Non-Surgical Management of Canine Degenerative Joint Disease

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Disclosure

- Dr. Jaffe is a paid speaker on behalf of Nutramax Laboratories
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Presenting Complaints by owners

- *"My dog is not as active as he used to be"*
- *"She doesn't get up as much as she used to"*
- *"We can't go for walks like we used to"*
- *"He gets tired really easily"*
- *"I want him to run with me again"*
- *"We can't take him on long walks anymore"*
- *"She seems painful"*
- *"We bought a new puppy to play with him and he's not interested"*

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Signs of arthritis in dogs

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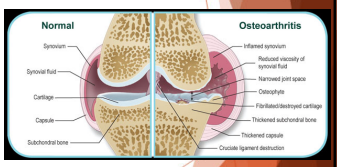
Osteoarthritis

- A form of arthritis caused by inflammation, breakdown and eventual loss of cartilage in the joints
  - Synonymous term DJD
- Arthritis: Inflammation of a joint
- We have to think of this as an *inflammatory condition*
  - Inflammation not due to leukocytosis
  - Mechanically-driven but chemically-mediated
  - Proteases derived from synovial tissue and cartilage result in cartilage matrix degradation
  - MMP's and aggrecanases result in cartilage catabolism



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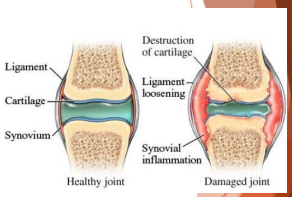
Why is arthritis painful?

- Cartilage damage
  - Subchondral bone exposure?
- Joint effusion
  - Stretch of joint capsule
- Thickened joint capsule
  - Loss of ROM
- Muscle atrophy
- Fibrosis of periarticular muscles and tissue



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Broad causes of arthritis

- Normal forces imposed on an abnormal joint
- Abnormal forces imposed on a normal joint
- Pathologic changes in the cartilage are reversible up to a point
  - Cartilage has the potential for endogenous repair, but once compensatory repair mechanisms are exhausted the damage becomes permanent

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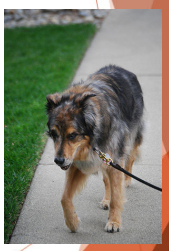
Broad categories of causes of lameness

- Orthopedic
  - Often ruled out radiographically
- Neurologic
  - Should be easy to rule out with a good neuro exam
- Soft tissue
  - The hardest category to get a diagnosis in some cases
- "Metabolic"
  - Includes immune-mediated, infectious, etc.
  - Very challenging to diagnose in many cases



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Two broad categories of management

- Surgical
  - No really great options, salvage procedures
  - Oftentimes for extreme cases….but should it be?
- Non-surgical
  - Multimodal management
  - Needs more attention and is the focus of treatment for most cases

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Diagnostics

- Good physical exam
  - Make a complete neuro exam standard
- Orthopedic Exam
  - Localize the site of pain
- Imaging
  - Rads
  - CT
- Arthrocentesis
  - Cytology
  - Cultures
- Bloodwork
  - Serum titers where indicated

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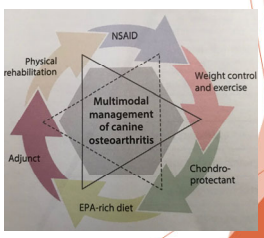
Multimodal Management of Osteoarthritis

- Anti-inflammatory drugs
- Chondroprotectives
- Weight management
- Controlled exercise
- Fatty acids
- Adjunctive therapies



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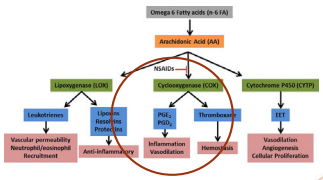
Anti-inflammatory medications

- The mainstay of treatment for inflammation
- NSAID's will reduce inflammation along the inflammatory pathways
- COX2 inhibition most common



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COX2 drugs: Q and A

- Effective, expensive, but there are side effects
- Does it benefit the arthritic joint?
- Or are the effects more peripheral?
  - More effective at reducing inflammation in the periarticular soft tissue
- Bottom line is they work and are a necessary part of the treatment regime
- But can we do better?

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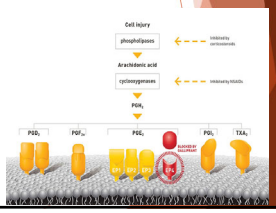
PGE2 inhibitors and EP4 antagonists

- PGE2 is the principal pro-inflammatory prostanoid in the arachidonic acid cascade
- Contributes to inflammation and pain hypersensitivity
- EP4 is a major receptor in mediating pain associated with OA and rheumatoid arthritis
- EP4 antagonism is as effective as COX2 inhibition
  - **Few side effects and wide safety margin**



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Chondroprotectives

- Glucosamine, chondroitin sulfate, MSM, Omega-3 fatty acids, others
- Nutraceuticals – extracted form of non-drug substances to provide agents required for normal body structure and function
- Egg-shell Membrane
  - **Multicenter, randomized, double-blind, placebo-controlled study**
  - Reduced joint pain and improved joint function rapidly and demonstrated a lasting improvement in joint pain leading to an improved quality of life compared to placebo

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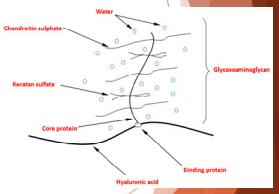
Glucosamine/Chondroitin Sulfate

- ***Provides precursors of cartilage matrix that favors matrix synthesis and repair of articular cartilage***
- Glucosamine – precursor of glycosaminoglycans
- Chondroitin sulfate – a glycosaminoglycan that is a normal constituent of cartilage
- MSM (Methyl-sulfonyl-methane)
  - Strengthens connective tissue and also helps to increase the permeability of the joint and muscle membranes allowing the release of excess fluid.
  - Results in a relief of swelling as well as drainage of inflammatory toxins.



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Essential Fatty Acids

- Polyunsaturated fatty acids that contain Omega-3 fatty acids
  - EPA and DHA
- Omega-6 FA part of cell membrane is broken down in osteoarthritic joints
  - AA Metabolizes to form inflammatory mediators
- ***Omega-3 FA's compete with and replace Omega-6 FA's in cell membranes***
  - ***Thus reduces the inflammatory response***
- 50 mg EPA + DHA (combined) per kg body weight recommended
- Safe for puppies

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PSGAG's

- Polysulfated glycosaminoglycans, i.e. Adequan, Legend
- Inhibit catabolic enzymes which have increased activity in inflamed joints
  - Enhance the activity of anabolic enzymes
- ***Inhibit enzymes that play a role in the interleukin-1 mediated degradation of cartilage, collagen, proteoglycans, and hyaluronic acid***
- Also inhibits PGE synthesis
- Best started when early OA, less effective in advanced OA

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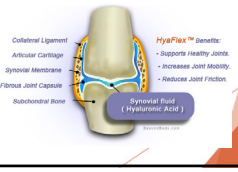
Hyaluronic Acid

- Intra-articular injections
- Viscosupplementation to improve rheologic properties within the joint
  - ***Improves joint fluid viscosity***
- Benefits:
  - Slows progression of OA
  - Decreases inflammation
  - Chondroprotective effects
- Once per week for 3 weeks
  - ~70% response for 6 months
- New oral HA product now available



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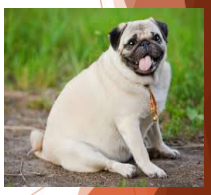
Weight management and diet

- One of the most important aspects, yet most difficult to accomplish
- Purina life-long diet study in Labs proved the importance of this management aspect
  - ***Dogs on a restricted diet and who have a leaner body mass have less OA!***



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Controlled exercises

- Leash walking must be a controlled activity
  - Slow pace
  - Short leash
  - Come home from walk still fresh
- Swimming
  - Laps
  - Floatation vest
  - Assisted
- Stairs/hill climbing exercises
- Hill walking

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How to walk an arthritic dog

- Slow pace!!
  - Pets will find it less strenuous to walk on 3 legs at a quick pace than on 4 legs
- Short leash
  - Better control, "shortens" their walk, allows slower pace
- Come home still fresh
- Make use of Slings and Help 'em Up Harnesses as needed
- Gradually extend the walk as able
- Pet *must* place foot at every step
- End the walk if not using the leg or painful

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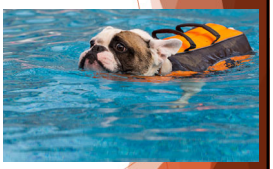
Swimming

- It must be non-traumatic to the patient!
- Good non-weight bearing activity
  - Encourages range of motion
  - Promotes muscle use in non-walking manner
- Can use flotation vests or assisted by owner
- Good for strengthening and endurance exercises
- Short duration, doesn't need to be a long swim



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Surgical management

- Joint replacement
- Osteotomies
- Ostectomies
- Other

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Alternative management options

- Adjunct drugs
  - Tramadol – does it work?
    - In very few cases
    - Sedative effects
  - Gabapentin – best for neuropathic pain
    - Not advised for OA
    - Sedative Effects
  - Tylenol 4 – useful for pain management but doesn't treat the underlying issue
    - 1-2 mg/kg PO q8h
  - Amantadine 3-5mg/kg SID, 2-3 weeks
    - NMDA antagonist
    - GI side effects possible

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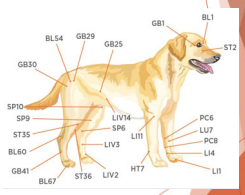
Other conventional treatment options

- Rehabilitation practices
  - Physical Therapy
- Regenerative therapies
  - Stem cell
  - PRP
- Alternative therapies
  - Herbal therapies
  - Acupuncture – reduce pain and inflammation



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Herbal therapies

- CBD
  - Controlled studies
    - Cornell Study[1]
  - Mechanism of action
    - May affect pain receptors in brain
  - Chroniquin
    - Veterinary product
    - Hemp oil, minimal traces of THC[2]
    - Once daily (2mg/kg), long serum half-life
- Boswellia
  - Synergistic with ASU+glucosamine+chondroitin
  - Suppresses PGE2 in cell culture
- Turmeric
  - Curcumin
  - Anti-inflammatory effects through down-regulation of COX-2
  - Dosage?
- ASU
  - Avocado/soybean unsapponafiables
  - Suggested to promote OA cartilage repair by chondrocyte and subchondral osteoblasts
- Phycocyanin
  - COX-2 inhibitor
  - Anti-oxidant and anti-inflammatory effects

1. Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs, Gamble et al. , Frontiers, 2018
2. Boothe, et al. The Disposition of Cannabidiol (CBD) in Dogs after Single Dose Oral Administration (abs), 2020

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Muscle Atrophy

- Often is pronounced in chronic osteoarthritis patients
  - Disuse atrophy due to pain and soreness
  - Decreased ROM of joints prohibits full muscle contracture and promotes fibrosis
- Self-propagating effects
- *Sarcopenia* – age-related decline in skeletal muscle mass and function
  - Multifactorial pathogenesis
- Fortetropin *delays* muscle atrophy
  - Demonstrated in healthy dogs to decrease serum myostatin levels
    - Myostatin – extracellular cytokine, plays a negative role in regulating skeletal muscle mass and growth
  - Does *not* rebuild muscle
- Can reverse to some degree with exercise but controlled PT/Rehab much more effective

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Regenerative therapy

- IA injections of autogenous mesenchymal stem cells into inflamed joints, will reduce inflammation
- Injections generally need to be repeated every 7-8 months
- 1 minor surgical procedure to harvest adipose tissue
- Injections given with PRP to potentiate stem cell anti-inflammatory effects
- Many patients are able to decrease or discontinue medications
  - Owners must have realistic expectations though
- 70-90% success rate
- Advantage: multiple joints can be treated concurrently
- Disadvantage: costly, but costs are spread out over time after initial start-up

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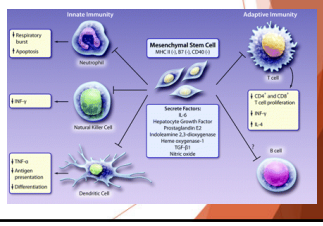
Five main mechanisms of action of adult stem cells

- Trophic support - growth factors and cytokines
- **Anti-inflammatory**
- Differentiation into tissue
- Homing to injury site
- Immune System Modulation



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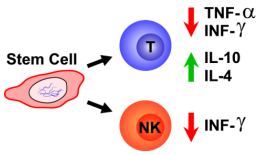
Anti-Inflammatory Effects

- Decrease pro-inflammatory mediators
- Increase anti-inflammatory mediators



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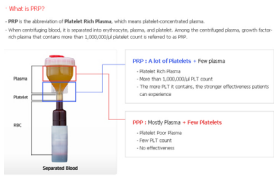
Platelet-Rich Plasma

- Autogenous fluid concentrate composed primarily of platelets and WBC's used to accelerate healing of tendon, ligament, bone, and other tissues.
- Platelets contain growth factors (PDGF, TGF-B, VEGF, EGF) that stimulate tissue healing
  - PDGF stimulates mitogenesis, angiogenesis, and activation of macrophages
  - TGF-B accelerates production of collagen, and is chemotactic and mitogenic for pre-osteoblasts



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Rehabilitation therapies

- Laser
- E-stim
- Ultrasound
- Underwater treadmill
- Strengthening exercises
- Stretching/PROM
- Massage
- Other, i.e. acupuncture, shockwave

- Improves mobility and helpful in weight loss

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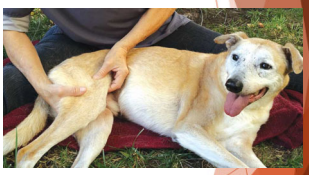
Massage therapy

- Prevents adhesions of muscles, tendons, and ligaments
- Reduces muscle spasm, swelling, and joint stiffness
- Improves tissue relaxation, muscle flexibility, and blood flow
- Maintains muscle mass while decreasing pain



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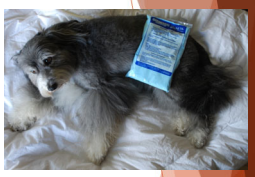
Cold therapy



- Post-op swelling or pain (post-*acute* injury)
- Musculoskeletal trauma
- **After exercise to reduce edema and pain**
- Vasoconstriction
  - → decreased edema formation
  - → decreased inflammation
  - → decreased hematoma formation following acute injury
- Decreased nerve conduction velocity → decreases pain in superficial nerves
- Decreased muscle spasm
  - Due to decreased muscle spindle activity

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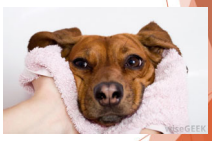
Heat therapy

- **As a warm-up, often prior to massage or exercise**
- To decrease muscle spasms
- More often used in chronic cases
- To improve lymphatic flow when edema is present
- Increases metabolic rate and chemical activity
- Decreased pain
  - Counter-irritant effect
- Improved nerve conduction velocity
- Increased extensibility of connective tissue
  - Decreased joint stiffness



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Next Generation therapies *Radiosynoviorthesis (RSO)

- Tin-117m – radioisotope of tin (Sn 117-m) combined with a homogenous colloid
- Synoviorthosis – IA injection of a compound that diminishes the degree of synovial hypertrophy -> decreases pain and inflammation -> decreases chondromalacia
- Microparticles of Synovetin OA® selectively target the source of inflammatory mediators through dual cellular targeting (macrophages, activated synoviocytes)[1]
- **Radionuclide particles phagocytized by inflammatory synovial macrophages to deactivate them**
- 14-day half-life
- Purported to provide up to 1 year of relief with 1 single injection

1. Donecker JM, Stevenson NR. Radiosynoviorthesis: A new therapeutic and diagnostic tool for canine joint inflammation. Technical Bulletin. Exubrion Therapeutics, July 2019.

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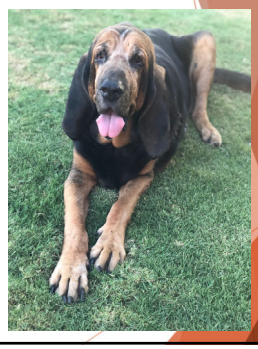
Otis

- 11 year old MN Bloodhound
- Two previous right stifle surgeries 4 years ago
- Weight 1 year ago 139# (BCS 7/9)
- Exhibits stiffness after rest, exercise intolerance, muscle atrophy in right rear leg
  - Rx Rimadyl prn
- Goals:
  - Lose weight, target 120# (~15% wt. loss)
  - Improve mobility and comfort
  - Rebuild leg strength and stamina



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Otis's Plan

- Weight loss diet
  - Metabolic and Mobility diet
  - Strict measured portions
  - Eliminate table snacks (mostly)
- NSAID
  - Switched to Galliprant
- Chondroprotectives
  - Dasuquin Advanced, EFA's
- Controlled Exercise
  - Twice daily leash walks
- PT
  - PROM exercises
  - Muscle massage
  - Heat/Cold

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Otis's Outcome

- Lost weight over a 6-8 months period
- Improved mobility and comfort
  - Able to do 2-mile morning walks and 1-mile evening walks without limping
- Significantly increased thigh circumference, muscle strength, and stifle/hip joint mobility
- Switched to j/d diet for maintenance
- Continued Galliprant daily (as needed)
- Continued Dasuquin Advanced daily
- Maintain exercise plan
- Dramatically more comfortable and mobile
- Greatly improved QOL

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Let's not forget cats!

- More common than previously believed
- Signs include reluctance to jump, decreased activity, lameness
- Orthopedic exam may be challenging
- Hip, stifle, tarsus, and elbow most commonly
- Older cats had higher incidence
- Radiographs
  - Osteoarthritis in up to 90% of cats older than 12 years old screened[1]
    - Only 50% had clinical signs
  - 22% of cats greater than 1 year old had radiographic changes consistent with OA[2]
    - Most had no clinical signs

1. Hardie, et al. **Radiographic evidence of degenerative joint disease in geriatric cats: 100 cases (1994-1997). *JAVMA* 220:628-632.**

2. Godfrey DR. Osteoarthritis in cats: a retrospective radiological study. 2005. *JSAP.* 46:425-429.

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Treatment

- Weight management
- Nonsteroidal anti-inflammatory drugs
  - Onsior?
- Adjunctive drug therapy
- Joint supplements
- Environmental modifications
- Physical rehabilitation
- Surgical techniques

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Solensia (frunevetmab)

- Cat-specific monoclonal antibody recently approved by FDA for use in cats with chronic disease such as osteoarthritis
- Blocks **nerve growth factor (NGF)** which is elevated in arthritic joints
  - Attaches to NGF that's involved in pain regulation
  - Prevents the pain signal from reaching the brain
- NGF is released secondary to an inflammatory stimulus
  - NGF is in higher concentrations in the arthritic joint
- Cats that received Solensia did better than those that didn't receive the drug
  - Data reported to the FDA is based on owner's observations of their cats seeming more active
- Most common *side effects*: vomiting, diarrhea, injection-site pain, scabbing on the head and neck, dermatitis and itchy skin
  - Effects were relatively mild and did not require a halt to treatment
- Injection given once per month based on cat's weight

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Questions?

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