# Nonsurgical Management of Osteoarthritis in Dogs

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**KEYWORDS**

- Osteoarthritis • Nonsteroidal anti-inflammatory drug
- Disease-modifying agent of osteoarthritis • Physiotherapy
- Medical management • Evidence-based

Occam's razor is a philosophical statement that is often used as a guideline in the practice of medicine. Originally referred to as the Law of Parsimony, it essentially states that the simplest explanation of a problem is frequently the best.[1] In medicine, it is often used to suggest that a patient's clinical signs can usually be explained by one disease process instead of a complex interaction of multiple disease processes. By extension, it is often suggested that the abnormality is treated in the least complex manner possible.

Although Occam's razor can be used to explain how a multitude of clinical signs can be attributed to a condition like osteoarthritis (OA), it does not necessarily extend to the treatment of this condition. OA, although superficially considered to be deterioration of the joint associated with pain and dysfunction, is actually quite a complex condition. When considering treatment of OA, a multitude of biochemical, physical, and pathologic alterations must be recognized.[2] Because our knowledge of OA and factors contributing to its development suggest that OA has existed for as long as the diarthrodial joint has existed, and because no known cure or even universally accepted treatment for OA exists, it is probably safe to assume that a single simple treatment does not exist. This does not seem to hinder the quest to find one, however. The search for the Holy Grail of OA treatment continues, and is likely to continue, well past the career longevity of the authors of this article.

Treatment for OA is effectively limited to the available products. The number of products proved to provide safe and effective treatment does not change rapidly. The approved pharmaceutic agents are the most extensively reviewed products. There is a constant search to find new and improved treatments, however, and

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nonpharmaceutic treatments are often suggested and embraced despite a lack of proved efficacy or safety. Journal articles, podium presentations at major and minor veterinary meetings, and popular press articles frequently address the treatment of OA. Seemingly, most of these presentations are based on the same data, or include that author's or speaker's opinion variably based on scientific data or anecdotal experience.

In practice, the decision of when and how to treat OA is often based on a combination of factors. These factors include the available data regarding efficacy but also incorporate the frequency of administration, product formulation, cost, promotions and advertisements by the manufacturer or distributor of the drug or supplement, personal experience, and success or failure of prior treatments used by the client and patient. Treatment is further influenced by the ability or willingness of the client to understand or implement weight control, exercise modification, and physical therapy as part of the management strategy. This article presents a review of the published material regarding various treatments for OA. When there are no data regarding a specific treatment or when a statement is the opinion of the authors, such a deficiency is identified.

## TREATMENT OF OSTEOARTHRITIS

Treatment of OA has traditionally been directed toward palliation of the painful symptoms associated with the condition. It is generally recognized that a variable degree of pathologic change, including bone and soft tissue alterations, exists, and the degree of pathologic change and clinical signs associated with OA must be considered on a continuous scale. The severity of discomfort, often manifest as lameness, can be inconsistent with the degree of pathologic or radiographic change. Furthermore, the severity of the associated symptoms may be related to recent use, or stress, placed on the articular and periarticular tissues. The combination of these variables may lead to chronic pain, often characterized as a dull ache, or acute pain, more typically characterized as a sharp shooting pain. The wide range of factors affecting joint health and pain status makes it difficult to provide a specific recommendation for the treatment of OA that is applicable in all situations. Part of the challenge of OA treatment is that the goal is often variable between patients or within an individual patient. As a result, multimodal therapy is often necessary to address this complex problem.

## NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently recommended treatment for OA. The popularity of this class of drugs is typically attributed to the effectiveness of NSAIDs for palliating the painful symptoms associated with OA and their relative ease of administration. An excellent thorough review of NSAIDs approved in the United States for use in small animals was recently published.[3] It is not the intention of this article to repeat such an extensive review but to focus on the use of these products for the treatment of OA.

Although acetaminophen, an analgesic, is often recommended for the treatment of OA in human beings because of a decreased side effect profile, NSAIDs remain popular despite well-known side effects that may occur with their use.[4–6] When used by people who have OA, NSAIDs are generally considered to provide a greater global relief score than does acetaminophen.[7] A greater global relief score is generally a result of treatment effect (including decreased pain, improved functioning, or both), decreased side effects, and patient (or client) expectation.[8] Although use of acetaminophen is

considered to be an option for the treatment of OA in dogs, no controlled clinical trials have been performed to evaluate the safety and efficacy of this drug.[9]

The efficacy of NSAIDs, when compared with placebo administration, for the treatment of OA is unquestioned. Studies comparing one NSAID with another NSAID for the treatment of people with OA most frequently demonstrate that each NSAID is superior to placebo with respect to pain relief but that no significant difference exists among NSAIDs.[10] Although some studies using veterinary-approved NSAIDs suggest a difference with respect to analgesic quality,[11] it is generally accepted that, when comparing large groups of patients, there is little difference among the approved NSAIDs with respect to the level of symptom relief. Nevertheless, there is evidence, through n-of-1 studies published in the human literature, that one NSAID is often more beneficial than another for a specific individual.[12] It is reasonable to presume that dogs have a similar response to NSAIDs. Veterinary NSAIDs are often prescribed based on convenience of dosing, product formulation, risk or concern for the patient developing side effects, marketing issues (including manufacturer support and promotional efforts), cost, and demonstrated efficacy for an individual.

A recent review article by Aragon and colleagues[13] identified the evidence-based literature related to clinical trials evaluating the treatment of OA in dogs. This review included NSAIDs in addition to other treatments. Articles published since that review are included in the following discussion. The rating system used by Aragon and colleagues[13] is included in the Appendix.

### *Aspirin*

There have been no clinical trials assessing aspirin for the relief of painful symptoms associated with OA in dogs. The recommended dosage of aspirin, based on pharmacologic studies and clinical experience, is 10 to 25 mg/kg administered orally two to three times daily. In the authors' clinical experience, vomiting is often associated with a dosage of 25 mg/kg administered orally three times daily, whereas 10 mg/kg administered orally one or two times daily is better tolerated.[9] Endoscopic studies have documented that aspirin is more likely to cause gastric bleeding and erosions than most other NSAIDs.[14–16]

### *Carprofen*

Carprofen was the first of the newer NSAIDs to be approved for canine use. Aragon and colleagues[13] evaluated five clinical trials designed to assess the use of carprofen to alleviate the clinical symptoms associated with OA. They concluded there was a moderate level of comfort that the substance and disease relation is scientifically valid. Since that evaluation, three more clinical trials have been published evaluating carprofen for the treatment of OA.[17–19] These three trials support the efficacy of carprofen for the treatment of OA. The strength of evidence ranking is likely to increase from moderate to high as the number of clinical trials supporting carprofen use for the treatment of OA increases.

The recommended dosage of carprofen is 2.2 mg/kg administered orally twice daily or 4.4 mg/kg administered orally once daily. Adverse effects reported with carprofen include gastrointestinal toxicity and idiopathic hepatocellular toxicosis. Because of different methods of reporting, it is difficult to assess the incidence of adverse effects related to the hepatic and gastrointestinal systems. Clinical trials evaluating the administration of carprofen for 60 days or longer suggest a combined incidence of approximately 6% or less.[17,20,21] A study directly comparing firocoxib and carprofen reported the incidence of health problems (including adipsia, anorexia, anxiety, constipation, diarrhea, emesis, and polydipsia) associated with firocoxib and carprofen

use as 20% and 34%, respectively, but there was no statistical difference between the two treatment groups.[19] The study did not include an untreated group for comparison with the overall incidence of health problems in the study population.

One experimental study[22] suggested the possibility of decreased cartilage damage and subchondral bone remodeling in dogs with cranial cruciate ligament transection. This finding has not been evaluated in a clinical trial.

### *Etodolac*

Etodolac was the second veterinary NSAID to obtain the approval of the US Food and Drug Administration (FDA). It was demonstrated to be effective for alleviating the painful symptoms associated with coxofemoral OA in one randomized placebo-controlled study.[23] Based on this study, Aragon and colleagues[13] concluded there was a moderate level of comfort that the substance and disease relation is scientifically valid. Etodolac was used as a noninferiority comparator in a clinical study of dogs with OA.[24] Although evaluation of the efficacy of etodolac was not the primary emphasis of that study, etodolac seemed to be effective for the treatment of OA. The recommended dose of etodolac is 10 to 15 mg/kg orally once daily.

Keratoconjunctivitis sicca (KCS) has been reported with etodolac administration.[25] The mean duration of etodolac administration before the development of KCS was approximately 8 to 9 months. Most dogs that developed KCS did not respond to treatment. The incidence of KCS development is unknown.

The product prescribing information states that oral administration of etodolac at a daily dosage of 10 mg/kg (4.5 mg/lb) for 12 months, or at 15 mg/kg (6.8 mg/lb) for 6 months, resulted in some dogs showing a mild weight loss, fecal abnormalities (loose, mucoid, mucosanguineous feces or diarrhea), and hypoproteinemia. Diarrhea was reported to occur in 2.6% of dogs receiving etodolac in the clinical trial reported by Budsberg and colleagues[23] and in 8.3% of dogs evaluated by Hanson and colleagues.[24]

### *Deracoxib*

In one scientific abstract, deracoxib was reported to be effective for alleviating lameness associated with OA in dogs.[26] The recommended dosage is 1 to 2 mg/kg administered orally once daily for chronic pain. Deracoxib has been reported to cause gastrointestinal ulceration, although most cases reported were associated with concurrent administration of prednisone, another NSAID, or administration of deracoxib exceeding the recommended dose.[27] Because no clinical trials have been published regarding deracoxib use, Aragon and colleagues[13] were not able to evaluate the clinical evidence regarding deracoxib for the treatment of OA.

### *Meloxicam*

Meloxicam has been evaluated in four clinical trials targeting dogs affected with OA.[20,28–30] All four of these studies are classified as type I.[13] In all studies, meloxicam was demonstrated to be effective for alleviating clinical symptoms. Aragon and colleagues[13] evaluated these four clinical trials and concluded there was a high level of comfort that the substance and disease relation is scientifically valid.

The recommended dosage of meloxicam is 0.1 mg/kg administered orally once daily. Administration of a single loading dose of 0.2 mg/kg administered orally can be given to hasten establishment of steady-state blood levels. The product insert for meloxicam indicates an incidence of diarrhea of approximately 12%. Two clinical trials[29,30] suggest an approximately 12% incidence of mild gastrointestinal side effects, although two other clinical studies[20,28] suggest that adverse gastrointestinal

events occur less frequently. Meloxicam has been demonstrated not to affect gastrointestinal motility or gastrointestinal mucosa permeability when administered for 6 or 8 days, respectively.[31,32]

### *Tepoxalin*

Tepoxalin is a unique member of the stable of drugs available to the small animal practitioner. It is classified as a dual inhibitor of cyclooxygenase (COX) and lipoxygenase (LOX). Tepoxalin inhibits the LOX pathway of arachidonic acid (AA) metabolism, and therefore decreases the production of leukotrienes, specifically $LTB_4$, which is a potent chemoattractant for neutrophils and other inflammatory cells.[33] Leukotrienes are known to increase the production of proinflammatory cytokines, such as interleukin-1β.[34] It is speculated that inhibition of the COX and LOX pathways provides greater analgesia than inhibition of COX inhibition alone. Despite the attractiveness of this theory, there are no published clinical studies demonstrating efficacy of tepoxalin for the treatment of OA in dogs. The recommended dosage is 10 mg/kg administered orally once daily. A loading dose of 20 mg/kg may be given to hasten increasing plasma levels to a minimum effective concentration. Commercially, tepoxalin is available as a rapidly dissolving tablet.

### *Firocoxib*

Firocoxib is the most recently approved NSAID for the canine market. Three clinical trials have demonstrated that firocoxib is effective when administered to dogs with OA.[19,24,35] These trials were not evaluated by Aragon and colleagues.[13] Two of these trials[19,24] were study design type I, and one[35] was study design type III. Using the criteria employed by Aragon and colleagues,[13] the authors conclude there is a moderate level of comfort that the substance and disease relation is scientifically valid for firocoxib. The recommended dose is 5 mg/kg orally once daily.

The incidence of vomiting, diarrhea, or both was reported as 4.7% or less in one study evaluating firocoxib use.[24] The incidence of an adverse health event, not necessarily related to the gastrointestinal tract, was 20% by Pollmeier and colleagues[19] and could not be determined from the information presented in the study by Ryan and colleagues.[35]

## ANALGESICS USED AS PART OF MULTIMODAL THERAPY

Because of the complex neurobiology of pain,[36] it is reasonable to believe that multimodal pharmacologic and nonpharmacologic therapy is advantageous for the treatment of OA.[4,37] Similarly, it is often suggested that the dosage of any drug be decreased to the lowest effective dose, particularly when used as part of multimodal therapy, to avoid potential side effects. However, since demonstrating efficacy of a single drug or modality for the treatment of OA is challenging, demonstrating the efficacy of an altered dosage, or the addition of a subsequent treatment or a combination of treatments for a condition with such variable pathologic and clinical signs as OA is more challenging and requires a considerable investment of time and resources.[37] Therefore, there are few clinical studies documenting the efficacy of an altered dosage of a single drug or the use of a combination of drugs. The following analgesics have been suggested based on a sound understanding of the neurobiology of chronic pain. Although these drugs may be used clinically in human beings and dogs, further studies are required to confirm efficacy.

### *Tramadol*

Tramadol is considered to be an opioid analgesic that is unlike typical opioid analgesics. The mechanism of action is through weak inhibition of opioid receptors, along with interference of the release and reuptake of noradrenaline and serotonin in the descending inhibitory pathways.[38] Central inhibition of proinflammatory cytokines and nuclear factor (NF)-κB may also occur with tramadol use,[39] and tramadol may also work by influencing various neuronal cation channels and other receptors.[40] A once-daily formulation of tramadol has been demonstrated to be effective for treatment of OA in people.[41,42] The use of the combination of tramadol and an NSAID or paracetamol has been demonstrated to be effective for the treatment of OA in people.[43–46]

Although the combination of an NSAID and tramadol is commonly used clinically in veterinary medicine, no published clinical trials have demonstrated clinical efficacy of this combination for the treatment of OA in dogs. One study of the combination of ketoprofen and tramadol has been reported in abstract form.[47] Although no clinical trials have confirmed a safe dosage range, clinical use at a dosage of 2 to 5 mg/kg administered orally every 8 to 12 hours has been effective in the authors' experience.

Side effects reported with the use of tramadol in human beings include nausea, vomiting, constipation, dizziness, drowsiness, and seizures.[48] Infrequently, tramadol has been associated with serotonin syndrome, a condition of excessive serotonergic activity producing cognitive behavioral changes, neuromuscular hyperactivity, and autonomic activation.[49] Serotonin syndrome has been reported in human beings with tramadol alone, or when coadministered with other drugs that may inhibit reuptake of serotonin, such as tricyclic antidepressants.[49] Because of the possibility of this interaction, coadministration of tramadol and a tricyclic antidepressant, such as amitriptyline, should probably be avoided.

### *Amantadine*

Amantadine inhibits the *N*-methyl-D-aspartate (NMDA) receptor. NMDA receptors are found in the dorsal spinal horn. Activation of these receptors is associated with chronic pain. When aδ and c fibers are chronically stimulated, glutamate is released from the afferent terminal. Glutamate then activates the NMDA receptor in the dorsal spinal horn, resulting in transmission of an ascending impulse along the second-order neuron.[36,50] Despite sound theory suggesting that NMDA receptor blockade results in decreased pain, a truly effective NMDA inhibitor has not been identified for treatment of neuropathic pain in human beings.[51] Although an NMDA inhibitor may not be an effective primary analgesic, it may provide benefit if coadministered with an opioid or other analgesic.

An interesting study by Lascelles and colleagues[52] demonstrated that administration of meloxicam to dogs with OA resulted in significant improvement in client-specific outcome measures. Additionally, it was demonstrated that the combination of amantadine (3–5 mg/kg administered once daily) and an NSAID (meloxicam), given for 21 days, provided greater treatment effect than meloxicam alone. This is the first clinical trial in human beings or dogs to demonstrate an effective analgesic effect of an NMDA inhibitor for the treatment of OA.

### *Gabapentin*

It has been speculated that other drugs, such as gabapentin, may also be beneficial adjunctive treatment for OA. Gabapentin is structurally similar to γ-aminobutyric acid (GABA). Although the mechanism of action was initially thought to be through

GABAergic transmission, it is now believed to be through the blockade of voltage-gated calcium channels.[53] Gabapentin is thought to work primarily by influence within the central nervous system and is recognized as being beneficial for the treatment of neurogenic pain. To the authors' knowledge, no studies have been published evaluating the use of gabapentin for the treatment of OA in dogs.

### *Amitriptyline*

Amitriptyline is a tricyclic antidepressant that has been used to treat chronic and neuropathic pain in human beings. Amitriptyline is thought to act centrally by inhibiting neuronal reuptake of norepinephrine and serotonin.[54] The result of this action is an increase in the activity of the descending inhibitory pathways that modulate afferent nociceptive input.[55,56] Amitriptyline may also act peripherally by inhibiting sodium channels.[54,57] There are no published clinic trials evaluating the use of amitriptyline for the treatment of OA in dogs.

## ADDITIONAL THERAPEUTIC AGENTS

### *Polysulfated Glycosaminoglycan*

Polysulfated glycosaminoglycan (PSGAG) is approved for use in dogs as a disease-modifying agent of osteoarthritis (DMOAD). Two studies are published providing information on the treatment of OA in dogs using PSGAG.[58,59] One study[58] was a type I study. The study subjectively suggested a potential positive effect without statistical significance. Aragon and colleagues[13] gave the study a quality rating that suggests some uncertainties exist relating to the scientific quality. The study does provide information to conclude there was some suggestion that the effect is physiologically meaningful and achievable. A more recent study[59] was a type II study and was not evaluated by Aragon and colleagues.[13] Using the criteria as applied by Aragon and colleagues,[13] this study receives a good quality rating. The overall rating of the strength of the evidence concludes that one can have a moderate level of comfort with the results of these two studies.

Although numerous dose recommendations have been reported for the use of Adequan Canine (Novartis Animal Health US, Inc., Greensboro, North Carolina) in dogs, a dosage of 5 mg/kg administered intramuscularly twice weekly for 4 weeks is the current labeled dosage in dogs. No data are available in regard to dosing beyond 4 weeks. PSGAG is a heparin analogue, and its use in animals with bleeding disorders should be avoided. Concurrent use with NSAIDs that exhibit strong antithromboxane (COX-1) activity should be avoided in all patients.

### *Pentosan Polysulfate*

Pentosan polysulfate (PPS) is approved in human medicine to treat interstitial cystitis. It is also an antithrombotic/lipidemic agent and has had recurring popularity as a potential DMOAD. Two trials in dogs with OA have been published.[60,61] Both studies were prospective in design, were randomized, and are classified with a type I rating.[13] One study subjectively showed a positive effect,[61] and the other subjectively showed no positive effect.[60] Aragon and colleagues[13] gave the studies a quality rating that suggests some uncertainties exist relating to the scientific quality and a low consistency rating, meaning the results were inconsistent. The studies do provide information to conclude there was some suggestion that the effect is physiologically meaningful and achievable. An overall rating of the strength of the evidence concludes that one can have a moderate level of comfort with the results of the aforementioned studies.

### *Hyaluronan*

Hyaluronan (HA) is a nonsulfated glycosaminoglycan that is a major component of synovial fluid. It is administered primarily by intra-articular injection, although a form of HA for intravenous administration is available for use in horses (Legend, Bayer HealthCare, LLC, Shawnee Mission, Kansas). One experimental study evaluated OA progression 32 weeks after intra-articular administration of HA.[62] This prospective nonrandomized study is rated as a type III study. No clinical improvement or preventative effects were identified. The study received a negative quality factor rating, which means it did not adequately address issues of scientific quality.[13] The influence of intravenous HA on synovial fluid quality was evaluated in one clinical trial.[63] Although this study was not a clinical trial assessing functional outcome, it did demonstrate that HA had no influence on the synovial fluid parameters assessed. Another study evaluated intra-articular sodium hyaluronate in dogs with naturally occurring OA.[64] Although not evaluated by Aragon and colleagues,[13] this study is considered to be a type III study with a negative quality factor rating. Based on the available evidence evaluating the use of HA in dogs, the overall rating of strength of the evidence concludes that one can have a low comfort level with the results of these studies.

## NUTRITIONAL SUPPLEMENTS

### *Chondroitin Sulfate and Glucosamine Hydrochloride Preparations*

Two trials were identified describing the use of compounds, with chondroitin sulfate and glucosamine hydrochloride as major components, for improving clinical signs associated with OA in dogs.[18,20] Both study designs were prospective, were randomized, and received a type I classification.[13] One study[18] subjectively showed a positive effect, whereas the other[20] showed no positive effect. Examination of the quality of the studies showed that they had adequately addressed issues of scientific quality relating to data collection, analysis, bias, and generalizability. There is a low consistency rating, meaning that the results were inconsistent between the studies. The studies do provide information to conclude there was some suggestion that the effect is physiologically meaningful and achievable. An overall rating of the strength of the evidence concludes that one can have a moderate level of comfort with the results of the aforementioned studies.

### *Green-Lipped Mussel Preparation*

Two trials were identified by Aragon and colleagues[13] as evaluating use of a compound in which the main ingredient was green-lipped mussel (*Perna canaliculus*) for the treatment of OA in dogs.[65,66] Both studies were prospective and randomized in design and received a type I rating. Although both studies subjectively showed a positive effect, these studies were assigned a quality rating that suggests some uncertainties exist relating to the scientific quality. Two other studies[67,68] were not evaluated by Aragon and colleagues.[13] Using the criteria of Aragon and colleagues,[13] these studies were classified as type I studies but had questionable quality ratings. Of the four studies addressing use of green-lipped mussel, three studies suggested mild to moderate improvement, whereas one suggested no difference between placebo and treated groups. Therefore, there is a moderate level of consistency between the studies. The studies do provide information to conclude there was some suggestion that the effect is physiologically meaningful and achievable. An overall rating of the strength of the evidence concludes that one can have a low level of comfort with the results of the aforementioned studies.

### *P54FP*

P54FP is an extract of the Indian and Javanese turmerics *Curcuma domestica* and *Curcuma xanthorrhiza*. A randomized, blind, placebo-controlled, parallel-group clinical trial of P54FP as a treatment for OA of the canine elbow or hip was performed.[60] This study is classified as type I study.[13] The study subjectively suggested a potential positive effect. Examination of the quality of the study showed that the issues of scientific quality relating to data collection, analysis, bias, and generalizability had been adequately addressed. The study does provide information to conclude there was some suggestion that the effect is physiologically meaningful and achievable. An overall rating of the strength of the evidence concludes that one can have a moderate level of comfort with the results of the aforementioned study.

### *Resin Extract of Boswellia Serrata*

One trial with a herbal dietary supplement consisting of a natural resin extract of *Boswellia serrata*, a tree that grows in the hills of India,[69] was conducted to evaluate the effect on OA in dogs.[70] The study is classified with a type III rating. Subjective clinical improvements were identified. As for a quality rating, the study did not adequately address important issues of scientific quality as defined by Aragon and colleagues.[13] Using the criteria of Aragon and colleagues,[13] a low overall rating of the strength of the evidence is given for *B serrata*, indicating that one can have a low level of comfort with the results of the aforementioned study.

### *Omega-3 (n-3)–Based Diets*

Increased omega-3 (n-3) fatty acid dietary supplementation has been advocated as an adjunctive therapy to degenerative and inflammatory arthritic conditions. The theory behind this idea is based on the fact that polyunsaturated fatty acids (PUFAs) are incorporated into cell membrane phospholipids. The amounts of PUFAs in cell membranes depend on dietary fatty acid content. AA is the predominant PUFA in cell membranes; however, supplementation with increased levels of n-3 fatty acids results in increased eicosapentaenoic acid (EPA) content in membrane phospholipids.[71] When eicosanoid metabolism is induced, the EPA competes with available AA as a substrate for the COX enzymes, altering the levels and even the particular inflammatory mediator produced.[71–73] The metabolism of EPA produces relatively less inflammatory prostaglandins (eg, $PGE_3$). Classic Western diets (human and canine) contain an abundance of n-6 PUFAs and a rather low proportion of n-3 PUFAs. Several canine food products that have a high n-3–to–n-6 fatty acid ratio, and are touted to be of therapeutic benefit in dogs with OA, have recently entered the market. Although most of the data supporting these diets is anecdotal, one abstract presented recently found significant increases in ground reaction forces in dogs with OA after 90 days of the feeding trial.[74]

### *Weight Control and Weight Loss*

Weight reduction has been shown to ameliorate the clinical signs associated with OA in dogs.[75–79] In a nonblind prospective study of 9 overweight dogs with hip OA, Impellizeri and colleagues[75] found that an 11% to 18% reduction in body weight significantly decreased the severity of hind limb lameness. Mlacnik and colleagues[78] reported the results of a prospective randomized clinical trial in which 29 overweight dogs were treated with a combination of caloric restriction and physiotherapy. This treatment was shown to improve patient mobility and facilitate weight loss. Kealy and colleagues[76] reported that the prevalence and severity of OA were less in dogs

with long-term reduced food intake (25% less food than control dogs). In another study, Kealy and colleagues[77] reported that long-term 25% restriction in food intake delayed the onset of signs of chronic disease, including OA, and also increased the mean lifespan in these dogs. In a longitudinal cohort study, Smith and colleagues[79] found that a restricted diet delayed or prevented development of radiographic signs of hip joint OA in a population of Labrador retrievers. These studies indicate that weight control is an important aspect of managing osteoarthritic dogs and that weight loss alone may substantially improve clinical signs in overweight dogs with OA.

## PHYSICAL REHABILITATION FOR PATIENTS THAT HAVE OSTEOARTHRITIS

Physical rehabilitation is the treatment of diseases and injuries with physical agents, such as heat, cold, water, sound, electricity, massage, and exercise.[80] Its benefits may result from increasing blood and lymph flow through the affected area, resolving inflammation, preventing or minimizing muscle atrophy, preventing periarticular contraction, and providing positive psychologic effects for the patient and owner.[80] There is a paucity of scientific literature documenting effectiveness of physical rehabilitation techniques in small animals. Much of the available information is extrapolated from human physiotherapy, knowledge, and experience and is based on an understanding of basic physiology and pathophysiology. In recent years, however, interest in veterinary physical therapy has grown substantially. On the coattails of this increasing interest, more and more objective research is underway to develop physical therapy techniques specifically for animals (and for specific medical conditions) and to better understand the mechanisms by which rehabilitative techniques may benefit veterinary patients. Until this body of scientific literature increases, currently established physiotherapy techniques are used to manage canine patients that have OA and may reduce pain, control inflammation, improve strength and balance, increase range of motion, prevent muscle spasms, and help to restore more normal joint function.[81–87] In many cases, physiotherapy also helps to reduce the dose of analgesics necessary to maintain patient comfort.[87] Rehabilitation for patients that have OA generally consists of a combination of modalities.[81,82,86,87]

### *Cryotherapy*

Cryotherapy, or local hypothermia, is used in acute inflammation. It promotes vasoconstriction and skeletal muscle relaxation and decreases nerve conduction.[88–93] Vasoconstriction limits blood flow into the area, thereby reducing edema. Muscle relaxation can decrease edema formation by improving venous return and by preventing endothelial damage caused by local acidosis. Decreased nerve conduction produces mild analgesia.

Cryotherapy is applied to osteoarthritic joints using ice packs, ice wraps, and cold compression wraps (**Fig. 1**). A ‘‘ziplock bag’’ containing a solution of two parts water and one part alcohol works well as a reusable cold pack.[82] Multiple-use ice packs and cold water circulating systems are also available. A light bandage can be applied to the limb after treatment.[89] Use of a compression bandage, such as an elastic wrap, can further lower the temperature of the deeper tissues.[89,91]

Superficial cryotherapy can penetrate to a tissue depth of 1 to 4 cm, with the greatest temperature change occurring to a depth of 1 cm.[82] Treatments usually last no more than 30 minutes and should be performed two to four times daily. Longer treatment times may lead to lower temperatures, resulting in protective vasodilation and local edema.[90]

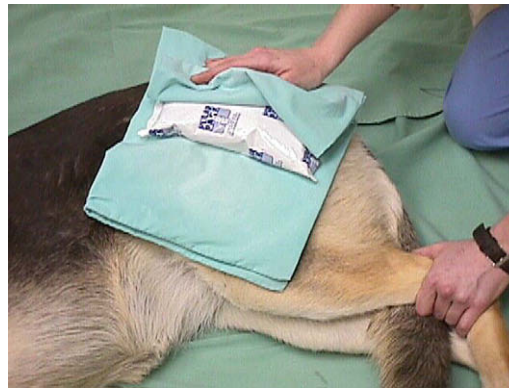

**Fig. 1.** Cold compress is applied to a dog's limb.

### *Moist Heat*

Moist heat is typically used in chronic cases of OA after acute inflammation has resolved and is often applied before stretching, massage therapy, passive range-of-motion (PROM) exercises, or active excercise.[81,82,87] It has been shown to reduce muscle spasms and increase blood flow to the region.[89,93–95] Superficial hyperthermia reaches a tissue depth of 1 to 2 cm, causing vasodilation, mild sedation, relief of muscular pain, resorption of extravasated fluids, and increased local circulation.[94] Increased circulation enhances local metabolism and improves the delivery of nutrients. Heat also increases the compliance of joint capsules, tendons, and scar tissue and reduces joint stiffness, thereby countering much of the stimulus for pain.[92]

Moist heat is typically applied using moist hot packs, warm baths, warm towels, or hydrocollators.[96] It is applied directly over the affected joints for 15 to 20 minutes two to three times daily. The temperature of the heat source should be between 104°F and 109°F (40°C–45°C).[89] Electric heating pads can burn the patient's skin and are not recommended. The skin should be monitored every 2 to 3 minutes; if hot to the touch, more insulating towels should be applied. Heat is often combined with other forms of physiotherapy; specifically, massage and passive exercise if reduced swelling is the goal. Mild exercise in ambulatory patients within 1 hour of the hyperthermia leads to prolonged and increased effects from the treatment.[93] Superficial hyperthermia is contraindicated in the absence of skin sensation, because the patient can neither sense nor respond to the heat. Premature application of heat (during acute inflammation) may lead to increased edema and pain in the injured area.

### *Passive Range-of-Motion Exercises*

PROM exercises are effective when performed appropriately and help to restore more normal joint motion in patients that have OA. The objective is to advance the joint through a comfortable range of motion. At no time should the patient experience discomfort from strenuous manipulation of the limb, because this can lead to reflex inhibition, limited use of the limb, fibrosis, and, ultimately, delayed return to function.[84] In many cases, analgesics are administered before PROM therapy to improve patient comfort. The patient should be muzzled before any manipulations.[80]

During PROM therapy, the therapist moves the joints without effort on the part of the patient (**Fig. 2**). It is intended to maintain normal range of motion in joints, prevent contracture, improve blood and lymphatic circulation, and stimulate sensory

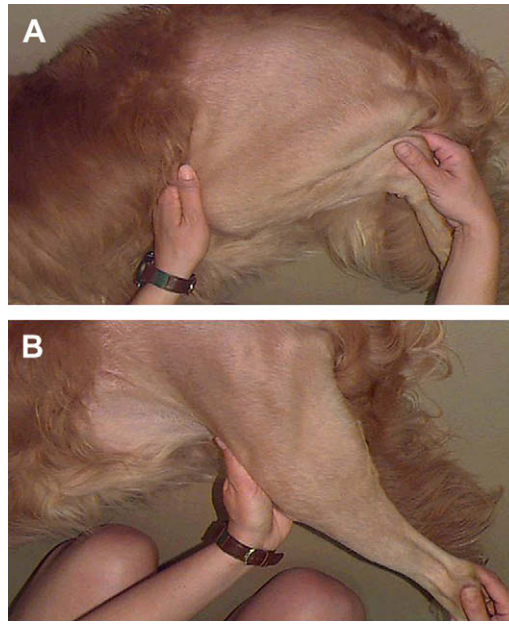


**Fig. 2.** PROM of the left stifle. The limb is placed in flexion (*A*) and extension (*B*).

awareness. Passive motion has been shown to reduce the catabolic effects of immobility on articular cartilage.[95,97] PROM therapy is commonly used whenever a patient has a lack of motor control or is unwilling to use the limb because of pain. The therapist moves a joint through an unrestricted pain-free motion for 10 to 15 repetitions two to three times a day.[98] It is important that passive motion be performed slowly with the muscles relaxed. The joint is grasped on either side and gently manipulated until the desired flexion or extension angle is reached.[85] After treatment of the individual joints, the entire limb is moved through a range of motion similar to that of ambulation for a minimum of 10 times.[95] A recent study by Crook and colleagues[83] evaluated the effect of passive stretching on the range of motion in osteoarthritic joints of 10 Labrador retrievers. After 21 days of passive stretching (10 repetitions performed twice daily), the range of motion in the affected joints was significantly increased.

### *Stretching Exercises*

Stretching exercises are used to increase tissue extensibility and are performed several times daily after the application of moist heat or therapeutic ultrasound therapy. The muscles are stretched and held for 10 to 30 seconds. This procedure is repeated 10 times during each session.[95,96]

### *Balance and Proprioception Exercises*

Balance exercises focus on weight shifting and are performed several times daily when possible.[95] This can be achieved by moving the standing patient, such that weight is shifted from limb to limb. Alternatively, the therapist can encourage weight shifting by exercising the patient on an uneven surface. Commonly, rocker boards are used to improve balance and proprioception.[81,87]

### *Massage Therapy*

Massage therapy is often combined with other therapeutic techniques. Massage is used to increase arterial, venous, and lymphatic flow; to stretch and breakdown adhesions; to provide muscle relaxation; and to produce analgesia. Massage has no effect on muscle mass, strength, or rate of atrophy.[99] The five components of massage are rhythm, rate, pressure, direction, and frequency. The rhythm should be even. If the intent is to improve circulation, reduce edema, and provide relaxation, the rate should be slow.[100] The rate is increased when friction massage is used to loosen adhesions and break down fibrin clots in deeper structures. The appropriate pressure applied during massage also varies. Light to moderate pressure is used to achieve relaxation or reduce edema. Firmer pressures are used in frictional massage. Pressure also varies over the course of a massage, beginning with light pressure and proceeding to moderate pressure at the end of the session.[101]

There are many types of massage. Two commonly performed techniques in dogs are effleurage and pétrissage.[82,89] Effleurage is performed by running the hands gently over the surface of the skin beginning distally and moving toward the heart. The therapist maintains light contact with the skin, allowing the skin to glide gently over the underlying fascia, which reduces adhesions.[100] Pétrissage is performed by lifting and kneading the soft tissues and rhythmically squeezing the deeper muscles. Intermittently, small circles are made with the heel of the hands at a moderate rate with increasing pressure.[101] A massage session may last 10 to 20 minutes, beginning with effleurage and proceeding to pétrissage. After pétrissage, effleurage is again used to aid in blood and lymph flow from the treated area. Therapy may be performed every 24 to 48 hours.

### *Therapeutic Ultrasound*

Therapeutic ultrasound can be used if heating of deeper tissues is required to help control pain and improve tissue extensibility. The sounds waves are converted to heat as they are absorbed in the muscles.[101] A depth of 5 cm can be reached, causing an elevation in temperature to 40°C to 45°C. Ultrasound is also thought to promote healing by stimulating fibroblastic activity, increasing cellular metabolism, improving circulation, and increasing the strength and pliability of tendons.[95] Nonthermal effects include increased cell membrane permeability, calcium transport, removal of blood cells from the interstitial space, and increased phagocytic activity of macrophages.[102,103] Ultrasound is frequently used to treat muscle injuries and OA and can be delivered at 1 MHz or 3 MHz.[81] The 1-MHz probe penetrates 3 to 5 cm and is used for deep tissues, primarily muscle. The 3-MHz probe achieves only superficial penetration and is used over bony areas. The units have a continuous mode and a pulsed mode.[93]

Ultrasound therapy begins by clipping the area and applying gel to promote ultrasound transmission. Various protocols may be used, depending on the condition being treated. Typically, pulsed ultrasound is applied (0.5–1.5 W/cm$^2$) to painful areas and continuous ultrasound is applied to stiff joints and muscles two to three times per week.[81]

### *Laser*

Application of laser (light amplification of stimulated emission of radiation) energy in the red and near-infrared light regions may help to reduce pain and inflammation.[96] It has been shown to be effective in controlling OA pain without side effects.[104] The laser probe is held directly over the painful region. The number of joules applied depends on the size of the area and the condition being treated.

### *Electrical Stimulation*

Electrical stimulators are used to increase muscle strength, improve joint range of motion, re-educate muscles, and decrease edema and pain.[105] The stimulator can be pulsed alternating current (biphasic) or pulsed direct current (monophasic). Transcutaneous electrical nerve stimulation (TENS) is used to treat the area of pain and to combat muscle atrophy.[96] One electrode is placed over the motor point of the muscle, and the other is placed along the muscle belly, after shaving the appropriate sites (**Fig. 3**). Typically, treatments last 20 to 30 minutes.[82]

The neuromuscular stimulator can be set with a specific frequency (hertz, pulses per second), amplitude, and pulse duration. The amplitude and the duration of the pulse should be adjusted to make the workout more comfortable for the patient. The location of the electrodes on the skin is marked so that they can be placed in the same location for each treatment. Research has shown that at a frequency of 50 pulses per second at a duration of 175 microseconds, a muscle may contract up to 50% of the normal isometric contraction.[106] Often, the stimulator is set so that the muscle contracts for 10 seconds and relaxes for 50 seconds (duty cycle), for a total of 10 cycles.[95] The optimal duty cycle depends on the condition being treated, however. One study found that neuromuscular stimulation effectively promoted an early return to function and reduced the amount of OA in dogs undergoing cranial cruciate repair.[107,108] This study used 35 pulses per second at 250 microseconds with a duty cycle of 12 seconds on and 25 seconds off for 30 minutes, 3 seconds ramp up, and 2 seconds ramp down.

### *Active Exercise*

Active exercise improves muscular strength, endurance, cardiovascular function, and coordination while reducing joint stiffness and muscle atrophy.[81,82,87,109] It also helps to control body weight. Exercise also provides periodic cartilage loading, which may increase cartilage metabolism and synthesis of proteoglycans.[85,109] Low-impact exercises are preferred, such as leash walking, treadmill walking, jogging, swimming, or climbing stairs or ramps.[81,87] Initially, several shorter sessions (three 20-minute periods) are preferred over a single long session.[87] At first, exercise may be accomplished using active assisted exercise, in which the therapist assists the patient to overcome the force of gravity. Slings, harnesses, ''towel walking,'' or aquatic therapy is commonly used.

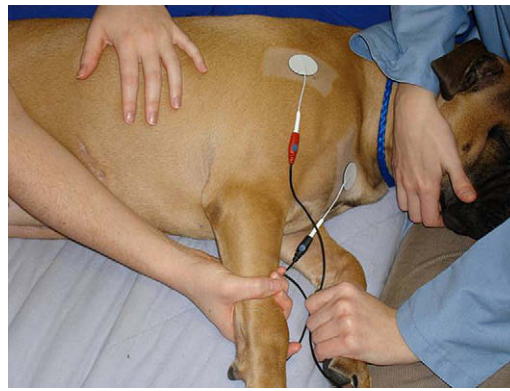

**Fig. 3.** Electrical stimulator is applied to a dog's right front limb to treat the shoulder.

Aquatic therapy is a special form of active exercise and was developed to help reduce the amount of weight that the patient supports during activity. The amount of weight bearing can be adjusted by varying the depth of the water in which the animal is placed. A water depth to the patient's midthorax promotes walking, whereas deeper water encourages swimming.[89] Swimming promotes the use of all limbs, whereas buoyancy permits mass muscle movement patterns that have instinctively low synaptic resistance pathways in the central nervous system.[110] Underwater treadmills are an increasingly common form of aquatic therapy and can be used for walking and swimming exercises.[87] If the water depth reaches the level of the greater trochanter, the weight borne by the dog is reduced by more than 50%.[96] The speed of the treadmill is typically set at 0.5 to 5 mph. Aquatic therapy using an underwater treadmill enhances cardiovascular endurance, improves muscle strength, reduces pain, and improves balance and range of motion.[87] The patient must be monitored closely during aquatic therapy to prevent exhaustion and hyperthermia.[82]

Active resistive exercises, in which the patient is required to perform specific tasks, are used to restore the animal's strength, stamina, and coordination. Examples include sit-stand exercises, wheelbarrowing, dancing, and approximation.[82,85,87] Approximation involves applying downward pressure over the limbs as the animal is standing, approximating the forces generated while walking. Figure-of-eight exercises may be used to develop medial leg muscles. Other resistive exercises include the use of a physioball to strengthen the forelimbs or hind limbs, and cavaletti rails to improve range of motion and proprioception (**Fig. 4**).[96] Stair climbing and leash walks are also useful resistive exercises and can be gradually increased in duration as the patient improves.

### *Therapy Monitoring*

Rehabilitation programs are customized for individual patients and should be designed to encourage increased weight bearing, to enlarge muscle mass, and to reduce body fat, thereby breaking the cycle of disuse often seen in patients that

**Fig. 4.** Patient uses a physioball for active resistance therapy.

have OA.[82,85,87] It is important to maintain a consistent level of activity on a daily basis and to avoid intermittent bursts of activity surrounded by long periods of rest.[80,87] The program should be monitored regularly to determine the efficacy of treatment. Monitoring may include subjective and objective observations, such as goniometric assessment of range of motion, measurement of limb circumference (girth) to assess muscle mass, lameness scoring, documenting changes in muscle mass using CT, dual-energy x-ray absorptiometry (DEXA) analysis, and force plate gait analysis.[82]

**APPENDIX**

***Evidence-Based Classification from Aragon and Colleagues[13]***

***Study design rating***

Type I: randomized controlled interventional trials
Type II: prospective observational cohort studies
Type III: nonrandomized intervention trials with concurrent or historical controls, or case-control studies
Type IV: cross-sectional studies or analyses of secondary disease end points in intervention trials or case series

***Quality factor rating***

\+ study has adequately addressed the issues of scientific quality relating to data collection, analysis, inclusion and exclusion, bias, and generalizability
ø some uncertainties exist relating to the scientific quality
− study has not adequately addressed issues of scientific quality

The total body of evidence rating[13] is a rating given on a combined evaluation of quantity, consistency, and relevance to disease risk reduction (RDRR), with each ranked according to the following criteria:

Quantity

*** numbers of studies (type I, type II, and + only) and individuals tested are sufficiently large enough to generalize comfortably to the target population
** sufficient numbers of studies and individuals, but uncertainties remain regarding generalizing
* numbers of studies and individuals are insufficient for generalization

Consistency

*** sufficient numbers of studies of high quality (+) that are type I or II studies and have consistent results
** moderate consistency across all study types
* results are inconsistent

RDRR

*** magnitude of the effect observed in the studies (type I, type II, and + only) is physiologically meaningful and achievable
** some suggestion that the effect is physiologically meaningful and achievable
* magnitude of the effect in the studies is not likely to be physiologically meaningful or achievable

Strength of evidence ranking

High level of comfort: indicates that qualified scientists agree that a specific claim is scientifically valid. This highest level of ranking indicates an extremely low level of

probability of new scientific data overturning the conclusion that the relation in question is valid or significant. This rank is based on relevant high-quality studies of study design types I and II with sufficient numbers of individuals, resulting in a high degree of confidence that the results are relevant to the target population.

Moderate level of comfort: indicates that a relation is promising but not definitive. The claim is based on relevant high- to moderate-quality studies of study design type III and higher and sufficient numbers, resulting in a moderate degree of confidence that the results could be extrapolated to the target population.

Low level of comfort: ranking indicates a low consistency. The relation is based on moderate- to low-quality studies of study design type III and insufficient numbers of individuals tested, resulting in a low degree of confidence that the results could be extrapolated. Uncertainties exist as to whether the proposed benefits would be physiologically meaningful and achievable.

Extremely low level of comfort: ranking indicates extremely low consistency. The relation is based on moderate- to low-quality studies of design type III and insufficient numbers, resulting in an extremely low degree of confidence that the results could be extrapolated.

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