

Treatment of canine osteoarthritis

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KEY POINTS

- Osteoarthritis is a complex condition involving not only the articular cartilage but also all surrounding joint tissues.
- Weight control, exercise modification, and physical rehabilitation should be addressed in the management of every osteoarthritic patient.
- Further treatment recommendations should be based on the needs of the individual dog and the client's expectations for quality of life.
- Non-steroidal anti-inflammatory drugs are traditionally the mainstay of pharmacological treatment. However, these drugs should be administered with caution and clients need to be informed of potential adverse reactions.

Introduction

It has been estimated that as much as 20% of the canine population over one year of age in the USA is affected by some form of osteoarthritis (OA) (1). Osteoarthritis is a slowly progressive, low-grade inflammatory syndrome that affects all articular and periarticular tissues, including joint capsule, synovium, articular cartilage (Figure 1), and subchondral bone. Damage to the articular cartilage and stiffening of the subchondral bone may be initiating events or consequences of OA. Regardless, it is apparent that a combination of biochemical and biomechanical events are involved in the pathogenesis of this complex syndrome. Disruption to the joint triggers collagen breakdown, proteoglycan loss, and chondrocyte death. Cytokines, metalloproteinases and other degradative enzymes released from chondrocytes and synocytes mediate these events. The progressive changes that result include cartilage erosion, joint capsule fibrosis, and bone remodelling (Figure 2).

The exact mechanisms of OA are not well understood. Joint instability, trauma, and developmental orthopaedic diseases are possible causes of OA, although often the aetiology remains unknown (2). Clinical manifestations of OA include pain and limited mobility in one or multiple joints. Owners

Normal cartilage components:

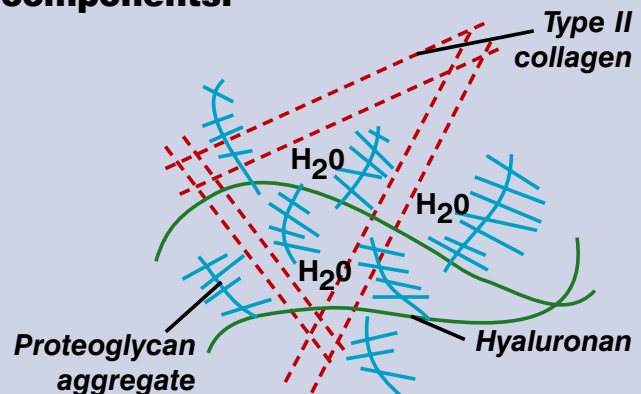


Figure 1 Components of normal articular cartilage.

may complain of a chronic intermittent lameness that is exacerbated by exercise, extended rest or cold weather. Palpation of affected joints on physical examination may reveal pain, swelling, poor range of motion, capsular thickening and crepitus. The degree to which dogs with OA are affected ranges from an occasional mild lameness to complete disability. Often, older dogs with OA will have concurrent or underlying neurological, metabolic, or cardiopulmonary disease and, therefore, a thorough general examination is essential before deciding on the optimum management.

Diagnosis of OA is made primarily on the basis of history, clinical signs, and radiography. Radiographs may demonstrate joint effusion, osteophyte formation, subchondral sclerosis and bone remodelling (Figures 3a and 3b). Other diagnostic modalities, such as CT scan (Figure 4), MRI, kinematic gait analysis and nuclear scintigraphy, may provide additional information, especially in the mildly affected dog.

Changes within the joint that result from OA are irreversible. However, early recognition gives the owner more options for treatment with the aim of slowing progression and ameliorating the pain and disability associated



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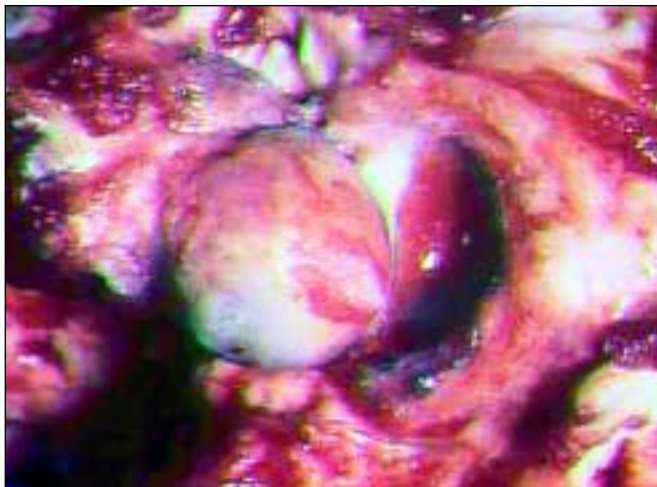


Figure 2 Gross pathology of a coxofemoral joint demonstrating cartilage erosion and bony remodelling.

with this disease. Locating and surgically addressing an underlying cause before marked changes have occurred in the joint offers the best prognosis for minimising OA. In general, treatment of canine OA should be tailored to the needs of the individual dog and based on the owner's expectations for the dog's quality of life. The stage of OA (early vs. late, acute vs. chronic) will also dictate treatment decisions.

Overall, the goals of therapy are:

- to relieve pain.
- to reduce inflammation.
- to improve joint mobility.
- to increase activity level.
- to prevent further cartilage degeneration.
- to improve quality of life.

Management options

Management of OA has become multifaceted, especially with the increasing acceptance of alternative treatment modalities.

The five general categories for the treatment of the osteoarthritic dog are:

- Nutrition/weight control
- Exercise modification/physical rehabilitation
- Drug and nutraceutical administration
- Surgery
- Alternative methods

Pharmacological therapy continues to be the mainstay of treatment, although modifications of diet, exercise, and body weight should be addressed in every patient. Surgical options should be given where appropriate, and alternative methods should be offered if available and if the client is receptive.

Medical

Nutrition/weight control

Obesity has been shown to be a risk factor for OA in humans and dogs (3). Increased loads placed on an arthritic joint contribute to cartilage deterioration. Weight control may alleviate the severity of the clinical signs of OA by decreasing the amount of abnormal force put on the joint and avoiding obesity is essential. Owners should be informed of their dog's ideal body weight, from which it is possible to recommend a daily calorific requirement. The weight of the dog and its body condition score (BCS)



Figure 3a Radiograph of a shoulder joint with severe chronic osteoarthritis.



Figure 3b Radiograph of an elbow joint with moderate to severe chronic osteoarthritis.

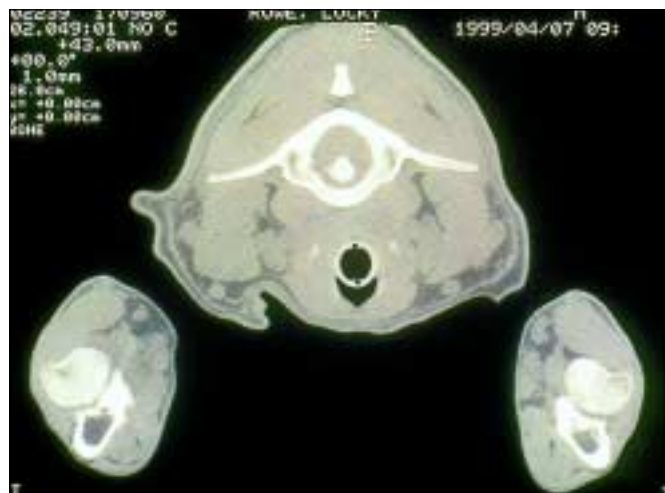


Figure 4 CT scan of elbows demonstrating fragmented medial coronoid process and secondary changes of the left elbow.

Table 1

5-point body condition score system for dogs*

Score	Area of Evaluation	Description
1 – thin	Ribs	Easily palpable with no fat cover
	Tailbase	Prominent raised bony structure with no SC tissue
	Abdomen	Severe tuck with accentuated hourglass shape
2 – underweight	Ribs	Easily palpable with minimal fat cover
	Tailbase	Raised bony structure with little SC tissue
	Abdomen	Noticeable tuck with marked hourglass shape
3 – ideal	Ribs	Palpable with slight fat cover
	Tailbase	Smooth contour of some thickening; bony structures palpable under thin layer of SC fat
	Abdomen	Noticeable tuck; well-proportioned lumbar waist
4 – overweight	Ribs	Difficult to palpate; moderate fat cover
	Tailbase	Smooth contour of some thickening; bony structure remain palpable
	Abdomen	Little or no abdominal tuck or waist; back slightly broadened
5 – obese	Ribs	Very difficult to palpate; thick fat cover
	Tailbase	Appears thickened; difficult to palpate bony structure
	Abdomen	Pendulous ventral bulge; no waist; back markedly broadened; trough may form where epaxial areas bulge dorsally

*Lund E. M., Armstrong P. J., Kirk C. A. et al (17)

should be recorded at each visit. Various BCS systems have been developed for dogs – a five-point system is presented in **Table 1**. Theoretically, weight reduction can be accomplished through food restriction, increased exercise or behaviour modification. In reality, reducing calorific intake is the only practical option in most circumstances and great care must be taken to ensure that good communications are maintained. Commercial foods such as WALTHAM® Veterinary Diet Calorie Control are ideal. Failure most often comes from poor owner compliance. Thus, anything that increases compliance is helpful and regular monitoring of body weight is mandatory. Clinicians should bear in mind that failure to lose weight may reflect an underlying metabolic condition, such as hypothyroidism.

Most developmental orthopaedic disorders will lead to some degree of OA later in life. Preventive measures should be taken in fast-growing, large breed puppies that risk facing such problems by avoiding nutrient excesses and rapid development. Restricting food intake has been shown to slow growth rate without significantly affecting adult body size and may help to prevent the development or decrease the severity of certain skeletal diseases, such as hip dysplasia and osteochondrosis.

Exercise modification/physical rehabilitation

All dogs with OA should have some regular exercise. The principles employed in physical therapy in human medicine can be applied in veterinary medicine. Benefits of physical rehabilitation include decreasing pain and discomfort, increasing muscle strength, increasing range of motion in the joint, improving limb function and reducing the necessity for drug administration. However, exercise is to be avoided in cases of acute exacerbation of OA accompanied by marked joint inflammation. In most cases, after a period of rest, an exercise regimen can be slowly reintroduced. High-impact activity, such as ball fetching, should be avoided but controlled leash walks and swimming should be encouraged, although there is a lack of controlled studies documenting the efficacy of physical rehabilitation in veterinary patients. Aside from low-impact exercise, other forms of physical rehabilitation include passive range-of-motion exercises, cold therapy, heat therapy, muscle and joint massage, ultrasound and electrical stimulation.

Swimming is an ideal means of exercise as it increases muscle strength and joint fluidity in a low-weight-bearing environment. A balanced exercise programme, which provides therapeutic benefits but avoids episodes of discomfort, needs to be developed for the individual dog.

Range-of-motion exercises can be taught to owners to allow for some



Figure 5 Acupuncture with electrical stimulation of a dog with bilateral hip dysplasia and lumbosacral disease.

physical rehabilitation at home. Passive exercises involve gently flexing and extending the limbs in non-weight-bearing position. The aim of these exercises is to stretch soft tissues and to improve joint mobility. These exercises should be well-tolerated by the animal, although owners should take care not to cause any pain or discomfort by forcibly moving the limbs. Active exercises encourage controlled activity to improve muscle strength and limb function. Examples include, but are not limited to, treadmill walking, incline training on hills or stairs, and sit-to-stand exercises.

Cold application causes local vasoconstriction that reduces the effects of inflammation. Cold therapy is indicated in instances where there is marked swelling or oedema in order to decrease haemorrhage and inflammation.

Heat application increases local blood flow, decreases pain and muscle spasm, and improves joint mobility. Heat should not be applied if there is acute swelling or oedema, because increased circulation may aggravate the condition.

Massage therapy minimises adhesion formation, decreases muscle spasm, and increases vascular and lymphatic circulation. This helps to reduce oedema, improve blood flow, and decrease muscle stiffness.

Therapeutic ultrasound is a form of deep heat that can be administered in continuous or pulsed mode. Continuous mode has both thermal and

Table 2

Dosages of selected drugs for the treatment of osteoarthritis

Generic name	Dose
Aspirin*	5–10 mg/kg PO q12–24 h
Polysulphated glycosaminoglycans	4 mg/kg IM q3–4 d
Carprofen	2.2 mg/kg PO q12 h
Hyaluronic acid	7 mg Intra articularly q7 d
Etodolac	10–15 mg/kg PO q24 h
Pentosan polysulphate	3 mg/kg SQ, IM q7 d
Piroxicam	0.3 mg/kg PO q48 h
Acetaminophen and codeine	0.5–2 mg/kg codeine PO q6–8 h
Meloxicam	0.2 mg/kg PO q24 h
Doxycycline	1.75 mg/kg PO q24 h

*Some authors quote 10–25 mg/kg q8–12 h for anti-inflammatory activity but the lower dose should be tried first. In most cases a licensed NSAID would be preferred as first-choice treatment.

non-thermal effects, while pulsed mode has only non-thermal effects. Thermal effects occur when the tissues are oscillated at high frequencies and produce heat, resulting in increased blood flow and decreased pain to the treated area. Non-thermal effects occur at the cellular level and include increases in cell membrane permeability, intracellular calcium, protein synthesis and angiogenesis (4).

Electrical stimulation increases muscle strength and joint range of motion while decreasing swelling and pain, and promoting wound healing (5) (Figure 5). Low-frequency, pulsed currents are most commonly utilised to improve muscular function in the affected areas. Unfortunately, electrical stimulation units are not widely available for use in veterinary patients and the cost may be prohibitive for the owner.

Drug and nutraceutical administration

The goals of pharmacological therapy in the osteoarthritic patient are to relieve pain, subside inflammation, improve joint function, and protect the joint from further damage. Commonly administered medications include non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids and parenterally administered disease-modifying agents, such as hyaluronic acid (HA) and polysulphated glycosaminoglycans (Table 2).

NSAIDs are the most frequently administered medications for OA in human and veterinary medicine. The primary mechanism of action for most NSAIDs is reversible inhibition of cyclo-oxygenase to prevent synthesis of prostaglandins (5). Prostaglandins not only mediate inflammation, but also increase vascular permeability and potentiate the effects of histamine, bradykinin, serotonin and other inflammatory mediators. The major adverse effects include gastrointestinal irritation, ulceration and acute nephrotoxicity. The occurrence and severity of adverse reactions can vary between individual agents and individual patients. The discovery of two isoforms of cyclo-oxygenase (COX-1 and COX-2) may explain the differences in efficacy and toxicity among agents. COX-1, the constitutive form is responsible for normal physiological functions dependent on prostaglandins (renal blood flow maintenance and gastrointestinal mucosal protection) while COX-2, the inducible form (6), is activated in inflammation (Figure 6). Greater inhibition of COX-2 by NSAIDs is associated with decreased potential for adverse reactions and selective COX-2 inhibitors – for example, carprofen – are now being marketed. [Budsberg, *WALTHAM Focus* 1999; 9(2) Current and future trends in the use of NSAIDs for the treatment of osteoarthritis in dogs].

Aspirin remains one of the most commonly prescribed medications for treatment of OA. It is a very effective analgesic and anti-inflammatory drug for most musculoskeletal disorders. Reports of side-effects are frequent, primarily consisting of gastrointestinal irritation. Vomiting, melaena or haematochezia are typical clinical signs seen with intolerance; however,

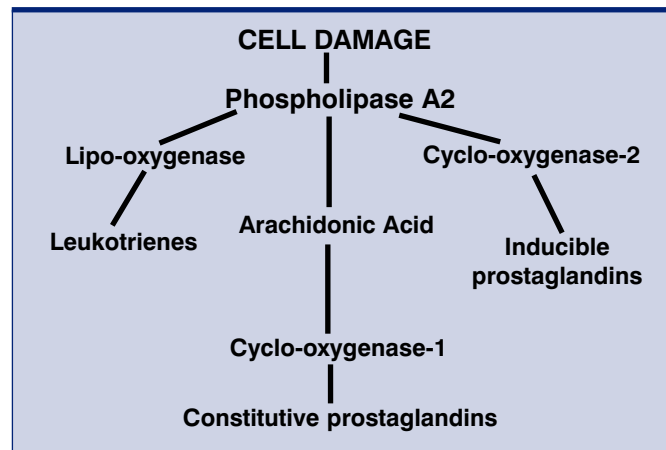


Figure 6 A diagrammatic representation of the arachidonic acid cascade.

resolution usually occurs with discontinuation of the drug. Administration of buffered preparations or concurrent administration of misoprostol, a synthetic PGE1 analogue, at 2–5 mcg/kg q8–12 hr may reduce the incidence of adverse reactions.

Carprofen is an agent in the propionic acid class of NSAIDs that is equivalent to indomethacin in potency, but substantially less likely to cause bleeding in the gastrointestinal tract due to a favourable COX-2:COX-1 ratio. Since its approval for use in the USA in January 1997, over 2,000,000 dogs have been prescribed carprofen. A variety of adverse effects have been reported, yet the incidence is small. Gastrointestinal signs predominate, although a subset of dogs was reported to have hepatic necrosis secondary to carprofen administration (7). This adverse reaction is believed to be idiosyncratic and cytotoxic and could occur with the administration of any NSAID.

Etodolac is a pyranocarboxylic derivative reported to also have a favourable COX-2:COX-1 ratio. Etodolac had potent analgesic and anti-inflammatory effects and causes minimal gastrointestinal side-effects. A prolonged half-life and extensive enterohepatic circulation allow etodolac to be administered on a once-a-day basis.

Piroxicam, an oxamic derivative, is an extremely potent NSAID. However, it has been associated with a high incidence of gastrointestinal ulceration. The recommended dose administered on a daily or alternate-day basis is thought to minimise the occurrence of adverse reactions. Piroxicam is effective in controlling pain and inflammation associated with OA. However, its analgesic properties may also provide relief from pain associated with cancer, as well as having potential chemotherapeutic properties.

Meloxicam is in the same class of NSAIDs as piroxicam and has been shown to have powerful anti-inflammatory effects with minimal toxicity. The preferential inhibition of COX-2 may explain the marked difference in the incidence of side-effects between piroxicam and meloxicam.

Ketoprofen is a member of the propionic acid class and is available in injectable and oral preparations. It seems to be more effective and safer when administered on a short-term basis for post-operative pain. Ketoprofen has the potential to inhibit both prostaglandins and leukotrienes and has a high incidence of side-effects.

Naproxen is also a propionic acid that, as well as being a potent anti-inflammatory, may have chondroprotective properties. However, due to its prolonged elimination and narrow therapeutic window in dogs, there is a high incidence of adverse reactions and its use is not recommended.

Ibuprofen, while highly effective in humans, has marked ulcerogenic and nephrotoxic potential in dogs due to different pharmacokinetics. Its use in the treatment of OA is highly discouraged.

Phenylbutazone is approved for use in dogs in the USA. However, in addition to potential gastrointestinal and renal side-effects, phenylbutazone may cause bone marrow suppression and blood dyscrasias. This drug is now rarely used, given the advantages of COX-2 inhibitors outlined above.

Meclofenamic acid is another NSAID that is approved for use in dogs in the USA. It is reportedly twice as potent as aspirin, but there is a high incidence of gastrointestinal adverse reactions.

Chondroprotective agents

Chondroprotective agents are more accurately labelled as slow-acting, disease-modifying agents that can be orally or parenterally administered. Nutraceuticals are orally administered non-pharmaceutical products that are considered nutritional supplements. Products directed toward the treatment of OA contain cartilage precursors that are believed to be chondroprotective and help rebuild the cartilage matrix. Although the use of oral disease-modifying agents is common, scientific data regarding their efficacy are limited. More is known about the injectable preparations, especially about their effects in the equine joint. Application of these agents in small animal medicine is becoming more frequent.

Polysulphated glycosaminoglycans (PSGAGs), when administered intramuscularly, have an anabolic effect on arthritic cartilage by inhibition of inflammatory mediators and destructive enzymes. A PSGAG preparation was recently approved in the USA for use in dogs, and is perhaps most effective when used early in the course of disease. When administered before the onset of arthritic change in very young dogs (six weeks to eight months of age) dysplastic puppies showed improved radiographic conformation (8). The only reported side-effect in dogs is prolongation of clotting times due to its structural similarities to heparin.

HA formulations are available for intravenous or intra-articular injection. The mechanism of action of exogenously administered HA is unknown, but it is believed to increase synovial fluid viscosity, to increase endogenous production of HA, and to scavenge oxygen free radicals. Reports of adverse effects in humans and equine are uncommon, therefore its use in dogs is thought to be relatively safe.

Glucosamine and chondroitin sulphate are the predominant components of most nutraceuticals. Recent clinical trials have shown subjective efficacy of one veterinary supplement containing glucosamine, chondroitin sulphate and manganese ascorbate in dogs with cranial

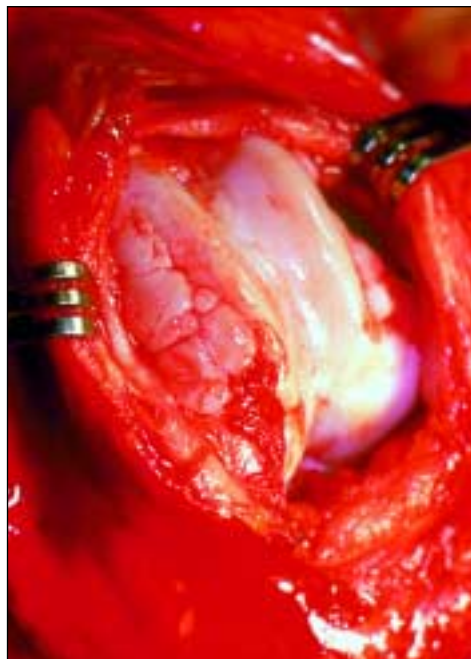


Figure 7
Stifle with cranial cruciate ligament rupture and moderate to severe chronic osteoarthritis.



Figure 8 *Radiograph of bilateral hip dysplasia with unilateral total hip arthroplasty.*

cruciate ligament rupture and in horses with navicular syndrome (9, 10). However, there are still limited scientific data supporting the effectiveness of most of these products or the bioavailability to the joint.

Pentosan polysulphate is a polysulphated polysaccharide composed of semi-synthetic polysulphated xylan. It may be administered orally or parenterally to improve synovial and subchondral blood flow, to limit cartilage matrix degeneration, and to stimulate HA and proteoglycan synthesis. Several experimental and clinical studies have demonstrated efficacy of pentosan polysulphate in decreasing articular cartilage damage and improving limb function (11, 12). However, availability of this drug is limited.

Other agents

Other agents that may be of benefit for the treatment of OA include glucocorticoids, tetracycline, omega-3-fatty acids and antioxidants.

Glucocorticoid administration for the management of OA remains controversial. Systemic side-effects and exacerbation of cartilage deterioration limits the use of steroids as long-term relief. However, systemic or intra-articular administration may provide immediate short-term relief for dogs that are refractory to NSAID therapy, have acute intermittent pain, or have end-stage joint disease.

Acetaminophen is known to be potentially fatal when administered to cats, although the incidence of side-effects in dogs is relatively minimal. Its potent analgesic effects, especially when combined with codeine, have made acetaminophen a popular drug for management of OA.

Doxycycline is a bacteriostatic broad-spectrum antibiotic that has also been shown to have anti-inflammatory effects due to its ability to inhibit

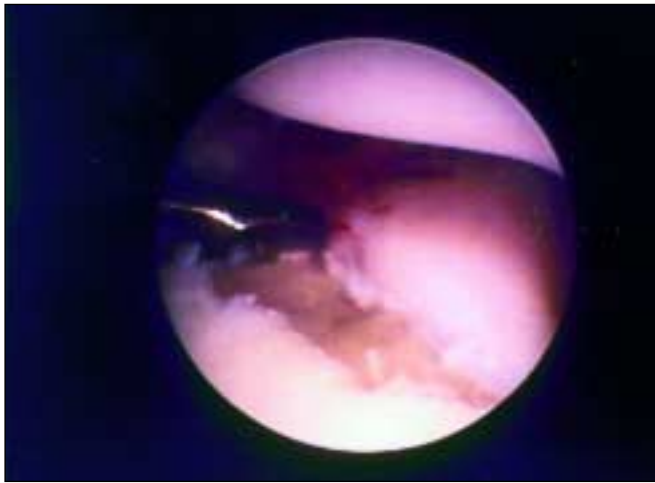


Figure 9 Arthroscopic view of fragmented medial coronoid process and cartilage debridement.

metalloproteinases. Its use might be of most benefit when used prophylactically. A decrease in cartilage degeneration in dogs with cranial cruciate ligament transection was documented in one study where doxycycline was administered twice a day for eight weeks (13). Further studies are warranted to evaluate its role in the management of OA.

Polyunsaturated fatty acid (PUFA) supplementation has been reported to reduce pain and discomfort levels in human rheumatoid arthritis patients. It has also been reported that arthritic dogs receiving PUFAs for dermatological problems have had noticeable subjective improvement in the degree of joint stiffness and lameness (14). PUFA supplementation replaces arachidonic acid in eicosanoid synthesis, producing enzymes that are potentially less inflammatory than prostaglandin-E2 and leukotrienes. Side-effects associated with PUFA supplementation, such as diarrhoea, are minimal.

Antioxidants are thought to be beneficial in osteoarthritic patients because free radicals contribute to the progression of cartilage degeneration by cellular oxidative injury. Proanthozone is an oral nutraceutical with potent antioxidant effects. Its efficacy has been evaluated in clinical trials and while results are favourable (15), further investigation is warranted. Vitamin C supplementation has been recommended by some due to its role in collagen synthesis. However, since dogs make vitamin C endogenously, exogenous administration is controversial. Superoxide dismutase also appears to be beneficial in treatment of chronic OA due to free radical scavenging and profound anti-inflammatory effects. The bioavailability of oral superoxide dismutase has not been demonstrated; therefore, only the injectable form should be considered (16). Adverse reactions to exogenous antioxidant supplementation are uncommon.

Surgery

The role of surgery in the management of OA depends on the stage of disease and the joint affected. Developmental conditions and traumatic injuries need to be recognised and corrected early if progression is to be slowed or OA prevented (**Figure 7**). As degenerative changes progress, surgery is indicated when conservative treatment fails. The initial goal of surgical treatment is to relieve pain and inflammation while maintaining a functional joint. Salvage procedures are often performed when a more favourable surgical option is not available, not affordable, or has already failed [Montgomery, *WALTHAM Focus* 2000; **10**(1) Decision making in the management of canine hip dysplasia].

Total joint arthroplasty is the ideal surgical salvage treatment for

alleviation of clinical signs and complete return to function [Massat, *WALTHAM Focus* 1995; **5**(4) Canine cemented total hip arthroplasty]. However, the coxofemoral joint is the only site at this time that is amenable to such a procedure with good to excellent clinical results (**Figure 8**). Total stifle and elbow arthroplasty are currently under scientific and clinical investigation with fair to good results to date.

Excisional arthroplasty is an acceptable salvage procedure for the coxofemoral joint. A pseudoarthrosis is created that has limited range of motion relative to a normal joint. Better functional outcomes are achieved in smaller dogs. However, larger dogs will also benefit from relief of the pain and disability.

Arthrodesis creates a permanently fixed joint angle and eliminates the motion between degenerate articular surfaces, thus reducing pain and discomfort. Arthrodesis is a good surgical option for distal joints, such as the carpus and tarsus. This procedure can also be performed successfully at the level of the shoulder, elbow or stifle with good to poor functional outcomes.

Arthroscopic debridement is becoming more common, especially with regards to the elbow (**Figure 9**). Arthroscopy is preferable to arthrotomy as there is minimal joint destabilisation, lower post-operative morbidity and faster post-operative recovery. The long-term benefits of arthroscopic debridement are not yet known.

Other treatment modalities

Acupuncture is applied in a wide variety of problems in small animal medicine (**Figure 10**). Acupuncture is most commonly requested for OA and chronic spinal disorders. It is thought to help the body heal itself and this is accomplished through nerve stimulation, increased blood circulation, muscle spasm relief, and endorphin and endogenous cortisol release. Acupuncture is thought to be beneficial as an adjunctive therapy to other treatment modalities or used in cases that have become refractory to medication. Acupuncture is claimed to provide long-term analgesia, decrease inflammation and increase circulation to affected areas.

The beneficial effects of other modalities of alternative medicine are not well known. Homeopathy, chiropractic adjustments and herbalism are just a few forms of holistic medicine that clients may inquire about. In general, conventional means for treating OA should not be ignored in favour of alternative medicine. However, alternative modalities can be complementary to traditional approaches and may provide some benefit to



Figure 10 Acupuncture demonstration.

the individual animal. If alternative methods are offered to a client, a specialist familiar with or trained in veterinary medicine should be consulted.

The future

Advancements in the treatment of canine osteoarthritis are happening rapidly and appear to follow trends set in human medicine. Future directions for the management of OA include:

- The development of more preferential COX-2 inhibiting NSAIDs.
- NO-NSAIDs – these are NSAIDs bound to nitric oxide, a mucosal protective agent.
- Cartilage resurfacing agents.

Awareness of new developments will also help the veterinarian to educate the client better and to make rational decisions together with the client for the care of each individual dog suffering from OA.

Summary

Osteoarthritis can be a frustrating condition for dogs and their owners, and the treatment of canine OA can be as complex as the disease itself. While treatment modalities are numerous, an understanding of the owner's goals and expectations of therapy will help the veterinarian make appropriate recommendations. Weight reduction and exercise modification should be implemented in every therapeutic regimen for OA. Long-term administration of NSAIDs is not ideal, due to the risk of adverse reactions. However, coupled with surgery, disease-modifying agents, physical rehabilitation, and/or alternative methods, the need for chronic medication may be reduced.

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