Clinical Perspectives on Canine Joint Disease

Presented at
The North American Veterinary Conference
Orlando, Florida, USA
January 17, 2001
Contents

Summary of Contents .................................................. 2

Author Profiles .......................................................... 6

Articular Cartilage in Health and Disease .......................... 8
Allan J. Lepine, PhD; Michael G. Hayek, PhD

The Benefit of Weight Management in Dogs with Joint Problems .... 18
Mark A. Tetrick, DVM, PhD; Joseph A. Impellizzeri, DVM; Peter Muir, BVSc,
M VetClinStud, PhD, M A C V Sc, D A C V S, D E C V S

Physical Therapy for Dogs with Joint Disease ..................... 22
Darryl L. Millis, MS, DVM, Diplomate ACVS

Pathophysiology and Diagnosis of Intervertebral Disk Degeneration .... 28
Takayoshi Miyabayashi, BVS, M S, PhD, Diplomate ACVR

Balanced Management of Osteoarthritis in Companion Animals .... 32
Steven A. Martinez, DVM, MS, Diplomate ACVS
CHAPTER 1: ARTICULAR CARTILAGE IN HEALTH AND DISEASE

Allan J. Lepine, Michael G. Hayek
Pages 8–17

Summary. Nutritional management of articular cartilage health requires an understanding of the changes that normally occur during life, as well as the alterations caused by disease or injury.

Findings.
- Components of articular cartilage extracellular matrix
  - Proteoglycans – comprised of various glycosaminoglycans
  - Hyaluronan
  - Chondroitin sulfate and dermatan sulfate
  - Heparan sulfate
  - Keratan sulfate
  - Collagen
- The ability of articular cartilage to respond to compressive stress depends on the characteristics and interrelationships between proteoglycans and collagen
- Significant structural changes occur during the maturation of articular cartilage
  - Amounts and proportions of collagen types change
  - Proteoglycans become smaller and enriched with keratan sulfate
  - Result of aging changes is a reduced ability to withstand normal joint functioning forces
- Three types of articular cartilage damage
  - Microdamage or blunt trauma
  - Chondral fractures
  - Osteochondral fractures
- Osteoarthritis – noninflammatory degenerative joint disease
  - Changes in proteoglycan amounts and ratios
  - Matrix degradation often exceeding synthesis
  - Cytokine release stimulates production of degradation enzymes and suppresses protein biosynthesis in chondrocytes
- Nutritional management of articular cartilage health
  - Eicosanoid production can be manipulated by dietary fatty acids and thereby assist in inflammation management
  - Dietary glucosamine and chondroitin sulfate may help increase cartilage biosynthesis and decrease degradation

Application. Dietary fatty acids and chondroprotective nutrients such as chondroitin sulfate and glucosamine may be useful in maintaining joint health and managing joint injury or disease.

CHAPTER 2: THE BENEFIT OF WEIGHT MANAGEMENT IN DOGS WITH JOINT PROBLEMS

Mark A. Tetrick, Joseph A. Impellizeri, Peter Muir
Pages 18–21

Summary. An observable improvement in lameness can be achieved when overweight dogs lose body weight.

Findings.
- Lameness severity was significantly influenced by weight loss in overweight dogs with hip osteoarthritis and lameness.
Findings. (continued) • Rapid or prolonged increases in blood glucose and, therefore, insulin secretion may promote greater weight gain and fat deposition. Specially formulated foods containing a blend of barley and grain sorghum may help improve glucose tolerance and stabilize blood glucose levels in overweight dogs • Dietary carnitine addition resulted in lower fat mass and greater lean body tissue in dogs during weight loss • Diets containing chromium tripicolinate may lead to an improvement in glucose tolerance and blood glucose stability in overweight pets

Application. Weight loss can influence lameness severity. A achieving weight loss in dogs can be facilitated by the use of specially formulated diets containing carnitine, chromium tripicolinate, and a blend of barley and grain sorghum.

CHAPTER 3: PHYSICAL THERAPY FOR DOGS WITH JOINT DISEASE
Darryl L. Millis
Pages 22–27

Summary. Joint disease is a common problem in dogs. Patients with osteoarthritis (OA) can have restricted activity, limited ability to perform, pain and discomfort, and decreased quality of life. Physical therapy can enhance or supplement other treatments for OA.

Findings. • Although mechanical stress can cause biochemical, histological and biomechanical changes in articular cartilage, a lifetime of regular low-impact exercise in dogs with normal joints did not cause significant alterations • Older dogs may be more vulnerable to articular cartilage changes from mechanical stress than younger dogs • The goals of therapeutic exercise should be to reduce body weight, increase joint mobility, and reduce joint pain through the use of low-impact weight-bearing exercises designed to strengthen supporting muscles • Exercise should be performed only after correction of major OA risk factors, such as joint instability or obesity • The ideal exercise program is one that provides sufficient benefits without causing discomfort • Initially, antiinflammatory drugs should not be administered prior to exercise so that the proper level of exercise can be determined • Suggested exercise methods include swimming, controlled exercise on a leash, and treadmill walking • Physical agents that can be useful aids in physical therapy include:
  - Superficial heat modalities
  - Cryotherapy
  - Massage
  - Ultrasound
  - Neuromuscular Electrical Simulation
• Progress should be documented to assist in further treatment decisions and help maintain the dog owner’s enthusiasm for the program

Application. Physical rehabilitation is a valuable, but underused part of the management of dogs with OA. It can be used in combination with nutritional, medical, and surgical management to reduce pain and lameness and improve quality of life.
CHAPTER 4:
PATHOPHYSIOLOGY AND DIAGNOSIS OF INTERVERTEBRAL DISK DEGENERATION
Takayoshi Miyabayashi
Pages 28–31

Summary. Intervertebral (IV) disk disease is a common neurological condition in dogs that causes pain and motor dysfunction. The age-related degeneration of IV disks in dogs cannot be avoided but it may be possible to delay the process. Research in chondrocyte metabolism and its relationship in degeneration should help in finding ways to maintain canine IV disk health for as long as possible.

Findings.
- Intervertebral disks have two distinct components, which work together to act as a shock absorber
  - Anulus fibrosus – stretches evenly to distribute force
  - Nucleus pulposus – contains proteoglycans that can hold high water content
- Degenerative changes of canine IV disks with age are unavoidable
  - Loss of proteoglycans is initial step
  - Eventually fissures form within the anulus fibrosus
  - Nucleus pulposus protrudes through fissures
  - IV disk space narrows
  - Spondylosis deformans develops around vertebral end-plates
  - End-plate sclerosis and malalignment may develop
  - All IV disk tissues herniate from the IV disk space
  - Further bony remodeling at end-plates
  - Finally, protruded nucleus pulposus undergoes endochondral ossification.
- As dogs live longer, more severe degenerative changes may be observed that may be confused with discospondylitis or neoplasia, even though the associated motor dysfunction is minor
- MRI is the diagnostic method of choice in human radiology but plain radiography and myelography are still the most commonly used imaging methods in diagnosis of IV disk disease in veterinary medicine
CHAPTER 5: BALANCED MANAGEMENT OF OSTEOARTHRITIS IN COMPANION ANIMALS

Steven A. Martinez
Pages 32–37

Summary. No single treatment will adequately manage osteoarthritis (OA) in all dogs. A combination of three treatment components should be considered when medically managing a dog with OA: 1) weight control, 2) exercise/activity, 3) pharmacological/disease-modifying osteoarthritic drugs. Exclusion of one or more of these components from a treatment protocol will usually result in an overall poorer clinical response.

Findings. • Weight Control
- Obesity is a major risk factor for the development of OA
- Achieving weight control can be challenging
- Dogs with OA that inhibits movement cannot utilize consumed or stored fat efficiently
- Dogs with underlying endocrine disorders have a tendency to maintain body fat even on a reducing diet
- Estimations of dog's ideal weight and energy requirements are often inaccurate
- Owners may not be willing to be proactive in helping dogs reduce weight
- All weight-control programs should include an exercise program

• Exercise
- Controlled exercise is an important aspect in the management of OA in dogs
- High-impact activities may over-stress damaged joints and increase inflammation
- Low-impact activities are thought to reduce loads on an OA joint and result in less discomfort for patient while maintaining good muscle strength/mass and joint function

• Pharmacologics
- The primary goal of the pharmacological management of OA is to relieve the patient of discomfort associated with joint movement
- Toxicity concerns are present with long-term, chronic therapy with NSAIDs; therefore, they probably should be administered only on a PRN basis, especially for the dog that has only intermittent discomfort due to OA.
- Glucosamine and chondroitin sulfate reportedly have a positive effect on cartilage matrix; they enhance proteoglycan production and inhibit catabolic enzyme production or activity in arthritic joints

Application. Osteoarthritis can be a debilitating disease for dogs; however, new concepts in a balanced management of OA can result in an acceptable quality of life for the OA patient. Medical management must be considered beyond pharmacological treatment to include a balance with exercise/activity and weight control management. Failure to consider this treatment “triad” concept will usually result in a poorer clinical response to therapy and quality of life as perceived by the owner of the arthritic dog.
Author Profiles

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Dr. Martinez received his MS degree in Comparative Pathology in 1984 and his DVM degree in 1985 from the University of California at Davis. After completing a small animal internship at California Animal Hospital from 1985-1986 and a small animal surgical residency at Michigan State University from 1986-1989, Dr. Martinez accepted an academic appointment as Assistant Professor of Small Animal Surgery at the Atlantic Veterinary College at the University of Prince Edward Island, Canada from 1989-1990. Dr. Martinez returned to Michigan State University and served as Assistant Professor of Small Animal Surgery from 1990-1997. Dr. Martinez has been serving as an Assistant Professor of Small Animal Orthopedic Surgery at Washington State University since 1997. His current research interests include bone grafting, cytokine delivery systems in bone, and gait analysis in dogs.

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Articular Cartilage in Health and Disease

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INTRODUCTION
Understanding the changes in the physiologic and morphologic relationships of articular cartilage during normal life stages, as well as during more dramatic events such as joint trauma or disease, can allow for the application of nutritional management to minimize negative outcomes. Nutritional interventions can include managing growth in those breeds prone to joint problems, decreasing incidence and symptoms of obesity, and providing nutrients such as omega-3 fatty acids and chondroprotective agents that aid the inflamed or damaged joint. A review of the structure and function of articular cartilage is important in order to better understand the control and management of companion animal joint health.

STRUCTURE AND FUNCTION OF ARTICULAR CARTILAGE

Synovial Joints
Synovial joints (diarthroses) are composite structures consisting of articular cartilage, a joint capsule filled with synovial fluid, and underlying osseous structures (Figure 1). A physiologically normal synovial joint provides a virtually wear-resistant and friction-free articulating surface that can withstand considerable compressive, tensile, and shear forces. Cells that line the synovial membrane of the joint capsule produce synovial fluid, a clear and viscous substance. Synovial fluid serves as a protective barrier by providing lubrication to the opposing articular surfaces and preventing contact between surfaces. It also supplies nutrients to the cells of the articular cartilage and removes waste products. Without an adequate protective barrier, rapid joint degeneration can occur when forces, especially weight bearing forces, are applied.


Components of the Articular Cartilage
Extracellular Matrix
Proteoglycans. Proteoglycans, a primary component of the articular cartilage extracellular matrix, are comprised
of numerous glycosaminoglycan chains that are covalently linked to a central core protein (Figure 2). Glycosaminoglycans are repeating disaccharide units in which one of the saccharides in each disaccharide is generally a sulfated amino sugar.

Four primary glycosaminoglycans associated with proteoglycans are: (1) hyaluronan, (2) chondroitin sulfate and dermatan sulfate, (3) heparan sulfate, and (4) keratan sulfate. These glycosaminoglycans are distinguished by the specific sugar residues included, the type of linkage between these residues, and the number and location of sulfate groups. Hyaluronan is a repeating disaccharide of glucuronate and N-acetyl glucosamine and is the only glycosaminoglycan that is nonsulfated. Chondroitin sulfate is a repeating disaccharide of glucuronate and N-acetyl galactosamine; dermatan sulfate is derived from chondroitin sulfate by the epimerization of glucuronate to iduronate. Keratan sulfate is a disaccharide of galactose and N-acetyl glucosamine; heparan sulfate contains iduronate and N-acetyl glucosamine. While the majority of these glycosaminoglycans are covalently bound to a core protein to form proteoglycans, hyaluronan does not bind to a core protein.

Aggrecan, the most common and well-defined proteoglycan in articular cartilage, is comprised of a core protein to which as many as 100 glycosaminoglycan chains are attached. The attachment to the core protein is at a serine residue and is stabilized by a link tetrasaccharide. While the majority of the glycosaminoglycans in aggrecan are chondroitin sulfate and keratan sulfate, they are not randomly attached to the core protein but are located within specific binding regions. This generally results in aggrecan having a greater chondroitin sulfate content than keratan sulfate since the keratan sulfate-rich binding region is located closer to the NH₂ terminal end of the core protein while a larger, chondroitin sulfate-rich binding region is more distal.

Aggrecan is generally found as a large aggregate with as many as 200 aggrecan molecules covalently bound to a single hyaluronan molecule. This linkage to hyaluronan is

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**Figure 2.** Proteoglycan, one of the 2 main classes of the articular cartilage extracellular matrix, is a complex structure formed by glycosaminoglycan (GAG) chains covalently linked to core proteins, which are then bound to form the proteoglycan, aggrecan. (Used with permission. Lepine AJ. Structure and function of articular cartilage. In: Reinhart GA, Carey DP, eds. Recent Advances in Canine and Feline Nutrition, Vol. III: 2000 Iams Nutrition Symposium Proceedings. Wilmington, OH: Orange Frazer Press, 2000; 481-494.)
stabilized by a small glycoprotein referred to as link protein. The link protein is homologous with the NH₂ terminal region of aggrecan, thus allowing hyaluronan to covalently bind to both link protein and aggrecan. These bonds serve to stabilize the aggrecan aggregate. To provide further stabilization, cross-links between the link proteins and the core protein are also present.

Collagen. Collagen, a second primary component of the extracellular matrix, is composed of a triple helix of polypeptide α-chains (Figure 3). These polypeptide chains of collagen are unique, relative to other proteins of animal origin, due to high proportions of hydroxylsine and hydroxyproline residues. The collagen molecules self-assemble into collagen fibrils. Within those fibrils, interchain hydrogen bonds and covalent intramolecular cross-links form between modified lysine residues of adjacent triple helices. These bonds and cross-links help to stabilize not only the triple helix, but ultimately the collagen structure. Collagen fibrils then aggregate into a single collagen fiber.

Several collagen variations are distinguished by the composition of the α-chains that form the triple helix. In articular cartilage, approximately 90-95% of the collagen is type II, with the remaining collagen types reported to be types V, VI, IX, and XI. The incorporation of these minor amounts of collagen types into the collagen matrix may be important to the physical organization of the matrix. For example, type IX collagen is located at the surface of the type II collagen fibril linked by a lysine-derived hydroxypyridinium cross-link. Two regions of the type IX collagen, the COL3 arm and the NC4 domain, project out from the surface and are suspected to serve as binding sites for other matrix components. It is also speculated that fibril thickness is controlled by Type XI collagen which is present within the type II fibrils.

Function of Extracellular Matrix Components

The unique physiologic relationship between the proteoglycans and collagen makes articular cartilage a biphasic material with a porous-permeable fiber-reinforced solid phase and a freely flowing fluid phase. It is precisely because of this biphasic nature that articular cartilage has the biomechanical properties necessary to withstand the stresses associated with normal joint functioning.

The proteoglycans are hydrophilic in nature and thus provide an extremely high hydration capacity. Proteoglycans swell as water is attracted to the matrix, however, the degree of swelling is limited to about 20% of the maximum potential since the proteoglycans are imbedded in a matrix of collagen fibers. Inherent in the fibrillar structure of collagen and enhanced by the cross-links between collagen molecules, collagen fibers exhibit maximal tensile strength. The tensile stress imposed upon the collagen network by the swelling pressure of the proteoglycans demonstrates the importance of the tensile strength of collagen. One important outcome of this functional relationship is that the collagen network holds the proteoglycan molecules within the extracellular matrix and prevents their escape (Figure 4). This is particularly important since there are no covalent links between collagen and the proteoglycans and it is solely the size of the hydrated proteoglycans that maintains them within the articular cartilage.

The ability of the articular cartilage matrix to respond to compressive loads is dependent upon the characteristics and interrelationships between proteoglycans and collagen. The compressive force placed on articular cartilage upon loading forces the fluid phase to flow through the permeable solid phase. As the compressive force increases, the hydraulic pressure increases. This is due to decreased pore size as the solid matrix is compressed causing increased resistance to fluid flow until an equilibrium is reached with the compressive force...
resulting in a ceasing of cartilage deformation. Further contributing to this equilibrium is the increasing negative charge density within the matrix as water is extruded from the matrix following increased compression. After compression ceases, water and nutrients reenter the cartilage matrix, thereby allowing the proteoglycans to swell and the cartilage to recover to its nondeformed conformation.

As cartilage deformation occurs in response to compressive forces, considerable tensile forces are placed upon the collagen network. Without adequate resistance to tension by the collagen fibers the cartilage would rupture as the compressions increase. The experimental removal of glycosaminoglycans from bovine articular cartilage clearly demonstrated the importance of the proteoglycan–collagen relationship in articular cartilage. In this study, the compressive strength of the cartilage was largely eliminated but the rupture strength of the cartilage was only slightly reduced.

**DEVELOPMENT OF MATURE ARTICULAR CARTILAGE**

"Zones" are descriptive reference points for the organizational layers that encompass the thickness of mature articular cartilage (Figure 5).

**Zone 1** — Superficial or tangential zone. Contains flattened, elongated chondrocytes and collagen fibrils that are parallel to the articular surface.

**Zone 2** — Transitional or intermediate zone. Chondrocytes are oval or round, are distributed randomly, and contain greater numbers of mitochondria, rough endoplasmic reticulum, and golgi apparatus. Collagen fibrils are more oblique and appear less organized.

**Zone 3** — Radiate or deep zone. Chondrocytes are large and rounded, arranged in columns perpendicular to the articular surface.

**Zone 4** — Calcified zone. Farthest removed from the articular surface. The “tidemark” delineates zones 3 and 4. The few chondrocytes observed are necrotic due to the calcified matrix.

Within the transitional and deep zones, chondrocytes are the most metabolically active and have the capacity to synthesize and degrade all components of the extracellular matrix, including the precursors for collagen and the proteoglycans. A ggreca, link protein, and hyaluronan are extruded into the extracellular matrix where they spontaneously aggregate. The collagen fibrils in zone 3 are arranged perpendicular to the articular

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surface. The deep zone forms an interlocking network that anchors the cartilage to the bony substrate. The concentration and composition of collagen and proteoglycans varies depending on the specific articular cartilage zone. For example, the concentration of collagen is highest in the superficial zone and decreases by approximately 15% within the deep zone. In contrast, proteoglycan concentration is lowest in the superficial zone and highest in the deep zone. Furthermore, the proteoglycan composition varies across these zones with less keratan sulfate apparent in the superficial zone as compared to the deeper zones.

Significant structural modifications occur during the maturation process of articular cartilage. It is interesting to note that developing cartilage does not exhibit the zone distinctions observed in mature articular cartilage. The zones seen in adult articular cartilage are not entirely distinguishable, as shown in research in the young rabbit (6–8 weeks of age). At 6–7 weeks of age, a surface zone (likely encompassing both the surface and transitional zones) and the deep zone layers are present. By 8 weeks of age a distinction is apparent between the surface and transitional zones but tidemark is not seen until 12–14 weeks of age.

The composition of the extracellular matrix continues to change during growth and development. Proteoglycans become smaller as the body matures, most likely due to a decreased chain length of the chondroitin sulfate and possibly also decreased core protein length. This reduced proteoglycan size is likely due to the action of extracellular matrix proteases. The proteoglycans become proportionately enriched with keratan sulfate as a result of the decreased chain lengths of chondroitin sulfate and core protein. The specific chondroitin sulfate chains that are present within the articular cartilage also are altered with maturity. Immature cartilage has a ratio of chondroitin-4-sulfate to chondroitin-6-sulfate of 1:1 with this ratio decreasing as age increases. These maturational changes are likely of functional significance since the stiffness of the cartilage and the resultant resistance to deformation are dependent upon the fixed charge density and glycosaminoglycan content. In this respect, keratan sulfate influences stiffness to a greater degree than chondroitin sulfate, thereby providing a potential advantage to keratan sulfate-rich proteoglycans in articular cartilage subjected to high load such as is the case in the adult.

The amounts and proportions of collagen types changes throughout development. A study of fetal and neonatal rabbits revealed that the cartilage of a 17-day-old rabbit fetus contained collagen types I, III, and V but no type II collagen. By day 25, the fetal articular cartilage still contained type I collagen but no type II. It was only by 6 weeks postnatally that type II collagen was present and type I collagen disappeared. Furthermore, the concentration of hydroxyproline increased 2-fold in the chicken through 22 days of age indicative of an increased concentration of collagen in the articular cartilage of the young animal. These collagen changes are likely due to structural modifications that are necessary as the stresses on the articular cartilage are increased.

An important aspect of appropriate maturation in response to increasing joint-related forces is the ability of articular cartilage to develop differentially from growth plate cartilage, structures that are similar during early life. A primary difference is in the maturation of the chondrocytes of these two cartilage types. In contrast to articular cartilage chondrocytes, growth plate chondrocytes undergo hypertrophy and maturation as the extracellular matrix matures. Although the mechanism by which this distinction occurs remains equivocal, evidence exists that tenascin-C, a large glycoprotein found in the extracellular matrix of some embryonic and adult tissues (also called cytoticin or hexabrachion), may have a role in assembly and restructuring of the cartilage matrix. It is suggested that tenascin-C may promote a stable phenotype (round) of the articular cartilage chondrocyte while the absence of tenascin-C in the growth plate may allow flattening, proliferation, and maturation of the chondrocytes and thereby the replacement of the cartilage with bone. The presence of tenascin-C throughout life in the articular cartilage, albeit at decreasing concentrations with increasing age, allows functional chondrocytes to be maintained throughout life in contrast to epiphyseal bone growth.
PHYSIOLOGIC CHANGES ASSOCIATED WITH AGING

It is normal for articular cartilage to undergo physiological changes throughout the aging process. Swine studies have shown age-related decreases in hydration, collagen (dry matter basis), glycosaminoglycan concentration (especially chondroitin sulfate), and proteoglycan size. Although the total glycosaminoglycan concentration may not vary much with increased age, the ratio of keratan sulfate to chondroitin sulfate does increase. With respect to chondroitin sulfate it was also noted that the 4-sulfated compound decreased while the 6-sulfated compound increased. The alteration of proteoglycan composition and size is most likely the result of proteolytic cleavages that are not limited to the period of growth and maturation but appear to occur throughout the aging process in all species. The link proteins are also subject to proteolytic cleavage as aging progresses. This is likely a normal component of aging and could contribute to the destabilization of the proteoglycan component of the extracellular matrix. The inherent result of these normal age-related changes of the articular cartilage will be a matrix of reduced capability to withstand the forces associated with normal joint functioning.

EFFECTS OF JOINT DISEASE/INJURY

Articular cartilage injuries are characterized by the degree of involvement of the extracellular matrix composition and resultant damage to the chondrocytes and generally fall into three categories.

- **Microdamage or blunt trauma** — Microdamage may be caused by a single impact or repetitive blunt trauma and is characterized by a loss of matrix components, most notably proteoglycans, without chondrocyte damage. If the traumatic event is short in duration, the chondrocytes may be able to repair the cartilage by restoring the lost proteoglycans and matrix components. Damage resulting from sustained blunt trauma, however, may eventually become irreversible.

- **Chondral fractures** — Chondral fractures result from a penetrating traumatic event disrupting the articular surface not effecting the subchondral plate. The pathophysiologic response of articular cartilage surrounding the injury results in chondrocyte proliferation and synthesis of extracellular matrix protein. Unfortunately, since chondrocytes cannot migrate to the lesion, these efforts do not result in complete repair.

- **Osteochondral fractures** — This injury is considered a full thickness defect and is characterized by an insult crossing the tidemark into the underlying bone, resulting in chondrocyte damage and marrow cell involvement. Since vascular structures are now involved, inflammation occurs. This is in contrast to the lack of inflammatory response to less traumatic articular cartilage injuries resulting from the inherent avascular nature of this tissue. Following a full thickness injury, fibroblasts differentiate into chondrocytes and repair of the tissue is attempted, but the fibrocartilaginous repair tissue produced is not “normal” articular cartilage. After several phases of remodeling, the repair tissue has a lower proteoglycan content and a substantial component of type I collagen rather than type II. Therefore, the resulting repair is often of suboptimal quality resulting in compromised joint function.

EFFECTS OF OSTEOARTHRITIS

Osteoarthritis is defined as a noninflammatory degenerative joint disease characterized by degeneration of the articular cartilage, hypertrophy of the bone at the margins, and changes in the synovial membrane. Chondrocytes are normally able to synthesize the proteoglycans, collagen, fibronectin, and other components needed to maintain joint homeostasis and integrity due to the relatively low turnover of the extracellular matrix. When chronic trauma or disease disrupts this homeostasis, however, the articular cartilage may progressively degenerate, ultimately resulting in the development of osteoarthritis.

During the initial stage of osteoarthritis, responses similar to those seen in subchondral injury of the articular cartilage occur. Chondrocyte proliferation is observed with subsequent increased synthesis of extracellular matrix. In early osteoarthritic cartilage the concentration of keratan sulfate is decreased, the length of the chondroitin sulfate side chain is reduced and the ratio of chondroitin-4-sulfate to chondroitin-6-sulfate is increased. The newly synthesized proteoglycan subunits do not demonstrate normal aggregation with hyaluronic acid.

Concurrent with the increased synthetic response by the chondrocyte is matrix degradation, often proceeding at a rate exceeding that of synthesis. Proteoglycan and collagen breakdown is mediated by an increase in matrix metalloproteinases, serine proteases, lysosomal enzymes and other proteases at the articular surface early in the degenerative process and are responsible for the extensive matrix degradation associated with osteoarthritis. In healthy articular cartilage the activity of the metalloproteinases is low. Enzyme activity is regulated by the presence of tissue inhibitors of metalloproteinases (TIMPs) resulting in a low turnover of extracellular matrix proteins. During the osteoarthritic disease process the production of metalloproteinases greatly exceeds the ability of heightened release of TIMPs to maintain...
homeostasis. 28 Cytokines such as IL-1 and TNF-α stimulate chondrocytes to synthesize metalloproteinases and serine proteases that subsequently further degrade the extracellular matrix components. 25, 26 The cytokines also serve to suppress protein biosynthesis by the chondrocytes, further depleting the extracellular matrix. 29 Both IL-1 as well as TNF-α can cause substantial loss of matrix molecules, presumably by inducing proteolytic degradation. 30 The presence of fibronectin fragments and possibly other peptides further enhance catabolic activity and levels of cytokines. 29 IL-1 also stimulates chondrocytes and synovial cells to release arachidonic acid metabolites such as PG E2, leukotriene B4 and thromboxane. Inflammation of the synovium is present in established osteoarthritis although the inflammatory response is considerably less than would be expected in other joint diseases. 27

One of the earliest changes seen in an experimental model of osteoarthritis was an increase in hydration (2–3%) in the entire cartilage of the joint. 31 This hydration appears to be the result of the cleavage of type II collagen by collagenase. The functional collagen network is disrupted thereby permitting the proteoglycans, the hydration capacity of which are no longer restricted by the collagen network, to bind increased amounts of water resulting in the cartilage swelling described in early osteoarthritis. 26, 28, 32

Chondrocyte necrosis is evident as osteoarthritis progresses. The synthesis of extracellular matrix ceases while degradative activity remains elevated. The collagen network becomes increasingly disorganized and disintegrated. The content of several extracellular components including collagen and proteoglycans are progressively reduced. 26 The removal of functional proteoglycans from the extracellular matrix results in decreased water content of the cartilage and a subsequent loss of biomechanical properties, such as resilience and elasticity. As a result the chondrocytes are subjected to increasing mechanical stress and trauma thereby accelerating the osteoarthritic process. 26

NUTRITIONALLY MANAGING THE EFFECTS OF JOINT DISEASE AND INJURY

Eicosanoids. Eicosanoids are local chemical mediators (leukotrienes, thromboxanes, prostaglandins, and prostacyclins) produced by the actions of cyclooxygenase and lipooxygenase or arachidonic acid (an omega-6 fatty acid) and eicosapentaenoic acid (an omega-3 fatty acid). 33 Eicosanoids mediate inflammation, pain and fever, blood pressure, blood clotting, several reproductive functions, and the sleep/wake cycle. 33

NSAIDs and Corticosteroids. Administration of NSAIDs or corticosteroids is often included in treatment regimens for patients with traumatic and degenerative joint problems. Both drug therapies are aimed at reducing the production of arachidonic acid metabolites, which are released as a result of cell membrane damage and cause inflammation and pain. 34 These drugs act directly to inhibit the enzymes that help produce these eicosanoids (Figure 6).

Dietary Fat. Dietary fatty acids can also effectively manipulate eicosanoid production. A total dietary approach alters the substrates presented to the enzymes which dictate the types of eicosanoids produced. For instance, feeding omega-3 fatty acids results in the replacement of arachidonic acid (omega-6) in the cell membrane with eicosapentaenoic acid. 35 The eicosanoids derived from arachidonic acid (prostaglandin E2, leukotriene B4, leukotriene C4, and thromboxane A2) are proinflammatory, 36, 37 whereas eicosanoids synthesized from eicosapentaenoic acid (prostaglandin E3 and leukotriene B3) are less inflammatory.

It has been reported that feeding dogs a diet that contains an omega-6 to omega-3 fatty acid ratio between 5:1 and 10:1 results in decreased leukotriene B4 and increased leukotriene B5 secretion in skin and neutrophils compared to dogs fed higher fatty acid ratios (25:1, 50:1, 100:1).
Glucosamine and chondroitin sulfate have not produced reports of safety concerns. One study found that glucosamine and chondroitin sulfate (2 capsules, PO, q 12; daily dose of 800 mg sodium chondroitin sulfate; 1,000 mg glucosamine hydrochloride; and 152 mg manganese ascorbate) administered to 13 clinically normal Beagles for 30 days produced statistically significant but clinically unimportant changes in hematocrit, hemoglobin, WBC, segmented neutrophils, and RBC; however, no changes were seen in the prothrombin time, activated partial thromboplastin time, or mucosal bleeding time.48

In considering oral supplementation of glucosamine and chondroitin sulfate for management of joint problems one must be cognizant of the route of supplementation. If capsules or pills are utilized owner compliance may be an issue of concern. Inclusion of these compounds in a total diet will eliminate any concerns for compliance.

CONCLUSION

The structure/function relationship of articular cartilage is clearly demonstrated in the structural modifications observed during growth and development of the joint in response to the increasing forces naturally applied during this period. It is also clear that traumatic injury or disease can substantially disrupt the normal architecture of the joint by altering the concentrations of glycosaminoglycans, proteoglycans, collagens, and associated structures within the cartilage. Failure to correct such damage can allow for the progression to advanced joint disease from which complete reversal may not be possible.

An overall regimen for treatment of primary and secondary joint diseases should include weight management (discussed elsewhere in these proceedings), exercise modification, and administration of nonsteroidal antiinflammatory drugs (NSAIDs), glucocorticoids, or polysulfated glycosaminoglycans (GAGs).49 Several of these treatments either directly require or may be influenced by nutritional management. The provision of nutritional compounds that decrease cartilage degradation, increase matrix synthesis, provide matrix precursors, or assist in the control of the inflammatory response must be a primary directive in the control and management of joint health of the companion animal.


The Benefit of Weight Management in Dogs with Joint Problems

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INTRODUCTION
Obesity is recognized as an important factor influencing the clinical expression of osteoarthritis in humans. The incidence of obesity in the canine population has been estimated to be on the order of 25% and likely affects at least this proportion of dogs with osteoarthritis. While veterinarians have used nutritional therapy to achieve weight reduction in overweight osteoarthritic dogs, no data describing the effect of weight loss on lameness severity or the effect of weight loss on the prevalence or progression of osteoarthritis in dogs has been described. Because osteoarthritis of the hip joint is an important cause of lameness in dogs of all ages, we selected naturally-occurring cases of obese dogs with hip osteoarthritis to evaluate the hypothesis that lameness severity would be significantly influenced by weight loss.

A RECENT STUDY: INFLUENCE OF WEIGHT MANAGEMENT ON JOINT HEALTH
The influence of weight reduction on pelvic limb function was prospectively examined in 9 overweight client-owned dogs with hip osteoarthritis and lameness. Dogs studied were at least 10% over their ideal body weight. Dogs were screened using a serum chemistry panel with thyroid screen and complete blood count to rule out concurrent systemic disease. A numerical rating scale (NRS; Figure 1) and a visual analog scale (VAS; Figure 2) were used to subjectively assess lameness (by JI) prior to the dogs beginning a weight loss program. The weight loss program included Eukanuba Veterinary Diets® Nutritional Weight Loss Formula™ Restricted-Calorie™/Canine fed at 60% of maintenance calories for initial body weight.

Lameness assessment was repeated at the mid-point and end of the 10- to 19-week weight loss period. The effect of time on lameness and body condition were evaluated using repeated-measures analysis-of-variance and the Friedman test. Differences were considered significant at P<.05. Over the weight loss period, dogs lost between 11 and 18% of their initial body weight. Body weight decreased linearly over time (P<.001) and body condition score improved (P<.05). Numerical rating lameness scores improved significantly with time (P<.05) and there was also a linear improvement in VAS scores with time (P<.005). Visual analog scale assessment scores for lameness improved 76% over the study period. No dog was withdrawn from the study because of worsening lameness.

**Figure 1.** Numerical rating scale (NRS).

**Figure 2.** Visual analog scale (VAS) score using a 100 mm horizontal line. This method is considered to be a more sensitive assessment method.
Data from this study support the hypothesis that lameness severity can be significantly influenced by weight loss (Figure 3). Weight loss alone can result in a significant decrease in lameness. Increased emphasis should be placed on normalizing body weight in dogs with hip osteoarthritis. Although not examined in this study, normalization of the body weight of the osteoarthritic patient also has the potential to slow disease progression.

Current medical treatments for the management of dogs with osteoarthritis are primarily symptomatic. Longer treatment courses using nonsteroidal antiinflammatory drugs should not be given without using a concurrent nutritional program to normalize the dog’s body weight. Many overweight dogs with lameness due to hip osteoarthritis may not require drug treatment after excess weight has been lost.

ACHIEVING WEIGHT LOSS

Weight loss in dogs can sometimes be difficult to achieve. As in this study it is advisable to thoroughly evaluate the patient before beginning an obesity management program.

Diet History. Start with a dietary history to determine the types and quantities of food fed. Include feeding patterns such as the times fed per day and who feeds the pet. Also evaluate the activity level and overall lifestyle of the pet. You may need to continue to probe to get a complete picture of the situation — does anyone else (a neighbor?) feed or treat the dog? A physical exam, including a serum chemistry panel with thyroid screen and urine tests, is important to rule out medical conditions such as diabetes, hyperthyroidism or hypothyroidism, hyperadrenocorticism, and heart disease.

Weight Assessment. Next evaluate the patient’s weight. Comparing the dog’s weight to breed standards where appropriate can be a first step to evaluating the degree of obesity. Given the wide ranges within breeds and the popularity of mixed breed dogs, assigning a Body Condition Score (BCS) may be a more practical approach to determining level of obesity. Determining a BCS requires a visual and tactile evaluation of the ribs, spine, pelvis, waist, and abdomen (Figure 4). If you don’t put your hands on the dog you have not completed an accurate BCS!

Figure 3. Body weight and visual analog scale ratings of lameness during weight loss for lame, overweight dogs.

Figure 4. Clinical Perspectives on Canine Joint Disease (TNAVC 2001)
**Owner Involvement.** One of the most important factors in achieving successful weight loss (including the weight loss in this study) is to involve the owner. The owner must want the pet to lose weight. Recognition of the dog’s obesity is a big step in enlisting the owner’s commitment to weight loss. Demonstrate to the owner using visual cues or palpation that the dog is overweight. Ensure that the client understands the health risks associated with obesity.

For the purposes of this study specific weight loss goals, timelines, and periodic weigh-ins were established and agreed to from the beginning. The same holds for any successful weight loss program. Setting short- and long-term weight-loss goals with target dates for the owner allows for interim goals with positive reinforcement. These weigh-ins can be every 1–2 weeks at first to ensure the program gets off to a good start and can be less frequent as the program progresses.

**Diet.** Determine the daily caloric allotment that will achieve the targeted degree of weight loss and ultimate BCS. Be sure the client understands that this allotment may change during the program, depending on the amount of exercise and/or metabolic adaptations that occur. Make the client responsible for restricting the food appropriately. Encourage them to measure and record all food given. Involve everyone in the household who provides treats or food for the dog.

**Exercise.** Although an exercise regime was not included as part of this study, exercise can play an important role in weight loss. Varying degrees of exercise can be prescribed, depending on the health of the client and the patient. Goals can be set for increasing duration and intensity of exercise, but keep it reasonable. Exercise is just one additional facet of the entire weight loss program.

**Client Support.** Provide support and positive reinforcement. Celebrate success. For the purposes of this study, rewards (such as a leash) for reaching certain study weight loss milestones were provided. Rewards need not be expensive. Inexpensive but meaningful rewards such as a certificate documenting the target weight loss and progress toward that goal serves both as a reminder and a reward.

**DIETARY CONSIDERATIONS**

The major contributing factor to obesity is excess caloric intake in relation to the dog’s caloric requirements. In this study Eukanuba Veterinary Diets® Nutritional Weight Loss Formula® Restricted-Calorie™/Canine (Restricted-Calorie) was fed at 60% of maintenance calories for initial body weight. Several features of this diet help to acceptably reduce caloric intake.

By replacing some dietary fat with carbohydrate instead of fiber, the caloric density of the Restricted-Calorie diet is reduced while maintaining a high level of nutrition. Carbohydrate contains less than half the calories of fat, which allows clients to feed an amount of food they perceive as adequate while reducing calories consumed by the pet. Reduced quantities of fat necessitate attention to the type and quality of the dietary fat. Ensuring that the ratio of omega-6:omega-3 fatty acids is between 5:1 and 10:1 will help promote healthy skin and coat during weight loss.

Likewise, it is important to carefully select the starch sources used to replace fat in the diet. The carbohydrate component of pet foods provides the primary source of the increase in blood glucose after a meal. Starch sources behave very differently in the way that they influence blood glucose and insulin responses. Grain sorghum and barley are utilized as starch sources in the Restricted Calorie diet. This results in lower postprandial blood glucose levels and lower blood insulin levels than if other starch sources such as wheat or rice are used as the source of starch. By minimizing postprandial increases in blood glucose and insulin, specially formulated foods containing a blend of barley and grain sorghum may help improve glucose intolerance and stabilize blood glucose levels in overweight pets.

Caloric density of the diet may also be reduced by the addition of fiber to the diet. The Restricted-Calorie diet contains normal levels of moderately fermentable fiber instead of high levels of nonfermentable fiber such as cellulose. Increased nonfermentable fiber levels can result in increased stool volume, poor skin and coat quality, and ultimately result in poor client compliance.

**ENHANCING WEIGHT LOSS**

Other dietary approaches, beyond feeding a low-fat, low-calorie diet to assist with canine weight management is to affect the way nutrients are metabolized to help promote weight loss and improve body composition. Chromium can help optimize body composition during weight loss. Dogs fed diets containing supplemental chromium (as chromium tripicolinate) had greater loss of fat mass compared with that from feeding a diet supplemented with carnitine only (data on file; The Iams Company). In addition to its role in improving body composition during weight loss, dogs fed diets supplemented with chromium tripicolinate had improved glucose tolerance and an increased rate of glucose removal from the bloodstream after intravenous glucose infusion. By enhancing tissue use of glucose, diets containing...
chromium tripicolinate may lead to an overall improvement in glucose tolerance and blood glucose stability in overweight pets.

Another dietary component that can affect nutrient metabolism is carnitine. Carnitine is a water-soluble, vitamin-like compound made in the body from the amino acids lysine and methionine. It is naturally present in animal-based protein ingredients. By forming acyl-carnitines, carnitine “escorts” fatty acids into the cells’ mitochondria for oxidation and energy production. In this way, carnitine helps reduce body fat storage and blood lipid levels. When added to a canine weight-loss diet, carnitine resulted in a tendency for lower fat mass and greater lean body mass, even with greater energy intake\(^\text{11}\) (Figure 5).

**CONCLUSION**

Achieving weight loss in overweight dogs can be challenging. However, successful weight loss can be achieved by engaging the owner, agreeing to achievable weight loss milestones with positive feedback, and by using diets with dietary features that can help achieve the desired weight loss. Additional motivation for successful weight loss can also be derived from the observable improvement in lameness as lame overweight dogs lose weight.

**REFERENCES**


**Figure 5.** Greater weight and body fat loss in dogs with carnitine, even with ad libitum feeding.\(^\text{12}\)
INTRODUCTION

Joint disease is a common problem in dogs. Patients with osteoarthritis (OA) have restricted activity, limited ability to perform, pain and discomfort, and decreased quality of life.1-3 As animals reduce their activity level, a vicious cycle of decreased flexibility, joint stiffness, and loss of strength occurs. Traditional management of dogs with OA has included weight loss, antiinflammatory and analgesic drugs, changes in lifestyle and exercise habits (usually restricted), and surgical management.

Advances in the management of human OA by physical modalities have reduced the severity of symptoms and reliance on medications to control pain and discomfort.4,5 Some of the benefits include increasing muscle strength and endurance, increasing joint range of motion (ROM), decreasing edema, decreasing muscle spasm and pain, and improving performance, speed, quality of movement, and function.

EXERCISE AND OSTEOARTHRITIS

Although the exact relationship between exercise and OA is uncertain, several factors have been identified in people, and most of these likely apply to animals.6,7 It is generally believed that mild to moderate exercise and training in normal humans and dogs do not cause OA by themselves, but biochemical, histologic, and biomechanical changes do occur in articular cartilage. Cartilage of dogs regularly subjected to high levels of stress shows a higher proteoglycan (PG) content and is stiffer than cartilage exposed to low stress levels. Most studies of running exercise have indicated that this activity produces no injury to articular cartilage, assuming that there are no abnormal biomechanical stresses acting on the joints. Running exercise of 4 km/day for 15 weeks in young Beagle dogs caused a 6% increase in stiffness of cartilage of the stifle joint.8 Thickness of the cartilage also increased so it is likely that moderate exercise has an anabolic effect on the physiological properties of cartilage, and may diminish the chance of developing OA. Using the same model, running exercise of 20 km/day for 15 weeks did not further improve the mechanical properties of articular cartilage.

Another study evaluated whether an increased level of low-impact lifelong weight-bearing exercise causes degeneration of articular cartilage by exercising dogs on a treadmill at 3 kilometers per hour for 75 minutes, 5 days/week for 527 weeks while wearing jackets weighing 130% of their body weight.9 Ten control dogs were allowed unrestricted activity in cages for 550 weeks. No joints had ligament or meniscal injuries, cartilage erosions, or osteophytes. Furthermore, tibial articular cartilage thickness and mechanical properties did not differ between the two groups. These results suggest that a lifetime of regular low-impact exercise in dogs with normal joints does not cause alterations in articular cartilage.

Heavy training programs may result in changes which predispose to the development of OA. In one study, dogs underwent a gradually increasing treadmill exercise regimen of up to 40 km/day, while control dogs lived normally in their cages.10 The articular cartilage response to training was site dependent. After the year-long exercise period, stiffness of the cartilage decreased by 12-14 percent in the lateral, but not in the medial condyles of the femur and tibia. Similar changes were seen in glycosaminoglycan content of the superficial zone of cartilage, confirming the role that PGs have in modulated cartilage stiffness. Although there was no overt cartilage damage, the softening of the cartilage may jeopardize the ability of the cartilage to maintain its normal structural and functional properties over time. In another study, strenuous running of old dogs at 6-8 mph with 20 degrees uphill inclination for 1 hour per day, 6 days/week for 8 months, led to accelerated matrix degradation in the femoral head. Proteoglycan content decreased and there was irreversible...
destruction of collagen fibrils. Older dogs may be more vulnerable to mechanical stress changes than younger animals. Therefore, although mild to moderate training protocols have an anabolic effect on cartilage, rather severe training protocols may result in detrimental alterations in cartilage.

Certain activities are associated with OA of particular joints, presumably because of the chronic impacts on joints which may not be biomechanically sound or are placed under abnormal loads. For example, Huskies tend to have more OA of the hips and shoulders associated with pulling sleds. Young dogs with coxofemoral joint laxity develop OA over time if corrective surgery, such as triple pelvic osteotomy, is not performed to improve joint biomechanics. Pathologic motion in a joint, such as cranial drawer as a result of a ruptured cranial cruciate ligament, results in progressive OA changes. Humans with normal joint conformation appear to be predisposed to OA, while humans with normal joint conformation do not.11,12

Although initiating an improper exercise program in a patient with abnormal joints may hasten the progression of OA, a well-designed training program increases muscle strength and tone, which may help stabilize joints, and possibly decrease abnormal stresses on joints. Human patients with knee OA in a supervised walking program walk farther in a period of time, have decreased pain, and use medication less frequently to control pain.13 Patients that exercise have improved strength, ROM, function, and decreased need for medication.14

THE ROLE OF OBESITY IN OSTEOARTHRITIS

Obesity is strongly associated with the development of OA in people and its management is important in the treatment of OA.15 Heavy people are 3.5 times more likely to develop OA than light people, and loss of 5 kg decreases the odds of developing OA by over 50%.16 This may have implications on the initiation of exercise programs for obese animals with OA. Overloading joints should be minimized by performing activities such as walking and swimming until weight loss occurs. In man, weight loss results in less joint pain and a decreased need for medication to treat OA. After weight loss, 90% of people in one study had complete relief of pain in one or more joints.17 A similar report exists in veterinary medicine, in which overweight dogs with hip dysplasia underwent weight reduction.18 Losses of 11–18% of body weight resulted in significant improvements in body condition scores and the severity of hind limb lameness. Currently, I do not perform total hip replacements in obese patients with hip dysplasia. Rather, these patients are placed on a weight loss program combined with a low-impact exercise program of walking, jogging (if tolerated), and swimming if possible. Antiinflammatory medications are also prescribed as needed for comfort. Body composition is documented to establish the percent body fat. That, combined with the weight of the animal, gives the veterinarian and the owner a target to reduce a specific amount of body fat. In general, our goal is to reduce fat composition to 20–25% of body weight. In many cases, the owners feel that the dog is doing well enough clinically after weight loss and the initiation of an exercise program that they no longer wish to pursue surgery.

THERAPEUTIC EXERCISE

The goals of therapeutic exercise should be to reduce body weight, increase joint mobility, and reduce joint pain through the use of low-impact weight-bearing exercises designed to strengthen supporting muscles.19 Muscle disuse results in atrophy and weakness. Muscles also act as shock absorbers and strengthening of periarticular muscles may help protect joints. Mild weight-bearing exercise also helps stimulate cartilage metabolism and increases nutrient diffusion. Exercise may also increase endogenous opiate production and relieve OA pain.

Exercise should only be performed after correction of major risk factors, such as joint instability or obesity. Exercising a dog with an unstable cranial cruciate ligament speeds the development of OA. An initial exercise program should consist of several short periods interspersed with rest periods throughout the day. The exercise periods should be evenly spaced throughout the day. Regular intermittent cartilage loading may increase cartilage metabolism and glycosaminoglycan synthesis as compared to constant loading or very slow loading. It is best to have regular exercise periods throughout the week, rather than compacting all of the weekly activity into a weekend. Increased levels of exercise should occur gradually and progressively.

The ideal exercise program is one which provides sufficient benefits without causing discomfort. If joint pain is greater after exercise than prior to exercise, the length of activity should be decreased by half. It is important to differentiate joint pain from muscle soreness. Some muscular discomfort may be expected early in exercise programs. The level of exercise must be prescribed for each individual based on the severity of OA, response to concurrent therapy, the patient’s pain tolerance, and the owner.

Ideally, antiinflammatory drugs should not initially be administered prior to exercise because it is important to determine if the level of exercise is too great and causes joint pain following a training period. After titrating the appropriate level of exercise so that pain is not worsened with exercise, oral antiinflammatory drugs should be administered about 1 hour prior to exercise. Treatment with an antiinflammatory drug allows a small increase in
activity and stress to the tissues to gradually increase function. As training events are stepped up over time, antiinflammatory agents are withheld to allow a true evaluation of the patient without the aid of medication. The goal is to reach the desired level of function and maintain that level without the aid of long-term antiinflammatory drugs. Early in the training program, however, antiinflammatory drugs may help address minor muscle and joint soreness as tissues adapt to the new stresses placed upon them.

**Type of Exercise**

Exercise programs must be tailored to account for the typical course of exacerbations and remissions of OA. The animal should not be forced to exercise during times of aggravation. Vigorous exercise may increase inflammation. During pain-free times, low-impact exercises are beneficial to maintain muscle strength, joint mobility and function. Stretching of affected muscle groups and joints during a warmup period is recommended. A application of superficial heat may relax tissues and the dog and allow more effective stretching of muscles, tendons, ligaments, and joint capsules.

Common activities include controlled activity on leash, treadmill walking ([Figure 1](#)), swimming, going up and down stairs or ramped inclines, and holding either the front or rear half of the dog up and encouraging the other half to exercise. Long leash walks provide good low impact, aerobic forms of exercise. The length of walks should be titrated so there is no increased pain after activity. It is better in the early phases of training to provide three 20-minute walks than one 60-minute walk. The walks should be brisk and purposeful, minimizing stopping. In prescribing the activity, owner compliance must be considered, and an exercise prescription should accommodate the owner's schedule and benefit the animal. Light jogging on grass may be added as the dog tolerates increased activity. For additional muscle strengthening, 1–2 pound strap-on weights may be fastened to the lower limbs ([Figure 2](#)). A back-pack with weights may also be used. Walking up and down inclines or stairs are good low-impact activities that are easily incorporated into a walking program and improve muscle strength and cardiovascular fitness. If strengthening the pelvic limb muscles is desired in dogs with hip dysplasia, repeated rising from a sitting position may be beneficial. Some assistance may initially be required in the form of sling support. High-impact exercises should be avoided.

If facilities and climate allow, swimming is one of the best activities for dogs. The buoyancy of water is significant and limits impact on joint surfaces, while promoting muscle strength and tone, joint motion, and cardiovascular fitness. Clean lakes or pools may be used. Self-contained tubs with whirlpool action are also available. Careful patient monitoring and assistance are important to prevent excessive thrashing. Fear of water must be addressed to avoid injury. Initially, dogs may swim for 1–3 minutes once daily, for 3 to 7 days per week. As strength and stamina improve, dogs may swim 5–10 minutes per session. When done carefully, swimming is an effective, functional exercise.

We have been using an underwater treadmill for dogs with OA and have been impressed with the results ([Figure 3](#)). In general, a 2-week training period in the

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**Figure 1.** A variable speed ground treadmill is useful to provide a consistent pace and footing for exercising dogs.

**Figure 2.** Strap-on weights can be fastened to the limbs to aid in muscle strengthening.

**Figure 3.** An underwater treadmill is useful to exercise dogs with joint osteoarthritis.
underwater treadmill may increase peak weight-bearing forces by 5–15%, which is similar to that typically achieved with medication. We have performed force plate analysis of gait and documented a 10% increase in weight-bearing immediately following exercise, which carries over for a period of time. The length of the workout, speed of the treadmill, and the height of the water may be adjusted as training progresses (Figure 4). Even dogs which fear water generally perform well in this unit because the water rises around the dog, rather than lowering the dog into the water.

Following exercise, a 10-minute warmdown period is necessary to allow muscles to cool down. The first 5 minutes may be spent walking at a slower pace after a brisk walk or swimming. Range of motion exercises may be repeated for the next 5 minutes. Finally, ice may be applied to painful areas for 15–20 minutes to control post-exercise inflammation. Massage is commonly used to decrease pain, swelling, and muscle spasm.

**PHYSICAL AGENTS**

**Superficial heat modalities**

Superficial heating agents typically heat the skin and subcutaneous tissues to a depth of 1–2 cm. The tissue is usually heated to 40–45°C for 15 to 20 minutes. Superficial heating agents include hot packs (moist and dry), circulating warm water heating blankets, and warm baths. Heat increases blood flow to the area, promotes tissue extensibility, decreases pain, muscle spasm and joint stiffness, and causes general relaxation. Heat is contraindicated if swelling or edema are present.

**Cryotherapy**

The application of cold decreases blood flow, inflammation, hemorrhage, and metabolic rate. Commercially available cold packs or ice wrapped in a towel may be applied to an area for 15 to 20 minutes, 3 to 6 times daily (Figure 5). An entire limb or limbs may be immersed in a cold water or water and ice bath to decrease inflammation. Most studies of cryotherapy treatment for OA indicate that patients experience positive benefits, including less stiffness and pain, and improved joint ROM, although some discomfort is initially associated with application of cold.

**Massage**

Massage is the systematic and scientific manipulation of soft tissues. The different types of massage include effleurage, vigorous cross-fiber friction over muscles or ligaments to break up adhesions, Swedish massage, deep tissue massage, neuromuscular massage, accupressure, myofascial release, and reflexology.

The beneficial effects of massage include relaxation of soft tissues, decreased muscle spasm and trigger points, increased muscle flexibility, improved venous and lymphatic flow with reduction of edema, and increased local blood flow to an area. Massage has been used to increase blood flow to muscles to “warm up” the area before activity, and to decrease stiffness after activity.

**Ultrasound**

Ultrasound (US) has been used to treat OA, rheumatoid arthritis, and bursitis (Figure 6). The most
common frequencies are 1 and 3 MHz. Most US units have continuous and pulsed modes. Ultrasound has thermal and non-thermal effects. These effects are related to the treatment time, intensity, frequency, and the area being treated. Thermal effects include decreased pain, and increased blood flow, metabolic rate, and tissue extensibility. Non-thermal effects include increased cell membrane permeability, calcium transport across cell membranes, nutrient exchange, and phagocytic activity of macrophages.

Ultrasound is capable of heating tissues deeper than superficial heating agents, heating tissues 5 cm deep to 40–45°C, without overheating the superficial tissues. Generally, 10 minutes of US application to a small area adequately increases tissue temperature. Because the tissue temperature increase is short-lived, stretching of joints and tissues should be performed during the latter half of treatment or immediately after. The indications, contraindications, and physiological effects must be thoroughly understood.

Neuromuscular Electrical Stimulation

A wide variety of neuromuscular electrical stimulators (NMES) are available (Figure 7). Neuromuscular electrical stimulators provide benefits, including increasing muscle strength and joint ROM, decreasing edema and pain, and helping to improve function. Pulsed AC units are the most useful for increasing muscle strength and joint ROM, and decreasing edema and pain. The commonly used TENS (transcutaneous electrical nerve stimulation) refers only to a particular type of electrical stimulator that is applied for pain control, but is not used for muscle strengthening or other applications.

In general, neuromuscular electrical stimulation appears to relieve pain in human patients with OA as long as the treatment is continued. Its role in pain relief of OA in animals is unknown, but it appears to attenuate muscle atrophy following some surgical procedures.

**THE ROLE OF THE ENVIRONMENT IN THE MANAGEMENT OF OSTEOARTHRITIS**

Animals with severe OA require modifications in their habitat. The principles of environmental modification for dogs are similar to those of people. Whenever possible, animals should be moved from a cold, damp outdoor environment to a warm, dry inside environment. A soft, well-padded bed or waterbed should be provided. A circulating warm-water blanket under the blankets provides heat which may reduce morning stiffness.

The playful activities of other pets may be a source of irritation to dogs with moderate to severe OA. Affected animals may attempt to keep up, and in the process, become more lame and painful. In some instances, however, play with other animals stimulates activity and provides a welcome break in the exercise routine.

Severely affected patients may no longer be able to negotiate stairs. Changes may be necessary to minimize stair climbing. Steps are negotiated easier if they are wider and spaced farther apart. A ramp may be used instead of steps. In climates with ice and snow, walks should be shoveled and ice cleared to minimize the risk of falling.

**SUMMARY**

Physical rehabilitation is a valuable, but underused part of the management of dogs with OA. The veterinarian, physical therapist, veterinary technician, and owner are vital to determine and carry out an appropriate therapeutic regimen. A variety of physical rehabilitation techniques are available to supplement and enhance other treatments for OA. To maintain enthusiasm for the program and to help with decision-making for further treatment, progress should be documented.
REFERENCES


INTRODUCTION

Intervertebral (IV) disk disease is a common neurological disease that causes pain and motor dysfunction. Results of complete clinical history and thorough physical examination facilitate neuroanatomical localization of a lesion. In addition, results of neurological examinations further localize the lesion. Then, imaging examinations are in order to confirm the neuroanatomical location of the lesion, not only longitudinal (for example, at C6-7) but also transverse (for example, extradural, intradural and extramedullary, intramedullary) location. Plain radiography, myelography, computed tomography, and magnetic resonance imaging have been used to accomplish this. A additional examination such as cerebrospinal fluid analysis assists ruling in and out of certain differential diseases such as neoplasia and infection (for example, meningitis).

Among many different causes of spinal cord dysfunction, extradural spinal cord compression due to IV disk protrusion or extrusion is the most common cause. In this presentation, pathophysiological changes of IV disk degeneration are reviewed along with radiographic abnormalities. In this discussion, an aging model is used. Furthermore, a type III IV disk degeneration pattern is introduced and fully discussed with differential diagnoses in aged dogs.

ANATOMY AND PHYSIOLOGY

Intervertebral disks have two distinctive components: anulus fibrosus and nucleus pulposus. The anulus fibrosus is in the outer layer, encasing the gelatinous nucleus pulposus (Figure 1). Although anulus fibrosus implies a circular structure, it is not a concentric ring-like structure. The dorsal aspect is thin and incomplete. Thus, nucleus pulposus is located in a dorsal location. The anulus fibrosus and nucleus pulposus work together to act as a shock absorber. The anulus fibrosus can stretch to evenly distribute a force due to their alignment of collagen fibers or fibrous tissues. The nucleus pulposus contains proteoglycans that can hold high water contents. The results of biochemical analysis of the anulus fibrosus and nucleus pulposus show their similarity to articular cartilage. As seen in the articular cartilage, IV disks lose their proteoglycans with aging or degeneration. This is most likely caused by altered metabolic function of chondrocytes. However, compared to articular cartilage, information regarding metabolic function of chondrocytes is limited in canine IV disk research.

SIGNIFICANCE OF PROTEOGLYCANS

A significance of proteoglycans can be readily demonstrated in a chemonucleolysis study of IV disks. Normal IV disk widths are maintained by healthy anulus fibrosus and nucleus pulposus. When proteolytic enzymes such as collagenase, chymopapain, and chondroitinase ABC are injected directly into the nucleus pulposus, the proteoglycans are lost. Consequently, the IV disk spaces collapse. This chemical change can be readily noted on...
magnetic resonance imaging (MRI) (Figure 2). It is reasonable to assume that these chemical changes are developing in a more subtle fashion in clinical situations most likely modulated by altered metabolic function of chondrocytes. Yet, again the information is limited in the literature.

Figure 2. Sagittal T2-weighted magnetic resonance image. Note decreased signal in an intervertebral disk that was treated by chymopapain (chemonucleolysis). Due to a loss of water-rich proteoglycans, the signal intensity is not as bright as the rest of normal intervertebral disks.

DEGENERATION OF IV DISKS AND SIGNIFICANCE OF BREEDS

Unfortunately, degenerative changes of IV disks are unavoidable. With aging, the composition of proteoglycans changes, causing a loss of water contents. A wear-and-tear occurs in IV disks, and eventually fissures form within the anulus fibrosus. This may be called a progressive aging pattern.

In a study using a colony of Beagle dogs, the following aging pattern was noted (Figure 3). Gross pathological change developed around 5 years of age. Orientation and order of the anulus fibrosus was altered and mild dorsal protrusion of the anulus fibrosus occured around 7 years of age. A narrowed IV disk space was also noted with this change. A sagittal section of the vertebrae showed disorientation of the anulus fibrosus and fissure tracts through which the nucleus pulposus protruded dorsally. Color of the nucleus pulposus was whitish and opaque. Around 9 years of age, further dorsal bulging of the anulus fibrosus was noted. The anulus fibrosus lost its layered appearance, and it was blended with protruded nucleus pulposus. Further degenerative changes were noted in the spine of a 10-year-old dog. The dorsal bulging of IV disks was seen with disorientation of the anulus fibrosus with separation of layers in the ventral side and fissure in the dorsal area. The nucleus pulposus appeared as blended with the anulus fibrosus. There was collapse of the IV disk space with dorsal and ventral protrusions of both anulus fibrosus and nucleus pulposus. The protruded nucleus had yellowish discoloration. Cartilaginous end-plates were not present, leaving smooth ground surfaces of the bony or vertebral end-plates. This change was seen most prominently in the ventral half of the vertebral end-plates which had thickened, whitish plate of bones. Along the ventral surfaces of vertebrae, new bone was formed adjacent to the cortex as spondylosis deformans. Malalignment of the adjacent vertebrae was also noted.

These changes were noted in both cervical and lumbar vertebrae. The most common and severe changes were centered around C5-6 and C6-7 in the cervical spine and T13-L1 through L2-3 in the lumbar spine.

The pattern described above can be called as Hansen type II degeneration and develops commonly in non-chondrodystrophic breeds. Since IV disks lose their proteoglycans gradually, the onset of IV disk disease is usually gradual and at middle ages. Good examples of these that become clinically significant are seen in the cervical spine of Dobermans and as a cauda equina syndrome at a lumbosacral junction in large breed dogs.

Hansen also noted much earlier degeneration of IV disks in chondrodystrophic dogs such as Dachshunds, Miniature Poodles, etc. Histologically, these breeds of dogs showed degenerative changes as early as 4 months of age. In addition, “chondroid” degeneration occurred with early calcification of the nucleus pulposus. Calcification of IV disks or nucleus pulposus does not allow IV disks to work as a shock absorber. Thus, unusual force can cause extrusion of the nucleus pulposus. This process is acute and causes severe spinal cord damage leading to paralysis of legs (Figure 4). Here, it is imperative to remember that chondrodystrophic dogs have a narrow spinal canal that tightly accommodates the spinal cord. Thus, even a minor extrusion can cause severe clinical signs.

Figure 3. Sagittal histology slides of lumbar intervertebral disks of Beagle dogs. Disruption of anulus fibrosus and dorsal herniation of nucleus pulposus are expected aging changes.
Plain radiography and myelography are still the most commonly used imaging modality in diagnosis of IV disk disease in veterinary medicine. Although the degree of degeneration cannot be directly assessed with these studies, it is often possible to suspect the site based on abnormal radiographic findings in light of clinical signs. For example, a 4-year-old Dachshund is presented with acute hind leg paralysis. Plain lateral and dorsoventral radiographs showed a narrowed IV disk space at L1-2 with an increased opacity in the intervertebral foramen and narrowed facet joint at the same level. Since this is a relatively young dog with acute history of paraparalysis, this is most likely due to IV disk disease. If the surgery is desired, myelography can confirm the site and lateralize the lesion. Decompressive surgery such as hemilaminectomy can certainly facilitate the recovery of motor function. However, if this is a 10-year-old Dachshund, the imaging diagnosis can be confusing at best with narrowed or collapsed IV disk spaces in many levels with moderate spondylosis deformans.

**IMAGING DIAGNOSIS OF IV DISK DEGENERATION**

We need to assume that IV disks are degenerated in aged animals. Currently, MRI is the diagnostic modality of choice in human radiology. Degenerated IV disks do not contain water-rich proteoglycans, and thus they appear hypointense on T2-weighted images compared to normal IV disks. In addition, sagittal and transverse images can delineate the dorsal border of the protruding disks and spinal cord compression. This modality is also exclusively used for detection of spinal diseases in some veterinary institutions, but its availability is limited. Most veterinary specialists agree to use this modality in a cauda equina syndrome, ruling in and out IV disk protrusion at the lumbosacral junction (Figure 5).

**TYPE III IV DISK DEGENERATION PATTERN**

The aging or degenerative pattern described above is progressive. With the life expectancy of dogs prolonged, we are now facing a drastic degenerative change in IV disks. This change can be referred to as the type III degenerative change.

Radiographically, the IV disk degenerative changes develop as a narrowed IV disk space, sclerosis of vertebral end-plates, and spondylosis deformans. With time, this further progresses to a collapsed IV disk space with severe spondylosis. At the same time, remodeling of vertebral bodies may result in malalignment or kyphosis. At older ages, around 15 years or so, the IV disk spaces are totally collapsed and a mineralized mass appears in the spinal canal. This mass is a protruded or extruded IV disk tissue (mainly nucleus pulposus) that is subsequently calcified and ossified (Figure 6). The ossification is the result of endochondral ossification of the protruded nucleus that...
contains chondrocytes and neovascularization. At the same time, severe vertebral end-plate changes are recognized (Figure 6). Protrusion of the IV disk tissue through the vertebral end-plates can occur (Schmorl’s node). In one Beagle dog that had extrusion of calcified disks at 2 years of age, the dog eventually developed a large bony bridge on the dorsal aspect of the vertebral body within the spinal canal. A gain, endochondral ossification was the apparent cause of this change.

Clinical significance of type III IV disk degeneration is the recognition of the condition. The type III disk degeneration appears so severe that this can be confused with discospondylitis or even neoplasia. The condition can also make remodeling changes of the pedicles due to long-standing presence of a mass at the spinal canal. The spinal cord is certainly misshapen due to the presence of the mass. Yet, a gradual onset appears to allow the spinal cord to adapt to the condition, causing only mild motor dysfunction. Decompressive surgery may not be indicated in these cases.

CONCLUSION

Pathophysiology of IV disk degeneration involves biochemical changes developing in IV disks. A loss of proteoglycans appears to be the initial step to degeneration. A predictable course follows with disruption of anulus fibrosus and protrusion of nucleus pulposus through these fissures. As a result, the IV disk space narrows, and this can be readily detected by radiography. With persistent instability, spondylosis deforms develops around the end-plates. The end-plates sclerosis and malalignment may develop. With advanced aging, all IV disk tissues escape from the IV disk space. Spondylosis deformans continues to develop. Further remodeling occurs at the end-plates. Dorsally protruded nucleus pulposus undergoes endochondral ossification. The spinal cord adapts to this gradual process of spinal cord compression. The mineralized mass can be readily detectable on radiographs. This should not be confused with discospondylitis or neoplasia.

It is important to understand that the degenerative process of IV disks cannot be avoided. Yet, it is possible to delay the process. Research in chondrocyte metabolism and its relationship with degeneration should broaden understanding of maintaining healthy IV disks.

REFERENCES

INTRODUCTION

Osteoarthritis (OA, syn. osteoarthrosis, degenerative joint disease, DJD) is a syndrome that affects synovial or diarthrodial joints and may manifest its presence by causing pain in association with degeneration of articular cartilage (loss of extracellular cell matrix and chondrocytes, inflammatory response of synovium, and critical changes in proteoglycan ratios within matrix and synovial fluid) and changes in periarticular soft tissues. Since typically a low-grade inflammatory process is associated with the development and maintenance of the degenerative process of articular cartilage, the underlying subchondral bone response (eg, sclerosis), intra and periarticular response (eg, synovial hypertrophy, fibrosis), the term "osteoarthritis" describes the disease process of the diarthrodial joint better than the older term "degenerative joint disease". Typically, OA is an insidiously progressive, degenerative condition that targets high motion synovial joints. Etiologies may include infectious (eg, septic arthritis) or noninfectious (eg, immune mediated, trauma, developmental/congenital) environment development within the joint. This discussion will be limited to medical management of secondary low-inflammatory-based OA or what has been classically labeled "secondary degenerative joint disease" or non-infectious, nonimmune-mediated osteoarthritis.

Micro and macroscopic changes within the synovial joint may result in the clinical signs of lameness due to joint pain (synovitis, microfractures of subchondral bone, osteophytes, and joint effusion/distention). The clinical signs associated with OA vary from patient to patient and may range from subclinical to a severe functional disability. Fundamentally, no one treatment will be all encompassing for all patients with OA. A balance of a "triad" of treatment components must be considered when medically managing a patient with OA: 1) weight control, 2) exercise/activity, 3) pharmacologic/disease modifying osteoarthritic drugs (Figure 1). Exclusion of one or more of these components from a treatment protocol will result in an overall poorer clinical response from the patient.

WEIGHT CONTROL

Obesity is a major risk factor for the development of OA \(^1,2\) while weight loss can reduce the symptomatic effects of OA.

Typically, osteoarthritis is an insidiously progressive, degenerative condition that targets high motion synovial joints.
Obesity is a major risk factor for the development of osteoarthritis.

Until recently, it was assumed that the same held true in other animals. A recent clinical study investigating the effects of obesity on dogs with hip dysplasia concluded that overweight dogs that achieved an 11–18% body weight reduction were significantly less lame compared to their pre-weight reduction lameness scores. Currently, Washington State University is performing a study to examine the effects of obesity on the clinical expression of OA in dogs with canine hip dysplasia.

Weight control can be one of the most challenging aspects of the medical management of OA in dogs for several reasons. Any one or a combination of the following factors will maintain a patient in an obese condition indefinitely.

1. A patient that is clinically inhibited by moving an OA joint(s) will not be able to utilize consumed or stored body energy efficiently and will instead increase body stores of energy (fat) when given a constant caloric intake.

2. Dogs with underlying endocrine disease (e.g., hyperadrenocorticism, hypothyroidism) will have the metabolic propensity to maintain body fat stores even in the face of a reducing diet.

3. Dogs that are in a multi-pet household (e.g., other dogs and cats) are more prone to consume greater volumes of food than dogs in single-pet households.


5. Inaccurate estimation of animal’s energy requirements.

6. Most critical is the owner’s lack of willingness to be proactive in trying to reduce their pet’s body weight.

Prior to starting a weight-reducing program, a complete physical exam should be performed. If the clinical history (attempted weight reduction in the past with poor results, lethargy, “heat seeking”, PU/PD, etc.) and physical exam findings (pendulous abdomen, symmetrical alopecia, recurrent dematopathy, etc.) indicate, a complete minimum data base (CBC, serum chemistry profile, UA) should also be obtained.

Weight reduction can be obtained in healthy patients by simply reducing current caloric intakes; using reductions by 1/2 to 1/2 of the “normal” volume of the regular diet, calculating caloric content of regular diet and caloric needs based on basal metabolic rates, or using specially formulated commercial diets with recommended intake volumes per the manufacturer, and avoiding additional calories in the form of table scraps or “dog treats”. Also important is the frequency of feeding. Dogs on weight-reducing plans appear to be less hungry if fed a divided volume of the reducing diet over the course of the day. In addition, feeding in-between “snacks” of low calorie and high fiber quality (raw carrot sticks, raw celery sticks, non-flavored rice cakes) or ice cubes will satisfy most dogs. An appropriate caloric restriction should result in the loss of 1–2% of body weight per week.

All weight reduction/control programs must include an exercise program to ensure constant weight loss and eventual body weight maintenance. To encourage activity in the debilitated OA patient, regular pharmacologic treatment may be required for a short period until the patient becomes more ambulatory.

MODIFICATION OF EXERCISE AND ACTIVITY

It is known from the human literature that exercise is very important in maintaining strength, stamina, joint range of motion, and reducing dependency on medication when OA patients are allowed to exercise. It is assumed that the same is true in other animals as well and supported by a recent study in hamsters. Therefore, an important aspect in the management of OA in animals should be a controlled exercise. Depending on the animal’s activity history, it may be necessary to modify a patient’s regular level and type of activity that is part of that animal’s daily exercise regime.

It may be intuitive that an OA animal should not be allowed to have hard-impact, prolonged exercise activity, but controlled clinical studies have not been performed to evaluate this recommendation; however, from clinical experience, practitioners are used to hearing the usual owner’s report of greater clinical signs in OA patients after hard, prolonged activity. It is known from kinetic and kinematic gait analysis that dogs with OA will modify their gait to reduce the load of weight-bearing and motion of the affected joint. It is therefore safe to assume that prolonged “over activity” should result in greater modification of gait due to exacerbation of the discomfort associated with an OA joint. Some recommendations for the duration of certain activities in dogs have been made, but recommendations for activity duration can also be based on “common sense” and the observations made by the owner of their pet’s apparent gait response/comfort level to an activity period.
Just as important as duration of activity is the type of activity involved with the animal's daily lifestyle. Low-impact activities (e.g., walking, cycling) have positive effects on human OA patients.7,8,17 In veterinary medicine, low-impact activities (walking, swimming) have been traditionally favored over hard-impact aerobic activities (jumping, hard starting/running, vigorous climbing/running on irregular terrain), which can over-stress degenerative joints. High-impact activities may over-stress degenerative joints and increase the inflammatory condition of OA. Low-impact activities are thought to reduce loads on an OA joint and result in less discomfort for patients in maintaining good muscle strength/mass and joint function. Walking under controlled conditions (leash restraint) and/or swimming can be recommended to the owner with further instructions to eventually attempt to have the patient increase the duration of these activities gradually so long as the animal appears to remain comfortable in doing so.

PHARMACOLOGIC/DISEASE-MODIFYING OA AGENTS TREATMENT

The primary goal with the pharmacologic management of OA is to relieve the patient of discomfort associated with joint movement. Ideally, this would involve oral or injectable agents with analgesic, anti-inflammatory, and potential condromodulating properties (disease-modifying OA agents, aka “DMOA”). Such agents would ideally biochemically block the inducible cyclooxygenase-2 (COX-2) and lipoxygenase pathways. Nonsteroidal anti-inflammatory drugs (NSAID) have been developed for this purpose (Table 1) but generally, do not all selectively block mainly the COX-2 pathway18-20 or leukotrienes production from the lipoxygenase pathway.21-23

Two NSAIDs (carprofen, etodolac) have been recently approved for use in dogs. These NSAIDs are considered to have a low COX-2:COX-1 ratio, but have toxicity potential as with any NSAID. Concerns are present with long-term, chronic therapy with NSAIDs. Hepatic toxicosis due to NSAID administration has been reported24; however, all NSAIDs have a toxicity potential especially if a patient has underlying hepatic or renal disease, or a thrombocytopenia. Several in vivo studies using chondrocyte cell cultures or cartilage explants have reported a decrease in proteoglycan synthesis in those tissues incubated with selected NSAIDs.25-28 It would appear to be a wiser clinical practice to administer NSAIDs on a PRN basis especially for the patient that has only intermittent discomfort due to osteoarthritis.

Disease-modifying osteoarthritis agents (DMOA) have recently been developed for the treatment of human and veterinary OA patients. These agents have become common-place in the treatment of OA despite the lack of definitive scientific studies confirming their efficacy. Most of these products contain mixtures of glucosamine and chondroitin sulfate, which supposedly enhance cartilage health by providing the necessary precursors to maintain and repair cartilage. Glucosamine and chondroitin sulfate reportedly have a positive effect on cartilage matrix, enhance proteoglycan production, and inhibit catabolic enzyme production or activity in OA joints. These properties have contributed to the labeling of these agents as “condroprotective”.29 With the exception of one product which is a true pharmaceutical by definition (Adequan®, Luitpold Pharmaceuticals, FDA approved in

Table 1. Selected nonsteroidal anti-inflammatory drug doses for the dog

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route Route</th>
<th>Strength Strength</th>
<th>Side Effects Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>carprofen (Rimady)</td>
<td>2.2 mg/kg q 12 hr</td>
<td>PO (inj. soon)</td>
<td>25, 50, 75, 100 mg tablets</td>
<td>Vomiting, diarrhea, changes in appetite, lethargy, behavioral changes, constipation</td>
</tr>
<tr>
<td>etodolac (Etogesic)</td>
<td>10-15 mg/kg q 24 hr</td>
<td>PO</td>
<td>150, 300 mg tablets</td>
<td>Vomiting, lethargy, diarrhea/loose stool, hypoproteinemia, behavior change, uticaria, anorexia, regurgitation</td>
</tr>
<tr>
<td>ketoprofen (Oquidis)</td>
<td>1-2 mg/kg loading (once) 1 mg/kg q 24 hr (maint.) 1 mg/kg q 24 hr</td>
<td>PO</td>
<td>12.5 mg tablets</td>
<td>Vomiting, diarrhea, serum increase of creatinine</td>
</tr>
<tr>
<td>meloxicam (Metacam; approved only in Europe)</td>
<td>.1-.2 mg/kg q 24 hr</td>
<td>PO, SC Injectable</td>
<td>Suspension Injectable</td>
<td>Vomiting</td>
</tr>
<tr>
<td>piroxicam</td>
<td>0.3 mg/kg q 24 hr or once, e.o.d</td>
<td>PO</td>
<td>10, 20 mg capsules</td>
<td>Vomiting</td>
</tr>
<tr>
<td>rofecoxib (Vioxx)</td>
<td>5 mg/kg</td>
<td>PO</td>
<td>12.5, 25, 50 mg tablets</td>
<td>Vomiting</td>
</tr>
<tr>
<td>aspirin (Ascriptin)</td>
<td>10-20 mg/kg q 8-12 hr</td>
<td>PO</td>
<td>325 mg (w/ Malox)</td>
<td>Vomiting, lethargy, gastroduodenal ulceration</td>
</tr>
</tbody>
</table>

* currently not labeled for small animal use
Current research suggests that glucosamine and chondroitin sulfate products may be prophylactically beneficial in patients that are prone to develop osteoarthritis or patients that may aggravate preexisting osteoarthritis with activity.

Injectable forms of DM OA available are Adequan, which is a polysulfated glycosaminoglycans (PSGAG) product, and hyaluronic acid (HA), a non-sulfated GAG. The U.S. and European product (Arteparon) has been used in horses and dogs. Though conflicting evidence exists that PSGAG have a positive anabolic effect on hyaline cartilage, studies have shown that PSGAG may decrease hyaline cartilage catabolism. In one study, immature dogs prone to hip dysplasia administered Adequan developed better hip conformation than dogs that were not treated with Adequan. Coxofemoral joint assessment made post euthanasia was not significantly different from untreated dogs. A clinical study investigating the use of PSGAG on hip dysplasia patients found no significant difference in orthopedic scores (lameness, range of motion, pain on manipulation of hip joints) compared to PSGAG non-treated dogs. In a meniscectomy model in dogs, PSGAG provided partial protection to articular cartilage damage associated with the meniscectomy. Polysulfated glycosaminoglycan has been reported to have chondroprotective properties in joints with a chemically-induced articular cartilage damage model versus no effect on a physical articular cartilage damage model in horses. Recently, there have been anecdotal reports indicating that there may be a positive synergism between injectable PSGAG and oral glucosamine and chondroitin sulfate when administered concurrently to a patient.

Hyaluronic acid (sodium hyaluronate, HA) is a major component of synovial fluid. Hyaluronic acid is postulated to enhance joint health by increasing the viscosity of the joint fluid and by reducing inflammation and scavenging free radicals. A study using a Pond-Nuki model for OA in dogs followed by intraarticular injections of HA did not modify OA and reduced overall proteoglycan concentrations in treated stifles. Other products reported that have disease-modifying, anti-OA potential include pentosan polysulfate, tetracyclines (doxycycline, minocycline, and modifications of these molecules), S-adenosyl-L-methionine (SAMe), methylsulfonylmethane (MSM), capsaicin, and fatty acid ratio manipulation (omega-6:omega-3). To date, the limited number of studies conducted suggest that some of these products may eventually have a place as adjuncts to the treatment of OA in animals.

Adjuncts to pharmacologic, exercise/activity, and weight control treatment are the application of heat, cold, massage, hydrotherapy, ultrasound/diathermy, and electrotherapy. Although based on antidotal observations only, these adjuncts appear to help some patients. Well-controlled clinical trials are needed to test the supposition that these modalities are as positively effective in veterinary OA patients as they are in human OA patients.

**SUMMARY**

Osteoarthritis can be a debilitating disease for dogs; however, new concepts in a balanced management of OA can result in an acceptable quality of life for the OA patient. Medical management must be considered beyond conventional and nonconventional pharmacologic treatment to include a balance created with exercise/activity and weight control management. Failure to consider this treatment “triad” concept will usually
result in a poorer clinical response to therapy and quality of life as perceived by the owner of the OA patient. Excellent progress continues in the development of new pharmacologic agents and other agents to combat or even reverse the degenerative processes of OA. In contrast, research and development into exercise/activity management for the OA companion animal lags significantly behind that of human medicine, but since the mid-1990's, is beginning to grow in interest in veterinary medicine. Nonetheless, large controlled clinical trials are needed for developing balanced treatment protocols that will allow us to treat our OA patients beyond the "clinical experience".

REFERENCES


New concepts in a balanced management of osteoarthritis can result in an acceptable quality of life for the osteoarthritis patient.


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