combined D.V.M./M.S. at Kansas State University, an internship in small animal medicine and surgery at the the University of Missouri, a three-year residency in small animal surgery at the University of Florida, and training in canine rehabilitation by the Canine Rehabilitation Institute. Dr. Canapp currently practices orthopedic surgery and sports medicine at the Veterinary Orthopedic & Sports Medicine Group (VOSM) in Ellicott City, Maryland, and acts as a consultant to local zoos, police K-9 units, agility, flyball, and disc competition dogs. See additional information about Dr. Canapp at www.vetsportsmedicine.com.

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