Chapter 34

# Nutritional Management of Osteoarthritis

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*"I don't deserve this award,*
*but I have arthritis and I don't deserve that either."*
*Jack Benny*

## CLINICAL IMPORTANCE

Osteoarthritis, also referred to as degenerative joint disease, is a chronic, progressive disease characterized by pathologic changes of movable joints and clinical signs of pain and dysfunction. Osteoarthritis is associated with degeneration of articular cartilage and loss of proteoglycan and collagen, proliferation of new bone and a variable inflammatory response. In the United Kingdom, osteoarthritis is the most commonly observed nontraumatic orthopedic condition of dogs (Clements et al, 2006). Osteoarthritis has been estimated to affect up to 20% of dogs over one year of age in the United States.[a] This finding is supported by the fact that osteoarthritis was in the top 10 most common medical conditions reported in a 2006 survey of insurance claims in the United States.[b] The most common risk factors for osteoarthritis in dogs are developmental orthopedic diseases, trauma including cruciate ligament rupture and obesity.

The extent to which the general population of cats is affected by osteoarthritis is unknown but the disease is thought to be common. Radiographic surveys suggest that approximately 20% of cats older than one year may be affected (Godfrey, 2005). In a study of 100 well cared for cats over 12 years of age, 90% had radiographic evidence of osteoarthritis (Hardie et al, 2002). The most common sites of radiographic osteoarthritis in cats are the elbow, vertebral column and hips. In addition to age, obesity appears to be a risk factor.

Because osteoarthritis is a heterogeneous disease with diverse origins, it can present with a range of clinical manifestations. As a result, therapeutic recommendations should be customized for each patient. When appropriate, surgical correction of underlying conditions should be considered. After osteoarthritis is diagnosed, clients should be educated to foster realistic expectations. Osteoarthritis is usually irreversible but good management can minimize pain and slow progression of the disease. The goals of management include: 1) mitigation of risk factors, 2) controlling clinical signs and 3) slowing progression of the disease. Thus, effective treatment requires a multifaceted approach, of which therapeutic nutrition is an important component (**Figure 34-1**). Foods designed for patients with osteoarthritis should supply age-appropriate nutrition and specific nutrients that may help reduce inflammation and pain, slow the degradative process, complement prescribed medications and provide tangible improvement in clinical signs.

## PATIENT ASSESSMENT

### History and Physical Examination

Osteoarthritis in dogs and cats tends to be slowly progressive and clinical signs are often subtle early in the course of the disease. As a result, many owners are unaware that a problem exists or may attribute changes in their pet's behavior to normal

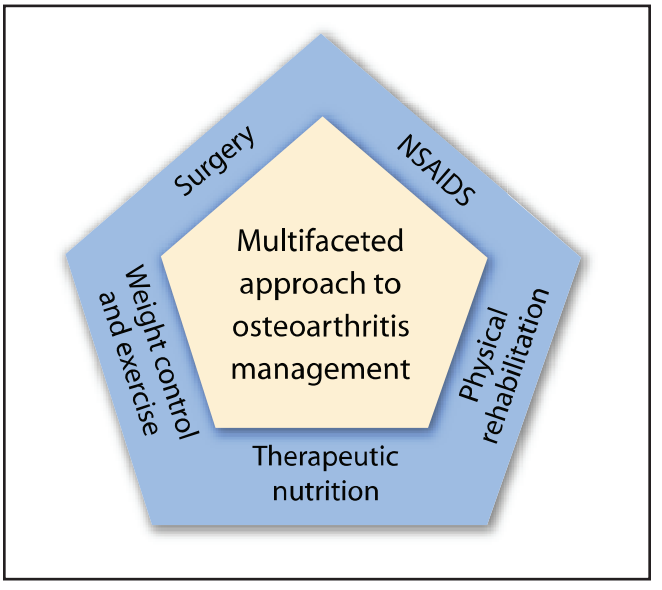


**Figure 34-1.** Treatment for osteoarthritis includes surgical correction, nonsteroidal antiinflammatory drugs (NSAIDs), physical rehabilitation, therapeutic nutrition and weight control and exercise. Most patients will benefit from a combination of these treatment options.

aging. Careful evaluation of pets whose owners report changes typically attributed to aging is warranted. Obtaining a complete history is important. The use of an owner questionnaire may facilitate recognition of these subtle changes (**Figure 34-2**) (Hielm-Bjorkman et al, 2003).

In dogs, clinical signs of osteoarthritis include reluctance to walk, run, use stairs, jump or play. Owners may also notice other signs including difficulty rising from rest, stiffness or lameness. They may describe their dog as lagging behind on walks or having decreased mobility that is attributed to age. Generally, signs of lameness are described as intermittent and progressive. Typically lameness or stiffness is worse after rest and improves with activity. The time it takes for activity to improve lameness or stiffness in affected dogs will frequently increase as the disease progresses. Pain is often difficult to assess and owners may be unaware of it unless a dog vocalizes (e.g., yelping or whimpering). Personality changes such as withdrawal or aggressive behavior may also be symptomatic of pain.

Clinical signs of osteoarthritis in cats are even more elusive. Most cats with osteoarthritis do not exhibit localizing lameness (Clarke and Bennett, 2006). The most common clinical signs are reduced activity and reluctance and/or inability to jump on or off elevated surfaces or travel up and down stairs. The inability to perform these activities may be related to the most common sites of osteoarthritis, which include elbows, vertebral column and hips. Many owners do not recognize decreased activity as problematic. Furthermore, if jumping or using stairs is not a normal part of a cat's daily routine its owners may not appreciate any abnormalities (Roe, 2006). Other behavioral changes that may be related to osteoarthritis include incomplete grooming, inappropriate elimination and aggression (Hardie, 1997). If

**Circle the index score that best represents your dog's behavior or locomotion.**

**1. Rate your dog's mood.**

| Very alert | Alert | Neither alert nor indifferent | Indifferent | Very indifferent |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**2. Rate your dog's willingness to participate in play.**

| Very willingly | Willingly | Reluctantly | Very reluctantly | Does not participate at all |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**3. Rate your dog's vocalization (audible complaining, such as whining or crying out).**

| Never | Hardly ever | Sometimes | Often | Very often |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**4. Rate your dog's willingness to walk.**

| Very willingly | Willingly | Reluctantly | Very reluctantly | Does not participate in action at all |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**5. Rate your dog's willingness to trot.**

| Very willingly | Willingly | Reluctantly | Very reluctantly | Does not participate at all |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**6. Rate your dog's willingness to run.**

| Very willingly | Willingly | Reluctantly | Very reluctantly | Does not participate at all |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**7. Rate your dog's willingness to jump.**

| Very willingly | Willingly | Reluctantly | Very reluctantly | Does not participate at all |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**8. Rate your dog's ease in lying down.**

| With great ease | Easily | Neither easily nor with difficulty | With difficulty | With great difficulty |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**9. Rate your dog's ease in rising from lying down.**

| With great ease | Easily | Neither easily nor with difficulty | With difficulty | With great difficulty |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**10. Rate your dog's ease of movement after a long rest.**

| Never difficult | Hardly ever difficult | Sometimes difficult | Often difficult | Very often difficult |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**11. Rate your dog's ease of movement after major activity or heavy exercise.**

| Never difficult | Hardly ever difficult | Sometimes difficult | Often difficult | Very often difficult |
|---|---|---|---|---|
| 0 | 1 | 2 | 3 | 4 |

**Figure 34-2.** Osteoarthritis pain assessment questionnaire. Dogs with total index scores greater than six are presumed to have chronic pain. (Adapted from Hielm-Björkman AK, Kuusela E, Liman KE, et al. Evaluation of methods for assessment of pain associated with chronic osteoarthritis in dogs. Journal of the American Veterinary Medical Association 2003; 222(11): 1552-1558.)

mobility and flexibility are reduced, cats may be unable to groom completely and be either unable or unwilling to navigate stairs to reach the litter box or to enter litter boxes with tall sides. Stroking or combing over arthritic joints may be painful. Some cats may resent this type of attention and even demonstrate aggression as a result of pain (Overall et al, 2005). **Table 34-1** summarizes common clinical signs for dogs and cats (Beale, 2004).

Physical examination should include neurologic assessment and a thorough orthopedic examination. Joints, muscles, tendons, ligaments and long bones should be palpated for evidence of swelling, heat or pain. Joints should be assessed for crepitus, range of motion, collateral stress, abduction and adduction (instability). Muscle atrophy, hypertrophy or asymmetry should be noted because these findings may indicate the most clinically affected joint.

## Radiography

Diagnosis of osteoarthritis generally requires a combination of history, physical examination findings and radiographic evidence. Clinical and radiographic signs of osteoarthritis are not always congruent. In one study, as few as 33% of cats with radiographic evidence of osteoarthritis also had clinical signs (Godfrey, 2005). In dogs, a study designed to evaluate the relationship between limb function and radiography of stifle osteoarthritis found that radiographic evidence of osteoarthritis did not correlate with clinical function (Gordon et al, 2003). Because the earliest changes in osteoarthritis occur at the level of the articular cartilage, and radiographs do not accurately assess this structure, changes may not be detected early in the course of the disease. As osteoarthritis progresses, typical radiographic changes include evidence of effusion, osteophytosis and subchondral sclerosis. Intraarticular ossific bodies are seen more commonly in cats. Synovial effusion and thickened periarticular soft tissue occur less commonly in cats than in dogs (Allan, 2000). Collapse of the radiolucent joint space and subchondral osseous cystic lesions may be observed in advanced cases of osteoarthritis.

Bony changes occur relatively late in the disease process and are largely irreversible. Early diagnosis of osteoarthritis by clinical signs and/or radiographic changes is hampered by the insidious onset and relatively silent progression of this disease. As a result, treatment that might prevent further cartilage destruction is often delayed. Recent efforts have concentrated on techniques to allow earlier diagnosis of osteoarthritis. Two methods of early recognition that have received considerable attention are radiographic predictors and biomarkers.

Because canine hip dysplasia (CHD) is one of the most common causes of osteoarthritis in dogs, it has been the focus of multiple studies designed to evaluate early predictors of osteoarthritis. Traditional subjective radiographic evaluations used to predict the presence of CHD include hip-extended radiographs evaluated by criteria established by either the Orthopedic Foundation for Animals (OFA) at two years of age or the British Veterinary Association Kennel Club (BVA/KC) scores at one year of age. Both underestimate the susceptibility to CHD and their use, therefore, has underestimated the development of osteoarthritis in affected populations (Kapatkin et al, 2004). As a result, these screening techniques have not reduced the incidence of CHD in affected populations when used as criteria for breeding selection. Hip joint laxity is a prominent feature of the pathogenesis of CHD; a variety of techniques to measure laxity have been described (Farese et al, 1999; Farese et al, 1998; Fluckiger et al, 1999; Smith et al, 1990; Todhunter et al, 2003). Several of these studies have documented that objective measurements of hip joint laxity such as the distraction index and dorsolateral subluxation score are better predictors of the presence of CHD and subsequent development of osteoarthritis than subjective evaluations. These techniques allow dogs to be evaluated as early as four months of age, which makes them more appropriate as screening tools for breeding populations (Adams et al, 1998; Lust et al, 2001; Smith, 1997; Smith et al, 1993; Smith et al, 2004; Todhunter et al, 2003a). One study evaluated the relationship between the presence of degenerative joint disease and radiographic measures of joint laxity in cats. Cats with increased laxity in the coxofemoral joint detected by objective measurements had an increased risk of osteoarthritis (Langenbach et al, 1998).

**Table 34-1.** Common clinical signs of osteoarthritis (OA).*

| Stage | Dogs | Cats |
|---|---|---|
| Mild OA | Stiffness, decreased activity, limping | Decreased activity |
| Moderate OA | Pain, muscle atrophy, difficulty rising | Reluctance to jump, climb stairs, groom |
| Severe OA | Loss of range of motion, vocalization, crepitus, lethargy, inappetence | Limping, muscle atrophy, inappropriate elimination |

*Adapted from Beale B. Orthopedic problems in geriatric dogs and cats. Veterinary Clinics of North America: Small Animal Practice 2005; 35: 655-674.

## Laboratory Information

Routine complete blood counts, serum biochemistry profiles and urinalyses serve as a baseline for evaluation of overall health. Synovial fluid analysis can help confirm the presence or absence of septic, immune-mediated, acutely traumatic or neoplastic processes (Harari, 1997).

## Biomarkers

Osteoarthritis biomarkers are molecules whose concentrations in a body fluid (synovial fluid, blood or urine) reflect a specific biologic or pathologic process, consequence of a process or a response to therapeutic intervention. Theoretically, biomarkers should be able to detect osteoarthritis at a very early stage. For biomarkers to successfully detect osteoarthritis, they must differentiate between arthritic and non-arthritic joints, be sensitive to change, have low variability and be reproducible. Although several candidates for osteoarthritis biomarkers exist for people, none have been found to be specific. Evaluation of a profile of biomarkers in combination with genetic analysis may prove to be more useful for risk assessment and evaluation of treatment effects (Haq et al, 2003). Most canine studies have examined the association of biomarkers with some aspect of the progression of either experimental or naturally occurring osteoarthritis (Arican et al, 1996; Budsberg and Bartges, 2006; de Rooster et al, 2000; Fujita et al, 2006; Fujita et al, 2005; Innes et al, 2005; Johnson et al, 2002; Matyas et al, 2004; Misumi et al, 2002; Trumble et al, 2004). Two articles have demonstrated changes in biomarkers as an indication of therapeutic intervention success in cats and dogs (Yamka et al, 2006; Yamka et al, 2006a). One obstacle to identifying reliable biomarkers is that most of the cartilage in the body is found in intervertebral disks and costochondral junctions. Joints typically affected by osteoarthritis represent a fraction of the total body cartilage and may develop only subtle biochemical changes in early disease. However, the expanding base of information about osteoarthritis-related biomarkers should positive-

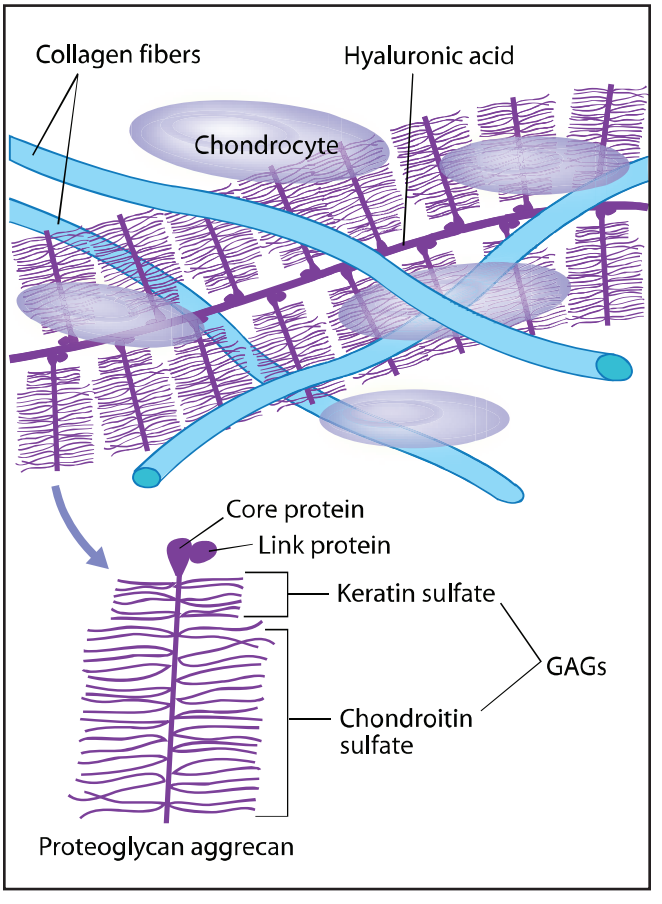


**Figure 34-3.** Microstructure of cartilage. Key: GAGs = glycosaminoglycans. (Adapted from White GW. DVM Best Practices. Nov. 2003.)

ly affect early diagnosis, development of therapeutics and ultimately clinical care.

## Risk Factors

### *Dogs*

Risk factors for developing osteoarthritis include age, breed (large or giant breeds), genetics, developmental orthopedic disease, trauma and obesity. Breeds with the greatest risk tend to be large and fast growing with genetic predispositions for developmental orthopedic diseases. These breeds include German shepherd dogs, rottweilers, Labrador retrievers and golden retrievers (Smith et al, 2001). Developmental orthopedic diseases are a heterogenous group of musculoskeletal disorders of growing dogs that can be affected by nutrition (Chapter 33). CHD, osteochondrosis, elbow dysplasia, fragmented medial coronoid process and ununited anconeal process are common developmental orthopedic diseases that can lead to osteoarthritis. The radiographic prevalence of CHD has been reported to be as high as 70% in golden retrievers and rottweilers (Paster et al, 2005). However, because CHD is a polygenic disease with complex inheritance, environmental factors such as nutrition and lifestyle can have a meaningful influence on its incidence and severity (Smith et al, 2006). Rupture of the cranial cruciate ligament is the most common cause of lameness in dogs and even with surgical correction, the most common traumatic cause of osteoarthritis in dogs (Hayashi et al, 2004; Wilke et al, 2005).

One long-term study documented that the prevalence and severity of osteoarthritis is greater in dogs with body condition scores above normal (Kealy et al, 2000). The mean age at which 50% of the dogs in this study required long-term treatment for clinical signs attributable to osteoarthritis was significantly younger (10.3 years, $p < 0.01$) for the overweight dogs compared to dogs with normal body condition scores (13.3 years) (Kealy et al, 2000). Traditionally, the mechanical stress of excess weight has been thought to be the primary perpetrator of the pathophysiology and progression of osteoarthritis. However, recent studies have documented metabolic activity in adipose tissue that may be of equal or greater importance. Adipocytes secrete several hormones including leptin and adiponectin and produce a diverse range of proteins termed adipokines. Among the currently recognized adipokines are a growing list of mediators of inflammation: tumor necrosis factor-α, interleukin-6, interleukin-8 and interleukin-10. These adipokines are found in human and canine adipocytes (Eisele et al, 2005; Trayhurn and Wood, 2004). Production of these proteins is increased in obesity, suggesting that obesity is a state of chronic low-grade inflammation. Low-grade inflammation may contribute to the pathophysiology of a number of diseases commonly associated with obesity including osteoarthritis. This might explain why relatively small reductions in body weight can result in significant improvement in clinical signs (Burkholder et al, 2000; Impellizeri et al, 2000).

### *Cats*

Overweight cats are reported to be 2.9 times more likely to present for lameness not associated with cat bite abscesses (Scarlett and Donoghue, 1998). In one study, cats older than 12 years were examined for reasons other than lameness. Ninety percent of the radiographs taken documented at least one area of degenerative joint disease (Hardie et al, 2002). Radiographic evidence of osteoarthritis was found in 22% of the general population of cats, greater than one year of age, evaluated at primary care cat clinics in the United Kingdom over a four-year period. The highest incidence of osteoarthritis was found in cats older than 10 years (Godfrey, 2005). In both of these studies, the highest frequency of disease occurred in the elbow, with the vertebral column and stifle being the next most common sites, respectively. One prospective study of osteoarthritis in cats documented the elbow and hip as most commonly affected joints (Clarke and Bennett, 2006). Additional risk factors for osteoarthritis in cats include age-related cartilage degeneration, developmental and traumatic causes of joint instability, chondro-osseous dysplasia of Scottish fold cats, the storage disease mucopolysaccharidosis, nutritional imbalances (hypervitaminosis A), neuropathic diseases (diabetes mellitus) and immune-mediated polyarthritides (Allan, 2000).

## Etiopathogenesis

The normal joint is composed of articular cartilage, subchon-

dral bone, joint capsule and supporting ligaments and tendons. The normal joint provides low friction motion and transfer of body weight across the articular surface during movement. Articular cartilage is made up of chondrocytes and extracellular matrix. Chondrocytes are terminally differentiated cells that are highly metabolically active throughout life (Roush et al, 2002). Normal cartilage is dynamic and is replaced over a one- to two-year period by the balance of the catabolic action of degradative enzymes on the extracellular matrix with the anabolic synthesis of matrix components by chondrocytes.

The extracellular matrix is composed of collagen, proteoglycans and water (**Figure 34-3**). Chondrocytes produce and maintain the extracellular matrix. Collagen fibrils (primarily collagen type II) provide structural support for the cartilage matrix. Proteoglycans are composed of glycosaminoglycan (GAG) chains attached to a central core protein. Chondroitin sulfate, keratin sulfate and dermatan sulfate are the most common GAGs in articular cartilage. Aggrecan is the shortened name for the large aggregating chondroitin sulfate proteoglycan. Aggrecan is the most common and well-defined proteoglycan in articular cartilage and is comprised of a core protein to which as many as 100 GAG chains are attached (Lepine and Hayek, 2001). Because GAGs are anionic and hydrophilic, they attract and hold water in a gel-like consistency. Aggrecans, with their hydrophilic GAGs, are normally contained within the framework of collagen fibrils, which limit their expansion when hydrated.

In the normal joint, cartilage must withstand both compressive and shearing forces. The unique relationship between collagen and proteoglycans provides the biomechanical properties necessary to withstand these forces. Collagen fibrils alone cannot resist compressive forces without collapse but tolerate tensile forces well, whereas hydrated aggrecan complexes weakly resist shear forces but withstand compressive forces (Johnston, 2005). When the normal distribution of collagen, proteoglycans and water is disturbed, the function of articular cartilage is altered, leading to changes typically associated with osteoarthritis.

Normal cartilage metabolism is a highly regulated balance between synthesis and degradation of the various matrix components. Osteoarthritis can be initiated by a variety of physical stresses that damage chondrocytes such as trauma, obesity or developmental orthopedic diseases. Despite the variety of initiating events, there seems to be common pathways that lead to the destruction of articular cartilage (Johnston, 1997). Once initiated, these molecular and cellular pathways interact to form a self-perpetuating cycle.

The instigating event of this cycle is thought to be loss of proteoglycans (aggrecans) (Caterson et al, 2000; Hegemann et al, 2002). Damage to chondrocytes causes up-regulation of catabolic enzymes, particularly aggrecanases (enzymes that cleave aggrecans at specific peptide bonds). This shift from anabolic to catabolic pathways is responsible for the loss of proteoglycans. Damaged chondrocytes also produce inflammatory mediators. Inflammatory cytokines contribute to the perpetuation and progression of arthritis by sustaining catabolic processes (Curtis et al, 2002). Initially, damaged chondrocytes attempt to compensate for this imbalance by producing increased quantities of proteoglycans and collagen. This may lead to an initial thickening of the articular cartilage; however, the quantity and quality of the proteoglycans and collagen produced are abnormal (Renberg, 2005). Eventually aggrecanases destroy proteoglycans faster than new ones can be formed. This imbalance escalates the deterioration of the extracellular matrix and cartilage's normal physiologic properties.

Without a healthy extracellular matrix, cartilage is unable to withstand the compressive forces of weight bearing. The net result is cartilage with decreased load bearing capacity and localized areas of softening (Vaughan-Scott and Taylor, 1997). Fibrillations and microfractures are early histopathologic changes. With progression of osteoarthritis, gross evidence of damage to articular cartilage becomes obvious. The normally smooth glistening surface becomes dull and rough. Fissures become evident and ultimately areas of cartilage erosion develop (**Figure 34-4**) (Renberg, 2005). Osteoarthritis affects not only the articular cartilage, but also the underlying bone and adjacent joint structures. Stiffening of the subchondral bone occurs concurrently with changes in the articular cartilage matrix. Osteoblasts in the trabecular portion of underlying bone begin to form new bone and the subchondral region is often thickened and sclerotic. Although changes in subchondral bone may not be necessary for the development of osteoarthritis, these changes may play an important role in the progression of the disease (Johnston, 1997).

Osteophytes are commonly associated with osteoarthritis. Generally, they develop at the periphery of the joint and are thought to form as a result of joint instability. Although they normally form over weeks to months, experimental models have demonstrated formation as early as three days after creation of instability (Johnston, 1997). However, osteophytes have been documented to develop in the presence of inflammation without instability, suggesting that synovial membrane inflammation may play a role (Johnston, 1997). Osteoarthritis and the accompanying inflammation also cause changes in the joint capsule. These changes may include thickening of the synovium and increased vascularity. Conversely, synoviocytes contribute to the progression of osteoarthritis by producing cytokines and leukotrienes, which attract inflammatory cells and the release of prostaglandins and other inflammatory mediators. This inflammation of the synovium contributes to decreased elasticity and viscosity of synovial fluid. Synovitis can either precede or follow observable cartilage changes and is likely secondary to exposure of neoantigens on the cartilage or release of inflammatory mediators by damaged synovium or chondrocytes (Renberg, 2005).

## Key Nutritional Factors

Besides supplying age-appropriate nutrition, foods designed for companion animals with osteoarthritis need to provide specific nutrients that may help reduce inflammation and pain, enhance cartilage repair, slow the degradative process, complement prescribed medications and provide tangible improvement in clinical signs. Because foods for osteoarthritis are fed in place of

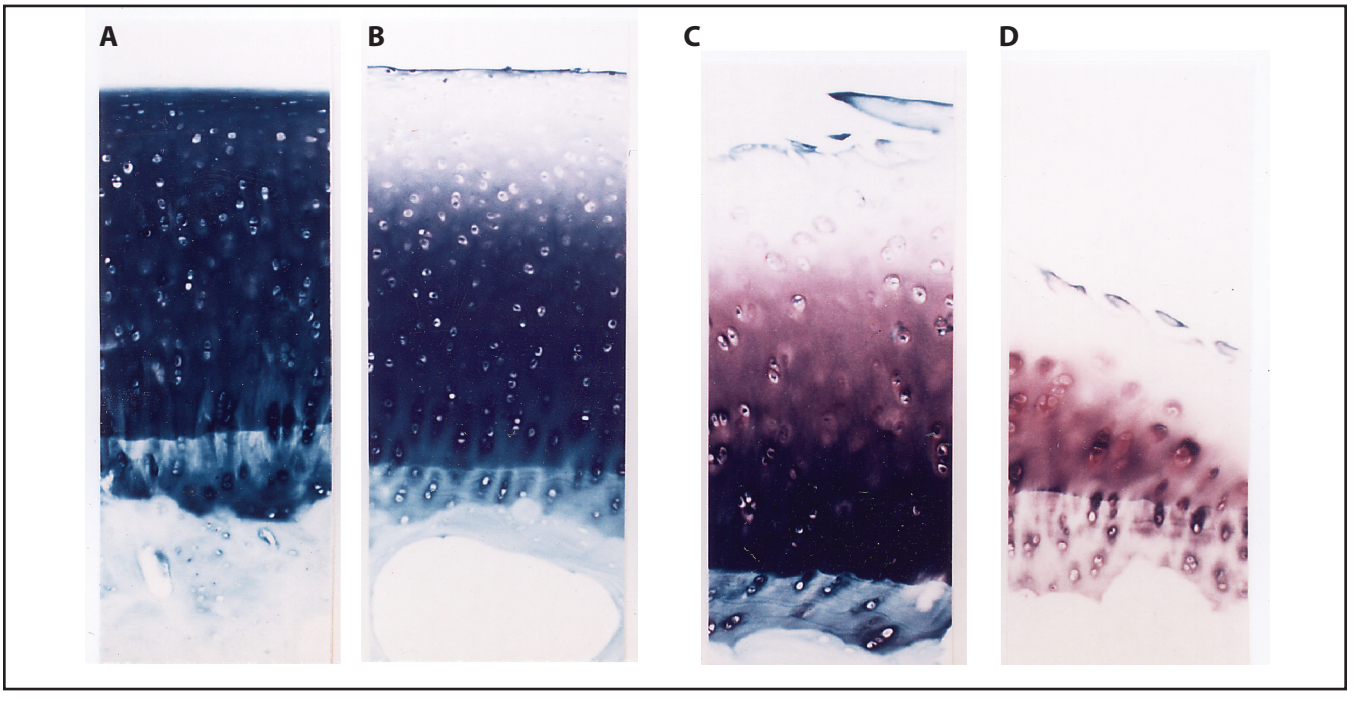


**Figure 34-4.** Toluidine blue-stained sections of canine articular cartilage from normal joints (A) and joints with early- (B), mid- (C) or late- (D) stage osteoarthritis (OA); the articular surface is at the top of each picture and subchondral bone is at the bottom. In the normal cartilage (A), the articular surface is smooth, the matrix (proteoglycans, collagen and water) is darkly stained and chondrocytes are visible in their lacunae. In early OA (B), proteoglycans and water are lost from the superficial layers (indicated by reduced stain uptake). As OA progresses (C, D), there is further loss of matrix accompanied by articular cartilage surface fibrillation and erosion due to collagen degradation and mechanical disruption of the tissue. (Used with permission from Caterson B, Flannery CR, Hughes CE, et al. Mechanisms involved in cartilage proteoglycan catabolism. Matrix Biology 2000; 19(4): 333-344.)

regular maintenance foods, several key nutritional factors are included due to their relationship to general health rather than specific benefits for osteoarthritis. Nutraceutical, or functional food additives, may also contribute to the management of osteoarthritis. **Table 34-2** summarizes key nutritional factors.

## *Omega-3 Fatty Acids*

All mammals synthesize fatty acids de novo up to palmitic acid, which may be elongated to stearic acid and converted into oleic acid. Plants, unlike mammals, can insert additional double bonds into oleic acid and produce the polyunsaturated fatty acids linoleic acid (LA, 18:2n-6) and α-linolenic acid (ALA, 18:3n-3). Linoleic acid and α-linolenic acid are considered essential fatty acids because animals cannot synthesize them from other fatty acids; therefore, they must be supplied by food.

In most animals, linoleic acid can be converted into arachidonic acid (AA, 20:4n-6) via desaturation and elongation. However, in cats, these conversions are greatly limited because of low Δ–6 desaturase activity (Bauer, 2006). As a result, cats are unable to synthesize other physiologically important long-chain polyunsaturated fatty acids, such as arachidonic acid and docosahexaenoic acid (DHA, 22:6n-3), in amounts sufficient for certain lifestages or processes. For cats, marine fish oils, rather than plant oils, are a more appropriate source of these fatty acids. Many marine plants, especially algae in phytoplankton, carry out chain elongation and desaturation of α-linolenic acid to yield omega-3 (n-3) fatty acids with 20 and 22 carbon atoms and five or six double bonds. Formation of these long-chain omega-3 fatty acids by marine algae and their transfer through the food chain to fish accounts for the abundance of eicosapentaenoic acid (EPA, 20:5n-3) and DHA in certain marine fish oils.

Arachidonic acid and EPA act as precursors for the synthesis of eicosanoids, a significant group of immunoregulatory molecules that functions as local hormones and mediators of inflammation. The amounts and types of eicosanoids synthesized are determined by the availability of the fatty acid precursor and by the activities of the enzyme systems that synthesize them. 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 oils containing 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 (**Figure 34-5**). Studies have documented that inflammatory eicosanoids produced from arachidonic acid are depressed when dogs consume foods with high levels of omega-3 fatty acids (Wander et al, 1997).

The effect of dietary fish oil on the expression and activity of matrix metalloproteinases (MMP), tissue inhibitors of MMP-2 and urokinase plasminogen activator in synovial fluid from

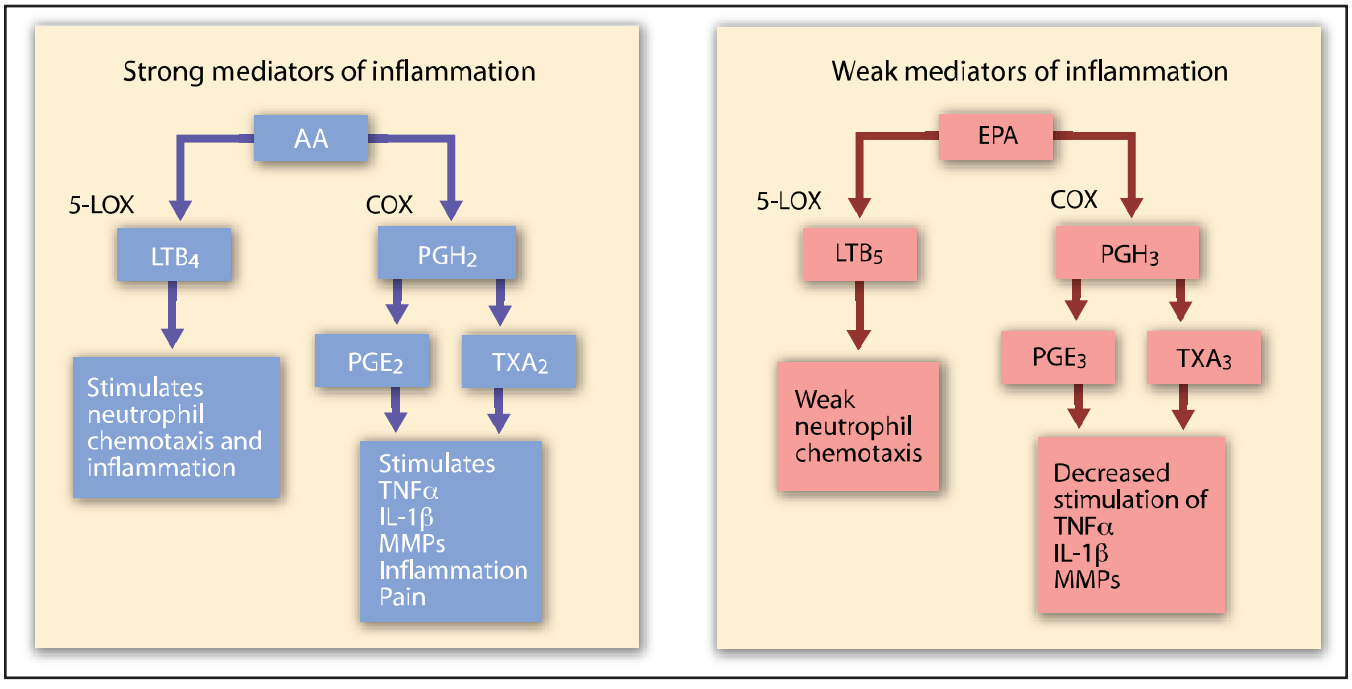


**Figure 34-5.** Eicosapentaenoic acid (EPA) competes with arachidonic acid (AA) for cyclooxygenase (COX) and lipoxygenase (5-LOX) pathways. Eicosanoids produced from AA are strong mediators of inflammation whereas those derived from EPA promote minimal to no inflammatory activity (sometimes referred to as antiinflammatory). Key: AA = arachidonic acid, LOX = lipoxygenase, COX = cyclooxygenase, LTB = leukotrienes, PGH/PGE = prostaglandins, TXA = thromboxanes, TNF = tumor necrosis factor, MMP = matrix metalloproteinase.

dogs with acute cranial cruciate ligament injury has been evaluated (Hansen et al, 2008). Two groups of 12 dogs with spontaneous cranial cruciate ligament injury were randomized to receive either a fish oil-supplemented food or control food from one week before surgery on the affected knee to 56 days post-surgery. The fish oil and control foods provided 90 and 4.5 mg of combined EPA and DHA/kg body weight per day, respectively. There were no changes in these biomarkers in the synovial fluid from the surgical joint at any time during the study. The authors suggested that the severe inflammation from cranial cruciate ligament injury and subsequent surgery was too great to be affected by the combined levels of EPA/DHA provided in the test food. However, dogs randomized to the fish oil food group had episodic but significantly ($p < 0.05$) decreased pro-matrix metalloproteinases and urokinase plasminogen activator and increased tissue inhibitors of MMP-2 in the synovial fluid from the nonsurgical knee. The fish oil food may have moderated the mild to moderate inflammation in the nonsurgical knee through suppression of inflammatory cytokines by EPA and DHA.

Reducing the production of proinflammatory mediators is only one mechanism by which omega-3 fatty acids promote the termination of inflammation and the return to homeostasis. Although it is true that the inflammatory response is essential to health and disease, sustained inflammatory responses are generally detrimental to the host. In people, in modern western civilization, unresolved inflammation has emerged as a central component of many diseases (e.g., arthritis, periodontal disease, cardiovascular disease, cancer and Alzheimer's disease) (Schwab and Serhan, 2006). Research has demonstrated that resolution of inflammation is an active, endogenous process aimed at protecting the individual from an excessive inflammatory response. The first endogenous local counter-regulatory mediators recognized were the lipoxins, which are derived from arachidonic acid (Serhan, 2005). Subsequently, two new families of lipid mediators derived from omega-3 fatty acids, resolvins and protectins, have been identified. Resolvins derived from EPA are denoted as resolvins of the E series (RvEs) and those derived from DHA acid are resolvins of the D series (RvDs) and protectins. These bioactive mediators have potent antiinflammatory, neuroprotective and pro-resolving properties (Schwab and Serhan, 2006). Further elucidation of the molec-

**Table 34-2.** Key nutritional factors for foods for canine osteoarthritis patients.*

| Factors | Dietary recommendations |
|---|---|
| Total omega-3 fatty acids | 3.5 to 4.0% |
| Eicosapentaenoic acid | 0.4 to1.1% |
| Omega-6:omega-3 fatty acid ratio | <1:1 |
| L-carnitine | ≥300 mg/kg |
| Glucosamine HCl | ≤0.10% |
| Chondroitin sulfate | ≤0.08% |
| Antioxidants | |
| Vitamin E | ≥400 IU/kg |
| Vitamin C | ≥100 mg/kg |
| Selenium | 0.5 to 1.3 mg/kg |
| Phosphorus** | 0.3 to 0.7% |
| Sodium** | 0.2 to 0.4% |

*All values are expressed on a dry matter basis unless otherwise stated.
**Dogs with osteoarthritis are often in age groups at risk for kidney and/or heart disease.

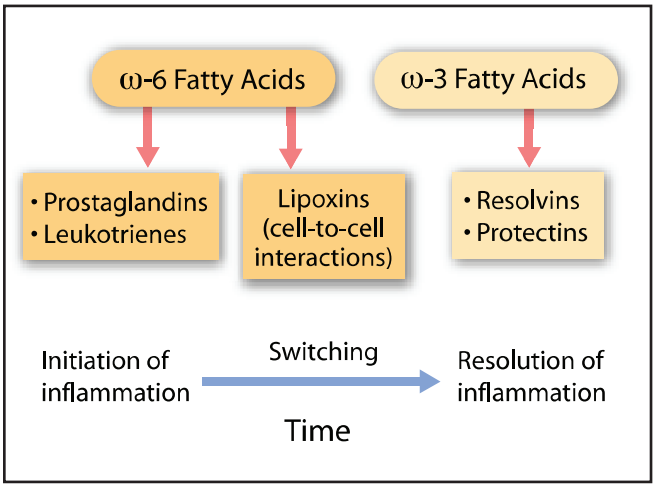


**Figure 34-6.** The role of omega-6 and omega-3 fatty acids in the initiation and resolution of inflammation over time. Resolution of inflammation is a progressive process involving a switch in the production of lipid-derived mediators over time. Pro-inflammatory products of omega-6 fatty acid metabolism (PGE2, PGE12, LTB4) are thought to initiate this sequence. Arachidonic acid-derived mediators foster the extravasation and homing of inflammatory cells at the site of the lesion. Cell-to-cell interactions exemplified by platelet-leukocytes within the vasculature and/or PMN-mucosal interactions enhance generation of lipoxins. With time, a class shift occurs towards domination by pro-resolving omega-3 derived mediators (resolvins, protectins). These mediators serve as endogenous stop signals by preventing inflammatory cell recruitment and stopping "cell entry" and promoting resolution by removing inflammatory cells from the lesion site through phagocytosis of PMNs and promotion of "cell exit." Key: PGE = prostaglandin, LTB = leukotriene. (Adapted from Schwab JM, Serhan CN. Lipoxins and new lipid mediators in the resolution of inflammation. Current Opinion in Pharmacology 2006; 6: 414-420.)

ular actions of these previously unappreciated families of lipid-derived mediators may shed light on the clinically recognized beneficial effects of omega-3 fatty acids (**Figure 34-6**).

The interaction between nutrients found in certain foods and the expression of genes responsible for certain disease conditions is known as nutrigenomics (Chapter 4). Progression from a healthy to a disease state occurs through changes in gene expression, which can be influenced through ingestion of specific nutrients. The capacity of specific omega-3 fatty acids (EPA in dogs) to alter the expression of genes responsible for progression of cartilage degradation is an example of one application of nutrigenomics to pet foods.

Mechanisms of cartilage metabolism in canine osteoarthritis and the potential role of omega-3 fatty acids to ameliorate the early events in the disease have been investigated using in vitro models. These studies identified some similarities and distinct differences between cartilage from dogs and other species in the response to catabolic agents and omega-3 fatty acids. Numerous catabolic agents significantly decreased canine cartilage proteoglycan synthesis. However, proteolysis and loss of aggrecan could only be stimulated by oncostatin M, leukemia inhibitory factor and retinoic acid. Stimulated aggrecan loss was associated with increased cleavage by aggrecanases and not matrix metalloproteinases. EPA was the only omega-3 fatty acid able to significantly decrease the oncostatin M-stimulated loss of aggrecan in the canine cartilage in vitro model (Caterson, 2005; Caterson et al, 2000; Curtis et al, 2002). In canine cartilage, EPA inhibits the up regulation of aggrecanases by blocking the signal at the level of messenger RNA (Curtis et al, 2000). Altering the expression of this messenger RNA signal by EPA is an example of how nutrigenomics can aid in the management of disease.

The application of nutrigenomic concepts can be applied to foods designed to aid in the nutritional management of osteoarthritis. Ideally, these foods should control clinical signs and moderate the progression of the disease and their efficacy should be demonstrated in well-controlled clinical studies. One veterinary therapeutic food[c] designed to aid in the management of osteoarthritis in dogs has been evaluated in multiple clinical studies. Specifically, four randomized, double-masked, controlled studies were completed in arthritic dogs fed either a control or test food. The foods had similar nutrient content with the exception of total levels of omega-3 fatty acids: 0.09% (dry matter [DM]) control vs. 3.48% DM test food and levels of EPA less than 0.01% DM vs. 0.38% DM, respectively. The ratio of omega-6 to omega-3 fatty acids was also markedly different in the two foods: 22.8:1 in the control vs. 0.7:1 in the test food (**Table 34-3**). Pet owners were given the option of feeding dry or a combination of moist and dry foods. One six-month and two three-month prospective studies were conducted in veterinary hospitals across the United States.[d-f] A fourth study was conducted as a three-month prospective study in two academic specialty practices in the United States.[g]

In all studies, osteoarthritis was diagnosed based on compatible history, clinical signs and radiographic evidence of arthritis in one or more joints of the clinically affected limb. To be eligible for inclusion, dogs had to be at least one year of age, weigh 12.5 kg or more, consume at least some dry dog food and be free of systemic disease as determined by history, physical examination, complete blood count, serum biochemistry analysis and urinalysis. Exclusion criteria included acute traumatic injuries, complicating disease conditions, preexisting conditions for which corrective surgery was anticipated during the feeding period and recent intraarticular injection or arthrocentesis.

Change in arthritic condition over time was evaluated in these studies and was based on owner observations of clinical signs and veterinary clinical evaluations. Variables were assessed at the beginning of the study and at set time intervals after onset of feeding the control or therapeutic food. Additionally, veterinary clinical evaluations were conducted at each time interval. These consisted of an orthopedic examination with a specific emphasis on lameness and pain, limitation in weight-bearing ability, range of motion of the affected joint(s) and willingness to bear weight on the most affected limb when the contralateral limb was elevated.

Investigators in the three studies conducted in veterinary hospitals[d-f] reported that the animals fed the EPA-supplemented food improved in several parameters throughout the studies. Veterinarians reported improvement in range of

motion and ability to bear weight, along with a decrease in pain (upon palpation of the affected joint) and lameness as compared to evaluations of these dogs before they participated in the studies. Dogs fed the EPA-supplemented food had significantly ($p < 0.05$) improved ability to rise from a resting position, in running and playing at six weeks and improvements in walking at 12 and 24 weeks compared to dogs fed the control food.

In the academic specialty practice clinical study,[g] variables were assessed at the beginning of the study and at 45 and 90 days after onset of feeding the control or test food. Additionally, gait analyses using a computerized biomechanical force plate were conducted at the same time intervals. For each dog, five valid force-plate trials were obtained during each test period for the most severely affected and ipsilateral limbs. Orthogonal ground reaction forces of peak vertical force, vertical impulse, braking and propulsion peak force and braking and propulsive force were measured and recorded. All forces were normalized with respect to body weight in kg. Data from valid trials for each limb were averaged to obtain a mean value at each time period.

On clinical orthopedic examination, a significantly ($p < 0.05$) greater percent of dogs consuming the test food were evaluated as "improved" vs. those consuming the control food. In addition, more dogs in the test group had a reduction in pain at the end of the 90-day trial when the affected joint was palpated. Vertical peak force was the key parameter measured to determine weight bearing of affected limbs. There was no significant change in mean peak force over the duration of the 90-day feeding trial for the control group. The mean vertical peak force increased significantly ($p = 0.01$) for the test group over the same time interval. The percent mean change in vertical peak force was also significantly ($p = 0.04$) different between groups, indicating that the test group increased weight bearing on the affected limb over the course of the study. Additionally, only 31% of dogs in the control group had improved weight bearing after the 90-day feeding trial, whereas 82% of dogs in the test group increased weight bearing; this difference was also statistically significant ($p = 0.003$).

These clinical studies indicate that nutritional management using a veterinary therapeutic food supplemented with omega-3 fatty acids helped improve the clinical signs of osteoarthritis in dogs as noted by pet owners, clinical orthopedic examination and gait analysis of ground reaction forces. Based on these studies, a food designed to aid in the management of osteoarthritis in dogs should provide levels of total omega-3 fatty acids between 3.5 to 4.0% DM and specifically 0.4 to 1.1% DM EPA. The omega-6 to omega-3 fatty acid ratio should be less than 1:1. Dogs consuming the therapeutic food should receive an average of 50 to 100 mg EPA/kg body weight/day.

Supplements have traditionally been used to provide a source of omega-3 fatty acids to pets. However, using supplements to provide levels of EPA documented to have a clinical effect may prove cumbersome. Many supplements designed to provide omega-3 and omega-6 fatty acids are available in both human and veterinary formulations. Concentrations in these supplements range from 50 to 375 mg of EPA per dose. To achieve EPA concentrations of 50 mg/kg body weight/day, a 27-kg dog would require four to 27 doses of a supplement (**Table 34-4**). Long-term compliance with this dosing regimen is likely to be poor. Providing a food with the recommended levels of EPA and total omega-3 fatty acids is preferable and likely improves compliance.

One study in osteoarthritic geriatric cats evaluated the effects of feeding an omega-3 fatty acid-supplemented food on cartilage protection (Yamka et al, 2006). Increased levels of EPA (3.2% DM), DHA (0.23% DM), methionine (1.32% DM) and manganese (104 mg/kg DM) and no synthetic glucosamine or chondroitin sulfate were associated with decreased values for arthritic biomarkers in these cats. Changes in clinical signs were not noted during the 60-day study.

Anecdotally, radiographic signs of osteoarthritis in cats have been managed with a combination of calorie restriction plus supplementation of the food with omega-3 fatty acids (75 to 110 mg/kg body weight/day). Over eight weeks of evaluation, there were no changes in radiographic appearance, but therapy resulted in a more natural gait and increased voluntary activity

**Table 34-3.** Nutrient comparison of control and test foods.*

| Nutrients | Control food | Test food** |
|---|---|---|
| Protein (%) | 23.2 | 20.0 |
| Fat (%) | 13.9 | 13.6 |
| NFE (%) | 54.7 | 53.3 |
| Total omega-3 fatty acids (%) | 0.09 | 3.48 |
| EPA (%) | <0.01 | 0.38 |
| Omega-6:omega-3 fatty acid ratio | 22.8 | 0.7 |

Key: NFE = nitrogen-free extract (digestible carbohydrate), EPA = eicosapentaenoic acid.
*All values are expressed on a dry matter basis unless otherwise stated.
**Prescription Diet j/d Canine dry. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

**Table 34-4.** Fatty acid concentration of a therapeutic food vs. supplements for a 27-kg dog.

| | Therapeutic food* (4 cups) | GNC Preventative Nutrition Multi Oil Formula (300 mg/capsule) | 3V Caps for Large & Giant Breeds (DVM Pharmaceuticals) (1,488 mg capsule) | Welactin (Nutramax) Liquid (1.5 ml/pump) |
|---|---|---|---|---|
| EPA content | 1,578 mg | 180 mg/capsule | 250 mg/capsule | 97-120 mg/pump |
| Amount/day to equal intake from j/d Canine | - | 9 capsules | 6 capsules | 13 pumps |

Key: EPA = eicosapentaenoic acid.
*Prescription Diet j/d Canine dry. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

(Saker, 2006). This treatment is similar to protocols recommended for management of dogs with osteoarthritis. Adverse effects on platelet function have been reported in cats fed a food with a 1.3:1 omega-6 to omega-3 ratio (1.03 g omega-3 fatty acids/kg food), but not in cats fed a food with 12:1 omega-6 to omega-3 ratio (0.07 g omega-3 fatty acids/kg food) (Saker et al, 1998). More studies are needed to confirm these findings; however, based on results in other species, providing enhanced levels of omega-3 fatty acids to cats with osteoarthritis seems promising.

### *L-Carnitine*

Maintaining a healthy weight throughout life will delay the onset and minimize clinical signs of osteoarthritis. Achieving an ideal body weight in dogs diagnosed with osteoarthritis will improve clinical signs and long-term management. Paradoxically, many dogs diagnosed with osteoarthritis are either overweight or obese prone as a result of breed, age and/or decreased activity. One key nutrient in weight loss and weight maintenance foods is L-carnitine. It plays a vital role in a variety of physiologic processes related to fat metabolism and energy production; specifically L-carnitine mediates the transfer of long-chain fatty acids into mitochondria. This action promotes oxidation of fatty acids as an energy source. Perhaps more importantly, weight-loss foods with appropriate levels of L-carnitine (≥300 mg/kg DM) aid in the retention of lean body mass during weight loss in dogs (Allen, 1998). Additionally, L-carnitine supplementation of obese-prone dogs led to a reduction in fat mass and increase in lean body mass through an extended feeding period (Gross, 1998). Obese cats supplemented with L-carnitine have been reported to lose weight faster and have less ketogenesis (Center et al, 2000), suggesting that increasing the L-carnitine level of foods for cats at risk for becoming overweight, such as after neutering, could be beneficial. Because lean tissue uses more calories than fat, increased lean body mass is desirable for long-term maintenance of an ideal body weight in dogs and cats. Achieving and maintaining a healthy weight is critical to the successful management of osteoarthritis.

Because many patients with osteoarthritis need support to achieve or maintain a healthy body weight and L-carnitine supports both weight loss and maintenance of weight after weight loss, foods intended for the dietary management of osteoarthritis should contain at least 300 mg of L-carnitine/kg DM.

### *Chondroitin Sulfate and Glucosamine Hydrochloride*

Chondroitin sulfate is a GAG consisting of repeating disaccharide subunits of glucuronic acid and N-acetylgalactosamine sulfate (Schoenherr, 2005). Commercially available chondroitin sulfate is generally derived from bovine cartilage. However, porcine and chicken cartilage and chondroitin from perna mussels and algae have also been used. Chondroitin sulfate decreases interleukin-1 production, blocks complement activation, inhibits metalloproteinases, inhibits histamine-mediated inflammation and stimulates GAG production and collagen synthesis (Beale, 2004). Both the molecular weight and species of derivation affect the bioavailability of chondroitin sulfate products. The low molecular weight form appears to be absorbed more readily. Some sources such as perna mussels contain only trace amounts of high molecular weight chondroitin sulfate and avian sources have not proven any more effective than placebo (Millis, 2006). **Box 34-1** contains additional information about commercially available glucosamine and chondroitin sulfate products.

Glucosamine hydrochloride is one of the basic sugar component precursors of the disaccharide units that make up all of the glycosaminoglycans in cartilage. Proposed mechanisms of action of glucosamine include a reduction of proteoglycan degradation and inhibition of the synthesis and activity of degradative enzymes (aggrecanases/matrix metalloproteinases) and inflammatory mediators (nitric oxide and prostaglandin $E_2$). Anabolic effects include stimulation of GAG and proteoglycan production (Neil et al, 2005). Glucosamine hydrochloride and glucosamine sulfate appear to be more efficacious than N-acetylglucosamine.

Glucosamine hydrochloride and chondroitin sulfate, taken in appropriate doses, are considered safe for dogs and cats. Safety studies of one proprietary formulation using oral administration in excess of the recommended daily dose for 30 days documented no clinically important alterations in hematologic indices or biochemistry and clotting profiles in dogs and cats (McNamara et al, 1996; McNamara et al, 2000). Although no coagulation abnormalities were recognized, because of the structural similarities of glycosaminoglycans and heparin, the concurrent use of other platelet inhibitors, such as phenylbutazone or aspirin, may be contraindicated. Some dogs and cats may experience mild gastrointestinal upset, which can be managed by offering the product with a meal.

Meta-analysis of randomized, double-blind, placebo-controlled studies evaluating the effectiveness of glucosamine and chondroitin sulfate supplements in people demonstrated moderate to large reductions of pain and disability in osteoarthritis compared with placebo; however, these effects may have been exaggerated as a result of publication bias. Greater effects have been detected for chondroitin sulfate than glucosamine (McAlindon et al, 2000). The Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) evaluated over 1,500 human participants with osteoarthritis of the knee who were randomly assigned to one of five treatment groups: 1) glucosamine alone, 2) chondroitin sulfate alone, 3) glucosamine and chondroitin sulfate in combination, 4) celecoxib or 5) a placebo. Patients were assessed at intervals over six months. Patients taking the positive control (i.e., celecoxib) experienced statistically significant pain relief vs. placebo. Overall, there were no significant differences between the other treatments tested and placebo. For a subset of participants with moderate-to-severe pain, glucosamine combined with chondroitin sulfate provided statistically significant ($p = 0.002$) pain relief compared to placebo. According to the researchers, because of the small size of this subgroup, these findings should be considered preliminary and need to be confirmed in further studies. For participants in the mild pain subset, glucosamine and chondroitin sulfate together or alone did not provide statistically sig-

## Box 34-1. All Nutraceutical "Chondroprotective Agents" Are Not Created Equal.

Veterinary nutraceuticals have been defined as "a non-drug substance that is produced in a purified or extracted form and administered orally to a patient to provide agents required for normal body structure and function and administered with the intent of improving the health and well-being of animals." Because the term nutraceutical has no regulatory definition and is not recognized by the FDA, these products are not subject to a pre-market approval process. As a result the safety, efficacy and manufacturing quality of these products cannot be ensured and there is evidence that this lack of regulatory oversight should be of concern to consumers.

In the United States, although there is no mandatory regulatory oversight, manufacturers of nutraceuticals can voluntarily submit their products for quality assurance. A variety of independent groups such as Consumer Laboratory (www.consumerlab.com) and the Institute for Nutraceutical Advancement (www.nsf.org) or trade associations such as the National Animal Supplement Council (www.nasc.cc) provide independent quality assurance testing and certification programs. The two substances most commonly used for treatment of osteoarthritis in veterinary medicine are glucosamine HCl and chondroitin sulfate either alone or in combination. Chondroitin sulfate is an expensive ingredient of many "joint" targeted products and serves as an example of the need for careful evaluation of these unregulated products.

A 1999 study partially funded by Nutramax Laboratories found that 26 of 32 (81%) commercially available human products contained less than 90% of the chondroitin sulfate stated on the label and 17 (53%) of those products contained less than 40% of label claim. This study documented that products costing ≤$1/1,200 mg chondroitin sulfate were critically deficient; on average less than 10% of the label claim. Interestingly, expense did not guarantee content because several of the most expensive products also contained less than 10% of label claim (**Figure 1**). ConsumerLab.com (accessed 11/16/06) found similar problems with glucosamine HCl/chondroitin sulfate combination products. Initially, on November 2, 2003, two of three veterinary combination products evaluated were found to have no chondroitin sulfate despite each displaying a "guaranteed analysis." One of these companies has since produced a re-formulated product that did pass Consumer Lab testing. Glucosamine hydrochloride, unlike chondroitin sulfate, is much more likely to be present in the amounts indicated on product labels. Information about specific products and testing procedures can be accessed at the Consumer Lab website for a fee. Because of these inconsistencies, consumers are cautioned against extrapolating results from clinical and experimental studies comparing one product to other similar products. Based on this information, when prescribing nutraceuticals, preference should be given to those products whose quality assurance and efficacy can be verified.

The Bibliography for **Box 34-1** can be found at www.markmorris.org.

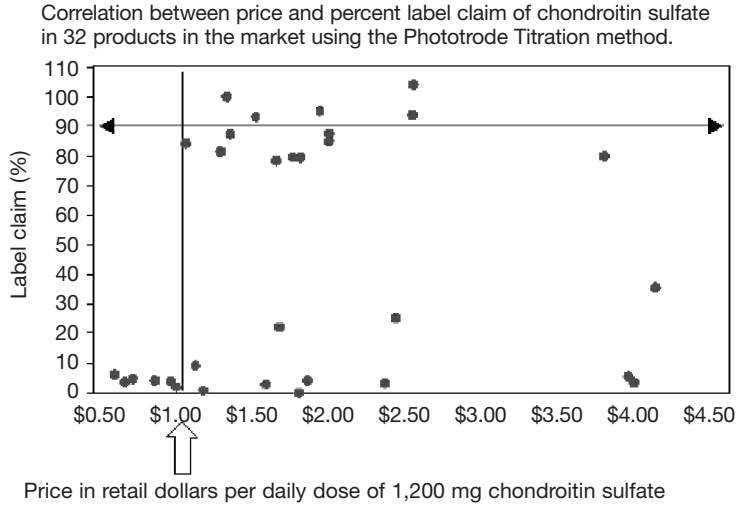


**Figure 1.** Relationship between products' label claims and standard retail prices. (Adapted from Adebowale AO, Cox DS, Liang Z, et al. Analysis of glucosamine and chondroitin sulfate content in marketed products and the Caco-2 permeability of chondroitin sulfate raw materials. Journal of the American Nutraceutical Association 2000; 3(1): 37-44.)

nificant pain relief (Clegg et al, 2006). The authors also noted that the elevated placebo response seen in this study may have dampened the ability to differentiate among the treatments (60% of patients receiving placebos had at least a 20% decrease in pain scores after 24 weeks) (Clegg et al, 2006). These studies suggest that glucosamine and chondroitin sulfate may offer clinically relevant reductions in pain for some patients with osteoarthritis. However, despite a large number of clinical trails in human medicine, there is still no consensus about the effectiveness of these compounds. In veterinary medicine, there is a lack of consensus and a lack of clinical trials to evaluate.

In veterinary medicine, claims of efficacy for glucosamine/chondroitin sulfate supplements are often based on subjective methods of assessment, in vitro testing or testimonials. Two studies evaluated the efficacy of supplements containing the combination of glucosamine/chondroitin sulfate in client-owned dogs with naturally occurring osteoarthritis compared to positive controls. These two trials evaluated 106 dogs with confirmed osteoarthritis. Nonsteroidal antiinflammatory drugs (carprofen and meloxicam) were used for positive controls. One study evaluated ground reaction forces and subjective owner and veterinary evaluations in 71 dogs randomized to receive meloxicam, carprofen, a combination glucosamine/chondroitin sulfate product or placebo (Moreau et al, 2003). After 60 days, dogs in the meloxicam and carprofen groups had improved ground reaction forces and clinical improvement. Owners

noted subjective improvement only in the meloxicam group; dogs in the glucosamine/chondroitin sulfate and placebo groups were not different on any evaluation at the conclusion of the study. In the second study, subjective veterinary and owner evaluations were used to assess 35 dogs randomized to receive either a combination of glucosamine/chondroitin sulfate supplement or carprofen for 70 days (McCarthy et al, 2007). Dogs in the carprofen group improved in all five parameters with the onset for some parameters occurring as early as 14 days. Dogs in the glucosamine/chondroitin sulfate group showed significant ($p < 0.001$) improvements at the conclusion of the study in pain, weight bearing and overall condition compared to pre-treatment evaluations, but no improvement in lameness or joint mobility. One explanation for the lack of improvement in lameness and joint mobility may be the insensitivity of the subjective scoring system in dogs with mild disease (low scores). The strong positive correlation ($rs > 0.55$) between the pre-treatment disease score and the Day 70 change score ($p < 0.02$) for all parameters independent of treatment group suggests that dogs with higher pre-treatment scores tended to have higher positive changes in their scores. The authors suggested that future clinical studies evaluating glucosamine and chondroitin sulfate should monitor dogs for a minimum of 70 days and include an objective measurement of lameness such as force-plate gait analysis. In addition to these two studies, numerous uncontrolled studies, anecdotal evidence and case reports support the use of glucosamine and chondroitin sulfate (Anderson et al, 1999; Hoffman, 2001; Lippiello and Prudhomme, 2005; Moore, 1996).

Beneficial effects of glucosamine and chondroitin sulfate alone and in combination have been documented in in vitro studies in several species, but to date, well-designed clinical studies in dogs and cats with naturally occurring disease are sparse. The current evidence suggesting beneficial effects warrants further investigation into the mechanism of actions, pharmacokinetics and possible disease-modifying activities of these compounds. Addition of glucosamine and chondroitin sulfate to a therapeutic food for dogs with osteoarthritis seems safe and potentially beneficial.

Dosages can be based on studies documenting positive effects with supplements. Currently the best evidence in dogs suggests that providing glucosamine HCl at approximately 25 to 50 mg/kg body weight/day and chondroitin sulfate at approximately 15 to 40 mg/kg body weight/day may benefit some patients with osteoarthritis (McCarthy et al, 2007; Moreau et al, 2003). Glucosamine HCl and chondroitin sulfate are not currently included in the federal GRAS (Generally Recognized as Safe) listing. Furthermore, the Association of American Feed Control Officials (AAFCO) does not provide limits for inclusion levels in commercial foods sold in the United States. However, at least one regulatory agency has provided upper limits for intake of these substances in foods sold in its state. On that basis, glucosamine HCl and chondroitin sulfate should not exceed 15 mg and 12 mg/kg body weight/day, respectively.[h] Based on anticipated food intake for dogs whose daily energy requirement (DER) is 1.8 times their resting energy requirement, and in a food with an energy density of 4 kcal/g DM, glucosamine HCl and chondroitin sulfate should not exceed 0.10 and 0.08% DM, respectively.

### *Antioxidants*

Free radicals are chemically unstable molecules that contain an unpaired free electron. Byproducts of mitochondrial respiration are the primary source of free radicals in mammals. In health, the potential destructive effects of free radials are mitigated by endogenous antioxidant systems. Imbalances between the concentrations of free radicals and availability of antioxidant defenses may be related to a variety of processes such as aging, cancer, diabetes mellitus, lupus and arthritis (Budsberg and Bartges, 2006). Chapter 7 discusses antioxidants in detail.

The generation of free radicals in synoviocytes and chondrocytes is an important factor in the development and maintenance of rheumatoid arthritis in people and animal models (Darlington and Stone, 2001). Free radicals are also implicated in aging of cartilage and in the pathogenesis of osteoarthritis. Increased oxidative activity in chondrocytes has a damaging effect on matrix, which may play an important role in matrix degradation, which is characteristic of osteoarthritis. Studies in animal models indicate that antioxidants can prevent matrix degradation and therefore may have a preventive or therapeutic value in osteoarthritis (Tiku et al, 1999). Clinical response to antioxidant supplements has been demonstrated in people with rheumatoid arthritis and osteoarthritis (Budsberg and Bartges, 2006). Methyl-sulfonyl-methane (MSM), a sulfur donor, and a normal oxidation product of dimethyl sulfoxide (DMSO), has not been studied in dogs and cats, but has been reported to be of benefit in the treatment of many human disorders including osteoarthritis (Parcell, 2002). The rationale for its use lies in the possibility of a dietary sulfur deficiency, with a resultant deficiency of sulfur-containing compounds in the body, such as antioxidants and chondroitin sulfate (Parcell, 2002). Additionally, organic sulfur as sulfur-containing amino acids can theoretically be used for the formation of connective tissue and repair of damaged protein. Damaged cartilage from osteoarthritic human patients has been shown to have approximately one-third the concentration of sulfur as normal cartilage (Rizzo et al, 1995). In a human study of 16 patients with osteoarthritis, 10 patients were randomly selected to receive 2,250 mg of MSM per day for a six-week trial; eight of the 10 patients experienced some relief of ostearthritis symptoms compared to placebo controls (Lawrence and Lignisul, 2002). A study in rats, administered MSM at 5 to 7 times the maximum recommended human dose as a single gavage of 2 g/kg or as a daily dose of 1.5 g/kg for 90 days, resulted in no adverse effects and was well-tolerated (Horvath et al, 2002).

Although there are no controlled studies in dogs or cats specifically assessing the efficacy of dietary antioxidants, there is a growing scientific rationale for their use as adjuncts in the treatment of inflammatory disorders including osteoarthritis. Thus, antioxidants are also recommended for inclusion in foods for general health.

The body synthesizes many antioxidants but relies on food

for others. The following discussion will focus on vitamins E and C and selenium as antioxidant key nutritional factors for foods for osteoarthritis because: 1) they are biologically important, 2) they act synergistically (e.g., vitamin C and selenium-containing glutathione peroxidase regenerate vitamin E after it has reacted with a free radical), 3) much is known about their safety and 4) information regarding inclusion levels in pet foods is usually available.

### VITAMIN E

Vitamin E is the main lipid-soluble antioxidant present in plasma, erythrocytes and tissues (NRC, 2006). It is one of the most effective antioxidants for protecting cell membrane constituent polyunsaturated fatty acids from oxidation. Vitamin E inhibits lipid oxidation by scavenging lipid peroxyl radicals much faster than these radicals can react with adjacent fatty acids or with membrane proteins (Gutteridge and Halliwell, 1994).

Research indicates that a level of vitamin E higher than the requirement confers specific biologic benefits (Hayes et al, 1969; Hall et al, 2003; Meydani et al, 1998; Jewell et al, 2002). Based on antioxidant biomarker studies in dogs and cats, for improved antioxidant performance, veterinary therapeutic foods for osteoarthritis should contain at least 400 IU/kg DM (dog foods) and at least 500 IU/kg DM (cat foods) (Jewell et al, 2000).

### VITAMIN C

Vitamin C is the most powerful reducing agent available to cells. Ascorbic acid: 1) regenerates oxidized vitamin E, glutathione and flavonoids, 2) quenches free radicals both intra- and extracellularly, 3) protects against free radical-mediated protein inactivation associated with oxidative bursts of neutrophils, 4) maintains transition metals in reduced form and 5) may quench free radical intermediates of carcinogen metabolism.

Although dogs and cats can synthesize enough vitamin C to fulfill minimum requirements (Innes, 1931; Naismith, 1958), in vitro studies indicated that both species have from one-quarter to one-tenth the ability to synthesize vitamin C as other mammals (Chatterjee et al, 1975). Whether or not this translates to a reduced ability in vivo is unknown. For improved antioxidant performance, and in conjunction with levels of vitamin E recommended above, foods for adult dogs and cats should contain at least 100 mg vitamin C/kg DM.

### SELENIUM

Glutathione peroxidase is a selenium-containing antioxidant enzyme that defends tissues against oxidative stress by catalyzing the reduction of $H_2O_2$ and organic hydroperoxides and by regenerating vitamin E. The minimum requirement for selenium in foods for dogs and cats is 0.13 mg/kg DM (Wedekind et al, 2002; Wedekind et al, 2003). Animal studies and clinical intervention trials in people have shown selenium to be anticarcinogenic at levels much higher (five to 10 times) than the recommended allowances for people or the minimal requirements for animals (Combs, 2001; Neve, 2002). Therefore, for increased antioxidant benefits, the recommended range of selenium for dog and cat foods is 0.5 to 1.3 mg/kg DM.

### *Phosphorus, Sodium and Urinary pH*

Because foods for osteoarthritis patients are fed in the place of regular maintenance foods and general health is the overall goal, key nutritional factors unrelated to osteoarthritis should also be considered. Besides being a risk factor for osteoarthritis, age is a risk factor for kidney and heart disease in dogs and cats. Phosphorus and sodium are considered key nutritional factors for apparently healthy adult dogs and cats for purposes of ameliorating or slowing the progression of subclinical kidney and heart disease. Phosphorus levels in foods for older dogs and cats should be within the range of 0.3 to 0.7% DM and 0.5 to 0.7% DM, respectively. Sodium levels should be between 0.2 to 0.4% DM for dog and cat foods. Urinary pH in older cats should be somewhat higher than for young cats (i.e., in the range of 6.4 to 6.6). For detailed discussions of the rationale for the inclusion of these key nutritional factors in foods for middle-aged to older dogs and cats, see Chapters 13 and 14 (dogs) and Chapters 20 and 21 (cats). These key nutritional factors are listed in **Table 34-2** along with the key nutritional factors for managing osteoarthritis.

## FEEDING PLAN

Providing appropriate nutrition during growth and maintaining a healthy weight throughout life will minimize the expression of underlying genetic tendencies for the development of osteoarthritis. Current evidence suggests that the manifestation of developmental orthopedic diseases is affected by rate of growth, specific nutrients, food consumption and feeding methods (Chapter 33). Nutrition during growth of large- and giant-breed dogs requires providing nutrients in appropriate amounts and balances for optimal bone development. Excesses of calcium and energy, together with rapid growth, appear to predispose dogs to certain musculoskeletal disorders such as osteochondrosis and CHD (Hedhammar et al, 1974; Meyer and Zentek, 1991). Refer to Chapter 33 for additional information about nutritional management to prevent developmental orthopedic diseases of dogs.

Developmental orthopedic diseases have also been recognized in cats. Because cats seldom present with clinical signs referable to hip lameness, hip dysplasia in cats has received little attention. However, hip dysplasia has been documented in cats. Over a 21-year period (1974 to 1995) 21% of 284 radiographs of Maine Coon cats submitted for evaluation to the OFA were judged dysplastic. A 6.6% incidence of hip dysplasia was documented in 684 cats of various breeds. Much like in dogs, the frequency appears to be breed dependent with increased risks in Siamese, Persian and Himalayan breeds (Keller et al, 1999). A cross-sectional prevalence study designed to evaluate simultaneous patellar luxation and hip dysplasia in 78 cats of various breeds reported a 32% incidence of hip dysplasia, 58% incidence of patellar luxation and 24% incidence of concurrent hip dysplasia and patellar luxation (Smith et al,

## Box 34-2. Physical Rehabilitation for Osteoarthritis.

The chronic pain associated with osteoarthritis often results in diminished use of the affected joints. With disuse, muscle mass, tone and function are typically reduced. As a result, added stress is placed on arthritic joints during locomotion. This creates additional pain and dysfunction, which may lead to immobility of the joint. Mobility is one of the most important aspects of a patient's quality of life and severe limitations may be a cause for elective euthanasia. Lack of mobility may also contribute to obesity or complicate weight-reduction protocols. Physical rehabilitation has been successfully used to manage pain and improve mobility in human osteoarthritis patients. In canine patients, physical rehabilitation has been evaluated and shown to be beneficial in laboratory and clinical settings.

The goals of physical rehabilitation programs include protecting and promoting mobility, assisting weight-reduction protocols and reducing joint pain. A variety of treatments are available including passive therapeutic options (cold therapy, heat therapy, stretching, massage and electrical stimulation), therapeutic exercises (land or water based) and the use of ambulation assistance devices.

Weight reduction in arthritic patients can be challenging. Successful weight-management programs typically include recommendations to increase exercise. This may be difficult for some arthritic patients. One study evaluated the effects of combining an intense physical rehabilitation program with a weight-reduction program in overweight dogs with osteoarthritis. The duration of the study was six months. Twenty-nine client-owned overweight dogs with clinical and radiographic evidence of osteoarthritis were randomized to participate in a weight-control program with a home-based physiotherapy protocol alone (Group 1) or a weight-control program with a home-based physiotherapy protocol with an additional intensive clinic-based physiotherapy program including transcutaneous electrical nerve stimulation (TENS) (Group 2). The combination of caloric restriction and intensive physiotherapy improved mobility as assessed by ground reaction forces and facilitated more effective weight loss. The authors attributed the more pronounced weight loss in Group 2 to enhanced owner compliance resulting from increased owner-patient-veterinary interactions and decreased pain sensations from TENS therapy, which promoted increased physical activity. Interestingly, even when dogs in both groups reached a goal of approximately 9% reduction in initial body weight, weight loss alone did not result in the same significant improvement of lameness as measured by ground reaction forces, in Group 1 compared to Group 2.

Physical rehabilitation should be considered as part of a multifaceted approach to the management of patients with osteoarthritis. Before initiating a rehabilitation program, patients should be thoroughly evaluated by a veterinarian and client education should include a clear understanding of the pathogenesis of the disease, typical disease progression and the anticipated benefits and potential complications of all treatment options.

The Bibliography for **Box 34-2** can be found at www.markmorris.org.

1999). Osteochondrosis dissecans was reported to occur in multiple joints of one cat (Ralphs, 2005). These sporadic reports suggest that developmental orthopedic disease may be more common in cats than previously thought. Increased awareness will undoubtedly lead to better characterizations of these diseases in cats. Appropriate nutrition in kittens should be focused on maintaining a healthy body weight and providing age-appropriate nutrition.

Although prevention of osteoarthritis is ideal, it is not always possible. After osteoarthritis is diagnosed, therapeutic recommendations should be customized for individual patients. The goals of management include: 1) mitigating risk factors, 2) controlling clinical signs and 3) moderating progression of the disease. These goals are best achieved by employing a multifaceted approach, which includes therapeutic nutrition, obesity management, analgesic medications, disease-modifying supplements and physical rehabilitation. The goals of nutritional management include reducing inflammation and pain, enhancing cartilage repair, slowing cartilage degradation and providing tangible improvement in clinical signs of osteoarthritis. After a patient has been diagnosed with osteoarthritis, or a condition that predisposes it to the development of osteoarthritis, initiating therapeutic nutrition is warranted.

Maintaining a healthy weight throughout life will delay the onset and minimize clinical signs of osteoarthritis. Achieving an ideal body weight in dogs diagnosed with osteoarthritis will improve clinical signs and long-term management. Although similar studies have not been conducted in cats, given that obesity is a risk factor in cats, similar effects can be expected. Obese patients diagnosed with either a concurrent risk factor or osteoarthritis should be managed with a weight-control program aimed at increasing mobility and restoring normal body condition. Weight control is best achieved by initiating an individualized weight-management program including the use of foods specifically designed for weight loss. Severely restricting the amount of a maintenance food to reduce energy intake will alter the intake and balance of other essential nutrients. It is important to remember that weight reduction alone may result in marked clinical improvement in patients suffering from osteoarthritis and should be a fundamental part of disease management. Refer to Chapter 27 for additional information about overweight/obesity and weight control.

Although calorie restriction is important, success in dogs and cats generally requires participation in an appropriate exercise program. Therapeutic exercise has been shown to help patients reduce body weight, increase joint mobility, reduce joint pain and strengthen supporting muscles. However, initiating an exercise program in overweight dogs suffering from osteoarthritis may be problematic (**Box 34-2**). If clinical signs are mild and reductions in body weight of 10% or less are necessary, patients can be managed with an appropriate therapeutic osteoarthritis food fed at approximately 80% of DER for the ideal weight (Table 27-3). If reductions greater than 10% of body weight are necessary or if clinical signs are severe, dogs

**Table 34-5.** Key nutritional factor content of selected veterinary therapeutic foods marketed for osteoarthritis in dogs compared to reommended levels.*

| Dry foods | Energy density (kcal/cup)** | Energy density (kcal ME/g) | Total omega-3 FAs (%) | EPA (%) | Omega-6: omega-3 ratio | Carn (mg/kg) | Gluc (%) | Chon (%) | Vit E (IU/kg) | Vit C (mg/kg) | Se (mg/kg) | P (%) | Na (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Recommended levels** | - | - | **3.5-4.0** | **0.4-1.1** | **<1:1** | **≥300** | **≤0.1** | **≤0.08** | **≥400** | **≥100** | **0.5-1.3** | **0.3-0.7** | **0.2-0.4** |
| Hill's Prescription Diet j/d Canine | 356 | 3.9 | 3.8 | 0.5 | 0.7:1 | 351 | 0.1 | 0.07 | 585 | 225 | 0.43 | 0.54 | 0.2 |
| Iams Veterinary Formulas Joint | 294 | 3.75 | na | na | na | na | 0.5 | na | na | na | na | 1.04 | 0.47 |
| Medi-Cal Mobility Support | 271 | na | na | na | na | na | na | na | na | na | na | 0.60 | 0.30 |
| Purina Veterinary Diets JM Joint Mobility | 351 | 4.2 | 1.07 | na | 1.8:1 | na | 0.14 | na | 1,073 | 133 | na | 1.07 | 0.39 |
| Royal Canin Veterinary Diet Mobility Support JS 21 | 322 | 4.2 | na | na | na | na | 0.1 | na | 725 | na | 0.44 | 0.60 | 0.29 |
| Royal Canin Veterinary Diet Mobility Support JS 21 Large Breed | 332 | 4.3 | na | na | na | na | 0.22 | na | 725 | na | 0.43 | 0.60 | 0.40 |

| Moist food | Energy density (kcal/can)** | Energy density (kcal ME/g) | Total omega-3 FAs (%) | EPA (%) | Omega-6: omega-3 ratio | Carn (mg/kg) | Gluc (%) | Chon (%) | Vit E (IU/kg) | Vit C (mg/kg) | Se (mg/kg) | P (%) | Na (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Recommended levels** | - | - | **3.5-4.0** | **0.4-1.1** | **<1:1** | **≥300** | **≤0.1** | **≤0.08** | **≥400** | **≥100** | **0.5-1.3** | **0.3-0.7** | **0.2-0.4** |
| Hill's Prescription Diet j/d Canine | 498/13 oz. | 4.2 | 4.24 | 0.85 | 0.7:1 | 316.8 | 0.07 | 0.04 | 698 | 128 | 0.81 | 0.56 | 0.19 |

Key: ME = metabolizable energy, FAs = fatty acids, EPA = eicosapentaenoic acid, Gluc = glucosamine hydrochloride, Chon = chondroitin sulfate, Se = selenium, Carn = L-carnitine, P = phosphorus, Na = sodium, na = not available from manufacturer.
*Dry matter basis unless otherwise indicated.
**Energy density values are listed on an as fed basis and are useful for determining the amount to feed; cup = 8-oz. measuring cup.
To convert to kJ, multiply kcal by 4.184.

may be unwilling or unable to engage in even mild exercise. For these dogs, it may be prudent to initially provide a combination of appropriate analgesia and therapeutic osteoarthritis food. The daily intake of the therapeutic osteoarthritis food should be based on 80% of the DER for an ideal body weight and fed for approximately one month. During this time chondrocytes will selectively concentrate EPA in their membranes, aiding in modulating the inflammatory process and minimizing the destruction of cartilage matrix by degradative enzymes. Based on clinical studies[d-g] with a commercial veterinary therapeutic food,[c] dogs can be expected to have increased mobility in approximately one month, facilitating initiation of an exercise program. At the end of the month, body weight, body condition and mobility should be reevaluated. If additional weight reduction is necessary, the dog should be transitioned to a food specifically designed for weight loss and an exercise program initiated. Rechecks should be performed at monthly intervals to assess body weight, body condition and mobility. The veterinary therapeutic food for osteoarthritis and the food designed for weight

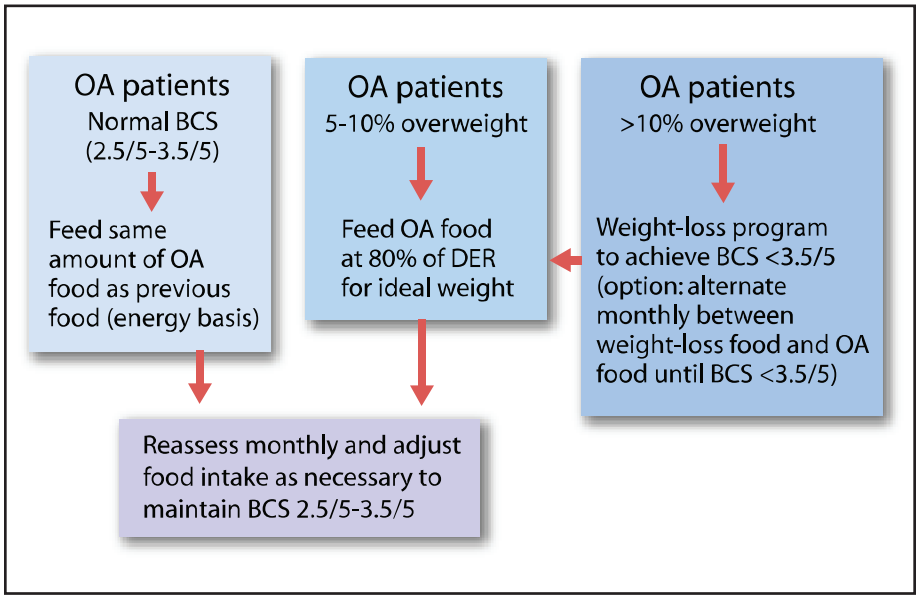


**Figure 34-7.** Overview of feeding regimen recommendations for osteoarthritis (OA) patients based on body weight/body condition scores (BCS). See Chapter 1 for methods for determining BCS. DER = daily energy requirement (Chapter 5).

### Box 34-3. NSAIDs and NSAID Dosage When Feeding a Veterinary Therapeutic Food Designed for Patients with Osteoarthritis.

Nonsteroidal antiinflammatory drugs (NSAIDs) are the most common class of analgesics used to control pain in canine patients with osteoarthritis. In dogs, the efficacy of NSAIDs for relief of clinical signs of osteoarthritis is well documented. However, in some patients, glucocorticoids, narcotic and non-narcotic medications may be indicated for control of pain and clinical signs. Pain control in cats is more challenging because of their limited ability to metabolize drugs requiring glucuronide conjugation. Currently in the United States, there are no NSAIDs labeled for long-term use in cats. However, with careful dosing regimens both aspirin and meloxicam have been used for management of chronic pain and osteoarthritis in cats. Although they are an effective part of multifaceted therapy, NSAIDs have not been shown to alter the progression of osteoarthritis. As a class, NSAIDs may cause side effects related to gastrointestinal, hepatic, renal and hematopoietic systems. Because of their unique metabolism, cats are more sensitive to these side effects than dogs. When NSAIDs are prescribed, owners should be made aware of clinical signs indicative of adverse side effects of these products. Careful titration of the dosage of NSAIDs is recommended for each individual patient. The addition of other therapeutic modalities may affect the appropriate NSAID dose. Dogs in the initial phases of physical rehabilitation will benefit from effective analgesia. Conversely, the initiation of appropriate therapeutic nutrition may allow for a reduction in the daily NSAID dose.

In a 90-day prospective, randomized (dietary treatments), double-masked, controlled study designed to evaluate the effect of a veterinary therapeutic food[a] on the dose of an NSAID (carprofen) required to manage clinical signs in dogs with osteoarthritis,[b] significant effects were noted in the dogs consuming the therapeutic food. Pet owners observed significantly greater pain reduction in dogs consuming the veterinary therapeutic food compared to the control food. Carprofen dose reductions were possible in 43% of dogs consuming the therapeutic food vs. 32% of dogs eating the control food. Carprofen dose increases were necessary in 11% of the dogs consuming the control food and in only 2% of dogs consuming the therapeutic food. For the group receiving the therapeutic food, the mean carprofen dose reduction was 25%. Significantly greater reductions in carprofen dose (mg/lb body weight) were possible in the dogs consuming the therapeutic food compared with the control group. This study indicates that nutritional management using a food with high levels of total omega-3 fatty acids and eicosapentaenoic acid may allow for reduction in the dose of NSAIDs necessary to control clinical signs in dogs with osteoarthritis.

**ENDNOTES**

a. Prescription Diet j/d Canine. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

b. Allen TA. A multi-center practice-based study of a therapeutic food and a non-steroidal anti-inflammatory drug in dogs with osteoarthritis. Hill's Pet Nutrition, Inc., Topeka, KS, USA. 2004.

The Bibliography for **Box 34-3** can be found at www.markmorris.org.

loss can be alternated at monthly intervals until ideal body weight is achieved. This approach will maximize the benefits of the weight-reduction food and the therapeutic food for osteoarthritis. Combining the foods (i.e., providing half the calories from each food each day) is not recommended and would be expected to compromise the benefits of both foods. **Figure 34-7** provides an overview of these feeding options.

## Assess and Select the Food

After the patient has been assessed and, if necessary, body condition returned to normal, an appropriate veterinary therapeutic food should be selected to aid in the long-term management of osteoarthritis. The steps to assessing foods include: 1) ensuring the nutritional adequacy of the food has been determined by a credible regulatory agency such as AAFCO (See product label.) and 2) comparing the food's key nutritional factors with the recommended levels. Because foods for the management of osteoarthritis are used in place of regular maintenance foods, the key nutritional factors include those for promoting long-term general health by managing nutrition-related risk factors for kidney and heart disease.

**Table 34-5** provides key nutritional factor profiles for selected commercial canine veterinary therapeutic foods marketed to provide an arthritis benefit and compares them to the key nutritional factors for osteoarthritis. Currently there are no veterinary therapeutic foods marketed in North America for cats with osteoarthritis. If the food in question cannot be found in this table, the manufacturer should be contacted. Manufacturers' addresses, websites and toll-free customer service numbers are listed on pet food labels. If the manufacturer cannot provide the necessary information, food selection should be limited to foods for which this information is available. Comparing a food's key nutritional factor content with the recommended levels is fundamental to food selection.

Another criterion for selecting a food that may become increasingly important in the future is evidence-based clinical nutrition. Practitioners should know how to determine risks and benefits of nutritional regimens and counsel pet owners accordingly. Currently, veterinary medical education and continuing education are not always based on rigorous assessment of evidence for or against particular management options. Still, studies have been published to establish the nutritional benefits of certain pet foods. Chapter 2 describes evidence-based clinical nutrition in detail and applies its concepts to various veterinary therapeutic foods.

Treats should not be fed in excessive amounts, if at all. It is best to limit treats to less than 10% of the total food fed on a volume, weight or calorie basis. Consider having owners switch to smaller treats or break larger treats in half and feed pieces instead of full treats. Too many treats will dilute the

beneficial effects of a properly formulated veterinary therapeutic food. The key nutritional factors important for osteoarthritis are not included in most commercial treats, particularly at the necessary levels.

### Assess and Determine the Feeding Method

It may not always be necessary to change the feeding method when managing a patient with osteoarthritis. However, a thorough assessment should be made to verify that an appropriate feeding method is being used. Items to consider include amount fed, how the food is offered, access to other food and who feeds the patient. If a new food is introduced, the amount to feed can be determined from the product label or other supporting materials. The food dosage may need to be changed if the caloric density of the new food differs from that of the previous food. The food dosage is usually divided into two or more meals per day. The food dosage should be altered if the patient's body weight and condition are not optimal.

For clinical nutrition to be effective there needs to be good client compliance. Ensuring compliance requires good client communication, both oral and written, regarding the benefits of, and instructions on, transitioning to the new food. Incorporating followup calls to clients within three days of initiating a new food and again in three weeks has been shown to dramatically improve client and patient acceptance of new foods (AAHA, 2003). Limiting the patient's access to other foods and providing both dry and wet products to satisfy owner and patient preferences may also promote compliance.

## REASSESSMENT

Clinical studies suggest that dogs with signs of osteoarthritis will respond to appropriate therapeutic foods within four to six weeks. Normal weight dogs should be evaluated for changes in lameness. Orthopedic examinations and owner quality of life assessments at this time can help determine the efficacy of the therapeutic food for osteoarthritis. After a response is noted, patients can be evaluated semiannually for overall health and disease progression.

Overweight dogs with osteoarthritis should be evaluated monthly to assess body weight, body condition and mobility until ideal body condition (~3/5) is achieved. After patients reach an ideal body condition they should be maintained on a veterinary therapeutic food properly formulated for osteoarthritis. These obese-prone patients should be evaluated every three to six months to assess body weight, body condition and mobility. Careful monitoring will encourage compliance and prevent weight regain.

Because management of osteoarthritis often involves a multifaceted approach, dosages of concurrent analgesics or supplements should be reevaluated within the first four to six weeks of initiating an appropriate therapeutic food (**Box 34-3**), weight loss or physical rehabilitation program. Adjustments to the dose of concurrent analgesics or supplements should be based on response to therapy.

Maintaining cats at a healthy body weight should be of paramount concern until additional options such as therapeutic foods are available. Cats participating in weight-loss programs should be evaluated monthly until ideal body condition is achieved then semiannually for overall health and disease progression.

## ENDNOTES

a. Proprietary market research. Veterinary sample size: 200. Data on file. Pfizer Animal Health, Exton, PA, USA. 1996.
b. www.press.petinsurance.com. Accessed September 2007.
c. Prescription Diet j/d Canine. Hill's Pet Nutrition, Inc., Topeka, KS, USA.
d. Allen TA. Dose titration effects of omega-3 fatty acids fed to dogs with osteoarthritis. Hill's Pet Nutrition, Inc., Topeka, KS, USA. 2004.
e. Allen TA. A multi-center practice-based study of a therapeutic food and a non-steroidal anti-inflammatory drug in dogs with osteoarthritis. Hill's Pet Nutrition, Inc., Topeka, KS, USA. 2004.
f. Dodd CE, Fritsch DA, Allen TA. Omega-3 fatty acids in canine osteoarthritis: A randomized, double-masked, practice-based, 6-month feeding study. Hill's Pet Nutrition, Inc., Topeka, KS, USA. 2004.
g. Allen TA. Effects of feeding omega-3 fatty acids on force plate gait analysis in dogs with osteoarthritis, 3-month feeding study. Hill's Pet Nutrition Inc., Topeka, KS, USA. 2003.
h. Eugster AK. Memorandum: Distributing Products Containing Glucosamine Hydrochloride and/or Chondroitin Sulfate. Texas Agricultural Experiment Station. The Texas A&M University, College Station, TX, USA. Office of the State Chemist. May 11, 1999.

## REFERENCES

The references for **Chapter 34** can be found at www.markmorris.org.

## CASE 34-1

### Lameness in a Labrador Retriever Mixed-Breed Dog

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### Patient Assessment

A six-year-old neutered female Labrador retriever mix, was examined for rear limb lameness of two years' duration. Clinical signs were mild to moderate in severity and included difficulty in rising from rest, limping, stiffness and reluctance to run, jump or play. The owner was giving no medications or supplements. The patient weighed 34 kg, but was considered overweight with a body condition score of 4 on a 5-point scale. The rest of the physical examination revealed no other abnormal findings. A thorough orthopedic examination disclosed the following abnormalities: slight left rear limb lameness at a walk, normal weight-bearing at rest, mild limitation in range of motion of the left hip joint and mild resistance to elevation of the right rear limb with full weight bearing on the left hind limb. Mild pain was elicited upon palpation of the left hip joint.

Results of a complete blood count, serum biochemistry profile and urinalysis were within normal limits. Radiographic changes were consistent with bilateral hip dysplasia and degenerative joint disease with the left coxofemoral joint more severely affected.

### Assess the Food and Feeding Method

The patient was fed a low-calorie dry dog food but had access to food sources for other dogs and cats in the household.

### Questions

1. What are the therapeutic goals for managing patients with osteoarthritis or degenerative joint disease of coxofemoral joints?
2. How might the overweight body condition contribute to the clinical problems in this dog?
3. Could this condition have been prevented with proper nutritional management?
4. Outline a comprehensive nonsurgical management plan for this patient.

### Answers

1. Therapeutic goals for managing chronic osteoarthritis or degenerative joint disease in the coxofemoral joints include: 1) eliminating underlying causes (e.g., femoral head and neck excision for aseptic necrosis of the femoral head), 2) setting realistic treatment outcome expectations with the patient's owner, 3) enhancing the dog's quality of life by reducing pain, maintaining or improving activity level and joint function and 4) slowing disease progression by modifying cartilage structure and function. Most patients with chronic osteoarthritis or degenerative joint disease have irreversible changes with no opportunity to eliminate or cure the condition. This makes client education very important. The patient's owner should be made aware that degenerative joint disease is controllable but not curable and that a comprehensive management plan needs to include long-term pain management. The goals are to alter disease progression and improve the patient's quality of life.
2. Osteoarthritis is often associated with abnormal forces acting on normal joints or normal forces acting on abnormal joints. Obesity may contribute to progression of degenerative joint disease and clinical signs by causing excess physical stress on either normal or abnormal joints. In addition, excess body fat is a source of inflammatory cytokines. Multiple studies have shown that weight loss helps decrease lameness and pain in overweight dogs with existing hip osteoarthritis. In these studies, even mild weight loss was associated with clinical improvement.

   Large- and giant-breed dogs are at risk for developmental orthopedic disease including hip and elbow dysplasia, osteochondrosis and other conditions associated with joint instability or incongruity. Nutritional risk factors for developmental orthopedic disease include excess energy, fat and calcium intake during growth. Use of foods specifically formulated for large-breed puppies and avoiding free-choice feeding helps manage these nutritional risk factors and ensure a normal, healthy growth rate. An overweight body condition is recognized as a risk factor for development of degenerative joint disease in dogs; maintaining a normal body condition can help reduce the incidence and severity of osteoarthritis. A study found that when at-risk puppies were fed free choice during growth, they exhibited an increased incidence and severity of hip joint laxity and hip dysplasia compared to puppies fed in a restricted fashion. Over time, those dogs fed to maintain a lean body condition throughout life exhibited reduced severity of osteoarthritis and a delayed need for medication compared to their heavier siblings.
3. Nonsurgical management of osteoarthritis should focus on three main aspects: 1) activity modification, 2) medications and supplements to modify joint pain and function and 3) nutritional management that emphasizes weight control and modifying joint inflammation and cartilage degradation. Previously, limiting activity levels in patients with osteoarthritis and degenerative joint disease was considered important. However, studies in human patients with osteoarthritis have shown the benefits of exercise including decreased pain scores and improved joint function scores. Furthermore, exercise reduced the need for analgesic med-

ications. Today, veterinary specialists recommend therapeutic exercise as a way to improve quality of life for dogs with chronic osteoarthritis. A variety of medications and supplements are available to manage pain and joint function. Responses to medications and supplements vary markedly in patients with osteoarthritis and specific products and doses need to be individually tailored for each dog.

4. New information has been generated about canine osteoarthritis from in vitro studies with cartilage models and clinical studies in dogs with various forms of arthritis. In vitro cartilage studies have shown that canine chondrocyte membranes selectively store the omega-3 fatty acid eicosapentaenoic acid (EPA), but not other omega-3 fatty acids. EPA is the most important fatty acid for helping manage inflammation in cartilage of dogs. EPA is also the only omega-3 fatty acid shown to inhibit activity of enzymes that degrade cartilage and helps turn off the signal to make degradative enzymes. Based on these in vitro studies, clinical trials were performed in dogs with arthritis using a veterinary therapeutic food enhanced with levels of EPA. The food also contained high levels of total omega-3 fatty acids, an omega-6 to omega-3 fatty acid ratio less than 1.0, high L-carnitine levels, added glucosamine hydrochloride and chondroitin sulfate, added antioxidant nutrients and added lysolecithin. Feeding this food to dogs with arthritis resulted in higher serum EPA concentrations, significant improvements in clinical signs observed by pet owners, improved clinical assessments of arthritis by veterinarians and improved weight bearing on affected limbs as measured by force-plate gait analysis. Many of the dogs in the studies were not receiving medications or supplements in conjunction with the food.

## Feeding Plan and Progress Notes

Prescription Diet j/d Canine dry food[a] was dispensed for the owners to feed. The amount of food was calculated for an obese-prone dog. The owners were encouraged to deny access to other sources of dog and cat food in the household. Controlled exercise was also encouraged using walks on a leash. Six weeks later the owners reported improvements in all clinical signs associated with arthritis and improvements in the patient's overall personality. The improvements observed by the owner continued at the three-month recheck and no pain was elicited on palpation of the left hip joint by the attending veterinarian. These improvements were noted without concurrent use of medications or supplements. Body weight and body condition score remained the same so client education focused on the importance of continued weight management with appropriate reductions in food, limiting access to other pet food and increased levels of exercise.

## Acknowledgements

Thanks to Drs. James Roush of Kansas State University, Manhattan, and Tara Enwiller of Gilbert, Arizona, for providing information about this patient.

## Endnote

a. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

## Bibliography

Budsberg S, Bartges J, Schoenherr B, et al. Effects of different n6:n3 fatty acid diets on canine stifle osteoarthritis (abstract). In: Proceedings. Veterinary Orthopedic Society Annual Conference 2001; 28: 40.

Burkholder WJ, Taylor L, Hulse DA. Weight loss to optimal body condition increases ground reactive forces in dogs with osteoarthritis (abstract). In: Proceedings. Purina Nutrition Forum; 2000: 74.

Caterson B, Flannery CR, Hughes CE, et al. Mechanisms involved in cartilage proteoglycan catabolism. Matrix Biology 2000; 19: 333-344.

Curtis CL, Hughes CE, Flannery CR, et al. N-3 fatty acids specifically modulate catabolic factors involved in articular cartilage degradation. Journal of Biological Chemistry 2000; 275: 721-724.

Curtis CL, Rees SG, Cramp J, et al. Effects of n-3 fatty acids on cartilage metabolism. Proceedings of the Nutrition Society 2002; 61: 381-389.

Dodd CE. Multicenter clinical study on the effect of an investigational food containing elevated omega-3 fatty acids on canine osteoarthritis clinical signs. Final report. Hill's Pet Nutrition Center, 2004.

Hansen RA, Allen KGD, Pluhar EG, et al. N-3 fatty acids decrease inflammatory mediators in arthritic dogs (abstract). FASEB Proceedings; 2003.

Impellizeri JA, Tetrick MA, Muir P. Effect of weight reduction on clinical signs of lameness in dogs with hip osteoarthritis. Journal of the American Veterinary Medical Association 2000; 216: 1089-1091.

Kealy RD, Olsson SE, Monti JL, et al. Effects of limited food consumption on the incidence of hip dysplasia in growing dogs. Journal of the American Veterinary Medical Association 1992; 201: 857-863.

Kealy RD, Lawler DF, Ballam JM, et al. Five-year longitudinal study on limited food consumption and development of osteoarthritis in coxofemoral joints of dogs. Journal of the American Veterinary Medical Association 1997; 210: 222-225.