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DIAGNOSIS AND CONSERVATIVE MANAGEMENT OF JOINT DISEASE.

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Joint disease is a very common reason for presentation in a small animal practice, and approximately 20% of the pet population has significant arthritis. While the canine patient is much more common, older cats have a high incidence of radiographic changes suggesting joint disease, and more in-depth evaluation of behavior changes might show that this is more significant than we realize. The diagnosis and treatment of joint disease is, therefore, a very important part of veterinary practice.

The primary cause of the joint disease may be difficult to identify as, after a period of degeneration, the process become self-perpetuating. It is also possible that the initial process – say a mild injury to a collateral ligament – recovers fully, but the associated cartilage damage results in clinical disease of the joint years later. This highlights the fact that, although direct injury to cartilage can be the cause of damage, in most cases, the joint degenerates due to continuing insult from the inflammatory process. Molecules of any type that are not supposed to be in the joint space are removed by the synoviocytes lining the joint space. This includes proteoglycans and Type II collagen released from damaged cartilage. If there is a continuous load of this debris, these cells are stimulated, release pro-inflammatory cytokines, and recruit a wider array of inflammatory cells into the synovial membrane, and, thus, into the joint space. Release of enzymes from these activated cells causes more breakdown of exposed cartilage collagen and proteoglycans. The process feeds upon itself.

To simplify matters, I categorize joint diseases into mechanical or inflammatory. The common mechanical causes are hip and elbow dysplasia, shoulder instability, patella luxation, cranial cruciate ligament disease, osteochondroses, ligament injuries, or intra-articular fracture. The inflammatory arthropathies are classified as infectious or immune mediated. In the infectious category, septic joints with bacteria are the most obvious. Joint involvement with tick born organisms such as *Ehrlichia* or *Rickettsia* are also in this category. The immune mediated category is complex, and specific categorization often difficult. Multiple joints are frequently involved, including those of the axial skeleton. Rheumatoid-like conditions are seen, though the specificity of canine rheumatoid factor does not appear to be high. Systemic Lupus Erythematosus (SLE) can also have joint involvement. However, in most cases, a specific cause for the inflammation can not be identified. It may also be that the primary cause is no longer present, and the immune response is to auto-antigens, like Type II collagen.

As there are many potential causes of joint disease, it is important to have a systematic approach to refining the differential and attempting to narrow the diagnosis. An accurate history is needed to assess the chronicity of symptoms. Because many conditions might have slow progression, clients often attribute reduced activity to “old age”. Questions that target specific activities like “How well does he jump into the car?” are more likely to reveal an issue than more general questions. Consideration of the signalment will direct the type of questions that are appropriate for the age and breed of the patient.

Physical examination requires an assessment of multiple features of the joint, and the anagram “**C R E P I**” can help.

- “**C**” is for crepitus – this can either be “soft”, indicating capsule and ligaments, or “hard”, suggesting eburnated cartilage and bone-on-bone contact.
- “**R**” is for range of motion – knowing the normal range is necessary for detecting early changes, and relying on the opposite side to be normal is not appropriate, because many conditions will be present bilaterally. Measuring and recording these angles can be helpful in assessing disease and treatment progression.
- “**E**” is for effusion, but also covers joint thickening due to periarticular fibrosis and osteophytes. Effusion can be difficult to detect in the more chronic joint.
- “**P**” is for pain – is the particular joint painful? This is very important, as not all diseased joints will be painful. In a patient with multiple joints involved, identifying the painful one will greatly improve your chances of successful treatment. The classic example is the dog that has reduced hip extension and marked degeneration on radiographs, but is limping due to rupture of the cranial cruciate ligament.
- “**I**” is for instability – the detection of abnormal motion due to developmental conditions, injury or severe degeneration is important for treatment planning.

Radiographs can provide information regarding the cause of the joint disease and its chronicity. *They do not tell you if the joint hurts !* They must be interpreted in light of your physical examination. Accurate positioning and at least two views are important for assessment of the articular surfaces. High quality images will enable identification of early bone changes. Films with good soft tissue detail may demonstrate effusion. Stressed views can be used to characterize suspected instability. In immune mediated polyarthropathies, they can help characterize the process as erosive or non-erosive.

Synovial fluid analysis can help determine the primary cause and quantify the intensity of the inflammatory process. The colour, volume and viscosity are assessed at the time of aspiration. Cell counts quantify the intensity of the inflammation. Normal joints can have up to 5000 cells/ml Large numbers of neutrophils ($> 10^5/\text{ml}$) may suggest an infectious process, particularly if there is cell degeneration. However, a very intense immunologic process can also attract neutrophils. Moderately high cell numbers and a high proportion of mononuclear cells suggests an immunologic process. Cell counts in chronic degenerative joint disease may be normal or slightly raised. Synovial lining cells may be seen occasionally.

Culture of synovial fluid is not always successful, especially when bacterial numbers are low. The viscous nature of the fluid and the effectiveness of the cellular response reduce the effectiveness of standard techniques. To improve the sensitivity, synovial fluid can be added to blood culture medium to encourage initial growth. Emulsification of synovial membrane tissue into media may expose organisms in otherwise “clean” joints.

Because joint disease may occur in conjunction with other systemic diseases, a thorough physical examination of all other systems, a CBC and chemistry panel may also provide diagnostic information. A “tick panel” is also routine for arthropathy cases at North Carolina. This includes *Ehrlichia*, *Rickettsia*, Lyme, *Bartonella* and *Babesia*. Canine Rheumatoid Factor can be assessed but levels can be raised in non-erosive arthropathies, so it is not specific for true rheumatoid arthritis. A positive ANA test and/or LE cells in a non-erosive polyarthropathy with anaemia, skin and/or renal disease suggests SLE.

Treatment of joint disease requires a multimodal strategy, and commitment from the veterinarian and the client. If the primary cause can be identified, and is treatable, it must be addressed. Infectious organisms must be targeted with appropriate antibiotics. Local treatment with joint lavage, with or without antiseptics or antibiotics, can help reduce bacterial numbers, dilute the damaging enzymes, and deliver high concentrations into the articular space. Stability should be re-established and cartilage flaps, damaged tissue or bone chips removed.

Immune mediate polyarthropathies often require aggressive therapy initially to suppress the immunologic response. Corticosteroids at 2 – 4 mg/kg daily for 3 – 4 weeks are used initially, and then the levels are tapered over the next 3 to 4 months. Success of therapy can be monitored by serial synovial fluid cell counts. Some patients will remain asymptomatic even when medications are stopped completely – others will require maintenance dosing. In refractory cases, other immune system modifiers, like azathioprine and cyclophosphamide, may be added.

When degeneration is already present, management techniques focus on maintaining patient mobility and quality of life. Weight loss, activity modification and anti-inflammatory and/or analgesic treatments are planned to suit the specific situation.

Achieving and maintaining an ideal body condition is one of the most important aspects of management of the arthritic patient, and one of the hardest for the client to really commit to. Continued emphasis of its importance, and positive reinforcement of progress, is essential. Regular free weight checks with progress displayed graphically in a very visible location in the home helps focus clients on the task. Prescription diets specifically for weight loss can be very helpful for the hungry dog and the guilty client.

Activity modification may be difficult to apply, as it may conflict with the desire to maintain quality of life – restriction from activities like hunting, or frisbie playing, or vigorous wrestling may not be something a client is prepared to do because the patient loves the activity too much. If possible, the impact level of activities should be reduced as much as possible. However, it is of equal importance that moderate exercise still be present. It is essential for maintaining joint health, muscle strength and tone, and is an important arm of weight management. The right balance must be found. Rehabilitation therapies can also be used to help or improve range of motion and to build muscle strength. Therapy can be targeted to a specific joint, or to general condition. Joint motion can be improved using massage and manipulation, or by specific exercises that require more joint movement than normal (e.g. cavaletti

course). Hydrotherapy, particularly with an underwater treadmill, can build condition and improve flexibility in a low impact environment.

Anti-inflammatory therapies are many – some might come under the “chondroprotective” or “nutraceutical” heading, others suppress the local inflammatory pathways (either the cyclooxygenase or lipoxygenase systems), while others modify pain perception, either locally or centrally.

Glucosamine and chondroitin sulphate products are popular in the US. Studies vary in the strength of their support for these products. There is debate regarding their real mode of action. It is likely that there are some situations in which they will help the patient, but we don't know enough about them, or may not be able to be specific enough in our diagnosis to separate out those with appropriate disease, to really select the right time to use them. The broader approach is to perform an n-of-1 trial on each patient, ideally with no other management changes and, after a 3 to 4 month period, critically evaluate the response. If the response is equivocal, discontinuing and assess for deterioration would confirm the lack of response. Pentosan polysulfate is used extensively outside of the US in a similar manner.

Modification of dietary levels of various fatty acids is also used to modulate the inflammatory response. Commercial diets are now available with various ratios of the different components, and further work is needed to see if there is an ideal combination. Oral supplements can also be used to add these fatty acids to the diet.

A wide range of non-steroidal anti-inflammatory drugs (NSAIDs) are now available for dogs. Some over-the-counter human products can be used, but they tend to be associated with higher rates of gastro-intestinal injury. Carprofen, etodolac, deracoxib, meloxicam and firocoxib are the primary veterinary drugs that are COX-1 sparing, and thus cause less gastric irritation. Tepoxalin has both COX and lipoxygenase pathway affects, which may be of benefit in some patients. Price and ease of administration often guide the initial choice, though, if a patient does not respond to the first choice, I try another just to see if they are just not specifically receptive to that particular NSAID. These drugs can be used either as-needed, or on a continuous basis.

Tramadol is added to an NSAID regimen when further analgesia is required. It is a weak opioid and also acts by enhancement of adrenergic and serotonergic descending pathways. It can be sedating in higher doses. Amantadine is an NMDA inhibitor that has shown benefit in some patients for central modification of pain. Gabapentin has been used in neuropathic pain in humans, and has had some success in some patients with chronic pain from arthritis.

Corticosteroids are used infrequently in non-immune-mediated joint disease in small animals, but should likely be considered more frequently. Intra-articular long acting compounds are very effective in humans and horses. While there are potential negative effects on general cartilage metabolism, and a risk of infection, the benefits of suppressing the inflammatory damage and improving patient comfort potentially outweigh the negative effects.