Options for Chronic Pain Management in Small Animals

If All You Have is a Hammer, Everything Looks Like a Nail

Old Dogs & New Tricks
What if I don’t feel like learning new tricks?
A Huge Professional Void

- Most of what needs to be done can be done without any major capital expenditures
- All you need is more understanding and a little more time
- You often gain 9 to 24 months if not many years of high quality life for your patients

Learning Objective

Understand the disease we call Chronic Pain

What Is This Thing Called Pain?
A Complex, Diverse Experience

No Pain No Gain?
- Physiologic pain is protective; a defensive mechanism
- An early warning system that minimizes injury

No Gain From Chronic Pain
- Pathologic pain – Jekyll & Hyde
  - Acute – can help us guard an injured area
  - Chronic – persists after the injury has healed
    - IT IS A CRUEL MALFUNCTION of the nervous system
    - IT IS A DISEASE in its own right
Brief Summary Of Pain History

It’s Complicated

It’s Complicated
Pain Amplification

Human vs. Animal Pain

- “it is appropriate to assume that a stimulus that is painful to people…is indeed painful to that animal”

Feline Perioperative Pain Management...Leigh Lamont. V CNA. July 2002
Chronic Pain Survey

• Is this list complete?
  • Osteoarthritis pain
  • Neck and back pain
  • Cancer pain

Chronic Pain Survey

• Myofascial pain
• Trauma related pain
• Chronic post-surgical pain
• Chronic inflammatory pain

Learning Objective

Understand the key components in optimal chronic pain therapy.
What We Want Chronic Pain To Be

- A straightforward problem with an easily correctable cause
- One that resolves quickly when you address the cause
- We want “a” target with “a” solution

What Chronic Pain Is

- A complex process
- A disease in its own right regardless of the original cause
- Even when we remove the initial cause, chronic pain may not resolve

One thing leads to another, and the next thing you know is that you now have two things.
Analg esic drug consumption increases after knee arthro plasty: a pharmacoepidemiological study

Chronic Pain: Its Own Disease
• 15% to 47% of patients undergoing hip and knee replacement continue to experience pain in the operated joint
• Patients… feel disabling pain despite a technically successful, uncomplicated procedure

Chronic Pain Therapy: What we want it to be
• Simple, safe, convenient, and profitable
Laser Therapy

• An excellent supportive modality: NOT a highly successful monotherapy
• Especially if the entire patient has not been adequately evaluated and ALL of the problem sites have not been identified

Power?

• Class IIIb?
• Class IV?

Real Power

Knowledge is power
Chronic Pain Therapy: What It Should Be

- An interdisciplinary process involving:
  - Pain medicine
  - Rehabilitation therapy
  - Needle therapy
  - +/- other supportive modalities

Optimal Diagnostics

- A thorough hands-on examination
- Imaging when possible
  - Radiographs, Myelograms, CT, MRI
- Help define rule outs
  - Neoplastic, infectious, OA
- Helps shape Rx
  - Bisphosphonates, antibiotics,
    OA support
Avoid Tunnel Vision

- Don’t just treat the 1st cause: treat the patient
- Don’t treat the radiograph: treat the patient
- Don’t find “a” problem: find “all” problems
- Collect a good history
- Look at the entire patient
- Palpate the spine, joints, and muscles
- Observe their gait - slow motion video

Create Hope!

- Patient has: Severe bilateral hip OA
- The 1st thing you need to do: Create hope!
- What you need to treat:
  - The front end and core!
  - Joint pain, Muscle pain, & Central sensitization
  - Compensatory components
  - Patient weight

Set High Goals

- Simply to have your patient survive?
- Or to regain the patient’s normal ADLs; to resume doing what they love to do
Expanding Possibilities

Expanding the Possibilities

Help’EmUp Harnesses

www.HelpEmUp.com
Help’EmUp Harnesses

www.HelpEmUp.com

Ramp Training


Learning Objective

Understand the basic issues associated with OA management.
OA’s Central Component

- 15% to 47% of patients undergoing hip and knee replacement continue to experience pain in the operated joint
- Patients… feel disabling pain despite a technically successful, uncomplicated procedure

Osteoarthritis & Central Pain

- http://www.vin.com/doc/?id=5949063&pid=7773
- VIN search: 5949063
Osteoarthritis

- Three key OA components
- Joint disease
- Chronic pain (its own disease)
- Broader impact
  - ROM, muscle strength and flexibility, fitness, balance
  - Myofascial disease - MTrPs
Foundational Joint Support

- Weight control
- Omega-3 FAs
- DHA + EPA @ 310
- Adequan/Zydax

Adipokines & Obesity-related Inflammation
Foundational Joint Support

- Natural anti-inflammatories/analgesics
- Dasuquin/Dasuquin Advanced
- Cosaquin ASU Active Lifestyle
- Cosamin ASU w/AKBA
- Glyde
- Duralactin
- Probiotics

Probiotics & Obesity-related Inflammation

- Role of bacteria/inflammation in the emotional and cognitive alterations displayed by animal models of obesity. Dalle Carbonare, Giorgio; La蒙, Angela; Elia, Emanuela; Panaccione, R; 2013. Am J Physiol Endocrinol Metab 304(6): E915-E923. doi: 10.1152/ajpendo.00330.2013

Foundational Joint Support

- Natural anti-inflammatories/analgesics
- Curcumin (Meriva/Theracurmin)
- Bromelain
- Devil’s claw
- Corydalis
- Conolidine

PEMF Therapy

- Pulsed electromagnetic fields therapy is safe and effective in improving knee osteoarthritis symptoms
- Pain threshold increases after pulsed electromagnetic field therapy in knee osteoarthritis patients compared with placebo

PEMF therapy can be used as adjuvant therapy to preserve cartilage from detrimental effects of high inflammatory cytokine levels during OA.
OA Pain Medicine Therapy

- NSAIDs
  - Piprant vs COX-2 selective
- NMDA antagonist
- Reuptake inhibitors
  - TCAs, SNRIs
  - Ca+ channel blockers
  - Microglial inhibitors

OA Pain Medicine Therapy

- Janus kinase inhibitors?
- NK-1 antagonists?

Invasive Options

- Mesenchymal Stem Cell Therapy
  - IA & IV
- IA therapies
  - IA botulinum toxin
- Surgical options
  - Joint denervation
  - Joint replacement
End Stage OA - Botulinum Toxin

- Human patients that failed treatment with oral and/or intra-articular medications and were not surgical candidates
- Up to 12 month pain relief
- Effect was repeatable
- Dog dose?
  - 25 Units per joint
  - 100 – 200 Units/dog in print

Crucial OA Therapies

- Physical rehabilitation therapy
  - The worst thing an OA patient can do is nothing
    - Office based UWTM program is ideal
  - Myofascial trigger point therapy
  - Laser
  - Needle therapy
  - Ca+ channel blockers; SNRIs

Asymptomatic Patient

- Adipose derived stem-cell therapy
- Pulsed electromagnetic field therapy
Mild OA Patient

- Stem-cell therapy
- PEMF therapy
- Intermittent NSAID
- Monitor myofascial status

Moderate OA Patient

- Stem-cell therapy
- PEMF therapy
- Intermittent use
  - Galliprant/NSAID
  - Amantadine
  - Pick one:
    - Amitrip/Dulox/Gabap
  - Needle therapy?

Advanced OA Patient

- Stem-cell therapy
- PEMF therapy
- Min dose to best effect:
  - Galliprant/NSAID
  - Amantadine
  - Amitrip/Dulox
  - Gabapentin
- Needle therapy
Advanced OA Patient

- Additional options:
  - Minocycline
  - Mexiletine
  - Apoquel
  - Cerenia

End-stage OA Patient

- IA therapies
  - Corticosteroids
  - HA
  - Botulinum toxin
  - Surgery
    - Replacement
    - Denervation/FHO

IA Injection Tutorials

- VetStem Biopharma
- www.VETSTEM.com
- ArthroDynamic Technologies
- www.youtube.com/channel/UCb5dvVm6bBEfA9tsC67ReMA
IA Injection Volumes

Case Report

- Reggie: 8 yo M/N Golden Retriever
- Progressive PWB right foreleg lameness; decreased attitude and appetite
- On examination we find severe right elbow enlargement; pain, crepitation on PROM
- Imaging shows advanced degenerative joint disease

Case Report

- Pain medicine Rx, needle Rx, and rehab Rx fully developed
  - Overall function improves but his right foreleg use remains somewhat limited
  - He wags his tail and acts energetic when his family returns from being away
  - Great appetite
Treatment Options

- Amputation?
- Euthanasia?

Case Report

- MacKenzie - 11 yo m/n Labrador Retriever
  - CCL Sx @ 5 & 10, thyroid adenocat @ 9
  - Daily NSAID + reuptake inhibitor
  - July 4th - acute crisis
  - Owners were thinking this was his time and it wasn’t a good time at all
  - Marked stifle pain, muscle pain, normal CP
Case Report

- Medication adjustments & additions
  - Reuptake inhibitor increased
  - NMDA antagonist added
  - Calcium channel blocker added
- Day 2 – better attitude, can walk 20 ft
- Day 6 – 50% improvement
- Day 17 – static

Case Report

- Radiographs – mild spinal changes, bilateral stifle DJD
- Increased calcium channel blocker, added Adequan, added PRT twice weekly
- 6 weeks later much better mobility, bringing owner ball, no problems on stairs
- Lost to GDV event 17 months after crisis

Learning Objectives

Understand the basic issues associated with bone cancer pain management.
Greg Ogilvie

• “All cancers are painful. Some more than others. Patient comfort anticipating pain, as you advocate, is paramount.”

Family Loss

• Grief normally ebbs 6 months after loss
• Grief persisted longer when death occurred within 6 months of a terminal diagnosis
• Less acceptance of death at 12 to 24 months
• Prolonged grief disorder

Canine Bone Cancer Facts

• 90% have pulmonary mets by the time you diagnose the disease
• Mets are only detectable in about 10% of the cases that do have mets
• Amputation does not reduce the frequency of metastatic disease
• Amputation has the potential to accelerate metastatic disease
Canine Bone Cancer Dogma

- Median survival with pain medications alone is only 1 - 2 months
- Median survival with radiation therapy alone is 2 to 4 months
- Median survival with amputation alone is 2.5 to 5 months
  - 10% alive at 1 year
  - 2% alive at 2 years

Canine Bone Cancer Dogma

- Median survival with amputation followed by chemo is 8 to 12 months
  - 40% are alive at 1 year
  - 20% are alive at 2 years
- Median survival with effective multimodal pain therapy coupled with chemotherapy?

Amputation or Euthanasia?
Arguments For Amputation

- Chance of cure
- You’re the 1 in 10 dog
- You’re a cat
- Complete disuse & perception that leg is inhibiting patient
- Unrelenting pain
- Pathologic fractures??

Arguments Against Amputation

- Cost (surgery + chemotherapy)
- General surgical complications
- Risk of CPSP, phantom pain
- Loss of metastatic suppression
- Angiostatin & endostatin
- Inability to function as a tripod

Angiostatin & Endostatin

- In cancer patients, dormant micrometastases are often asymptomatic and clinically undetectable, for months or years
- The metastases exhibited rapid growth when the inhibition of angiogenesis was removed
Angiostatin & Endostatin

- angiostatin fragments are present in urine of dogs with bone cancer…
- Importantly, these fragments were absent in urine collected from the same dogs after complete surgical removal of the primary tumor

Cancer Pain

- Cancer pain similar to neuropathic pain
- It’s never “just” cancer pain
- Check all muscles & joints
- Address all of the problems that you can

Cancer Pain Therapy

- Practical inpatient therapies
  - CRIs
  - Epidurals
    - Opioid +/- local anesthetic
    - Bisphosphonates
      - Pamidronate (90 mg $37)
Cancer Pain Therapy

- Pamidronate dose
  - Dogs - 1 to 2 mg/kg q 3 to 4 weeks
  - Cats - 1 to 1.5 mg/kg q 3 to 4 weeks
  - Dilute in 0.9% saline
    - Dogs - 250 ml over 2 hours
    - Cats - 50 ml over 2 hours

- Pamidronate benefits
  - Decreased pain
  - Anti-cancer
  - Reduced stress fracture risk
  - Pamidronate risks
    - Renal

- Top choices
  - Reuptake inhibitors (TCAs, SNRIs)
    - Amitriptyline, duloxetine (Cymbalta)
  - Ca+ channel blockers
    - Gabapentin, pregabalin (Lyrica)
  - NMDA antagonists
    - Amantadine
Cancer Pain Therapy

- Top choices
  - NSAIDs vs Corticosteroids
  - Piroxicam vs COX-2 vs EP4

Matrix Metalloproteinases MMPs

- MMPs are able to digest the extracellular matrix which allows blood vessels to invade the area and support tumor growth
- Inhibition of this process is the target of several drugs

Tetracyclines & MMPs

- Reduces tumor burden in a mouse model of breast cancer-derived osteolytic bone metastasis.
- MMP inhibition
- A negative effect on osteoclasts
- MMP-inhibitors significantly reduced OSA cell invasion
Cancer Pain Therapy

- Medications I avoid
  - Opioids
    - May facilitate neoplastic growth
    - May cause immunosuppression
    - Opioid tolerance
    - Opioid induced hyperalgesia
    - Regulatory issues

Supportive Therapies

- Low carbohydrate diet
- DHA supplementation
  - 30 mg/kg vs 100 mg/m^2*
- Curcumin
- Melatonin
- Herbal therapies
  - Stasis Breaker
  - Wei Qi Booster
Curcumin

- Acts as a chemosensitizer
- Acts as a radiosensitizer
- Has been shown to protect normal organs such as liver, kidney, oral mucosa, and heart from chemotherapy and radiotherapy-induced toxicity

Bone Tumor Patient Therapy

- Injectable therapy
  - Pamidronate q 3 to 4 wks
  - Analgesic CRI
  - Epidurals

Bone Tumor Patient Therapy

- Oral therapy
  - Reuptake inhibitor
  - Amitriptyline/Duloxetine
  - Calcium channel blocker
  - Gabapentin/Pregabalin
  - NMDA antagonist
  - Amantadine
Bone Tumor Patient Therapy

- Oral therapy
  - NSAID
    - Galliprant/COX2
  - Microglia/MMP inhibitor
  - Doxy/Minocycline

Her-2/neu Vaccine

- Amputation w/chemo & vaccine
- The median survival time for the HER2 treated dogs was 956 days
- The median survival time of the historical control group was 423 day
Supportive Therapies

- Physical rehabilitation therapy
- Office based UWTM program is ideal
- HEP (Home Exercise Program)
- Home environment & supportive appliances
- Needle therapy

Gus

- 12 yo F/S Airedale
- Sustains a comminuted pathologic femoral fracture while on a leashed walk 7-4-16
- Pulmonary mass on chest radiographs
- Prognosis?
  - With surgery?
  - Without surgery?
Case Report

- Pain medicine Rx, pamidronate infusions, anti-cancer therapy fully developed
- Overall function improves but his right foreleg use remains somewhat limited
- He wags his tail and acts energetic when his family returns from being away
- Great appetite

Case Report

- “Walking better than he has in years, kicking both feet after defecating, hasn’t done that in a long time, lifts R rear”
- “Running better than owner”
Case Report

- Mocha – 9 ½ yo m/n Great Dane Mix
- Marked foreleg lameness
- Proximal humeral neoplastic disease
- Pamidronate, NSAID, reuptake inhibitor, NMDA antagonist, calcium channel blocker
- Cancer suppressant therapy

Thoughtful Suggestions

- It’s not “amputation or euthanasia”
- Make a careful assessment regarding their ability to function on 3 legs
- Consider multimodal pain therapy coupled with chemotherapy?
- Reserve amputation for unrelenting unbearable pain

Thoughtful Suggestions

- When performing amputations utilize:
  - Epidurals
  - Analgesic CRIs
  - Complete nerve blocks
  - Extended multimodal pain therapy
  - Anti-cancer supportive therapy
  - HEU harnesses and ramps
Multimodal Pain Medications

- Multimodal inpatient options for tough pain
  - CRLs*
  - Opioid/lidocaine/ketamine
  - Epidurals*
    - Opioid +/- local anesthetic
    - Pamidronate infusions for bone cancer

Quick Read

- Outpatient Oral Analgesics in Dogs & Cats
- Beyond Nonsteroidal Antiinflammatory Drugs: An Evidence-based Approach
  Butch KuKanich. VCNA; Sept 2013

NSAIDs

- Anti-inflammatory analgesics well suited to:
  - Acute inflammatory injury
  - Chronic joint pain
  - Bone cancer management (antiangiogenic)
  - Often combined with NMDA antagonists, Ca+ chnl/AEDs, opioids, reuptake inhibitors
NSAIDs

- Expense
  - Generic – low; Branded – high
- Dosing
  - Dose to lean body estimate if overweight
  - Avoid doses above recommended dosing
  - Titrate to lowest effective dose
    - Liquid product facilitates this process
  - Aim for minimal intermittent use

Galliprant

- Anti-inflammatory analgesic
- Appears to have a superior safety profile
  - Free from high level renal, hepatic, or serious GI related concerns
  - “Unlike COX-2 inhibitors, EP4 antagonists appear to reduce pain without prolonging inflammation”.

Lin et al. Journal of Pharmacology and Experimental Therapeutics December 2006, 319 (3) 1096-1103
Galliprant

- Median peak plasma concentrations
  - Fasted: 1,598 ng/mL
  - W/food: 614 ng/mL
- Median time of peak concentration:
  - Fasted: 1.0 hour
  - W/food: 3.0 hours


Galliprant

- Concentrations remained higher than the concentration estimated to be the minimal effective concentration required to control pain in dogs


Galliprant

- Use with corticosteroids?
- Use with significant pre-existing hepatic Dz?
- Use with significant pre-existing renal Dz?
  - EP4 agonist a potential renal Rx

Galliprant

• Use after fracture repairs?
• EP4 agonist promote bone healing
• Use with significant GI disease?
• EP4 agonist a potential Colitis/ IBD Rx


Galliprant & Feline Patients

• 3, 9, or 15 mg/kg, administered PO once daily for 28 days
• No significant effects identified on body weight, food consumption, clinicopathologic variables, or gross or histologic necropsy findings

Longterm Robenacoxib Use

• Administered orally to healthy young domestic short-hair cats at
  • 5 and 10 mg/kg once daily for 28 days
  • 2, 6 and 10 mg/kg twice daily for 42 days
  • Not associated with any detectable toxicity

Longterm Robenacoxib Use

• Robenacoxib was well tolerated when given daily for 1 month in cats with evidence of concurrent CKD
• There was no clinical indication of damage to the gastrointestinal tract, kidney or liver.

Longterm Meloxicam Use

• Median maintenance dose was 0.02 mg/kg/day (range 0.015-0.033 mg/kg/day).
• There was no difference in sequential serum creatinine concentration or USG measurements between the 'non-renal group' treated with meloxicam compared to control cats not treated with meloxicam.
Longterm Meloxicam Use

- There was less progression of renal disease in the 'renal group' treated with meloxicam compared to the age- and IRIS-matched cats with CKD not given meloxicam.

NSAIDs

- Cautionary information
  - Hepatic, renal, GI
    - Monitor chronic use closely
  - Not effective for neuropathic pain
  - Avoid use in close proximity to corticosteroid
  - Washout between NSAIDs

NSAIDs

- General thoughts
  - One may provide better relief than another
  - One may be better tolerated than another
  - Piroxicam may be the best choice for bone cancer patient management
  - NSAIDs are the first medication class I “vote off the island” when managing stable chronic pain
NMDA Antagonists

- Desensitizing medications that turn down the pain “volume”
- No meaningful compatibility issues
- Expense - moderately high
- Amantadine dosing
  - 3 to 5 mg/kg PO SID to BID
  - Continually or 1 to 2 week pulsed therapy

NMDA Antagonists

- Cautionary information
  - Can cause GI effects (but not harm)
  - Reduce dose if significant renal dysfunction is present
- General thoughts
  - A foundational chronic pain medication

Ca\(^+\) Channel Blocking AEDs

- Broadly capable analgesics especially well suited to neuropathic/cancer pain
- No meaningful compatibility issues
- Expense
  - Gabapentin – low
  - Pregabalin – mod high
Ca\textsuperscript{2+} Channel Blocking AEDs

• Dosing
  • Gabapentin (nonlinear pharmacokinetics)
    • 10 to 200 mg/kg/day
      • Divided BID to TID
        • Asymmetric dosing may help with sedation and somnolence

• Pregabalin (linear pharmacokinetics)
  • 2 to 15 mg/kg/day
    • Divided BID to TID
      • Asymmetric dosing may help with sedation and somnolence

• May be able to gradually reduce to SID dosing if doing well after extended therapy
Ca\textsuperscript{2+} Channel Blocking AEDs

- Cautionary information
- Use of the gabapentin liquid not recommended
- Use the Amneal product
- Initial drowsiness for few days
- Eventually more "normal" on mu opioids as a rule

Ca\textsuperscript{2+} Channel Blocking AEDs

- Renal excretion
  - Reduce dose if significant renal impairment
- Do not stop abruptly
  - Withdraw gradually to avoid rebound pain

Ca\textsuperscript{2+} Channel Blocking AEDs

- General thoughts
  - One of the most easily administered long term feline pain medication
Reuptake Inhibitors

- Broadly capable analgesics - especially well suited to neuropathic/cancer/chemo pain
  - TCAs, SNRIs, tramadol
- Often combined with NSAIDs, NMDA antagonists, Ca* channel blockers/AEDs, opioids
- Expense
  - TCA generics – mod low
  - SNRI generics – mod low

Reuptake Inhibitors

- SNRIs – Duloxetine
  - Approved for human OA, muscle pain, and neuropathies
  - Canine toxicity studies
    - 3, 10, & 30 mg/kg daily for 12 months
    - 100 mg/kg acute dosing
Reuptake Inhibitors

• Dosing
  • TCAs - Amitriptyline, doxepin
    • 0.25 to 4 mg/kg PO BID
  • SNRI – Duloxetine
    • 0.25 to 1.0 mg/kg PO BID to TID

• Cautionary information
  • Do not combine with SSRIs, MAO inhibitors, and tramadol

Reuptake Inhibitors

• Cautionary information
  • Generally good safety margins at analgesic doses
  • Concerns regarding use/dose if Hx of seizures or hepatic dysfunction

Reuptake Inhibitors

• General thoughts
  • Reuptake inhibitors have fascinating properties beyond descending inhibition
    • Microglial cell inhibition
    • NMDA antagonism
    • Na channel blocker
    • Anti-inflammatory
Tramadol

- Species specific analgesic action
- Reuptake inhibition +/- mu agonist
- Often combined with NSAIDs, NMDA antagonists, Ca2+ chnl/AEDs, opioids
- Dose
  - Dogs: 3 to 5 mg/kg 4 to 6 times daily
  - 1 to 2 mg/kg BID does NOT cut it
  - Cats: 1 to 2 mg/kg BID in gel caps

Tramadol

- Cautionary information
  - Do not use with other reuptake inhibitors
  - Reduce dose if hepatic/renal concerns
  - Use cautiously if seizure patient

Tramadol

- General thoughts
  - Dosing frequency and bitter taste limit our use of tramadol
Opioids

- Less well suited to chronic pain therapy
- Buprenorphine
  - Transmucosal, SR preps
- Tramadol (cats)
- Oral opioids?
- Fentanyl patch?

Opioids

- Buprenorphine (never PO)
  - TM - Cats
    - 0.020 mg/kg TM BID to TID
  - Sustained release
    - Dogs - 0.05 to 0.1 mg/kg SQ q 72 hrs
    - Cats
      - Zoopharm - 0.12 mg/kg SQ q 72 hrs
      - Simbadol - 0.24 mg/kg SQ q 24 hrs

Oral Opioids

- Pharmacokinetic studies examining codeine, morphine, methadone, butorphanol, and oxycodone indicate that they are unlikely effective.
Oral Opioids

- Codeine may be more useful than we thought
- Codeine-6-glucuronide (C6G) may be produced in effective amounts in some dogs
- Hydrocodone may be effective in dogs

Opioids

- Simply less well suited to chronic pain therapy
  - Opioid tolerance
  - Opioid induced hyperalgesia (OIH)
  - Diversion
  - Constipation
  - May promote angiogenesis, cell proliferation, immunosuppression, and metastasis
Microglial Cell Inhibitors

• One of the major contributors to central sensitization and the chronification of pain are the microglia.
• Minocycline is a known microglial cell inhibitor.
• We add minocycline to the management of some of the tougher pain patients
• Dose: 5 to 20 mg/kg BID.

Microgliosis

• there is a potential role of glial cells in the central sensitization associated with OA, which may provide a novel analgesic target for the treatment of OA pain.

Microgliosis

• gabapentin with minocycline produced synergistic interaction in (pain test models).
• the combination provide a therapeutic alternative that could be used for human neuropathic pain management.
Acetaminophen
- Dogs only
- Analgesic only
- Dose
  - 10 to 15 mg/kg PO BID to TID for 5 days
    - Then up to 10 mg/kg PO TID if beneficial

Mexiletine
- Sodium channel blocker
  - “Oral lidocaine”
- Dogs only
  - 4 to 8 mg/kg PO TID w/food

NK1 Antagonist
- Cerenia 1 mg/kg
  - MAC reduction similar to 4 mg/kg carprofen during electrical stim study
  - Similar to 0.5 mg/kg morphine as premed for OHE surgery
  - Long-term oral dosing unclear
    - P450 saturation/prolonged 1/2-life
NK1 Antagonist

- Drug interactions
- CYP-450 enzyme
- Highly bound to plasma proteins
- NSAIDs, phenobarbital, xxxxconazoles
- Cost is a challenge

JAK1 Inhibitors

- Apoquel – broad cytokine/IL role
- Antipruritic & Anti-inflammatory roles
- No known drug interactions
- Inadequate understanding of dosing for OA
- Apoquel vs Corticosteroids

Monoclonal Antibodies (mAbs)

- NV-01 & NV-02 are mAbs that inhibit the activity of nerve growth factor (NGF)
- Antibodies against NGF are analgesic in rodent models and in humans with DJD
- No side effects were noted
- The magnitude of the effect appeared identical to that expected with an NSAID
Monoclonal Antibodies (mAbs)

- Results of this study suggested the evaluated anti-NGF mAb decreased (pain) scores for 4 weeks after administration.
- This treatment may be effective for alleviation of signs of pain in dogs with osteoarthritis for up to 4 weeks.

NV-01 & NV-02 mAbs

- For NV-01, our therapy in development for controlling canine osteoarthritis pain, we’re targeting a late 2018/early 2019 market launch.
- For NV-02, our equivalent therapy for cats, we’re targeting a market launch shortly thereafter.

Cannabinoids

Marijuana Legal Status Map
• Please give me a week to recover from my travels!
• Make sure “Milwaukee” is in the subject line
• Resend 7 to 10 days later if I don’t respond right away