**Osteoarthritis is the #1 cause of chronic pain in dogs**

Chronic pain; Decreased activity; An overall negative impact on the patient; Interferes with human-animal bond; Decreased food intake; Euthanasia for dogs that become non-responsive to treatment.

**Cartilage damage initiates osteoarthritis**

Chondrocytes are damaged and release matrix metalloproteinases (MMPs) and Nitric oxide and inflammatory cytokines. Nitric oxide causes further release of MMPs and release of inflammatory mediators. MMPs cause further damage to the cartilage.

**Other changes in OA**

Thickening of Joint Capsule; Remodeling of subchondral bone → sclerosis; Osteophyte formation; Joint is less able to bear stress and forces.

**Joint inflammation**

Mechanoreceptors – stretch and pressure, which allows the brain to know where the limb is in space; Neuroreceptors – noxious stimuli. Cartilage is anueral; cartilage damage alone is not painful; Neurogenic Inflammation is Also a Source of Pain in Osteoarthritis

**A comprehensive approach to treatment is required to break the cycle**

NSAIDs are a cornerstone for OA management, which also includes weight control and exercise to both treat the pain and inflammation of OA as well as the dysfunction of the joint.

**Diagnosis and treatment of osteoarthritis can be challenging**

Pain is a hallmark of osteoarthritis; signs may be subtle; often go unnoticed; Dog owners often do not mention as a problem; Dogs mask pain; pain not evident during physical exam; Often requires a thorough orthopedic examination; When a dog is diagnosed with OA, they are often experiencing chronic pain.

**Do the risks outweigh the benefits?**

The answer to that question is patient dependent and depends upon a number of factors.

“Lowest Effective Dose” FDA=Lowest effective dose for the shortest duration consistent with individual response. For idiosyncratic reactions, reducing the dose does not decrease the risk.

**Minimize the risk. Dogs at greatest risk**

Dehydrated or on concomitant diuretic therapy; Dogs with renal failure, cardiovascular and or hepatic dysfunction. Pet Owner Communication, Always provide a Client Information Sheet with prescription

**NSAIDs are safe & effective for vast majority of canines**

Safety and Efficacy of Using NSAIDs Long-term in Dogs with Osteoarthritis: the current evidence suggests that there is a clinical benefit of longer-term NSAID use for dogs with chronic osteoarthritis and that is associated with a low risk of serious adverse events” — Innes et al. “Review of the safety and efficacy of long-term NSAIDs use in the treatment of canine osteoarthritis.” Vet Rec 2010

**Rehabilitation (physical therapy)**

The goal of rehab is to: maintain muscle mass, build muscle support around joint, reduce pain, weight loss

**Adequan**

Polysulfated Glycosaminoglycan: FDA approved, disease modifying osteoarthritis drugs; for dogs and horses; water-based, for intramuscular Injection. MOA in vitro studies show: Inhibit serine proteinases; PGE2 synthesis; metalloproteases, hyaluronidases and others. Stimulate synthesis of protein, collagen, proteoglycans, and hyaluronic acid

Summary of ASU, glucosamine, and chondroitin sulfate’s effects: Combination inhibits expression & production of many mediators. Effects extend across species (including canine, feline, equine, and human cells) and to multiple cells in the joint – cells which may all contribute to cartilage breakdown by secreting the mediators responsible

**Amantadine**

Studied to treat canine osteoarthritis: In dogs with osteoarthritic pain refractory to an NSAIDs, addition of amantadine improved physical activity. Might be a useful adjunct therapy for the clinical management of canine osteoarthritis pain.

NMDA receptor antagonists. Amantadine is excreted, primarily unchanged, in the urine. Consider reduced doses, if used at all, for patients with impaired renal function. Dogs & Cats: 3 to 5 mg/kg SID PO Typically used for 21 days to “re-set” pain pathways
Gabapentin
An oral prescription medication capable of helping reduce neuropathic and other chronic pain states. Although its mechanism is unknown, it has been shown to affect central sensitization. Excreted unchanged in the urine reduce dose or discontinue in patients with renal dysfunction. Dogs: 10 +++ mg/kg BID to QID PO; Cats: 5.0 +++ mg/kg BID PO

Amitriptyline
Tricyclic antidepressants (TCA’s) have been used in humans and animals as adjuncts to other analgesics (especially opioids) for chronic pain. They act to inhibit serotonin and norepinephrine reuptake, though they may have other analgesic effects as well (including possible actions at opioid receptors and on nerve transmission). 1 – 3 mg/kg BID: typically start at 1mg/kg and increase after 1 week if needed.

Acetaminophen
10 – 15 mg/kg q 8 – 12 hours. CAUTION in hepatic or renal disease. Break through pain. Can use with corticosteroids or NSAIDs. Do not use in cats. Helpful to bridge from one NSAID to another

Tramadol
Dogs make negligible amounts of the o-desmethyltramadol (M1) metabolite, which is the metabolite known to have mu-agonist activity in humans and rodents; what little is produced has a very short T ½: 2.2 Hr. No clinical studies on oral tramadol, nor clinical studies on use in osteoarthritis

CereKin from kindred biosciences
Antagonist being developed to directly inhibit IL-1β synthesis and release in vitro and down modulates IL-1β induced activities.

Grapiprant – aratana
A new piprant chemical class drug. Instead of inhibiting the cyclooxygenase enzymes, grapiprant has a specific target: the EP4 receptor. Prostaglandin E2 normally binds this receptor, and this binding results in pain and inflammation. When grapiprant blocks the EP4 receptor, Prostaglandin E2 cannot bind, and this results in the blocking of the pain response.

Monoclonal antibody – NV-01 NexVet
A monoclonal antibody (mAb) that targets nerve growth factor, a potent mediator of pain in the body. Is classed as a ‘Biological’ agent; completely caninised, or “100% dog”, meaning the canine immune system does not regard it as foreign. NV-02: 100% feline monoclonal antibody to the same target.

ACVIM abstract
Efficacy of Canine Anti-nerve Growth Factor Antibody for the Alleviation of Degenerative Joint Disease-Associate Pain in Dogs. BDX Lascelles, et al

Capsaicin
Centrexion: synthetic version of capsaicin, which works on a site-specific basis; reduce osteoarthritic pain on average by approximately 70%; provide pain relief for up to six months for a single injection.

Osteoclasts
Bisphosphonate used as a preventative before chemically induced arthritis, completely prevented onset of the arthritic changes. In fact, cartilage was not different from controls. Needs to be used very early in disease to have positive effects. Other agents include calcitonin (need to use early) and strontium ranelate which shows more clinical promise in human studies
Targeting cartilage defects - severe OA

**Shock wave therapy:** effect of shock wave therapy on elbow OA in dogs
Pulsed magnetic field therapy: Enhanced cartilage repair; Increased collagen synthesis of tendon fibroblasts; Cell proliferation;
Synthesis of glycosaminoglycans by growth plate chondrocytes; Decrease production of inflammatory cytokines

**Superficial heat (moist heat)**
The tissue is usually heated to 40 to 45C for 15 to 20 minutes. Increases blood flow to the area, promotes tissue extensibility, decreases pain, muscle spasm and joint stiffness, and causes general relaxation. Heat is contraindicated if swelling or edema are present.

**Intra-articular hyaluronic acid**
In vitro evaluation shows clear superiority of high molecular weight HA but in vivo more complicated. High molecular weight (>3.5x10^6 Kda) has been shown to be more effective than low molecular weight hyaluronic acid in several studies (human, rabbit, horse). Low molecular weight in ankle study shown not superior to saline injection. Look at concentration of injection - Hycoat is 5mg/ml and is low mw, Legend and Hyalartin-V are 10mg/ml and high molecular weight

**Intra-articular injections – steroids**
Much information from equine and human medicine. Methylprednisolonone forms deposits (hydroxyapatite) in synovial fluid and on joint surface, Triamcinolone does not. With triamcinolone, only repeated injections suppress proteoglycan production, not single injection – this was shown to be chondroprotective (synovitis). Adding triamcinolone improves viscosupplementation (hyaluronic acid injections)

Always double check dosing when transcribing from lectures. Plumbs or North American Companion Animal Formulary.

Managing chronic osteoarthritis can be challenging: Diagnosis may occur later in the disease; Progressive nature of disease; Chronic pain aspects

Multimodal, comprehensive approach is recommended: Rehabilitation, Pharmacologics and Weight Loss

NSAIDs are currently the cornerstone of therapy: Benefits/Risks are assessed patient-by-patient; Appropriate patient selection and monitoring maximize benefits and minimize risks; Long-term therapy can provide progressive benefits for some.

More research is needed to assess adjunctive therapies

**References**

Ralph P. Webster, et al. AJVR, Vol 75, No. 6, June 2014.
DL Millis, DVM, DACVS, CCRP, DACVS MR et al, University of Tennessee, College of Veterinary Medicine . Conclusion “Shock Wave appears to be an efficacious addition to the multimodal approach to OA of the elbow”.