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Lecture Topic: Nutrition Supplements for the Canine Athlete

This presentation will review many of the individual components of available supplements for the canine athlete. A focus will be on joints, but muscle supplements will be discussed as well.

A brief review of the structure of joints, the extracellular matrix and the organization of chondrocytes will be done to orient the attendee on the goals of supplements in the chondroprotectant role. Components discussed for joint health will be:

- ⊙ Glucosamine
- ⊙ Chondroitin
- ⊙ Avocado/soybean unsaponifiables (ASU)
- ⊙ Long-chain Omega-3 fatty acids
- ⊙ Methylsulfonylmethane (MSM)
- ⊙ Egg Shell Membrane
- ⊙ Hyaluronic Acid
- ⊙ Green-lipped mussel
- ⊙ Boswellia serrata extract
- ⊙ Curcumin extract
- ⊙ Elk or deer velvet antler
- ⊙ Cetyl-myristolate
- ⊙ Hyperimmune milk factor (HIMF)

A review of eicosanoid production and the role of Omega-3 and Omega-6 fatty acids will be done.

Muscle recovery and strengthening supplements will then be discussed. These will include:

- ⊙ Creatine
- ⊙ Whey protein isolate/protein/specific amino acids (DL-methionine, L-lysine, L-carnitine)
- ⊙ Chromium
- ⊙ Dimethylglycine
- ⊙ Lecithin

Recent published research will be presented, including a brief look at a review of randomized clinical controlled trials. A brief review of over the counter supplements will be discussed. Patient assessment and implementation/selection of appropriate supplements, in the presenter's opinion, will then be discussed.

Selected References:

- 1) Millis D, Levine D, Canine Rehabilitation and Physical Therapy, 2nd edition, Elsevier, Philadelphia, 2014. P 254-262
- 2) McCarthy G, O'Donovan J, Jones B, McAllister H, Seed M, Mooney C., Randomised double-blind, positive-controlled trial to assess the efficacy of glucosamine/chondroitin sulfate for the treatment of dogs with osteoarthritis, *Veterinary Journal*, 2007 Jul;174(1):54-6
- 3) Boileau C, Martel-Pelletier J, Caron J, Msika P, Guillou GB, Baudouin C, Pelletier JP, Protective effects of total fraction of avocado/soybean unsaponifiables on the structural changes in experimental dog osteoarthritis: inhibition of nitric oxide synthase and matrix metalloproteinase-13, *Arthritis Res Ther*. 2009;11(2):R41

Nutritional Supplements for the Canine Athlete

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By the end of this lecture you will have a working knowledge of some common (and not so common) supplements for joint health, muscular recovery and strengthening, gastrointestinal system health, and immune support. You will also be able to observe critically and identify what I call “evidence vs. claims”. And finally, you’ll apply it to your own canine athlete.

The first step is to define what a nutritional supplement is. The United States Food and Drug Administration (FDA) defines it as “a product intended for ingestion that contains a dietary ingredient to add further nutritional value to the diet.” Said ingredient may be any one or a combo of the following: vitamin, mineral, herb/botanical, or amino acid.

Well that is pretty broad and nonspecific. How about we look at what a nutraceutical is. That is defined by the North American Veterinary Nutraceutical Council as “a non-drug substance that is produced in a purified or extracted form and administered orally to provide compounds required for normal body structure and function with the intent of improving health and well-being.” So we are looking for something that can help the body. That narrows it down (sarcasm font) since it is not a *drug* it is NOT regulated by the Food and *Drug* Administration. This is important and will come up later in our discussion.

Since we do not have specifics, we need to think critically. It is important to know the difference between evidence and claims.

Evidence – These are established facts.

Examples are:

- Double blind placebo controlled study
- Third Party Research
- A bibliography and sources referenced to back their statements
- A prospective study
- It appears in a peer-reviewed publication
- It utilizes the scientific method

Claims – This is a statement that something is the case, often without proof.

Examples are:

- Catchy terms on the label
- Copying one company’s research and using it as your own
- Proprietary blend --- don’t keep secrets. Tell us what’s in it
- Self-published
- Used for marketing
- “Organic”
- “Natural”

- “Guaranteed”

I put those last 3 in quotes because we see those used freely and there are no regulatory methods for them. While those words sounds straightforward, they can be very misleading.

On the other hand, I don't want you to be scared by big words. Dihydrogenmonoxide sounds scary right? But you need this every day. 65% of you is made of this. What is it? WATER!

So don't worry about big words on your supplements. But work to identify them and make sure they're valid and proven for your pet.

So why should we use a supplement? I think of it in “big picture” terms. We can potentially reduce or eliminate the need for medications with supplements. We want to use it as part of a whole body approach. This can include acupuncture, rehabilitation, surgery, exercise, diet (a well-balanced, appropriate feed with the CORRECT amount of calories), and use it with medications as well. We do need to use it SAFELY though. Over 22,000 trips to human emergency rooms occur EACH YEAR due to issues with supplements. So remember, you can have too much of a “good thing”.

Supplements for Joint Health

If we do that we need to understand what a healthy joint looks like and an arthritic joint as comparison. The picture on the left is what we want. It's what we are born with. The one on the right is what can happen. It is what we are trying to avoid. Or at least DECREASE those changes if they have already occurred.

Compounds for joint health:

- Glucosamine hydrochloride
- Chondroitin sulfate
- Avocado/soybean unsaponifiables (ASU)
- Long chain Omega-3 fatty acids
- Methylsulfonylmethane (MSM)
- Egg Shell Membrane
- Hyaluronic Acid
- Green lipped mussels
- *Boswellia serrata* extract
- Curcumin extract
- Vitamin D3
- **Pilose Antler Peptide**
- Cetyl-myrestolate

- Hyperimmune milk factor (HIMF)

And this is just the short list!

Glucosamine

Let's start with Glucosamine. This is an amino sugar found naturally in the body. It is a building block for the cartilage matrix. It stimulates cartilage cells positively. It is readily available and relatively cheap in the marketplace. Even though it sounds like glucose, it is NOT a factor in diabetic pets. There are studies (EVIDENCE) that show the sulfate form may be absorbed better than the hydrochloride. Perhaps because the hydrochloride is found in the joint. We do need a loading dose, which is 2x maintenance for 4-6 weeks to build up levels in the joints. What is maintenance? For a 75-pound (34kg) dog it's 500mg/day.

Many dog foods on the market will supplement with glucosamine. This needs to be carefully looked at. If the average 34kg Labrador Retriever eats 1400kcal/day and the food is 4.0 kcal/gram, then they eat 350 grams of food per day. Well if that food has 475ppm (parts per million) of glucosamine that equals 475mg per kg of food. That same food may have 250ppm chondroitin sulfate (foreshadowing!) that equals 250 mg/kg of food.

Our Labrador Retriever is only eating 350grams (1/3 kg). So, it's only getting 160mg of glucosamine and 85 mg of chondroitin. It SHOULD be getting 1000mg of each for 4-6 weeks and then 500mg daily. So we still need to supplement. We also don't know if it is absorbed the same when it is built into the food. So check your inclusion rates and do some math. Do not just trust the bag. It may contain glucosamine but not nearly enough to be a benefit.

Chondroitin Sulfate

Up next is chondroitin sulfate. It is also naturally occurring in the body. It helps to form the matrix that cartilage forms to support joints. Chondroitin inhibits cartilage-destroying enzymes. It can be difficult to get a reliable source and extract into an edible form. Therefore it will cost more than glucosamine. Again, we need a loading dose. Both glucosamine and chondroitin are inherently safe. Some dogs that eat too much of it can get mild gastrointestinal (GI) reaction (vomiting, diarrhea). If this happens, you should stop the supplement and immediately consult your veterinarian.

There is good evidence that glucosamine and chondroitin work together. In fact, the two have a synergistic effect. That means that $1+1>2$ in this case. They have been shown to lessen inflammation and lameness when given BEFORE a joint injury. Remember that these are *chondroprotectants*. That means they will PROTECT cartilage from damage. They can still help cartilage after an injury but work more

effectively as a pre-emptive agent. They help to maintain healthy cartilage metabolism.

Now to talk about a claim with regards to these products. I was recently on a checkout line at a pet store (Yes, I go to pet stores—I have fish.) and saw a box of dog treats that said “contains glucosamine”. Having a minute as I waited, I flipped the box over and started to do the math. Calculating how much was in each treat and how many treats they would need to reach MAINTENANCE levels per day. Our 75 pound Labrador Retriever would have to eat TWO BOXES of treats PER DAY to get the 500mg glucosamine it would need for its joints. Not only is that not financially smart, it is BAD due to the amount of calories that dog would be eating. Obesity and joint health is a whole topic for another day. So be smart in the stores and READ.

Avocado and Soybean Unsaponifiables

Moving on to our next joint supplement: Avocado and Soybean Unsaponifiables. Let's keep this simple and just refer to them as ASU. The ASUs are extracted out of the oils of the plants. These extracts have been shown to inhibit inflammation in the joint. They also complement the effects of glucosamine and chondroitin (1+1+1>3). Adding ASU decreases the amount of chondroitin needed which saves money in the long run for the consumer.

ASU supports cartilage matrix production and helps protect against cartilage damage. The safety has been widely demonstrated and there are even studies that show Dasuquin (made by Nutramax), which contains all 3 products, may be SIMILAR to the effect of non steroidal anti-inflammatory drugs (NSAID) in dogs for joint problems.

Omega-3 Fatty Acids

Next up, let's look at the long chain Omega-3 fatty acids. Get ready for more big words.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These are found in oil from wild caught COLD water fish (anchovies, sardines, salmon). The farm raised has low levels of omega-3 and high levels of omega-6.

Omega-3's have been shown to support heart health, joint health, skin and coats, the nervous system, the kidneys, and the immune system. GREAT! What's the catch, you ask? They work in all those different systems at DIFFERENT DOSES.

Let's look at some evidence for them. Studies in dogs with arthritis fed a diet with high levels of EPA and DHA had improved weight bearing on a force plate. They also had subjective reports from owners with regards to being able to walk and play more. Omega-3's can be used in the diet or as a supplement. They are safe and well tolerated. However, like anything in life, we can have too much of a good thing.

When we reach 500mg/kg/day we can run the risk platelet dysfunction. And before you ask: NO. Flax oil or coconut oil will not provide the same effects. In fact coconut oil has been shown to decrease the dog's ability to SMELL. So for you working dogs out there lay off the coconuts.

It's been a bit so let's do some math again. (I know. You love it as much as I do.) Let's use some round numbers to make it easier. A 100-pound (50kg) dog has arthritis. For arthritis we know that dogs need 80-120 mg/kg/day of Omega-3's. Let's go with the median dosage and use 100mg/kg/day which means our 50kg dog will need 5000 mg/day. (100x50). That equals 3 pumps of Welactin twice a day. 3 cups of Hill's J/D twice a day or up to TWENTY-FIVE omega-3 capsules TWICE a day. So, be careful with those over the counter gel caps. Are you really saving money? And as we will learn later, not all supplements have in them what they say they do.

Methylsulfonylmethane

MSM or Methylsulfonylmethane is up next. This is a sulfur-containing compound found in small quantities in the body as well as fruits, veggies, and grains. It is a byproduct of the breakdown of DMSO (dimethylsulfoxide). DMSO for those of you who haven't had the pleasure, smells like onions and garlic. It can be used in horses and dogs for neurological conditions and people for interstitial cystitis. (And before you ask, yes that means if your urinary bladder is inflamed we can make your pee smell like onions. Isn't medicine great?)

Thankfully, MSM doesn't have that special trait. There's good evidence with two studies in humans with knee arthritis that MSMs helps them. There's no published research in dogs yet. So this means we aren't sure on the dosage needed. But the safety in dogs has been shown. And like other supplements, we can have a bit of GI issues in some cases. But otherwise, no reported problems.

Eggshell Membrane

Moving on, we have eggshell membrane. (Anybody else getting hungry with all these supplements coming from food?) This is a new supplement. It's been shown to be of benefit to people. I'm contributing to research on it for dogs. A water soluble, (hydrolyzed) powder of the eggshell has been shown to contain elastin, collagen, desmosine, and isodesmosine. And yes, we are talking about the thin tissue paper like layer on the inside of the hard eggshell. It also contains glucosamine and chondroitin. So, if we can prove it beneficial in dogs, this could become another available supplement.

Hyaluronic Acid

Hyaluronic acid is our next joint supplement. It is naturally found in the body as a component of joint fluid. It can be given in the joint or in the vein in horses and dogs. It is given in the joint directly in people. There are some thoughts that it can be

orally administered but the one case report in German Shepherds shows that it had benefit, but those dogs were also on other joint supplements. Therefore we are not sure about it for oral routes at this time. However, it is one of my preferred therapies for injecting directly into problem joints.

Green-lipped Mussels

OK, back to food. Green-lipped mussels. These are a New Zealand shellfish. They are also known as *Perna canaliculus*. There are studies in dogs that suggest benefits, but the results are not consistent. They may contain Vitamins C and E, minerals, Omega-3's, and even chondroitin. So, we are not sure how they help. More research is needed.

***Boswellia serrata* Extract**

Boswellia serrata extract. You may also know this as frankincense. The bark of a tree found in India. It is a mix of boswellia acids that have an anti-inflammatory effect. The benefits have been seen in human arthritis patients. A study in dogs showed improved clinical signs with problems such as lameness, pain, stiff gaits. Is it good enough as a stand-alone therapy? No. But it can help.

Vitamin D3

Vitamin D3 is next. We know this helps support good bone health. Strong bones helps support good joints. Vitamin D3 also modulates the oxidative stress that can occur in the body. It also helps in immune responses (another subject of supplements later in this class). Finally, Vitamin D3 contributes to cell differentiation. So it helps to assign cells to be workers in different arenas. Definitely helpful, but a well-balanced dog food should have this already. A little extract can help but we want to avoid toxicity.

Curcumin Extract

OK, back to food. (Can you tell what drives me?) Curcumin extract. This is the active part of turmeric. We know turmeric from good cooking. The extract has antioxidant and anti-inflammatory effects. One study in dogs showed improvement in clinical scores. The standard extracts are not well absorbed by dogs, but particular ones are. And before you go "wait, I can just flavor my dog food with turmeric" don't bother, it will not work. Dogs can't process pure turmeric.

Pilose Antler Peptide

Let's talk about some antlers. The velvet parts of elk or deer antlers specifically. This is a Traditional Chinese Veterinary Medicine (TCVM) modality. It is from the antlers in a fast growing stage when the antler is CARTILAGE. We can use farmed deer or elk, but we have to consider the ethics of collecting this. What is the active

ingredient you ask? Good question. It is pilose antler peptide which is a good source of chondroitin sulfate, minerals, amino acids, collagen, and Omega-3 and Omega-6's.

Is there any evidence? Another good question. In dogs some gait parameters and owner assessments were good. The same dogs graded by veterinarians at the same time did not show any improvement. We have potential safety concerns with this too. Antlers can be chewed down and get stuck in the mouth, throat, or the GI tract. Use with caution and always under adult supervision.

Two more joint supplements and then we'll move on to muscle supplements.

Cetyl-myrestolate

Cetyl-myrestolate is a fatty acid found in Swiss albino mice. The mechanism of action is decreasing inflammation and joint lubrication. However there are NO STUDIES in dogs and we do not know how or why this MIGHT work.

Hyperimmune Milk Factor

We will end with (shocking) another food product. Hyperimmune milk factor is a natural component of milk. We can use it to manage inflammation. The cows that are immunized with intestinal bacterial agents grow the factor for us. The high molecular weight IgG and low molecular weight anti-inflammatory components aid in reducing inflammation by blocking the entry of neutrophil attachment to the endothelial wall of cells. The concentrated version of this factor is called MicroLactin and it is the active ingredient in Duralactin.

A study of 8000 people with arthritis was done and 80% reported considerable improvement in joint pain and 72% reported less stiffness in the morning. There are also studies in dogs that pet owners felt the dog moved better. These are subjective and more studies are needed but it remains a promising product.

Well, can't I just give my dog milk? Nope. This is a milk factor from specifically stimulated cows. On top of that, dogs lose the ability to digest lactose from a very young age. So, unless you want a lot of diarrhea and other GI issues for your dog, do not give it milk. Same goes for our feline friends.

Nutritional Supplements for Muscle Recovery

Moving on to nutritional supplements for muscle recovery and strengthening. While these are very popular for people we need to be very critical of them in dogs. Many of the muscle supplements will contain creatine, whey protein isolate, or specific amino acids; they can also contain chromium, dimethylglycine, or lecithin. Let us look at these individually.

Creatine

Creatine is an amino acid derivative in the body. It is found in skeletal muscle, heart, brain, and other organs. It is made via the anaerobic formation of ATP (Adenosine Triphosphate). Human studies show it may help performance and strength in repeated bouts of MAXIMAL exercise of short duration (<30 seconds): weight lifting, sprinting, cycling, etc. There are no studies in dogs at all. The biggest side effect is weight gain. This would not be helpful for dogs with arthritis. It would be borderline helpful in dogs trying to become pulling and working dogs to build muscle. I think there are better ways to do this (like rehab and conditioning and a proper diet plan).

Whey Protein Isolate

Whey protein isolate (Yep, curds and whey, just like in the nursery rhyme). This is made from milk. In human studies that looked at resistance training they had mixed results for muscle recovery, muscle mass, and strength. Again, we have no doses in dogs and, as I've mentioned earlier, we can't just offer them milk.

Chromium

Chromium is an essential trace mineral found in many foods: meat, cheese, whole grain foods, fresh fruits, fresh veggies, and brewer's yeast. It is needed for fat and carbohydrate metabolism. It can be helpful for people with diabetes but is not of benefit to diabetic dogs. The supplement is promoted for building muscle. There is absolutely no research that proves this claim in dogs or people.

Dimethylglycine

Dimethylglycine is an antioxidant that naturally occurs in the body, in cereal grains, and beans. It is marketed to support performance by decreasing lactic acid build up. Once again, we have absolutely NO research to back this up. There is conflicting research that it MAY support immune function.

Lecithin

Lecithin is a fat in the body that is also found in egg yolks and soybeans. It's an emulsifying agent, which is a substance that helps an emulsion become more stable. An emulsion is usually a mixture of two products such as oil and water that do not mix together or that are also referred to as immiscible. An emulsifying agent is added to an emulsion to prevent the coalescence of the globules of the dispersed phase. Lecithin may support the gut barrier and it is marketed to support athletic performance, but yet again, there's absolutely no data to support this.

We haven't talked about food in a while so let's talk about supplements for the GI system.

Nutritional Supplements for the GI and Immune Support

We'll first take review probiotics for GI and immune support, then review a variety of options for immune support specifically. Some I've listed earlier and some are new. New to the list are bovine colostrum, Vitamin A and C, L-glutamine, Echinacea, Reishi mushroom, Maitake mushroom, *Astragalus membranaceus*, Thymus (sweetbread) Coenzyme Q10, Zinc (which can be toxic in dogs), glutathione, and sulforaphane glucosinolate (broccoli). These may act as antioxidants or support the body's own production of them. They may reduce inflammation and they may directly affect immune cells.

Probiotics

These are beneficial bacteria used to help reestablish the normal GI microflora. They may be useful for stress diarrhea. The studies done in various brands have shown benefit in reducing the severity of diarrhea. More is BETTER in this case. We want multiple strains and high bacterial counts in our supplements. Much of the body's immune tissue is in the GI, so it may also support the immune system.

Bovine colostrum

Moving on to immune support, we have bovine colostrum. Yep, this is the third time we'll talk about cow's milk today. Colostrum is the "first milk" full of antibodies, growth factors, and hormones. Some research in humans has shown it can support the immune system of people when they are stressed by high intensity or prolonged exercise. Research has also looked at effects on performance in people – these have been contradictory. In dogs: no research.

Echinacea

Echinacea is a perennial herb used for centuries. It is potentially helpful for stimulating the immune system to fight off infections. You do need to take it early in the course of the disease if you are feeling sick in order to have any effect. In veterinary medicine, it is a short-term aid and not for chronic use. It is suggested in literature that chronic use creates tolerance.

Maitake mushrooms

Maitake mushrooms can be fractionated into a polysaccharide called D-fraction. This may have immune modulating effects. One study for lymphoma, a cancer of the lymph glands, in dogs, showed that when given ALONE it had no effect. I am not a big fan of this study because we have so many proven good options to help with cancer treatment. Maitake mushrooms can be used for general immune function support. It is commonly used in TCVM, Traditional Chinese Veterinary Medicine.

Astaxanthin

Astaxanthin (pronounced as-ta-zan-thin) is a potent xanthophyll carotenoid antioxidant. Here are big words again. It is not converted to Vitamin A in the body. Astaxanthin is found in microalgae, yeast, salmon, trout, krill, shrimp, crayfish, crustaceans, and the feathers of some birds. It provides the red color of salmon meat and the red color of cooked shellfish. It is used for enhanced immune response in dogs.

Chinese Herbs

A brief side note here for Chinese Herbs: I use them in my practice, but use only one specific company, Jing Tang Herbal, because they verify their source material and their compounds afterwards. Many herbs will have different combinations of mushrooms, antler, and other compounds in them. A trained professional is needed to advise in this area for your pet.

Conclusion

Well that is a lot of options right? How do we implement a plan? We need to look at the breed, job, goals, and medical record of each individual canine athlete. From there, we can identify certain risks and where certain supplements may be of benefit. Remember, many of these take time to have an effect and are not a quick fix. In fact, they work better as preventatives and therefore they will need to be on them consistently (read: DAILY) for weeks to months to have a benefit for your pet.

Another important fact is that the manufacturers are NOT held to the same standard as pharmaceuticals. We therefore have to question the accuracy of information on the label, and the purity and source of the material used. Are they free from contaminants? Do we have any PROOF or do we have CLAIMS?

Let's look at an example from the human literature. There was a study published in the Journal of the American Nutraceutical Association in 2000. It looked at the correlation between price and % label claim of chondroitin sulfate in 32 products.

We can see that separate from the price per DAY for a maintenance dose of 1200mg that only SIX of the 32 had at least 90% of what they claimed to have as far as chondroitin sulfate. This report did not look at the source or the efficacy of the product, but merely if there was chondroitin IN THE PRODUCT.

Yikes, so what should you do?

I recommend you contact the companies and ask for their research papers. You should also require that what's on the label is actually in the product. Also, do a background search on the reputation of the manufacturer. You don't always get what you pay for, and it's easy to be taken advantage of. In the chondroitin study above, all the very costly supplements FAILED to reach 90% of their claim.

You may want to know what I use for my dogs?

Penny is my 2-year-old pit bull. She is my running partner (already has done a half marathon) and is working on agility and mountain climbing. She's on Hills' Science Diet Healthy Mobility and Dasuquin Advanced.

Adelaide is my 14-month-old Newfoundland. She has mild hip dysplasia and had surgery for OCD lesions in each shoulder. She is on Hill's Prescription Diet J/D and Dasuquin Advanced. When she was growing (under a year of age), I fed her Hill's Science Diet Large Breed Puppy.

I hope that you have found this helpful. There is a lot of information out there and it is important to take time and review your options. Again, remember to consult with your veterinarian about specific needs for your dog. If you have questions, please leave them as comments so that everyone can see them.

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Conference Proceedings: Managing DJD: Beyond the NSAIDS

Osteoarthritis (OA) also known as degenerative joint disease (DJD) is the number one cause of chronic pain in dogs in the US. It has been concluded that 20% of dogs have some degree of OA/DJD. This results in decreased activity, weight gain, negative impact for the patient, a change in the human animal bond (negatively) and an increase in euthanasia in dogs that become refractory to treatment.

It is critical to have options to treat this disease. Identifying patients within your practice that have OA/DJD can be done quite easily. A complete, thorough physical exam and proper history on each and every patient coming in for an office call should be done. Asking questions about mobility (Trouble going up the stairs? Not playing as much? Slowing down?) should be included. Proper flexion and extension of all the joints of the limbs and palpation of the spine, flexion of the neck, checking for joint effusion and instability of joints can easily clue the clinician to finding potential OA patients. Signs such as muscle wasting, asymmetry, lameness should also be looked for. Cartilage damage occurs well before radiographic changes.

Initial trauma = fibrillation of cartilage surface, damage to chondrocytes, release of: Cartilage degradation products (CDPS), Matrix metalloproteinases (MMPs), Nitric oxide (NO) and inflammatory cytokines. MMPs/CDPS are engulfed by synoviocytes, which release: Inflammatory mediators: PGE₂, TNF, IL1 β and MMPs. All contribute to cycle of inflammation, degradation and pain of osteoarthritis.

Other changes that occur in the process are thickening of the joint capsule, remodeling of subchondral bone which leads to sclerosis. Osteophyte formation occurs via synoviocytes releasing Bone Morphogenetic Proteins (BMPs). Periosteum mesenchymal stem cell to differentiate into chondrocytes; initiate osteophyte formation from which a joint mouse or the osteophyte impinges on periosteum. Bottom line: OA becomes a vicious cycle. The joint is less able to bear stress and forces leading to further joint damage and the initiation of clinical signs.

This ongoing inflammation is the source of both the progressive nature and pain of OA. Prostaglandin E₂ (PGE) and other inflammatory cytokines lead to: progressive degradation of the joint and stimulation of nociceptors in synovium, joint capsule and subchondral bone. PGE is also released in dorsal horn and contributes to the pain signal.

The neural aspect of the joint is also a source of pain. Cartilage is aneural; cartilage damage alone is not painful. Inflammation stimulates nociceptors found in: joint capsule, synovium, subchondral bone and the periosteum. The joint nociceptors intimate pain.

Neurogenic inflammation is an additional step in the nociceptive pathway. Involve the antidromic release of neurotransmitters near the joint. Neurotransmitters such as Substance P trigger inflammatory mediators within the joint. This contributes to joint pain and inflammation.

In summary of OA inflammation: Osteoarthritis is a chronic progressively destructive disease that involves the entire joint. Inflammation is a key component of both joint destruction and pain. Acute pain resolves after the initial injury heals. Chronic pain involves structural changes of the dorsal horn, is more intense than acute pain and more difficult to control. Treatment considerations for osteoarthritis should address inflammation as well as pain.

A multimodal approach to OA management is needed. Non-Steroidal Anti Inflammatory Drugs (NSAIDS) represent the cornerstone of therapy, but other modalities include: nutrition, chondroprotectants, additional analgesics, physical rehabilitation, weight control, exercise, an EPA rich diet and many new and emerging options. Let's look through these individually.

Obesity is a growing issue in veterinary medicine. The effects of obesity on OA are twofold. Biomechanical stress contributes to clinical signs and progression of disease. Adipokines secreted by white fat cells contribute to the progressive inflammation of osteoarthritis. Leptin levels are elevated in obese dogs. In humans with osteoarthritis, increase leptin levels correlate with elevated MMPs and NO in synovial fluid. Adiponectin is anti-inflammatory, but levels are low in obese dogs. In human patients with knee osteoarthritis there is a significant correlation with adiponectin: leptin ratios.

Humans with increased body mass index (BMI) experience OA in non-weight bearing joints, which resolves with weight loss. Decrease in BMI, is associated with symptomatic relief from knee OA in man. Systematic review of canine studies found that preventing obesity decreases incidence of OA and weight loss reduces signs of OA. Additionally, diets rich in Omega-3 fatty acids have shown to be beneficial for both dogs and cats with OA. Additional nutritional supplements such as glucosamine, chondroitin, methylsulfonylmethane (MSM) and others have been shown potentially beneficial for our patients.

Physical rehabilitation has a multimodal approach within itself for managing OA. Physical modalities, manual therapies and therapeutic exercises can all be used to achieve relief from OA. Goals of rehab for the DJD patient include: maintaining or improving muscle mass, building muscle support around the arthritic joint (and all joints), reducing pain and weight loss (via exercise, when indicated).

Physical modalities can include thermotherapy (the use of cold and warm packs). The benefits of cryotherapy are established (pain relieving, vasoconstriction, etc.) and warm compresses can be used to relieve pain, cause vasodilation and also help to warm up stiff, tight tissues to begin other exercises.

Therapy LASERs (Light Amplification by Stimulated Emission of Radiation) have become very popular in recent years. There are different wavelengths, amplitudes, treatment times and other factors that must be considered. This process has also been called photobiomodulation. It has been proposed to activate cytokines and other tissue factors, decrease pain and inflammation and increased wound healing. Always use goggles for both the humans and patient to avoid damage to the eyes. It cannot be used over pregnancy or cancer.

Manual therapies are skilled hand movement techniques intended to: improve tissue extensibility, increase range of motion (ROM), induce relaxation, mobilize or manipulate soft tissues and joints, modulate pain and reduce swelling and inflammation. These can include massage and joint mobilizations. The basic principles of joint mobilizations work from physiologic motions and accessory motions. Physiologic motions are normal active motion that is available at a joint. Examples: flexion, extension, abduction, internal rotation, etc. Accessory Motions are movements that cannot be performed actively. Examples: distraction, compression, glides, spins and rolls. There are 4 grades of mobilization, and the manipulation (used in chiropractic) is a 5th grade. Grades 1-4 are passive movements, with 1 and 2 not reaching initial resistance of the joint end feel. Grade 3 moves through the initial resistance to the end feel, but does not exceed it. Grade 4 mobilizations are compact with in the first and second resistance points. Grade 5 (manipulations) exceed the normal end feel of a joint.

Therapeutic exercises are the “meat and potatoes” of rehabilitation. These are designed to work a patient from a recumbent position back to normal (or as close as possible) activity following injury or insult. Exercises in this group can include cavaletti rails, working on balance boards, disks or other core strengthening equipment. Once walking on a flat non-slip surface is achieved, adding varying degrees of difficulty (up hills, through different traction, etc.) can be included. Other modalities in this group can include walking on treadmills or underwater treadmills.

Disease modifying agents for OA are next to be discussed. Polysulfated glycosaminoglycan is FDA approved, disease modifying osteoarthritis drugs; for dogs and horses; water-based, for intramuscular injection Dosage: 2 mg/lb body weight, IM, twice weekly for up to 4 weeks (maximum of 8 injections). MOA: specific is not known; *in vitro* studies show; they inhibit serine proteinases; PGE2 synthesis; metalloproteinases, hyaluronidases and others. Stimulate synthesis of protein, collagen, proteoglycans, and hyaluronic acid. There are studies showing it reaches feline cartilage via subcutaneous injection. This is extra label usage for this medication. Also, maintenance injections have been anecdotally reported for

both dogs and cats. Clinical studies on PSGAGs showed both good efficacy and safety. Treated dogs had statistically significant improvement in range of motion and total orthopedic score over placebo treated control dogs. 2.1% of dog had adverse reactions including: transient pain at the injection site (1 incident), transient diarrhea (1 incident each in 2 dogs) and abnormal bleeding (1 incident). These effects were mild, self-limiting; did not require interruption of therapy. Do not use in dogs showing hypersensitivity to PSGAG, or in dogs with known or suspected bleeding disorders. Use with caution in dogs with renal or hepatic impairment.

Adjunct analgesics for OA are numerous. They are used in addition to or replacement for NSAIDs. Research is scant on some of them. Amantadine – only drug studied to treat canine osteoarthritis. In dogs with osteoarthritic pain refractory to an NSAIDs, addition of amantadine improved physical activity. Amantadine might be a useful adjunct therapy for the clinical management of canine osteoarthritic pain. It can be dosed at 3-5mg/kg SID. Gabapentin – Calcium channel modulator – 5-10mg/kg SID-TID. Amitriptyline 0.5-1.0mg/kg SID-BID – cats and dogs. Local anesthetics – Lidocaine, bupivacaine, mepivacaine. Acetaminophen can be used in dogs but not cats. Opioids – morphine, meperidine, methadone, oxymorphone, hydromorphone, fentanyl, fentanyl patches, butorphanol, pentazocine, nalbuphine, buprenorphine, codeine and tramadol.

Tramadol's metabolism and elimination is rapid and variable among dogs. When administered orally or intravenously to the dog, metabolism of tramadol and all metabolites is rapid. There is much variability between dogs, possibly breeds. Pain control did not necessarily correlate with plasma levels of the active metabolite (O-desmethyltramadol). Tramadol effects on α -adrenergic or serotonin receptors may contribute to analgesic effects in the dog. Regardless of mechanism of action, studies suggest oral dose should be 5 mg/kg q 6 hours or 2.5 mg/kg q 4 hours. In the author's opinion this is a very challenging drug to utilize effectively in practice due to these variables.

Galliprant is a first-in-class non-cyclooxygenase (COX) inhibiting, non-steroidal anti-inflammatory drug (NSAID) in the piperant class. Piperants are a newly recognized drug class, established and defined by the World Health Organization in 2013 as prostaglandin receptor antagonists (PRA). Unique mechanism of action by antagonizing the prostaglandin E2 (PGE2) EP4 receptor. PGE2 its physiologic effects through binding of four different receptors, EP1, EP2, EP3 and EP4. The EP4 receptor has been identified as the primary receptor responsible for mediating pain and inflammation associated with osteoarthritis. Galliprant selectively blocks the EP4 receptor, thus blocking PGE2 elicited pain.

Intraarticular medications can provide targeted therapy for OA. These can be easy to learn with practice. In the author's practice it is done under sedation, and after radiographs to verify the OA process. This also allows for elimination of infection or neoplasia as mimics of OA pain. Diagnostic arthrocentesis could be done if indicated. The same approaches to joints for diagnostic purposes can be utilized for treatment. Removal of some of the joint fluid allows space for the infusion of medication. These need to be done with sterile technique for obvious reasons.

Options for intraarticular therapies include corticosteroids, hyaluronic acid and regenerative medicine (platelet rich plasma or stem cell therapy). Corticosteroids can have deleterious effects to cartilage, but these are often used in palliative care, or if other options are not financially available. Methylprednisolone acetate has historically been used in these cases for both dogs and horses. A 20mg dose is used for most medium to large breed dogs. I prefer to use triamcinolone which has been shown to have less damage to equine cartilage than methylprednisolone. Additionally, if any systemic side effects happen from corticosteroids, triamcinolone's effects will be over faster than methylpred. This is especially important in patients with severe mobility issues (less chance of urine scald, accidents in the house) and potentially other metabolic diseases (renal, hepatic impairment).

Hyaluronic acid increases viscosity of joint fluid, is anti-inflammatory, analgesic and they induce production of synovial fluid. Many different options are available, and molecular weight is the primary variable among them. Cost can be variable as well, and some products are not currently available. In my practice Legend (10mg/ml) is used. Usually 20mg for large breed dogs, 10mg per joint for small breeds. It

can be combined with a steroid if needed for both a short term and long term effect. Repeating injections in a few weeks to months may be needed in some cases.

Regenerative medicine is an emerging field for both animals and humans. There are many variables with products and product preparation. In clinic and outside laboratory preparations are available. Each has their own pros/cons to be considered by the clinician. Currently either requires patient donation or baseline cells. An over-the-counter synthetic product is not yet available.

Platelet Rich Plasma has positive effects on angiogenesis and extracellular matrix remodeling, provides fibrin for matrix, a potent source of growth factors, cell proliferation and differentiation and stem cell recruitment and chemotaxis.

Stem cells can be of bone marrow or adipose tissue origin. Research is not clear as to which is superior at this time. Stem cells are reported to contribute to generating new tissue, chemotactic for progenitor cells, supply growth factors, make extracellular matrix, angiogenesis, anti-apoptosis, anti-inflammatory and are anti-fibrotic.

ESWT stands for extracorporeal shock wave therapy. Short duration acoustic waves at low frequency and high pressure. 100x atmospheric pressure is reached in microseconds. Mechanisms lacking – but reported is reduced inflammation, improved vascularity, neovascularization, increase bone formation, realignment of tendon fibers and enhanced wound healing. Improved weight bearing and comfortable ROM similar to NSAIDs. Heavy sedation or anesthesia usually required, and repeating treatment q 2-3 weeks for 3-4 treatments, and no concurrent NSAIDs during treatment.

PEMF is pulsed electromagnetic field therapy. This delivers a micro current that targets the body's own natural anti-inflammatory process. The electrical signal is deposited to the tissue that mimics physiological stimulus that occurs in healthy tissue, thus stimulating tissue repair. It enhances nitric oxide production to help speed healing of tissues. It can be used by the owner at home in between rehab sessions, or as an alternative if other modalities are not available.

TCVM or Traditional Chinese Veterinary Medicine has been available for thousands of years. While herbal and food therapy are options, the most research is available for acupuncture. Acupuncture, the placement of small sterile needles at points along meridians has been shown to have a pain relieving effect. Dry needling, aqua puncture (the placement of small amount of a fluid), gold bead therapy and electro acupuncture are all options for stimulating the acupoints. Acupuncture has been shown to release the body's natural endorphins and this is the method of analgesia.

Kinesiology taping is an emerging modality in people and animals. This tape lifts on the fascia and can improve blood flow, lymphatic return and pain relief. The proposed mechanism of analgesia is working along the gate theory, stimulation of nerve fibers by non-painful stimulation allows the body to "close the gate" to those nerve fibers transmitting pain from noxious stimuli.

A trial and error approach is sometimes needed to find the right combination of methods to control the pain of osteoarthritis. Having comfort with numerous, but not necessarily all, of these techniques can help the clinician and the patient.

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