Rethinking common geriatric neurologic and orthopedic issues

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Pain management services in human medicine

- Originated in 1950s on west coast
  - Dr. John Bonica, Seattle Washington
- Multidisciplinary centers dedicated to the patient's ability to function and quality of life
  - And return to work!
- Goal is to relieve, reduce or manage pain without classic surgical intervention or heavy reliance on any one medication, particularly opioid
- Concern is for overall quality of life
- the whole patient, vs. one organ system, is treated

Established pain management centers

- Human medicine:
  - Brigham and Womens Hospital, Boston
  - John Hopkins, Baltimore
  - University of Illinois, Chicago
  - Texas Spine and Joint hospital, Tyler
  - Massachusetts General Hospital, Boston
  - Pain Relief of Dayton, Ohio
- Veterinary medicine:
  - Oradell CARES program, Paramus NJ
  - Animal anesthesia and pain management center, Colorado springs, CO
  - Veterinary Pain Solutions, Santa Fe, NM
  - Center for veterinary pain management and rehabilitation, The woodlands, TX

What's unique about a good pain management hospital

- They don't claim to cure pain
- They are rarely solo medication or solo procedure oriented
- They are resourceful
- They have outcome data but they don't rely solely on evidence based therapies
  - Pain is what a person says it is
- They offer multi-disciplinary approach
- They offer support to the family

Top ten cases seen by Veterinary Pain Management Services

- Geriatric patients
  - Osteoarthritis axial and appendicular
    - Orthopedic with neurogenic component
- Orthopedic non surgery or post surgery
- Neurologic disease
  - Disability, inability, dysfunction, or pain?
- Oncologic disease/hospice
- Sports medicine/performance medicine
- Cases requiring advanced imaging
- Cases requiring diagnostics or therapies "outside the box" (normal therapies not working, unsuitable)
- Clients seeking complementary or alternative therapies

Issues discussed this evening

- Degenerative ortho and neuro disease beyond the NSAID
- Oncology palliative care

What is osteoarthritis?

- Degenerative joint disease
- Resulting from mechanical and biologic destabilization of
  - Articular cartilage chondrocytes
  - Extracellular matrix
  - Subchondral bone
  - Synovium
- Primary
  - rare
- Secondary
  - common
  - Results from initiating cause (joint instability, trauma, osteochondral defects, joint incongruity)

Peripheral sensitization OA pain

- Cytokines are released with tissue trauma
- TNF alpha
  - Stimulates further cytokine release
- IL-1B
  - Protease release from bone cells
  - Lysis of synovium
  - Further release of prostanoids from chondrocytes
- IL-8
  - Acts via adrenoreceptors to excite afferents

Goodrich LR, Nixon AJ, 2004

Central sensitization OA pain

- C fiber sensitization
- NMDA receptor becomes functional
  - Repeated activation of AMPA receptors
  - Magnesium "stoppers" dislodged
  - Sodium and calcium channels opened in AMPA and NMDA receptors

Neurogenic OA pain

- Conformational change in neuronal membrane
  - Due to
    - nerve compression
    - Inflammatory factors
  - Radiculopathy from mediators
    - Tachihara H, et al 2007
- Antidromic transmission
  - Pathologic dorsal horn reflex
  - Afferents release neurochemicals at initiating terminals
    - Sub P/cytokines

Further mechanisms of OA pain

- Physiologic
  - Muscle, tendon, ligament, fascial pain
  - Impaired NM responses
  - Increased Intraosseous pressure
- Psychosocial changes
  - Debilitation
  - Distress
- Environmental changes

Dieppe PA, Lohmander S, 2005

The art of locoregional blockade in small animaldiagnosis

- Performed in equine patients all the time
- An underutilized but great way to diagnose lameness in canine patients
- Mepivicaine 2.5mg/kg, Lidocaine 1mg/kg
- Intraarticular rarely helpful
- Trigger point, soft tissue or neural blockade beneficial
- Proximal to distal placement and evaluation

Thermography

Computer-assisted Skin Videothermography Is A Highly Sensitive Quality Tool in the Diagnosis and Monitoring of Complex Regional Pain Syndrome Type I

Eur J Appl Physiol 2004 (May); 91 (5-6): 516-524

The use of thermography in the diagnosis and evaluation of complex regional pain syndrome type 1 (CRPS1) is based on the presence of temperature asymmetries between the involved area of the extremity and the corresponding area of the uninvolved extremity.The interpretation of thermographic images is, however, subjective and not validated for routine use. The objective of the present study was to develop a sensitive, specific and reproducible arithmetical model as the result of computer-assisted infrared thermography in patients with early stage CRPS I in one hand.

From studies of OA pain…

- …important treatment concepts
  - A dynamic process offers opportunities
    - Multimodal therapy
    - Pyramid of therapy can begin early
      - NSAIDS though important are only part of picture
  - Compensation happens much before obvious symptoms often manifest
    - Consider earl(ier) intervention
  - Classic imaging signs may or may not be associated with severe disease
    - The irony of severe radiologic disease!
    - OA is both an orthopedic and neurologic disease

Interesting concepts in oa treatment

- Why tramadol may not be helpful
- Gaba-ergic drugs and their slow down potential
- Why adequan (cf. cosequin)
- Does doxycycline have a long term value
- Acetaminophen
- Topical/transdermal treatments for oa
- Herbal and homeopathic therapies
- Support hose…they aren't just for your grandma
- Trigger point assessment and injection
- Therapeutic ultrasound, laser, and hydrotherapy
- Acupuncture and aquapuncture
- Shockwave therapy
- Perineural injection therapy
- Intra-articular therapies (facet and appendicular)
- Radiation therapy
- Denervation surgery

Guidelines for safe and effective use of NSAIDs in dogs

B Duncan X Lascelles; J Michael McFarland; Heather Swann

Vet Ther. Fall 2005;6(3):237-51

NSAIDs are the most widely used analgesics in veterinary medicine, and all have some toxic potential. The most common adverse class effects are gastrointestinal, renal, hepatic, and coagulation disorders. When treating chronic pain associated with osteoarthritis, the effectiveness of NSAIDs can be enhanced by physical therapy, use of chondroprotective agents, certain adjunctive drugs, and diet and exercise to control weight. To treat acute perioperative pain, NSAIDs are more effective when used preemptively, in the context of balanced (multimodal) analgesia, and in well-hydrated patients with normal blood pressure and renal function. Screening and monitoring to identify high-risk candidates for NSAID treatment should include a physical examination and patient history, identification of preexisting diseases or conditions, obtaining baseline and periodic hematologic and clinical chemistry values, and ensuring that other NSAIDs or contraindicated drugs are not used concurrently. When switching a patient from one NSAID to another (when no side effects have been seen), a washout period of 5 to 7 days minimizes chances for adverse drug interactions. Informing clients of the potential adverse effects of NSAID therapy and signs of NSAID toxicity greatly increases the likelihood of safe use of this class of drugs.

Serotonin syndrome

- Common Mechanisms of serotonin toxicity ="syndrome"
  - Stress or amphetamine like drugs increase serotonin release
  - Inhibition of serotonin metabolism by mao inhibitors
  - L-tryptophan or L-tryptophan precursors increases 5-HT production
  - Increases in synaptic 5-HT via reuptake inhibition

N ENGL J MED 352;11 WWW.NEJM.ORG MARCH 17, 2005

Gabapentin & pregabalin

- Anticonvulsant
- GABA analogs
  - No direct GABAnergic action
- Mechanism of action
  - Modulation of subunit of Ca channel
    - Inhibition of Ca influx
  - Release of monoamines
  - Possible sodium channel modulation
- Well tolerated
- Gradual loading vs. effect dosing
- Inexpensive

Adebowale et al, 2000

- 14 products with glucosamine were tested along with 11 products with chondroitin using UV-HPLC method and titration
- Amounts of both compounds were found to be 0% to 115% deviations from label claims
- Purity of drug and proximity of label claims somewhat related to cost of pill
- The data showed NO relationship between cost and content

How do PSGAGs work?

- Inhibit catabolic enzymes that degrade synovial fluid and cartilage matrix components
  - MMPs
  - Serine proteases
  - Nitric oxide synthetase
- Rejuvenate the matrix
  - Competitive substrate for degenerative enzymes present in joint
- anabolic effects on diseased joint tissue
  - Stimulates proteoglycan synthesis
    - Proteoglycan – HA backbone with branches of keratin and chondroitin sulphate
  - Stimulates collagen synthesis
  - Stimulates synthesis of HA by synoviocytes

Pentosan polysulphate

- Derived from beech wood hemicelluloses
- Calcium and sodium products
- Beneficial effects
  - Promote the synthesis of proteoglycans
  - Improve subchondral bone blood flow
  - Stimulates release of t-PA, superoxide dismutase and lipases from vascular endothelium
- Oral and IM preparations available
- Evaluation of pentosan polysulfate sodium in the postop recovery from CCL injury in dogs: a randomized placebo controlled trial
  - Budsberg SC et al 2007

Tetracyclines

- Classic antibiotics
  - Tetracycline
  - Minocycline
  - Doxycycline
- Other Mechanisms of action
  - Decreased MMP activity
  - Diminished interleukin 1 effect
- Chemically modified tetracyclines
  - Removal of dimethylamine side groups
  - No antibiotic properties
  - Fewer side effects
  - Longer serum half life

Acetaminophen

Cannot be used in cats!

- Not an anti-inflammatory!
  - Grouped with NSAIDS
- Good analgesic in dog
- Excellent antipyretic in dog
- Will not cause GI ulceration, renal disease or platelet dysfunction
- Mechanisms:
  - cyclooxygenase inhibition
  - NO synthesis blockade
  - reinforcement of the serotonergic system.
- Hepatic function (glutathione) must be adequate

Compounded topical gels

Fallon Wellness Pharmacy

www.fallonpharmacy.com

- Bromelain
- Ketoprofen
- Piroxicam
- Dexamethasone
- Lidocaine
- Ketamine
- Clonidine
- Triamcinalone

Evaluating Complementary Therapies for Canine Osteoarthritis—Part II: A Homeopathic Combination Preparation (Zeel)

www.heelusa.com

Anna Hielm-Bjo¨rkman1, Riitta-Mari Tulamo1, Hanna Salonen2 and Marja Raekallio1

A homeopathic combination preparation (HCP) for canine osteoarthritic pain was evaluatedin a randomized, double-controlled and double-blinded clinical trial. Forty-four dogs with osteoarthritis (OA) that were randomly allocated into one of three groups completedthe study. All dogs were fed test products or placebo for 8 weeks. The dogs were evaluated atthe clinic four times, with 4-week intervals. Six different variables were assessed: veterinaryassessedmobility, two force plate variables, an owner-evaluated chronic pain index and painand locomotion visual analogue scales (VASs). Intake of extra non-steroidal anti-inflammatorydrugs was also evaluated. A Chi-squared test and a Mann–Whitney test were used to determine
significant improvement between groups. When changed into dichotomous responses of 'improved' or 'not improved' three out of the six variables showed a significant difference (P=0.016, P=0.008, P=0.039) in improved dogs per group, between the HCP group and the placebo group. The odds ratios were over one for the same variables. An extent of improvement in the variables from start to end of treatment, the HCP product was significantly
more improved in four (P=0.015, P=0.028, P=0.049, P=0.020) of the six variables, compared with the placebo. Our results indicated that the HCP Zeel was beneficial in alleviating chronic orthopedic pain in dogs although it was not as effective as carprofen.

Herbal remedies

- Ayurvedic plant preps
- Green tea extract
- Extract of ginger root
- Grape seed meal
- Curcuminoids
  - turmeric
- Proposed Mechanisms of Action
  - Inhibition of NF KB
  - Inhition of MMP
  - Inhibition of COX-2
- Ahmed S, et al. 2005

Biological Basis for the Use of Botanicals in Osteoarthritis and Rheumatoid Arthritis: A Review

Veterinary Herbal information

- Wynn, SG www.susanwynn.com
- Tilford GL www.theanimalherbalist.com
- Marsden S www.nphc.ca
- www.viim.org
- www.vbma.org
- www.ivas.org

Trigger points

- Diagnosed via
  - Local twitch along fascia, muscle body palpation or meridians
  - Presence of taut pain
- Mechanism
  - Motor endplate or spindle apparatus pathology
  - Excessive Ach release producing sustained depolarization
- Treatment
  - Classic rehab interventions
  - Acupuncture
  - Injection therapy (steroids, local anesthetics, b toxin, sterile water, homeopathic remedies)

Acupuncture for OA

- How does it cause analgesia?
  - Increasing local regulatory mechanisms
  - DNIC (Diffuse Noxious Inhibitory Control) = gate cell regulation
  - Endorphin, neuropeptide, hormone release centrally (hypothalamus) and peripherally (hypophysis)
  - Initially increased and chronically decreased sympathetic regulation

Controlled PT and Therapeutic Exercise for OA

- Low impact exercises are best
- Benefits
  - Reduced body weight
  - Improved catecholamine and endogenous opiate levels
  - Increased joint mobility
  - Strengthening of supportive muscles
  - Cartilage metabolism increases
- Improper program might hasten progression of OA
  - Tailor program to the individual

Water exercises

- Thermal effects
  - Heat or cold
- Buoyancy
- Lessened cartilage concussion
- Turbulence
  - Wound cleansing
  - DNIC
  - Conditioning
- Decreased chance of injury

Hudson S. 2008
Canine Rehabilitation and Conditioning Center of Texas

Therapeutic Ultrasound

- Capable of heating tissues up to depths of 5 cm
- Sound waves of high frequency
- Absorbed by tissues with production of heat
- Increases collagen extensibility
- Increases ionic exchange through membranes
  - Nutrients
  - calcium
- Increases blood flow

Laser therapy

- Class III lasers
  - "cold" lasers
- Class IV lasers
- Mechanisms
  - Acceleration of angiogenesis
  - Lymphocyte activity
  - Increased cellular metabolism
    - Activation of mitochondrial respiratory chain components

Extracorporeal Shock Wave Therapy

- high-energy sound waves, which are transmitted to the affected body part
- Stimulate osteoblast cytokine production
- Stimulate neovascularization
- produce marked analgesia
  - Decreased metabolism of neurons
  - Depletion of Sub P and CGRP in afferents
  - Barrage of sensory noise resetting input to dorsal horn
  - Short term (72 hours)

Shockwave indications

- Tendonitis
- Fascitis
- Osteoarthritis
- Post surgical?
- Non healing wounds
  - Decubitus
  - Lick granuloma
- Non unions
- Burns

IA steroids

- Most useful for severe chronic non infectious non septic inflammation
- Systemic effects likely but individual
- Repeated <2-3 X/year in human medicine
- Period of rest after injection important
- Detrimental to chondrocyte and subchondral bone turnover?
  - No more than saline in two large clinical trials

IA Hyaluronic acid

- **HA**
  - Linear polydisaccharide
  - Synthesized by synoviocytes
- Marketed drugs
  - Legend
  - Hylartin V
- Mechanisms
  - Restores joint fluid viscosity and content of HA
  - Anti-inflammatory effects
  - Direct analgesic effects on nerve impulses

Intra-articular injections with high molecular weight sodium hyaluronate as a therapy for canine arthritis
Hellström LE et al 2003

Acute non surgical disc or nerve root pain

- 1-2 days of slow down
- Muscle relaxants
  - Acepromazine
  - Methocarbamol
- Steroid or NSAID
- Oxycodone
- If possible, Localized rx
  - Menthol camphor
  - Lidocaine dmso
  - capsaicin
- brush
- Massage
- Jacuzzi
- Warm compresses >24 hours
- Gentle stretch via positive feedback

Chronic back pain

- Spondylopathy
- Facet oa
- Psoas disease

- Thermography
- Ultrasound

- Water therapy
- Chiropractic
- Adequan
- Ther US
- Injection rx
  - Epidural injection
  - Facet injection
  - Foramina injection
  - Nerve root injection

Use of a nerve locator for specific peripheral nerve blockade

- Microcurrent isolates nerve or plexus
- Local is delivered while twitch fades
- Reduces volume of local used
- Minimizes possibility of toxicity

Long term or neurolytic blockade constituents

- Local anesthetics
  - Butamben
  - Lidocaine 2 and 5 %
  - Bupivicaine
- Saline
- Microdose
  - alpha two agonist
  - steroid
  - NMDA antagonist

- Alcohol/phenol
- Glycerol
- Ammonium salts
- Sarapin

Palliative radiation as an analgesic

- Mechanisms of relief for osseous pain
  - Not well known
  - Cell kill?
  - Tumor shrinkage?
  - Inhibition of prostanoid secreting cells within microenvironment
  - Induction of TGF-B
- Basic approaches
  - Moderate dose regimen protracted
  - Low dose single shot

Denervation surgery for coxofemoral oa

Berl Munch Tierarztl Wochenschr. 2002 Jan-Feb;115(1-2):53-6.

10 years experience with denervation of the hip joint capsule for treatment of canine hip joint dysplasia and arthrosis

Kinzel S, Hein S, von Scheven G, Küpper W

Denervation of the canine hip joint capsule is described as a surgical therapy method in the treatment of canine hip joint dysplasia and arthrosis. The goal of this operation is a removal of the pain immediately and a reactivation of the dynamic active component of the hip joint in moving the body forward. Simple removal of the periosteum of the craniolateral acetabulum edge destroys the rami articulares of the cranial glutaeal nerve and the rami articulares dorsalis of the sciatic nerve. Within 10 years now we performed the denervation of the canine hip joint capsule. Evaluation of the post operative clinical course in 269 cases revealed an impressive improvement of lameness due to pain relief in almost 92% of the cases

Quality of life scoring for cancer patients

- **Validity of a health-related quality-of-life scale**
- **for dogs with signs of pain secondary to cancer**
- Karina V. B. Yazbek, DVM, and Denise T. Fantoni, DVM
- JAVMA, Vol 226, No. 8, April 15, 2005

- Appetite
- Mood
- Frequency of contact with family members
- Hygienic habits
- Sleep patterns
- Tiredness
- Energy
- Ability to ambulate
- Respiratory ease

Generalities of QOL care

- Lifetime nutritional management
- Supplements/nutraceuticals can really assist
- Eliminate environmental carcinogens
- Talk to the family, change the environment
- Prevent nausea, vomiting, diarrhea, constipation
- How is the bladder working?
- What is the animal's sleep and awake cycle?
- Prevent anorexia and cachexia; engage the nutritionist
- Assure mental stability; treat stress

Generalities of QOL care

- Complementary treatments imply just that
- Complementary treatments are useful
- Transdermal medications often work well
  - Despite lack of evidence!
- Home parenteral care may be needed
- Mucositis needs to be treated aggressively
- Dermatologic disease needs to be treated aggressively
- Watch your white blood cell counts
- Learn to embrace imaging modalities
- Prepare the owner for realistic outcomes

Useful appetite stimulants

- Food change and removal
- Enrichment
- Cyproheptadine
- Mirtazapine
- Moxa
- Diazepam
- Alprazolam
- Microdose propofol
- Caffeine

- Walking
- Play
- Brushing
- Acupuncture
- Antiemetics
- Antihistamines
- Steroids
- Anti-depressants

Anti-emetics

- Antihistamines
- Phenothiazines
- Benzamide
- Steroids
- ACTH
- Cannabinols
- Neurokinin antagonist
- Propofol
- Butorphanol

Urinary and defecatory assistance

- Urinary incontinence
  - Soy flavinoids
  - Ppa
  - DES
  - r/o uti
  - Testosterone
- Fecal incontinence
  - Performance foods
  - Acupuncture
  - Nsaids and steroids
  - Epidurals
- Chronic uti
  - Adequan
  - Interstitial infusion
  - Amitriptyline
  - Fluoxetine
  - Environmental arrangement
  - Nsaids or steroids
  - Phenoxybenzamine
  - Prazosin
  - Acepromazine
  - Antihistamines
  - Epidural

Oral opioids

- Tramadol 1-3mg/kg po tid to 3-5mg/kg po tid
  - Not that effective
  - Not for cats
- Codeine 0.1-1mg/kg po bid
  - Constipation in dogs
  - Combined with tylenol usually
- Hydrocodone 0.05-0.2mg/kg po bid
- Oxycodone 0.1mg/kg po sid-tid
- ER morphine 0.1mg/kg po sid
- Methadone 0.01-0.2mg/kg po sid-tid

Lidocaine infusion for chronic pain

INTRAVENOUS LIGNOCAINE INFUSION For
NEUROPATHIC PAIN IN CANCER PATIENTS– A PRELIMINARY STUDY

INDIAN JOURNAL OF ANAESTHESIA, OCTOBER 2002 360 Indian J. Anaesth. 2002; 46 (5) : 360-364

Dr. Anjum S. Khan Joad, Dr. Jyoti Burad, Dr. Charu Mehta

The effectiveness and duration of pain relief with a continuous lignocaine infusion was observed in 10 cancer patients. All the 10 patients were suffering from pain of neuropathic origin, having two or more of the symptoms: burning, aching, allodynia, reduced sensitivity to touch or pain, hyperaesthesia, nightly exacerbation and sleep disturbance. The patients received intravenous lignocaine in a dose of 5mgkg-1 in 1mlkg-1 of normal saline over 60 minutes. Significant relief in pain (t value> t at 0.01), dysaesthetic sensations, paraesthesias and nightly exacerbations were seen in the majority of patients upto 14 days. Statistical analysis were performed using the unpaired 't' test and analysis of variance (through application of x2 test).

Keywords : Lignocaine infusion, Neuropathic pain, Cancer pain.

Lidocaine infusion for chronic pain

Efficacy of 5-day continuous lidocaine infusion for the treatment of refractory complex regional pain syndrome.

Pain Med. March 2009;10(2):401-12.
Robert J Schwartzman, Mona Patel, John R Grothusen, Guillermo M Alexander

Chronic regional pain syndrome (CRPS) is a severe pain condition that usually results from an injury or surgical procedure. The pain in CRPS often spreads from the site of injury, and with time becomes refractory to conventional therapy. The present study was undertaken to evaluate the effects of 5-day continuous intravenous lidocaine treatment in patients afflicted with CRPS. METHODS: Intravenous lidocaine was administered in an escalating dose schedule to 49 severely affected CRPS patients in a monitored setting over 5 days. Evaluation of pain parameters and other signs and symptoms of CRPS were obtained during the infusion and at 1, 3, and 6 months following therapy. RESULTS: The majority of patients demonstrated a significant decrease in pain parameters and other symptoms and signs of CRPS. The pain reduction lasted an average of 3 months. Lidocaine may be particularly effective for thermal and mechanical allodynia. Less clinically significant effects were documented on the motor aspects of the syndrome. DISCUSSION: Intravenous lidocaine administration titrated to 5 mg/L demonstrated: 1) a significant decrease in mechanical and thermal allodynia for three months, 2) lessened associated inflammatory components of CRPS, and 3) only minimal side effects and no severe complications.

Plasma levels of a low-dose constant-rate-infusion of ketamine and its effect on single and repeated nociceptive stimuli in conscious dogs.

Vet J. November 2009;182(2):252-60.

Alessandra Bergadano'Ole K Andersen; Lars Arendt-Nielsen ; Regula Theurillat; Wolfgang Thormann; Claudia Spadavecchia

This study quantitatively investigated the analgesic action of a low-dose constant-rate-infusion (CRI) of racemic ketamine (as a 0.5 mg kg(-1) bolus and at a dose rate of 10 microg kg(-1) min(-1)) in conscious dogs using a nociceptive withdrawal reflex (NWR) and with enantioselective measurement of plasma levels of ketamine and norketamine. Withdrawal reflexes evoked by transcutaneous single and repeated electrical stimulation (10 pulses, 5 Hz) of the digital plantar nerve were recorded from the biceps femoris muscle using surface electromyography. Ketamine did not affect NWR thresholds or the recruitment curves after a single nociceptive stimulation. Temporal summation (as evaluated by repeated stimuli) and the evoked behavioural response scores were however reduced compared to baseline demonstrating the antinociceptive activity of ketamine correlated with the peak plasma concentrations. Thereafter the plasma levels at pseudo-steady-state did not modulate temporal summation. Based on these experimental findings low-dose ketamine CRI cannot be recommended for use as a sole analgesic in the dog.

Transdermal pluronic lecithin organogel preps

- Lidocaine
- Ketamine
- Clonidine
- Piroxicam
- Gabapentin
- Amantadine

Resiniferatoxin and capsaicin in vet oncology pain therapy

- Resiniferatoxin
  - Derivative of cactus Euphorbia
  - Long lasting (permanent?) blockade
- Capsaicin
  - Active component to chili peppers
- TRPV1 receptor agonists
  - Peripheral
  - DRG
  - ganglia
- Induce calcium cytotoxicity
- Blocks inflammatory hyperalgesia and neurogenic inflammation

Geppetti P,Trevesani M Br J Pharmaco 141, 2004

Resiniferatoxin

- naturally occurring, ultrapotent capsaicin analog
  - *Euphorbia resinifera*, a cactus-like plant, is a member of the euphorb family
- activates the vanilloid receptor in sensory neurons involved in transmission of pain signals
- Intravesicular instillation may assist with control of cystitis pain
  - **Therapeutic Effect of Multiple Resiniferatoxin Intravesical Instillations in Patients With Refractory Detrusor Overactivity: A Randomized, Double-Blind, Placebo Controlled Study.** Kuo H-C, Liu H-T, Yang W-C. J Urol 176, 641 - 645, 2006
- Intrathecal administration
  - **Physiologic and Antinociceptive Effects of Intrathecal Resiniferatoxin in a Canine Bone Cancer Model. Brown, Dorothy Cimino D.V.M.; Iadarola, Michael J. Ph.D.; Perkowski, Sandra Z. V.M.D., Ph.D.; Erin, Hardam D.V.M.; Shofer, Frances Ph.D.; Laszlo, Karai J. M.D.; Olah, Zoltan Ph.D.; Mannes, Andrew J. M.D.** Anesthesiology: November 2005 - Volume 103 - Issue 5 - pp 1052-1059
- Not commercially available….yet

Bisphosphonates for vet oncology pain therapy

- Inhibit osteoclast activity
  - Altered morphology
  - Via clinging (tightly) to calcium phosphate crystals in bone
- Best are administered IV over a 2 hour period monthly (pamidronate)
- Animal needs good renal function or diuresis to receive
- Also used to treat hypercalcemia of malignancy

http://www.roche.com/pages/facets/9/osteo.htm

Long term or neurolytic blockade constituents

- Local anesthetics
  - Butamben
  - Lidocaine 2 and 5 %
  - Bupivicaine
- Saline
- Microdose
  - alpha two agonist
  - steroid
  - NMDA antagonist
- Alcohol/phenol
- Glycerol
- Ammonium salts
- Sarapin