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JOINT HEALTH SPECIAL EDITION

Expert Opinion in Joint Disease Management By Dr. M. A. Hatekar (Page 2)

Launching Terbopet-M

Vivaldis takes pleasure to announce launching of an antifungal cream, TERBOPET-M, the safe and effective regimen in fungal attack. Terbopet-M contains Terbinafine hydrochloride and Mometasone furoate, The combination of a superior antifungal with a soft and potent anti-inflammatory gluco-corticosteroid.

A new gene therapy for dogs with osteoarthritis.

WESTMINSTER, Colo. (CBS4)–

Veterinarians are injecting a new gene therapy into dogs with severe cases of osteoarthritis. Six-year-old Knob, a Tibetan Mastiff who has had arthritis pain since he was a puppy. He has had multiple surgeries and has been on medication but his pain forced him into a sedentary lifestyle. University of Colorado Boulder Neuroscience professor Dr. Linda Watkins says scientists have learned how to replicate the Interleukin X gene, can be found in all living species and wards of inflammation and in turn alleviates arthritis pain. Sometimes animals do not produce enough of that gene. This gene therapy, given in an injection, apparently helps the body naturally create Interleukin X which eliminates pain in dogs. The success of therapy made FDA to approve the treatment for humans also. Watkins says that it could mean the end of knee and hip replacements in the future. One injection of this shot lasts for 1½ years or more in dogs.

Bayer announces its exit from Animal Health Business

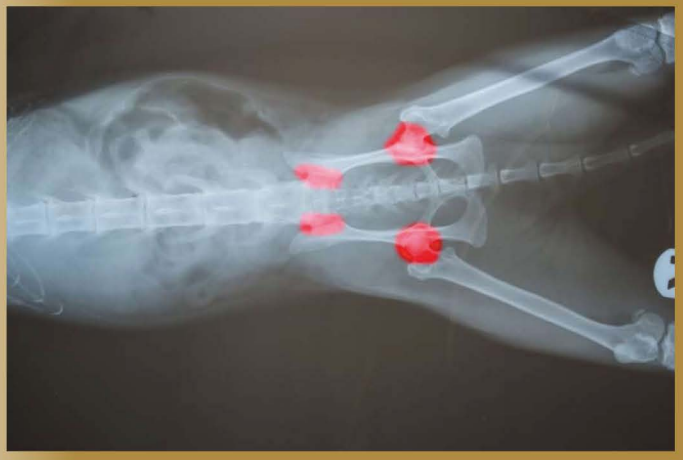
A recent statement, issued on December 2018, Bayer announced that the company intends to exit the animal health business.

The statement explained that they intend to allocate the investment resources necessary to support the Animal Health, to Bayer's core businesses of Pharmaceuticals, Consumer health and Crop sciences.

New Drug Available for Canine Osteoarthritis

By American Veterinarian Editorial Staff

Elanco Animal Health, a division of Eli Lilly and Company, and Aratanta Therapeutics Inc. announced the availability of Galliprant®—a new targeted drug for managing pain and inflammation in dogs with osteoarthritis (OA). Galliprant, a first-in-class piprant, is indicated for dogs with OA that are as young as 9 months of age and weigh at least 8 pounds. Dosing schedule as once a day with 1 or ½ tablet of the medication. This novel product acts by blocking the prostaglandin EP4 receptor, the primary mediator of OA pain and inflammation, while not inhibiting production of necessary prostanoids that maintain homeostatic functions. Galliprant was proven effective and safe and no clinically significant changes in liver, kidney, or coagulation parameters were seen. Likewise, there were no noticeable effects on food consumption, body weight, electrocardiography, organ weight, or hematology among study participants.



Expert Opinion in Joint Disease Management By

Dr. M. A. Hatekar

Founder of Pet Aid Clinic and a member of ESVOT, AOVET, WSAVA, PPAM, PDAP AND founder member of Veterinary Orthopedic Foundation.

Osteoarthritis is a common cause for lameness, although it is often secondary to a primary inciting cause, so treatment and management may need to address the primary inciting cause as well as the pain associated with the arthritis. Management of the condition involves a combination of medical and surgical options, and weight management can often be crucial in reducing pain and improving patient mobility.

Arthritis in the dog affects up to 20 per cent of the adult canine population. The susceptibility of any individual to osteoarthritis is related to factors such as genetics, age and systemic factors such as obesity. Superimposed on this inherent susceptibility are local factors such as instability and injury to the joint itself in growing stage or in an accidental injury.

Clinically, the major presenting signs are lameness, stiffness, exercise intolerance or an unwillingness/inability to climb or jump. The signs can be attributed to the primary inciting cause, pain associated with arthritis or a combination of both. Specific breed and age predilections so the signalment of an animal may help the clinician in reaching a diagnosis. For example, hip dysplasia is present in very young medium- to large-breed dogs and the secondary radiographic changes are evident from a very early age.

Ask following question for assessment:

Duration of lameness, clinical progression, response to any treatment; any history of trauma or other inciting causes, behavioral changes; response to amount of exercise performed; and effects of weather.

Inactivity stiffness: Owners report that their pet's lameness seems to resolve during exercise but then worsens after periods of rest following these bouts of activity. Other common presentations include a change in the animal's ability to climb, for example, the stairs, or jump, such as into the back of the car.

Physical examination

Osteoarthritis is usually secondary to a primary inciting cause so a diagnosis of osteoarthritis alone is usually insufficient and the clinician needs to identify the primary cause. A physical examination should be systematic and complete. It is useful to compare the contralateral limb when assessing the range of motion, and also when looking for soft tissue swelling and muscle atrophy. However, since the most common forms of orthopedic disease (eg. cruciate disease, elbow dysplasia and hip dysplasia) can frequently present bilaterally, this is not always useful.

A complete analysis of the gait should be performed. This is most commonly done in two ways:

•The patient can be examined while in the consultation room during the history taking. This can often reveal very subtle lameness and allows the clinician to monitor the animal lying down and standing up, as well when walking around the consultation room.

• Further analysis of the gait should be made in an area that allows the animal to be walked and trotted in a straight line. The animal should be observed walking away from and back towards the clinician, as pelvic limb lameness is often more obvious when walking away and thoracic limb lameness more obvious when walking back towards the clinician.

This gait analysis is usually performed before the physical examination as the lameness may be worsened by the examination, although repeated single joint examination followed by immediate gait analysis may help to localize lesions, especially in the most cases.

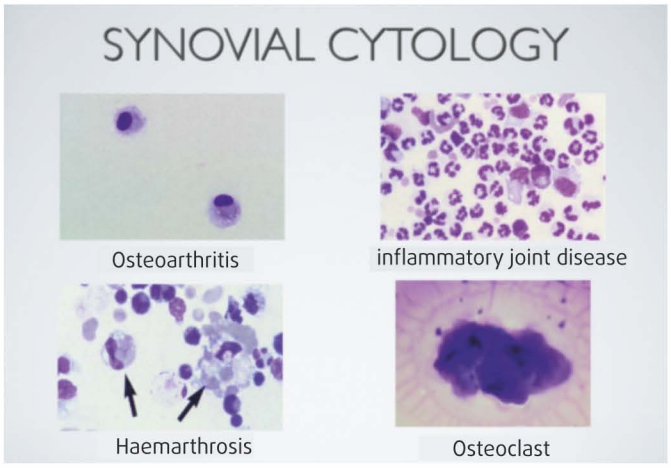
Although the presence of osteophytes can be used to diagnose osteoarthritis, there is a tendency for clinicians to focus on these osseous changes even if they do not necessarily correlate well to severity of disease or the clinical situation seen. Elbow dysplasia, for example, produces osteophytes very slowly whereas within three to four weeks of a cranial cruciate ligament rupture there will be radiographic evidence of osteoarthritis. It has also been shown that some breeds produce more osteophytes than others despite having the same degree of hip laxity (Smith and others 1995). For this reason, it is important to always evaluate the radiographs in line with the clinical situation in order to appropriately manage the cases.

Subchondral sclerosis is commonly quoted as an indicator of osteoarthritis although its sensitivity on plain radiography is limited, due to the wide variation in exposure factors that can lead to apparent differences in density. Care should be taken to not over interprete this radiographic finding because, taken in isolation, it is not a reliable indicator of osteoarthritis. However, if present in conjunction with other radiographic findings, it can be used to confirm the diagnosis.

Synovial fluid analysis

Synovial fluid analysis is an under used diagnostic test in clinical practice. With osteoarthritis, there are early changes that occur in the synovial fluid. In osteoarthritic joints the volume of fluid may be increased, cell counts, predominantly monocytes (>88 per cent),

are usually low (less than 5 × 109 white blood cells [WBC]/l) and can often be within normal limits (<2 ×109 WBC/l), and the colour remains clear to pale yellow. In the early stages of the disease viscosity is not reduced although, as the hyaluronic acid concentration diminishes over time, the viscosity decreases. Hydroxyapatite crystals are common features in the synovial fluid of human patients with osteoarthritis, but laboratories do not routinely test for them and the significance with respect to clinical outcome and treatment in dogs is unknown. We do not request hydroxyapatite counts from submitted samples. Biomarkers have been investigated as a possible way of diagnosing osteoarthritis and although several potential markers have been identified, none are validated in the dog.



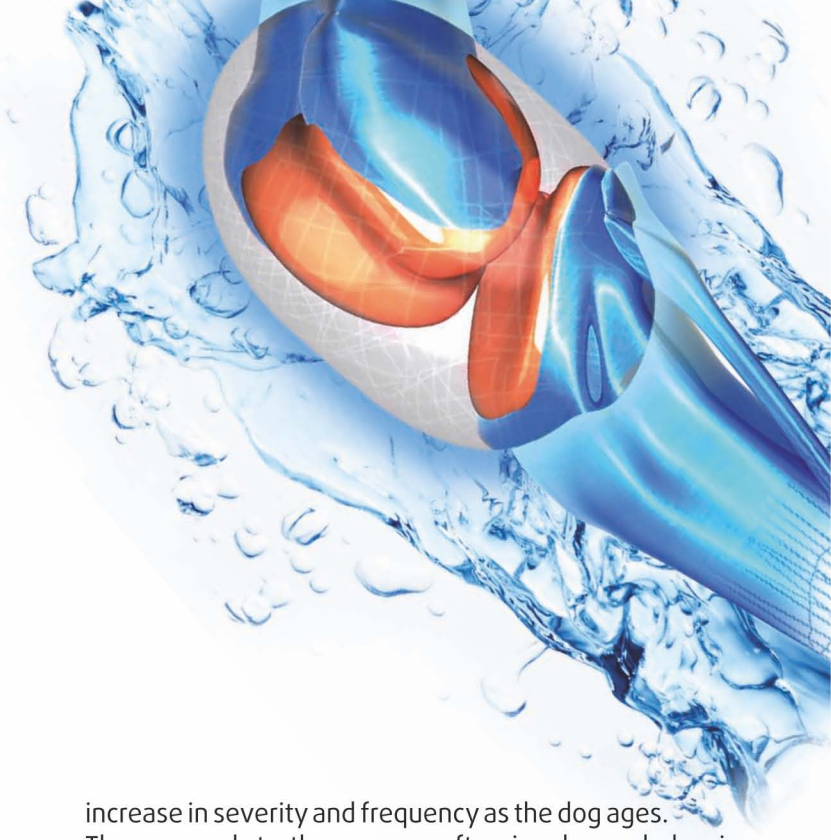
Advanced imaging

Advanced imaging modalities such as MRI and CT are becoming more routinely available to clinicians and, therefore, their use is increasing in the work-up of orthopedic cases. For patients with osteoarthritis, CT can be useful in the early stages of disease, as it may help to identify the primary lesion which may not be present or obvious on radiographs. This is particularly the case for elbow dysplasia, where the primary medial coronoid disease is often not visible on radiographs and progression of osteoarthritis may be so slow that radiographs appear normal when taken. CT is also much more useful than radiography when investigating complex joints such as the elbow, carpus and tarsus.

MRI can be useful as it gives better information about the articular soft tissue structures such as ligaments, menisci and the synovium. The main disadvantage of MRI, apart from its expense, is that canine cartilage is very thin and most of the magnets available to veterinary surgeons are not powerful enough to have a sufficient signal-to-noise ratio to allow accurate detection of cartilage lesions.

Management of osteoarthritis

The management of osteoarthritis may involve a combination of medical and surgical approaches. Owners need to be counselled from the outset that osteoarthritis is likely to be a lifelong process with flare-ups that may



increase in severity and frequency as the dog ages. The approach to these cases often involves a balancing act between exercise, medical management, weight management (if the dog is overweight), and surgery.

Exercise

Although one study demonstrated that a short period of exercise (1.20km of trotting) increased the degree of lameness when measured on a force platform, very little is really known about the effects of exercise on osteoarthritis. In people, it does seem that some exercise may be beneficial and certainly in canine patients exercise should be moderated but continued. Anecdotally, no exercise may be as detrimental as doing extremes of exercise. When advising owners on exercise levels for their dog it is important to advise them to try and avoid exuberant activities such as chasing balls, agility activities or other forms of high-energy exercise. When a flare-up of osteoarthritis has occurred for most patients the best course of action is to reduce the levels of exercise to short frequent lead walks which, if appropriate, are gradually increased over a period of weeks to previous levels of exercise.

Medical management

Drugs that are used to manage osteoarthritis can be divided into two main categories:
- symptom-modifying
- structure-modifying.

Symptom-modifying

The main drugs that can modify clinical signs are aimed at relieving the pain associated with osteoarthritis.
The symptom-modifying drugs used to manage osteoarthritis aim to relieve the pain associated with the condition, and include NSAIDs, codeine, oral opioids (e.g., buprenorphine, tramadol), amantadine; and corticosteroids.

Management plan

Start with medical management in conjunction with weight management, and closely monitor clinical status by assessing clinical signs at each revisit. At each stage, review the patient and consider the need for amending the plan. Aim to delay surgery for as long as possible, so as to maximize the amount of weight lost. NSAID therapy is started initially with a period of controlled lead-only exercise. The dog should be re-examined at regular intervals during the weight loss programme. A 15 percent reduction in weight should be sufficient to improve mobility, and should be achievable within a period of two to three months. Surgery after this weight loss is more likely to be successful, with less chance of complications. Further weight management can be scheduled after surgery, with improved mobility also being expected after surgery, which will aid the weight management process further. Use of weight management should always be considered in conjunction with other forms of medical management and surgery. The sooner a weight management protocol is started, the sooner the benefits will be observed. That said, because the process can take time, it should not be used as the sole strategy, as other medical therapies can alleviate clinical signs sooner. Indeed, combining weight management with other strategies might improve outcomes; for example, if analgesia alleviates chronic pain, mobility can be improved and this might help to promote weight loss. The timing of weight management in relation to surgery should also be considered. Successful surgery can improve mobility and again may improve the outcomes of weight loss; however, delaying surgery until after a period of weight loss may reduce the risks of complications of the procedure. It might also be that, as mobility improves, the need for surgery deceases. As a general guide for an overweight dog with concurrent osteoarthritis, we would suggest a short period of weight management (two to three months) before any surgical procedure, provided that this delay is appropriate. Such a period is a reasonable compromise since, as mentioned above, most dogs will successfully lose weight and measurable improvements in mobility will be expected.

Dietary management

Purpose-formulated weight loss diets should always be used because they tend to be supplemented in essential nutrients relative to energy content, which reduces the chance of malnutrition arising. These diets are often supplemented with protein and fiber, which is known to minimize signs of hunger in the pet thereby improving owner compliance. Food intake during weight loss should be accurately measured, with the exact amount fed depending upon the food used, the dog's sex and whether it is neutered. A recent study has also demonstrated that obese dogs with orthopedic disease need a greater level of energy restriction to achieve successful weight loss than dogs. It is critical for the owner to measure food portions precisely (eg, using electronic scales), because other methods (including the use of measuring cups) are unreliable and usually lead to overfeeding. Table scraps and treats should be avoided, although some treats (especially those with a purported health benefit such as a dental chew) can be allowed, provided that the energy content is considered within the feeding strategy.

Apart from weight loss regimens, few major joint chondroprotective nutrients that play vital role are Hyaluronic acid, Glucosamine and Chondroitin sulfate.

Hyaluronic acid is essential for the health of the synovial fluid. Hyaluronic acid plays a very important role in maintenance of synovial fluid within the joint and improves its viscoelasticity. It provides cushioning in the joints and helps carry nutrients to nourish and replenish cartilage. Hyaluronic acid is essential for the structure of the extracellular matrix. Supplementation with hyaluronic acid is crucial to maintain losses due to decreased synthesis in OA progression.

Chondroitin is a major constituent of the connective tissue known as cartilage, which helps cushion the joints and prevent bones from rubbing against each other. Chondroitin absorbs water and other fluids, which helps keep cartilage hydrated and healthy. Chondroitin sulfate and Glucosamine constitute the major GAG (glucosaminoglycans) in the joint. GAG serves as structural building blocks of articular cartilage. Chondroitin sulfate inhibits mediators of cartilage breakdown in chondrocytes and other cells of synovial membrane. Chondroitin helps in reduced pain and inflammation, and permits cartilage synthesis to occur. Chondroitin sulfate is beneficial in arthritis as it decreases synovitis and protects against cartilage degradation.

Glucosamine is an amino sugar and a prominent precursor in the biochemical synthesis of glycosylated proteins and lipids. It is one of the building blocks of cartilage. Like chondroitin, glucosamine is produced naturally and plays a role in joint health. It helps build and repair cartilage that connects the joints. Glucosamine has shown anti-inflammatory properties and may help relieve osteoarthritis pain.

EFFECTS OF ORALLY ADMINISTERED CHONDROITIN SULFATE ON JOINT FUNCTIONAL IMPAIRMENT IN SENIOR DOGS AFFECTED BY OSTEOARTHRITIS

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1: Bioibérica S.A., Barcelona, Spain. [2]: Centro Veterinario Indautxu, Bilbao, Spain

Study:
The mean age of dogs in study: 9.9 yrs
The mean weight of dogs in study: 26.5 kg
Evaluation done for: degree of pain, joint effusion, instability and cracking.
Evaluation done on: baseline, 40, 60, 80 days

Introduction

Osteoarthritis is a degenerative and inflammatory condition that results in joint alterations. The central element of this disease is cartilage degeneration together with difficulties in regenerating cartilaginous tissue and a remodelling of the subchondral bone with a secondary synovial reaction.

The main objective when treating canine osteo-arthritis is to relieve pain, restore the animal's functional status, prevent disability, improve the deformation and slow the progress of the disease. The therapeutic approach covers hygiene/dietary, pharmacological and surgical measures.

Different medicinal products and nutritional supplements, such as analgesics, anti-inflammatory and chondroprotectors, can be used during pharmacological treatment.

NSAIDs are the most widely used anti-inflammatory agents in dogs and exhibit their analgesic and anti-inflammaotry effect by inhibiting the arachidonic acid cyclooxygenase pathway. However, their main drawback includes, GI, renal and hepatic reactions and effect on vascular homeostasis.

Chondroprotectors (oral chondroitin sulfate and glucosamine, or intra-articular hyaluronic acid) increase the body's cartilage repair capacity, which is reduced in osteoarthritis.

Chondroitin sulfate is one of the most widely used oral treatments. This glycosaminoglycan acts by stimulating proteoglycan and hyaluronic acid synthesis whilst inhibiting the catabolic activity of the proteolytic enzymes responsible for degradation of the cartilage (collagenases, elastases, proteoglycanase), as well as nitric oxide and free-radical synthesis and chondrocyte apoptosis.
Its anti-inflammatory activity results from its ability to inhibit PGE2. It is also, well tolerated, and have fewer side effects as compared to NSAIDs

The improvement occurred in the degree of lameness when walking at days 60 and 80 (see figure 1), climbing stairs at day 60 (see Figure 2) and limitations in performing small jumps at days 40, 60 and 80 (see figure 3). As regards the physical examination undertaken by the vet, the degree of pain showed the best scores, with statistically significant differences at days 60 and 80 for the group treated with Chondroitin sulfate with respect to the baseline visit(see figure 4).

Figure 1. **Evolution of degree of lameness when walking for animals affected with osteoarthritis of the hip.**

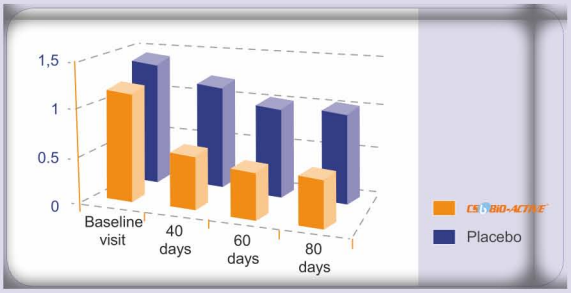


Figure 2. **Evolution of diffculty in climbing stairs for animals with osteoarthritis of the right hip**

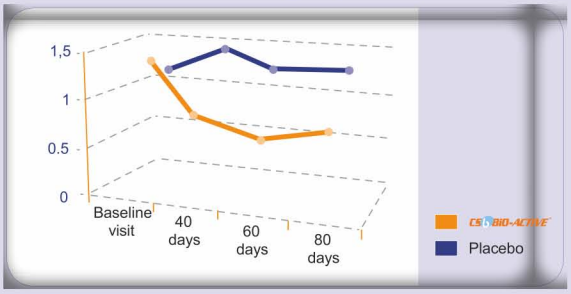


Figure 3. **Evolution of limitation in small jumps for animals with osteoarthritis of the right hip.**

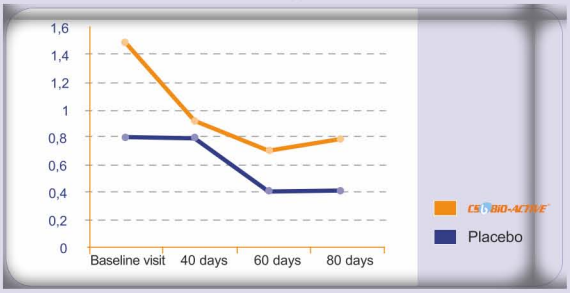
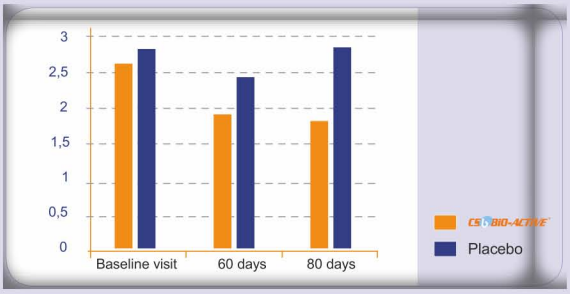


Figure 4. **Evolution of degree of pain in animals with osteoarthritis of the right hip.**



Result:
A study of the evolution of the scores on the overall functional scale showed that the percentage improvement was 29.4% at 80 days for the group treated with Chondroitin sulfate but 0% for the placebo group.

Discussion:
These results suggest that administration of Chondroitin sulfate may improve their functional limitations and degree of pain, implying a substantial improvement in QoL. It is important to note that no side effects were observed following the administration of Chondroitin sulfate.

Tailoring a plan: International opinion on nutraceutical and multimodal management of joint health in dogs and cats

A Roundtable Discussion
September 25, 2013, in Vienna, Austria

Osteoarthritis afflicts many dogs and more cats than most in the veterinary profession have previously recognized, and today many treatment modalities are available to veterinarians. As nutraceutical research emerges and veterinarians gain experience with these products, it is evident that a complementary role exists for nutraceuticals in clinically managing joint health in companion animals.

Role of radiography and overall scenario:

As per Dr. Beale:
In asymptomatic cats in the 0 to 5 yrs of age group, 80% of cats had radiographic arthritis. It climbed to 84% in 5 to 10 years age group and by the time cat reaches 10 years of age, the percentage with osteoarthritis was essentially 100%. This is observed in a cross sectional study done in cats.
Dr. Bruno Peirone, says that in dogs, there cannot be always a simple clinical correlation between amount of arthritis and clinical lameness.

Advancements in joint therapy:

A multimodal approach:
As per Dr Jerre, 15/20 years ago, NSAIDs was the main array of treatment in osteoarthritis. A lot many of dogs were then administered NSAIDs and that too for long term. Nutraceuticals came little later and specially designed food also entered into market for osteoarthritis.
Dr. Unger added that owners are much aware now-a-days and are aware of elbow and knee problems and other joint diseases. Overall approach towards joint diseases and techniques like arthroscopy and CT scanning or MRI is changing.
Dr. Bennett said that with changing owner's approach, newer NSAIDs and nutraceuticals are also entering into market. So veterinarians are also much aware about nutraceuticals now, than that of 10/15 yrs ago.

Dr. Michael Kowaleski added that:

All my patients with osteoarthritis receive nutraceuticals, regardless of their species, age, or activity level.

As per Dr. Bennett, one cannot expect improvement in patients receiving glucosamine until 4 to 6 weeks of therapy. Nutraceuticals are required to be given for much longer period of time. He further added that in cats, nutraceuticals help even in severe cases also.

Dr. Beale referred a human study as:
A study in people with symptomatic knee osteoarthritis compared the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scores for those receiving an NSAID with those receiving a nutraceutical. When analyzing the group as a whole, the NSAID group scored better than the nutraceutical group. But, surprisingly, individual group analysis based on baseline WOMAC pain scores (either mild or moderate to severe pain) revealed that the nutraceutical group scored better in the moderate to severe pain group.[3,4]

While discussing about Immune mediated polyarthritis, Dr. Bennett said that In these cases, inflammation persists for several weeks and cannot be controlled completely. Many times a chronic low grade inflammation persists. So in such cases, nutraceuticals are used as complementary because inflammation may lead to damaging the cartilage.

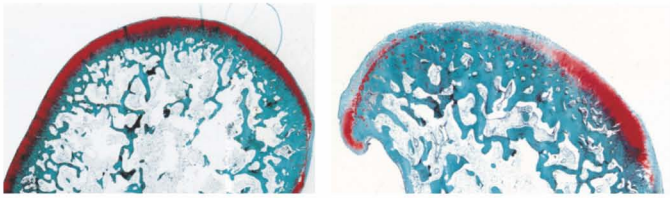
Dr. Michael Kowaleski discussed about the parameters of selecting a good nutraceutical:

1. **Types and quality of the active ingredients (especially, presence of chondroitin sulfate, glucosamine and ASU)**
2. **Evidence based supporting studies for efficacy and safety.**
3. **In vivo and in vitro studies carried out for active ingredients.**
4. **Label claim compliance**
5. **Using a low-molecular chondroitin is important to ensure better absorption**

Doctors strongly recommended combination of Glucosamine, Chondroitin sulfate and ASU (avocado soybean unsaponifiables)

Dr. Beale told no matter the product, focus on value rather than cost. One should look for product quality, amount of research work has been done to substantiate efficacy. It is always better to choose a product which is proven, tried and tested.
Dr. Jerre, while adding about Omega-3 fatty acids said that it is one of the essential supplement in joint diseases.
All of the participants agreed the important role of Hyaluronic acid in join supplements.

While discussing about weight management,
Dr. Bennett said that weight reduction is important if a cat is overweight, however a lot of older cats are not overweight. Also, NSAIDs don't go well in cats as 20% of the older cats have some degree of renal disease. So nutraceutical along with NSAIDs is always preferred in cat and dogs
In case of dysplasia, Dr. Unger said that treatment should be started right away with nutraceuticals and role of nutraceuticals should be explained to owners. A combination of NSAID and nutraceutical can also be used depending on the case.
Dr. Beale noted that the patients who are on chondroitin sulfate and glucosamine, less NSAIDs are needed. And Dr. Bennett agreed to it strongly.
Dr. Jerre shared his views on nutraceuticals as 'We begin by determining the treatment goal, we then initiate nutraceutical together with a joint health diet'.



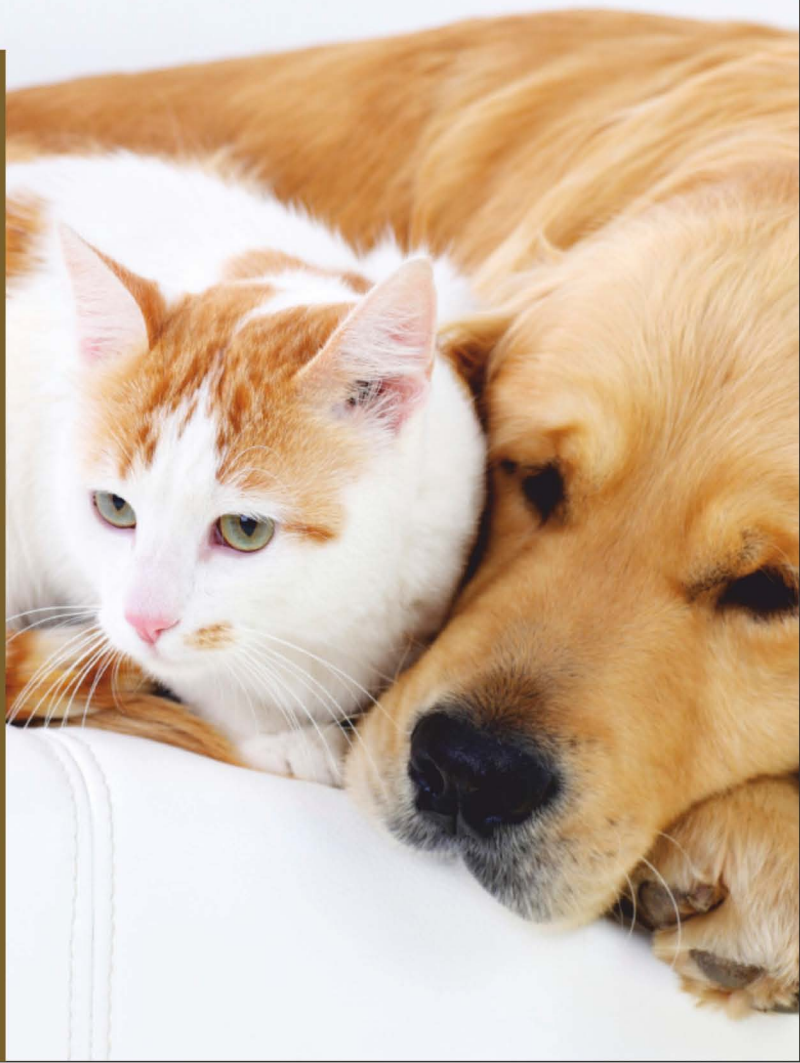
A B

Photomicrographs of histologic sections of the medial femoral condyle (from joints with surgically induced instability) from a rabbit in the combination group (A) and the control group (B). The safranin O dye has stained the glycosaminoglycan in the cartilage matrix. Note the loss of the cartilage layer in the control group (B).
(Reprinted with permission from Lippiello L, Woodward J, Karpman R, et al. In vivo chondroprotectionand metabolic synergy of glucosamine and chondroitin sulfate. Clin Orthop Relat Res 2000;381:229-240.)

Conclusion:
The research and clinical impression are that nutraceuticals can play a key supportive role in multimodal joint therapy for dogs and cats. Perhaps most importantly, veterinarians want to know what is in the products that they recommend and they prescribe for their patients are efficacious, safe, and of a consistently high quality.

A look at the research — Glucosamine and chondroitin sulfate

Numerous published controlled studies have shown that glucosamine and chondroitin sulfate can inhibit specific inflammatory mediators associated with osteoarthritis and protect against cartilage damage.
In an instability model of osteoarthritis in rabbits fed diets supplemented with FCHG49® glucosamine, TRH122 ®chondroitin sulfate, and manganese ascorbate, the combination of the three agents (as found in Cosequin® joint health supplement), compared with controls (no supplement), was best at protecting against the progression of cartilage damage.No severe and fewer moderate lesions were noted in the cartilage of the combination group (see photomicrographs below). In vitro, the combination of glucosamine and chondroitin sulfate synergistically increased glycosaminoglycan production. The study showed the benefit of using Cosequin over glucosamine or chondroitin sulfate alone. Results of a double-blind, placebo-controlled study in dogs showed that pretreatment with Cosequin had a protective effect against chemically induced synovitis as well as associated bone remodeling, as assessed by scintigraphy. Pretreatment also reduced lameness.



WSAVA, PPAM participation:

WSAVA, INDIA :

Vivaldis participated in WSAVA 2018 congress which was held at Ramoji Film City, Hyderabad. This event was organized in association with PPAT (Pet Practitioner's Association of Twin Cities). The event marked the presence of more than 750 veterinarians.

Dr. Clifford from University of Florida guided on 'Diagnostic imaging in companion animal practice' and Dr. Mike Petty discussed about 'Pain management in companion animal practice'.

Vivaldis could get chance to interact with more than 500 veterinarians. It was a good platform to interact with drs on innovative and path breaking brands like Denamarin, the 'Veterinarian Recommended No.1 Liver Support' brand and Atopivet, unique formula that helps to maintain skin integrity.

PPAM:

Vivaldis participated in PPAM, MEET THE INDUSTRY EVENT-10 held on 16th December 2018 at Hotel Express Inn, Thane. This event was organized by Pet Practitioners Association of Mumbai. The event marked the presence of more than 250 veterinarians.

During this event, participants attended the seminar on Feline Lower Urinary Tract Disease and the speaker was Dr. Afzal Mohamed, BVSc, DVCS (Australia).

We displayed our some of the innovative and path breaking brands like Denamarin, the 'Veterinarian Recommended No.1 Liver Support' brand, Relaxzyme, the proprietary blend of potent proteolytic enzymes designed to accelerate wound healing and recovery from inflammation, Terbopet with Terbopet-M, the undisputable leader in antifungals.

World No.1 Joint Care Product

OSTEOARTHRITIS & RHEUMATOID ARTHRITIS

- Analgesic
- Anti-inflammatory
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IN FRACTURES & BONE METABOLIC DISEASE

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