

# NON SURGICAL OSTEOARTHRITIS MANAGEMENT IN ANIMALS

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The most common form of arthritis in animals is osteoarthritis. Osteoarthritis is the #1 cause of lameness and chronic pain in animals. It's estimated that 20% of dogs over 1 year of age suffer from osteoarthritis and 90% of cats over 9 years of age have some form of osteoarthritis. The pathophysiology of OA involves a vicious cycle that is initiated by stress or damage to chondrocytes (cartilage cells). Most often, this stress is caused by trauma, developmental orthopedic diseases, or normal wear on abnormal joints or abnormal wear on normal joints. While NSAIDs and EPA-rich diets can help reduce inflammation, damaged chondrocytes up-regulate enzymes that cause cartilage degradation (aggrecanase enzymes), even in the absence of inflammation. So although patients are more comfortable, the cycle continues. Unless the vicious cycle can be interrupted, further degradation to cartilage causes damage to the cartilage matrix (infrastructure) and eventually leads to structural and functional failure of the joint. This discussion will focus on non-surgical modalities to manage dogs and cats with osteoarthritis.

The objectives that we will achieve today are to provide an overview of the multimodal approach to OA and:

- Discuss a case based approach to managing OA
- Outline the advantages of the multimodal approach for your patients
- Share tips on how to incorporate the approach into your practice
- Generate discussion and answer any questions you may have

It was once thought that OA was simply a result of wear and tear on the joint. We now know that it actually involves the interaction of a complex set of predisposing factors along with a patient's inability to repair joint damage.

For dogs, joint pain is the essential problem associated with OA. The synovium and subchondral bone are the major sources of OA joint pain; however, pain can also arise from ligaments, menisci, periarticular muscles, and the joint capsule. Eventually, OA involves *all* joint tissues, including the tendons, nerves, and blood vessels.

We now know that pain transmission involves multiple pathways, mechanisms, and transmitter systems. So it makes sense that a single class of drugs or a single therapeutic technique is not likely to provide complete analgesia. Clinical experience also proves this. To control perioperative pain, it's common to use two or more classes of drugs to provide more effective analgesia. The same theory can apply to managing OA pain: By combining analgesics with noncompetitive modes of action, we can produce a synergistic effect. The result? We can use smaller doses of these drugs and reduce the likelihood of adverse effects.

A multimodal approach to managing canine osteoarthritis and its associated pain and inflammation is rapidly becoming the new standard of care for several reasons:

First, chronic pain arises from a complex network of pathways, just as acute pain does. We now accept that effective control of post-surgical pain requires multiple blocking strategies and therapeutic techniques. Since OA pain processing is more complex than post-surgical pain, use of a multimodal approach to OA pain management is a reasonable conclusion.

Next, we want to avoid windup of the central nervous system through hypersensitization of the spinal cord's dorsal horn. Central nervous system hypersensitization and windup can lead to hyperalgesia, a pain state that is difficult to manage and reduces our patients' quality of life.

Finally, multimodal management of OA allows you to obtain the best possible results from the labeled doses of the analgesics used.

A multimodal approach to OA management incorporates both medical and nonmedical modalities to achieve therapeutic goals.

The medical component combines the use of a nonsteroidal anti-inflammatory drug (NSAID), a chondroprotectant (commonly referred to as a disease-modifying OA drug), and adjunct therapies, including

multimodal pain management as necessary (possible use of drugs in other classes).

The non-medical component includes weight management, exercise, a diet rich in the omega-3 fatty acid (EPA), physical rehabilitation, and new technologies, such as stem cell therapy.

For most dogs with OA, appropriate case management will involve a combination of these modalities in a program that is tailored to the specific dog and its owner. This is the best way to achieve success and can provide years of quality life for dogs with OA.

A multimodal OA treatment plan allows the veterinary healthcare team to achieve several therapeutic goals, including:

- Better control of pain and discomfort
- Reduction in drug dosages
- Mitigation of clinical signs of OA
- Slowing of progression of the underlying disease processes
- Promotion of repair of damaged tissue
- Improvement in strength, range of motion, and fitness

The multimodal approach to OA incorporates multiple treatment options as needed:

- NSAID to control pain and inflammation
- Chondroprotectant to safeguard and support cartilage and connective tissues
- An EPA-rich diet, which has been clinically proven to help improve joint health
- Weight control and exercise to avoid excessive stress on joints
- Adjunctive therapies to support the primary tools for managing pain and stiffness
- Physical rehabilitation to optimize comfort and mobility

It is important to recognize that all components of a multimodal approach to canine OA management may not be used every day for the remainder of a dog's life. Rather, some elements will be used initially or for a short time, while other components will ideally become part of the dog's and owner's daily routine.

The first component of multimodal involves an NSAID. When considering which NSAID to dispense, three categories of factors must be considered: drug, patient, and client. Drug-specific factors such as safety and efficacy are obvious considerations, but the availability of a specific drug in multiple formulations, flexibility in dosing, and palatability are also worth considering. Patient-specific factors, such as liver or kidney disease, concurrent medications, or previous NSAID intolerance, should also be factored into the decision-making process. Finally, client-specific factors, including an owner's ability to administer the medication and the cost of the medication, will influence your selection.

One option that can help us avoid potential side effects is to decrease the dosage of the medication to the lowest effective dose. This is especially true when a drug is used as part of multimodal therapy.

Be sure to ask your representative for the company's latest FDA-approved dosing charts if you use these drugs, and make sure you manually calculate the dose yourself for every weight of dog that is not specifically identified on the chart. Only two NSAIDs can offer specific dosing for most weight ranges. Metacam (meloxicam) can dose every dog accurately at a dose of 0.1 mg/kg PO q24h. However, Metacam does not have a flexible dosing range. Deramaxx (deracoxib) is the *only* tablet that can accurately dose every dog from 15 to 225 lb with a whole or half-tablet, and it is the *only* NSAID with an FDA-approved dosing range, meaning you can start at a dose that has been proven safe and you can titrate down to a dose that has been proven efficacious. No other NSAID can provide this flexibility.

It is also important to recognize that one NSAID may produce side effects in an individual dog, but another NSAID may not. In human medicine, it is common to try a different NSAID if the patient does not respond to the first one or experiences side effects. This strategy may work for some canine OA patients—provided that an appropriate washout period is observed when switching from one NSAID to another.

And finally, be sure to review the product labels of all the NSAIDs you prescribe. Don't assume you know what is on the label. Because NSAIDs are so commonly used in practice today, many veterinarians

don't review the product labels of the newer NSAIDs and mistakenly assume that all NSAIDs are the same.

Concurrent use of another NSAID (including aspirin) or steroid should be avoided. Concurrent administration of two NSAIDs or an NSAID and a steroid such as prednisone increases the patient's risk for an adverse reaction.

Ask the owner if the dog is taking any other supplements, including omega-3 fatty acids, glucosamine, chondroitin sulfate, or other nutraceuticals. During the initial NSAID trial period, it may be best to discontinue these medications so you can more clearly determine the effects of the NSAID as well as whether the other medications are still needed.

A 2-week trial period can be helpful in determining how a particular patient will respond to a given NSAID before settling on a specific drug for long-term pain management. Ask your pharmaceutical company sales representatives if the company offers trial samples that you can provide to owners of dogs with OA. These samples give you an opportunity to evaluate how your patient responds to a particular NSAID.

Don't forget that owners need to be educated about the potential side effects of these medications. Be sure to tell clients which physical signs suggest improvement or intolerance and encourage them to watch for those signs. Have one of your technicians follow up with the client by telephone 1 or 2 days after the appointment to assess how the dispensed NSAID is being tolerated.

Be sure to provide clients with an information sheet and review it with them. Since clients may only retain a small amount of what they are told in the clinic, the client information sheet can help remind them of your instructions on dosing and potential side effects.

While NSAIDs enable us to provide our patients with fast pain relief, the addition of another modality, such as a therapeutic food for arthritis, can help enhance joint function and mobility. As the benefits of the food take effect, it may allow us to reduce the NSAID dose required for pain relief. Today, there are a number of canine therapeutic foods for arthritis on the market, including Purina Veterinary Diets® JM Joint Mobility- Canine Formula, Hill's® Prescription Diet® j/d® Canine and Royal Canin- Mobility Support JS 21™ .

Only 1 is supported by published peer reviewed clinical trials in client owned dogs with naturally occurring disease; Hill's j/d canine

Inflammation plays a key role in the pathophysiology of OA. NSAIDs work by interfering with the production of inflammatory mediators from arachidonic acid. However, there are also effective non-pharmacologic mechanisms of reducing inflammation, such as EPA-rich diets.

Arachidonic acid and EPA act as precursors for the synthesis of mediators of inflammation. The amounts and types of eicosanoids synthesized are determined by the availability of the fatty acid precursor. In most conditions, the principal precursor for these compounds is arachidonic acid, although EPA competes with arachidonic acid for the same enzyme systems. The eicosanoids produced from arachidonic acid are proinflammatory and, when produced in excess amounts, may result in pathologic conditions.

In contrast, eicosanoids derived from EPA promote minimal to no inflammatory activity. Ingestion of foods containing high levels of omega-3 fatty acids results in a decrease in membrane arachidonic acid levels because omega-3 fatty acids replace arachidonic acid in the substrate pool. This produces an accompanying decrease in the capacity to synthesize eicosanoids from arachidonic acid. Studies have documented that inflammatory eicosanoids produced from arachidonic acid are depressed when dogs consume foods with high levels of omega-3 fatty acids.

Clinical studies document that dogs receiving a therapeutic arthritis food (Canine j/d®) were able to decrease the dose of NSAIDs by an average of 25%.

In addition to controlling inflammation, EPA plays a role in interrupting cartilage degradation by inhibiting degradative enzymes that break down cartilage matrix components. This is part of the new study of nutrigenomics, or nutrition affecting the genome. High levels of EPA have been shown to inhibit the upregulation of the genes responsible for increasing production of aggrecanase enzymes (degradative enzymes)

The use of Hill's® Prescription Diet® Canine j/d® for the management of OA has been supported by three grade-1 studies, which were randomized, double-blinded, controlled clinical trials using client-owned dogs.

Since the mechanism of action of j/d is high levels of n3 FA, owners may ask if they can simply supplement their dog's current food and get the same effect. There are no studies evaluating the efficacy of supplementing foods and perhaps most importantly, based on the j/d studies, for a 60 lb dog to get the same benefit from n-3 fatty acids supplements they would need to consume 13 GRAMS of total n-3 FA per day.

If an owner chooses to do this with supplements (even an inexpensive one) the cost, in addition to the food they will need to feed, will be ~ \$1,200 per year. More importantly, they will need to get 42 capsules into their 60lb

dog EACH DAY.

For a 60lb dog the recommended amount of Prescription Diet j/d is ~ 4 cups which costs ~ \$2.00 a day, \$60 a month and \$720 a year. Given that there are three Grade 1 studies supporting the use of j/d in dogs with OA and the reduced cost associated with providing n-3 FA in the food, this seems like both the most convenient and effective yet least expensive way to provide relief for dogs suffering with OA.

What about the overweight dog with OA? Will weight loss help?

In one study, 12 moderately overweight to obese dogs participated in a weight loss and exercise program that returned them to optimal body condition. The result was a significant improvement in lameness as assessed by force plate gait analysis and client perceptions. In a second study, researchers showed that in overweight dogs with hind limb lameness secondary to hip OA, weight reduction alone may result in a substantial improvement in clinical lameness.

These studies investigating the relationship between body weight and OA in dogs show that achieving and maintaining dogs in optimal body condition and weight reduces joint stress, enables more exercise, and ultimately leads to better quality of life for our arthritic canine patients.

To help overweight OA patients, we need to think of excess body weight and obesity as a disease and “diagnose” it. Unfortunately, studies show that obesity typically is not diagnosed or, at the very least, is underdiagnosed.

Ideally, every patient that enters a practice’s doors should be weighed. Monitoring and charting body weight can tell us if a dog is gaining or losing weight over time, but it doesn’t really determine whether the dog is too thin or too heavy for its skeletal frame and body type. That’s where body condition scoring can help.

Higher-than-ideal body condition scores can be used to diagnose obesity or excess body weight in patients just as you would use any abnormal laboratory value to aid or confirm the diagnosis of another health condition. Recording a patient’s body condition score in its health record allows you to monitor the pet’s condition over time.

“Prescribing” a therapeutic diet for your obese and overweight patients is another way to help them lose extra weight and allows you to more closely monitor your patients’ condition. It may also enhance practice revenue because, according to a survey of pet owners by Hill’s Pet Nutrition, 91% of pet owners want a pet food recommendation from their veterinarian.

In the past, exercise was often restricted or discouraged for patients with arthritis. We now know that mild to moderate exercise is beneficial for humans and dogs with OA. Exercise can help reduce pain and discomfort and improve overall quality of life. Frequent, mild, weight-bearing exercise over an extended period has also been shown to increase joint mobility and strengthen supporting muscles. It also helps reduce body weight, which helps decrease abnormal forces on joints. It is beneficial to first prescribe an NSAID to relieve the pain and inflammation that may limit exercise.

An exercise program must be tailored for the condition of each patient and each owner. An improper program could hasten the progression of OA. Overloading joints should be minimized by engaging in such activities as walking and swimming until weight loss occurs.

Associations between diet and disease have long been recognized through epidemiological studies.

The study of nutrigenomics provides a comprehensive understanding of the effects of just how diet can effect health and disease. Simply put, nutrigenomics is the study of the effect of nutrients on gene expression, proteins and metabolites.

Obesity is common among dogs in the United States, with 25% to 30% of adult dogs being overweight or obese. In fact, a common clinical presentation is the overweight dog with OA. We know obesity is a major risk factor for OA development in humans and dogs. Adipose tissue, once considered passive energy storage, is now recognized as an important endocrine organ that actively secretes several hormones and many cytokines. Among these cytokines are a host of inflammatory mediators. As fat mass increases, the production of these inflammatory mediators also increases. The result is a chronic, systemic, low-grade inflammation that is thought to exacerbate a variety of chronic inflammatory diseases including OA.

So, what does this mean for the overweight dog? A growing body of research suggests that changes in adipokine secretion provide the link between excess body weight and chronic health conditions, including canine OA.

Weight management and exercise are two of the most important lifestyle changes to implement as part of a multimodal OA management program, especially in the early stages of the disease. They are among the least expensive components of a multimodal OA management program.

As is always the case, an ounce of prevention is worth a pound of cure particularly in relation to OA since

obesity is a significant risk factor for OA in both humans and dogs. There is strong evidence from a prospective, randomized study that a lifetime of calorie restriction and maintenance of a lean body condition will delay the onset of radiographic evidence of OA in genetically similar dogs and the % of dogs requiring therapy for OA over their entire life span (50% vs 83%). In this study, over the life-span of these dogs, the median age of radiographic evidence of CHD/OA was significantly lower (6 years) in overweight vs. normal weight dogs (12 years).

The next component of a multimodal approach is disease-modifying OA drugs (or DMOADs), sometimes referred to as chondroprotectants. Hyaline cartilage has a limited ability to repair itself, so once lost, joint cartilage cannot be replaced or restored to its original condition. This makes cartilage preservation important to joint health and has spurred the search for a therapy or drug that can slow the progressive destruction of cartilage during OA.

Increasingly, veterinarians are recommending agents that may modify articular cartilage, synovial fluid, and the synovium of affected joints. Included in this group are parenterally administered polysulfated glycosaminoglycans (PSGAGs), pentosan polysulfate, and hyaluronic acid.

Although the exact mechanism of action is unknown, chondroprotectants are thought to encourage cartilage matrix synthesis, decrease the activity of degradative enzymes, and improve synovial fluid quality—all of which are beneficial for OA patients. However, it is essential to have viable cartilage present in the joint for these agents to exert their optimal effects, so using a chondroprotectant in the early stage of the disease is key.

In the United States, only one DMOAD is approved by the FDA\* for use in dogs: Adequan® Canine. Adequan® Canine contains PSGAG, primarily chondroitin sulfate that has a higher sulfur content to make this molecule more effective at inhibiting enzymatic activity. This agent is anti-inflammatory and *inhibits* enzymes that degrade glycosaminoglycans and hyaluronic acid (HA) within the joint. PSGAG increases concentrations of synovial fluid HA and inhibits complement activation, enzyme release from leukocytes, prostaglandin E<sub>2</sub>, and toxic oxygen radical synthesis.

Dogs of any age can develop OA and could benefit from the joint cartilage protection offered by PSGAG. Addressing joint cartilage health early in the disease process may help delay the need for additional drug therapy.

Studies have found that regardless of the surgical technique used to repair a ruptured cranial cruciate ligament, OA will likely progress. Many orthopedic surgeons have made PSGAG part of their postsurgical protocols because PSGAG treats the signs of traumatic arthritis that can occur after surgery, which helps those patients heal and get back on their feet. Certain drug therapies, including NSAIDs, may be contraindicated in some patients. PSGAG may help these patients by addressing the underlying causes of OA, which can improve comfort and mobility.

The lining of the joint capsule (intima) is normally only two cells thick, beneath which are free nerve endings (nociceptors). During the OA process, inflammatory mediators (metalloproteinases) are released into the joint fluid. It is, therefore, intuitive that the disease is painful, recognizing that inflammatory mediators are only two cells removed from free nerve endings. Since Adequan moderates the level of these inflammatory mediators, it is also intuitive that Adequan has an analgesic feature. Still, it's important to remember that the degenerative effects of hip dysplasia or any other kind of joint laxity can progress rapidly. That's why treatment is more likely to be effective when started *early* in the disease process.

Because OA of a single joint can lead to multiple joint disease through inactivity, physical rehabilitation is fast becoming an essential component of a multimodal approach to managing OA patients. Physical rehabilitation is a term used to define a broad spectrum of techniques from simple to complex. These treatments are used to address the secondary effects of OA, including loss of muscle strength and range of motion, while improving quality of life. The benefits of physical rehabilitation may include:

- Reduced joint pain and inflammation
- Increased joint range of motion
- Improved strength and balance
- Decreased muscle spasms
- More normal joint function
- Improved quality of movement

Sending clients home with a handout that describes how to incorporate specific physical rehabilitation methods will enhance at-home care and aid compliance.

A number of physical rehabilitation methods can be incorporated into a multimodal treatment plan.

Passive range-of-motion exercises help restore normal joint motion. The goal is to move the affected joint through an unrestricted, pain-free range of motion without effort on the part of the patient. This passive joint movement may help improve blood and lymphatic circulation and stimulate sensory awareness.

Stretching exercises are used after moist heat or therapeutic ultrasound therapy to increase tissue extensibility. Balance exercises focus on weight shifting to improve balance and proprioception. Massage involves applying comfortable pressure to tissues around affected joints. It can produce analgesia, improve blood and lymphatic circulation, loosen and break down adhesions, and relax muscles.

Therapeutic ultrasound can be used to heat deep tissues to help control pain and improve tissue extensibility. Sound waves are converted to heat as they are absorbed by muscles. Ultrasound is thought to promote healing by stimulating fibroblast activity, increasing cell metabolism, improving circulation, and increasing the strength and pliability of tendons.

Electrical stimulation agitates nerve endings in the affected area to control pain and help retrain muscles weakened by lack of exercise. It also can help improve joint range of motion and decrease edema.

Active exercise—leash walking, treadmill walking, jogging, swimming, and aquatic therapy—improves muscle strength, endurance, cardiovascular function, and coordination while reducing joint stiffness and muscle atrophy. It also helps control body weight.

Recommending a multimodal approach to OA is only half the challenge to achieving success; the other half is gaining client acceptance and compliance. In summary, let's look at steps you can take to help your clients understand your recommendations and ultimately to help your arthritic patients.

When discussing canine OA management with your clients:

- Provide specific, coherent, and consistent recommendations with conviction
- Deliver your recommendations both verbally and in writing
- Set appropriate expectations for the dog's improvement
- Stress the need for and the importance of progress or recheck examinations
- Establish clear expectations for the client of the financial obligations

The bottom line is to make it as easy as possible for your client to say yes to providing a high standard of care for your patient(s).