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### Medications for Degenerative Arthritis in Dogs and Cats

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## Pharmaceuticals and Nutriceuticals for Arthritis

There are numerous treatments and products available to manage joint pain and each one has proponents and detractors. One thing that is agreed on by experts is that arthritis management should be multimodal,

#### **Additional Resources**

- Normal Joints Look Like this in Dogs and Cats
- <u>Physical Therapy for Arthritic Patients</u>

which means best results come when many different approaches are used concurrently. (Not just a variety of medications and supplements but also other techniques such as weight loss and physical therapy.)

The goal of this page is to review the most common medications and supplements so you can more wisely choose how to cover multiple areas of the inflammatory cascade and achieve good pain-free mobility in your pet. But what should you choose? What products should you ask your veterinarian about when your pet's regimen is assembled? You want safety for your pet but also good effect and you certainly do not want to use incompatible products accidentally. We will divide options up into groups.

Degenerative joint disease is the number one cause of chronic pain in dogs and cats. The condition itself is the result of longterm stresses on a joint either as a result of old injury or of natural development of a poorly conformed joint in that individual. While surgery may be able to help in some situations, most of the time the degeneration of the joint cannot be reversed and treatment focuses on preventing progression of damage. Numerous products are available on the market; some are best combined with others and some cannot be combined. What we do know is that arthritis pain is best addressed by what is called



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a multi-modal approach, meaning that several approaches combined yield better results than any single therapy. The section presented here focuses on medications. Medications for arthritis pain are divided into two groups: fast-acting (non-steroidal anti-inflammatory drugs and cortisone-type drugs) and slow-acting drugs.

Expect your pet to need a combination of products. Make notes and ask your veterinarian about products in which you are interested. Your veterinarian will have some preferred products and will help guide you. Avoid a do-it-yourself approach as

you may accidentally create a dangerous medication interaction. Your pet may have a condition that precludes the use of certain products. Always check with your veterinarian before using any medications on your pet.

#### Cartilage and Muscle Support Supplements/Chondroprotectants

The body has natural mechanisms to rebuild damaged cartilage and improve muscle mass on its own but these mechanisms require raw materials. A common method of addressing arthritis, especially when it is in earlier stages, is to provide these materials orally as nutritional supplements. There are numerous supplement brands available both on the human and the pet retail markets, no prescription required. There are two important caveats:

- First, these products require weeks to build up in the body to a point where there is a detectable result. They are considered slow-acting, plus their effects are generally mild.
- Supplements are not regulated by the FDA in the same way that drugs are. Supplements are required only to be shown safe but not effective and quality control is not required. To be sure you are buying a legitimate product, look for the National Animal Supplement Council seal or ask for your veterinarian's recommendation.

#### <u>Glucosamine and Chondroitin Sulfate</u> (Dog Or Cat)

These products, often referred to as chondroprotectants, are cartilage components harvested chiefly from sea mollusks (i.e., cartilage is made up of chondroitin sulfate and glucosamine metabolites, among other things). By taking these components orally, the patient is able to have plenty of the necessary building blocks needed to repair damaged cartilage. It is also felt that these products may have some anti-inflammatory properties separate from their structural uses. A newer derivative of glucosamine (called N-Butyryl Glucosamine, GlcNBu, or Gluco Blu) has become available as well. This chemical change in the glucosamine allows for a more rapid onset of 2 weeks instead of 4 to 6 weeks.

#### Creatine (Dog or Cat)

Creatine is a substance contained mostly in muscle and is used in the body's natural recycling of ATP (stored energy). Taking supplements in modest doses will improve endurance and muscle strength.

#### MSM (Dog or Cat)

MSM stands for methyl sulfonyl methane and represents another nutriceutical antiinflammatory agent. MSM is in most plant and animal tissues and is a natural source of sulfur; however, for commercial sale, MSM is derived from DMSO (dimethylsulfoxide), a solvent that comes in both medical grade and industrial grade. One might wonder why a sulfur source would be helpful in treating arthritis. The glycosaminoglycans that enable cartilage to soak up water and thus act as a cushion for articulating bones, are all sulfates. The idea with this product is to provide nutritional building blocks for cartilage repair. Beyond this, MSM seems to have anti-inflammatory properties and may act as an anti-oxidant.

These materials are almost always included in anti-inflammatory supplement products (listed later) and may have anti-inflammatory features beyond simply being cartilage or muscle building blocks.

Fast-Acting Prescription Anti-Inflammatories (Non-Steroidal Anti-Inflammatories and the New Piprant Class)

Use only one medication from this group as they are not compatible with each other nor with corticosteroids.

As arthritis discomfort progresses, a product that acts in hours instead of weeks becomes important. This is where non-steroidal anti-inflammatory drugs (NSAIDS) come into play. These medications work by suppressing the effects of prostaglandins. Prostaglandins are important mediators of inflammation and pain in joints and we definitely want less of them. That said, there are "good" prostaglandins that one needs to maintain kidney and stomach circulation as well and we definitely want to keep those. So we want to hamper bad prostaglandins and leave the good ones alone.

#### Cox Preferential NSAIDs

Prostaglandins are created when certain fatty acids are liberated from our cell membranes and converted into prostaglandins by an enzyme called cyclooxygenase. There are two main forms of cyclooxygenase: COX-1 (which makes good prostaglandins) and COX-2 (which makes the bad ones). A huge development in pain management for pets as well as humans was the development of NSAIDs that preferentially suppress COX-2 over COX-1. Less suppression of COX-1 opened a new door in safety. Medications of this category are:

- <u>Carprofen</u> (dogs)
- <u>Meloxicam</u> (dogs, some controversy for cats)
- <u>Etodolac</u> (dogs)

#### Cox-Selective NSAIDs (The Coxib Class)

Soon there was a next generation in NSAIDS: medications that didn't just prefer COX-2 over COX-1; they only suppressed COX-2. Whether or not this advancement actually translates into even greater safety is of some controversy but theoretically, at least, it represents an advancement in maintaining good prostaglandins. There are numerous members of the coxib class available for pets:

- Deracoxib (dogs)
- Robenacoxib (dogs and cats)
- Firocoxib (dogs)

#### The Piprant Class

In 2017, a new pharmaceutical approach entered the scene: the piprant class. These antiinflammatories do not suppress either COX; instead they interfere with the EP4 receptor, a prostaglandin receptor involved in pain generation. This new way to address inflammation solves the issue of preserving COX-1 and solving some of the side effects issues that have been problematic for more traditional NSAIDs. At this time there is only one piprant on the market: <u>Grapiprant</u>.

The beauty of the prescription medications is that they work quickly (minutes to hours though since pets cannot talk, it may take a week or so before an obvious improvement in mobility becomes evident. They have reliable efficacy plus they also carry with them the background of thorough scientific testing for both safety and efficacy that go with FDA approval (at least for dogs).

#### A Word or Two on Aspirin and Human NSAIDs

Human beings are much more resistant to the problems caused by suppressing good prostaglandins. Some of us are sensitive and need special <u>NSAIDs</u> like Celebrex® but most of us can just grab a bottle of ibuprofen out of the medicine cabinet and take a couple of pills when we have inflammatory pain. The problem with the human over-the-counter NSAIDS is

that they suppress all prostaglandins both good and bad and this is not really optimal/safe pain treatment for dogs and is out of the question for cats. When it comes to NSAIDs in particular, it is crucial to consult your veterinarian.

#### The Feline Situation



Photo by Dr. Teri Ann Oursler

Cats are uniquely sensitive to these medications as the feline liver processes them extremely slowly. The products listed as approved for cats above are approved for extremely brief use (single use or a few days only) in the U.S. In Europe, these same medications are prescribed for long-term use. Same medication, same species (cat) but different legal medical standards to follow. In the U.S. there is some leeway given to prescribing off label medications where there is scientific publication supporting such use. Your veterinarian will use their judgment in making feline recommendations. For now, there is no approved NSAID for long-term feline use in the U.S.

### Straight Pain Relief Medications (Usually Adjuncts to the NSAIDs)

The anti-inflammatory pain relievers not only relieve pain but they do so by actually altering the disease process. Straight pain relievers do nothing for the disease process but they do help with the pain. They can be combined with each other and/or with any of the other medications/supplements listed here, assuming the patient does not have a condition precluding their specific use. These medications have some potential for drowsiness that will make a weak animal even weaker, so it is important to find the dose that relieves pain and improves mobility without making the pet sleepy (which would discourage mobility).

#### <u>Gabapentin</u> (Dog or Cat)

This medication is particularly beneficial for neurologic/spinal pain as it alters how pain is transmitted in the spinal cord. It also has anti-anxiety effects. It definitely has a drowsiness side effects and is used as a tranquilizer in higher doses especially in cats. It comes in a capsule which means it is hard to dose in small patients as the capsules cannot be cut accurately at home.

#### <u>Tramadol</u> (Cat)

In cats and people, this medication is split in the body into two active metabolites: a narcotic pain reliever and an anxiety relief medication. It should have good pain-relieving properties but can create sedation or mental alteration. It may be difficult to reduce the dose with accuracy as feline doses are typically quarter tablets and it is hard to cut pills smaller than this. Furthermore, tramadol is famous for tasting terrible, which creates additional difficulty in giving it to cats.

In dogs, the narcotic pain reliever is not created when tramadol is split and there is some controversy regarding whether the canine split products produce acceptable pain relief. At this time, tramadol is not considered a helpful choice for dogs.

#### Amantadine (Dog or Cat)

This medication helps reduce what is called wind-up pain in which chronic pain has sensitized nerves to a point where experiences that should not normally be painful become painful. This sensitization phenomenon happens after pain has gone unrelieved for a long time (exactly how long is of some controversy). Availability of a reasonably priced oral liquid has been helpful for administration to small patients, but there is some potential for sedation especially when combined with other medications on this list.

#### Supplements with Anti-Inflammatory Properties

There are a number of natural extracts and herbal products with anti-inflammatory properties. Some are anti-oxidants (which strike at the actual progression of arthritis) while others interfere with the inflammatory cascade to limit pain as well as the inflammation. Most are modest in their abilities. Some are fast acting while others must build up in the body for several weeks. Many have multiple therapeutic actions. As with all supplements, the FDA does not require proof of efficacy or quality control, only proof of safety so the reputation/certification of the manufacturer is important.

#### Green-Lipped Mussel Extract (Perna Canaliculus) (Dog or Cat)

As mentioned, inflammation is mediated by prostaglandins (produced by cyclooxygenase) and leukotrienes (produced by 5-lipoxygenase). Green-lipped mussel extract is inhibitory to 5-lipoxygenase. It's effect produces mild pain relief only and take several weeks to exert visible effects.

#### Omega Three Fatty Acids (Dog or Cat)

Certain dietary fats, typically from cold-water fish oils, have been found to have antiinflammatory properties. While this finding has primarily been used to treat itchy skin, many arthritic dogs and cats have also benefited from it. While there are no toxic issues to be concerned with, these products require at least one month to build up to adequate amounts. Effects are not usually dramatic but can be helpful.

Caution about flax seed oil: It should be noted that the flax seed oil is readily converted to omega three fatty acids in the human body. This conversion is not so easy in the canine or feline body (only about 10 percent of the oil is converted). It is somewhat wasteful to add flax seed oil to pet food; fish oils are needed. Numerous brands are available and the chances are your veterinarian stocks one. The appropriate dose is still somewhat controversial but the ratio of EPA (eicosapentanoic acid) to DHA (docosahexanoic acid) should be 3:2.

Caution about cod liver oil: Cod liver oil is especially rife with vitamin A. This sounds like a good thing but Vitamin A toxicity is a real problem for pets receiving cod liver oil supplements. It is probably best to use another type of fish oil.

#### Dried Milk Proteins (Dog or Cat)

To create an anti-inflammatory product, dairy cows are hyperimmunized so as to produce milk rich in assorted anti-inflammatory factors. These are refined into medical treats for dogs and cats. Unlike chondroprotectants, the onset of action is rapid (starts working in 4-7 days with maximum effect in 10-14 days) as they are anti-inflammatory biochemicals, and refilling a depleted store of cartilage building blocks.

#### Polyphenols: Phycocyanin, Grape Seed Oil, Green Tea Extracts, Turmeric (Dog or Cat)

Phycocyanin is one of the active ingredient in Phycox®. It is derived from Spirulina algae and appears to have antioxidant and anti-inflammatory properties. As described above, the NSAIDs act by suppressing the activity of different cyclooxyrgenase (COX) enzymes so that they cannot convert cell membrane fats into inflammatory prostaglandins. Similarly, phycocyanin interferes with the production of prostaglandins by suppressing the genes involved in making prostaglandins. Basically, it creates another way to achieve an anti-prostaglandin effect; however, these are potent anti-oxidants as well.

#### Avocado/Soybean Unsaponifiables, Often Simply Called ASU (Dog or Cat)

These are anti-inflammatory biochemicals extracted from avocados and/or soybeans leaving the fats behind. They promote cartilage repair and inhibit the inflammation-associated cartilage degradation that occurs in arthritis.

#### Cannabinoids (Dog or Cat)

These products are derived from the hemp plant, which contains multiple biochemicals with beneficial properties: they are anti-oxidants as well as immunomodulators (which makes them anti-inflammatory), plus they also decrease the perception of pain. There are obviously numerous legal and regulatory issues surrounding what products can be recommended for animals. At this time, only whole hemp-based products (with low enough THC levels to be legal) are sanctioned for animal use. Lack of research has been problematic as well. Cannabidiol, for example, is a potent liver enzyme inducer, which makes it capable of reducing the activity of many other medications. Since arthritis management commonly involves many products, it is important to be cautious where drug interactions are possible.

#### Miscellaneous Anti-Oxidants and Free Radical Scavengers

Free radicals are harmful biochemicals that can attack us from external sources (such as pollution, sunlight, etc.) or we make them ourselves as by-products of oxygen use. These harmful little molecules are highly reactive and attack our structural proteins as well as cause production of assorted inflammatory proteins. One prominent theory of aging centers on free radicals with the idea that the damage free radicals cause to our brains, skin, joints etc. is the foundation of age-related debilitation. Normally, our bodies use natural anti-oxidants to inactivate free radicals; by supplementing with additional anti-oxidants, age-related change can be retarded.

Anti-oxidants that are readily available include Vitamin C, Vitamin E, SAMe, Superoxide Dismutase (S.O.D.) and others.

#### **Injections and Specialized Products**

#### Adequan<sup>®</sup> Injections

Adequan® is an injectable polysulfated glycosaminoglycan (mostly chondroitin sulfate), which serves not only as a cartilage component used in healing but as an actual antiinflammatory agent. Adequan has numerous beneficial effects for the arthritis patient including the inhibition of harmful enzymes involving joint cartilage destruction, stimulation of cartilage repair, and increasing joint lubrication.

- Adequan is given as an injection and so is able to reach all joints, but it seems to have a special affinity for damaged joints.
- Adequan is best given as a series of injections, twice a week or so until a response is seen but not exceeding eight injections. After an effect is seen, Adequan injections are given on an as needed basis.

#### Platelet Rich Plasma

The concept here is to harvest blood from the patient and separate out the red and white blood cells leaving behind the plasma and platelets. The platelets would be active and in a concentration much higher than what is circulating in the regular bloodstream. The plasma is at this point said to be "platelet rich" and is injected into the patient's diseased joints.

Platelets are blood cells involved in blood clotting but it turns out they are also packed with growth and healing factors that are useful in inflammatory joint disease. This is a new therapy and how it compares to less exotic treatments is still in question but it does function as an

alternative to drugs. Possible pitfalls include the fact that virtually all the necessary blood processing equipment is made for human blood and the canine plasma quality that results is not consistent with what the same equipment produces for human samples. Also, the plasma must be injected directly into the joint so care must be taken not to introduce infection.

#### Stem Cell Therapy

This is an other regenerative therapy that yields a product that is made from the patient's own tissue (usually fat) and processed into a product that is injected into the patient's own joint. The necessary fat harvesting requires general anesthesia and is a surgical procedure. The fat is either processed in the animal hospital or sent to a laboratory for refinement. As with platelet-rich plasma therapy, stem cell use for arthritis is a new therapy and while it has been shown to have good effect, it has not been compared to less invasive/expensive modes of therapy.

#### Miscellaneous Injections

Injecting corticosteroids into joints is not a new practice, and neither is injecting hyaluronic acid (a natural portion of the cartilage structure). There is controversy regarding the effectiveness and risk of infection in these procedures.

#### In Conclusion

The arthritic pet has a large menu of medications to select from and while proper medication is an important part of therapy, weight control and proper exercise should not be forgotten. Proper exercise is excellent physical therapy for the arthritic pet, as it is crucial to maintain as much muscle mass as possible to support the abnormal joint. Remember, treatment for joint disease is likely to involve a combination of medications in addition to physical activities and to check with your veterinarian before attempting to assemble a regimen on your own.

#### **Related resources**

- Normal Joints Look Like this in Dogs and Cats March 17, 2021 🖻
- Physical Therapy for Arthritic Patients October 31, 2009 🖻

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