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CHRONIC PAIN: NEW THOUGHTS & INTERVENTIONAL TREATMENTS

PAIN PATHOPHYSIOLOGY, WHERE/HOW TO INTERVENE, CASE EXAMPLES

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- ▶ Pain assessment and treatment difficulties in veterinary patients
- ▶ Interventional Pain Management (IPM)
 - ▶ What is it?
 - ▶ History of IPM in human medicine and surgery
- ▶ Pathophysiology of pain
 - ▶ Windows of opportunity for IPM
- ▶ Case examples

OUTLINE OF TODAY'S PRESENTATION

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- ▶ Veterinary patient pain
- ▶ Why so difficult?
 - ▶ to diagnose?
 - ▶ and
 - ▶ to treat?

"Because owners may be unaware of or underestimate the presence of chronic pain, client staff education and owner engagement are critical to identification and treatment."
2022 AAHA Pain guidelines

....BUT SO NECESSARY TO ADDRESS

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- ▶ Owner and veterinary staff non education regarding pain
- ▶ Evolutionary suppression of overt pain "behaviors" in domestic species
- ▶ Assumption that medical and surgical procedures "fix" the patient
- ▶ Objective diagnosis of "veterinary patient pain" is difficult if not impossible
- ▶ Species, gender, breed, individual variations

DIFFICULTY OF CHRONIC PAIN DIAGNOSIS

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- ▶ Evolutionary suppression of pain
- ▶ Owner and veterinary staff non education regarding pain
- ▶ Assumption that medical and surgical procedures "fix" the patient
- ▶ Objective outcomes difficult
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DIFFICULTY OF CHRONIC PAIN DIAGNOSIS

DO PAINFUL SENSATIONS AND FEAR EXIST IN FISH? Smeets et al 2013

Group	Control - Analgesic	Control + Analgesic	Acid - Analgesic	Acid + Analgesic
Unimmobilized	~1.0	~1.0	~1.0	~1.0
Immobilized	~1.0	~1.0	~1.0	~1.0

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- ▶ Evolutionary suppression of pain
- ▶ Owner non education
- ▶ Assumption that medical and surgical procedures "fix" the patient
- ▶ Objective outcomes difficult
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- ▶ Specialty distraction
 - ▶ Leads to colunmal medicine
 - ▶ Global QOL picture is lost
 - ▶ Objectiveness not yet cost effective, validated, accessible
 - ▶ Diagnostics though improved still not "cage-side"
 - ▶ Non-linearity of pain not well established
 - ▶ Fear of Medical and surgical "fix" failure

"CURRENT" DIFFICULTY OF CHRONIC PAIN DIAGNOSIS

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- ▶ Anamnesis
 - ▶ Requires understanding of daily life of pet, role, family
 - ▶ TIME commitment during exam
 - ▶ Importance of critical owner questions
 - ▶ client specific outcome measures, functional questioning
- ▶ "Normal" behavior knowledge
- ▶ Sensitive physical exam techniques
- ▶ Diagnostic imaging advances
- ▶ Activity monitors, gait analysis, force plate data dependent on source of pain
- ▶ Importance of multidisciplinary team

DOES THE PATIENT HURT???

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PREVALENCE OF CHRONIC PAIN IN SMALL ANIMAL VETERINARY PATIENTS

- ▶ Muir W et al. 2004. Prevalence and characteristics of pain in dogs and cats examined as outpatients at a veterinary teaching hospital
 - ▶ 231 (20%) dogs and 92 (14%) cats had evidence of pain which could be categorized as "chronic" or "acute on chronic"
- ▶ Gruen ME et al. 2022. AAHA Pain Management Guidelines for Dogs and Cats
 - ▶ Chronic pain is ubiquitous in companion animals, most commonly as the result of OA, whose reported prevalence appears to be close to 40% in dogs and >50% in cats

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ROUSSEAU-BLASSÉ ET AL., 2020. PREVALENCE AND MANAGEMENT OF PAIN IN DOGS IN THE EMERGENCY SERVICE OF A VETERINARY TEACHING HOSPITAL

- ▶ **Chronicity of pain**
- ▶ Common reason for "acute" presentation
- ▶ not a "time" modality
- ▶ but instead from upregulation of some aspect of pathway
- ▶ Inappropriate initial treatment
- ▶ Ineffective overall treatment
- ▶ Ongoing medical or surgical disease

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OVERLAP BETWEEN PAIN AND DISEASE MARKEDLY HIGH

MARINO CL ET AL 2014

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CHRONIC PAIN ENCOURAGES ORGAN FAILURE

Pain and the stress response. From Handbook of Veterinary Pain Management, Gaynor & Muir, 1st ed.

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- ▶ Pain is
 - ▶ A Construct
 - ▶ A Multidimensional experience
 - ▶ A Uniquely individual experience
- ▶ Pathophysiology may be reversely correlated with "healing"
- ▶ Initial pathophysiology may respond to drugs
 - ▶ Ongoing pathology not as responsive
- ▶ Treating other dimensions requires "out of box thinking"

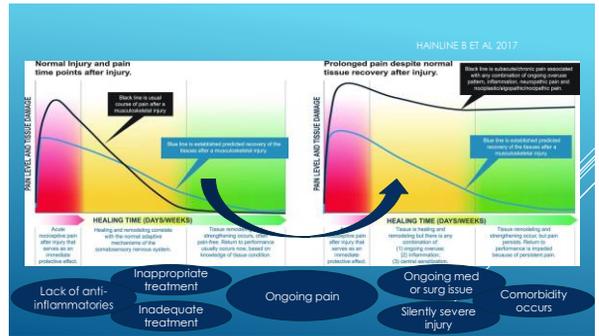
WHY CHRONIC PAIN IS DIFFICULT TO TREAT

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- ▶ “Transecting” a nerve will not only **NOT** alleviate pain
 - ▶ But **may also increase pain substantially**
- ▶ Daily examples of pain non linearity
 - Phantom pain post amputation
 - Increased pain with chronic opioid administration
 - Painful mobility of pets with radiographically “adequate” joints
 - Non painful mobility of pets with severe radiographic degeneration
 - Gentle touch triggering excruciating pain in “healed” surgical sites
 - Devastating wounds don’t always cause immediate pain

PAIN IS NOT LINEAR OR “HARD WIRED”

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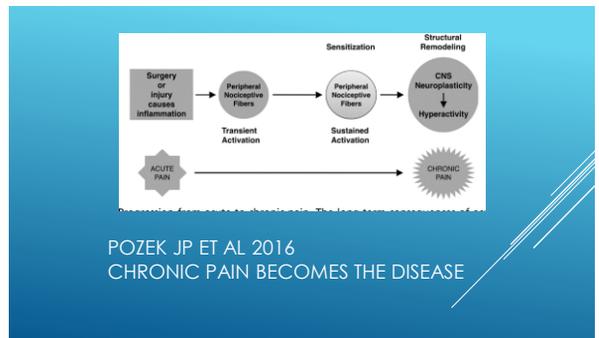
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Term	Bonick, 1952 ¹	Bonick, 1999 ²	Raffell, 1993 ³	Coslin, 1999 ⁴	Stallal and Coslin, 2004 ⁵	Nix and Dever, 2004 ⁶	Melback, 2005 ⁷	Coslin, 2007 ⁸	Tracey and Bushnell, 2007 ⁹	Dubois et al., 2009 ¹⁰
Pathologic pain	Pain arising from the physiologic system	Chronic pain that persists beyond the usual healing course of an acute injury or disease, or the pain recurring at intervals for months or years	Pain as a disease	Chronic pain	Persistent pain	Persistent pain	Chronic pain	Persistent pain	Chronic pain	Myalgia
Hypothesis			Dysfunction of the endogenous nociceptive system	Persistent pain causing physical effects involving the nervous system	Persistent pain expressing a specific physiopathologic constellation of symptoms	Association disease with som symptoms and a specific tissue physiopathologic	The source of the body self neuroimmune activating psychologic, hormonal, and behavioral programs alter injury, pathologic, or chronic stress	A self-perpetuating condition which may be due to biologic, psychologic, and environmental factors	A condition characterized by a nervous system changes in the nervous system	A neurologic condition characterized by pathologic changes in the nervous system
Evidences	Hypothesis grounded on clinical evidences	Clinical evidences	Hypothesis grounded on a theoretical idea and clinical evidences	Clinical cases and experimental studies	Literature review	Clinical and experimental evidences	Experimental and clinical evidences	Literature review	Literature review	Literature review

Pozek JP et al 2016

CHRONIC PAIN BECOMES THE DISEASE

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CURRENT OPTIONS FOR CHRONIC PAIN TREATMENT

- ▶ Oral
 - ▶ NSAIDs and Steroids
 - ▶ Gabapentinoids
 - ▶ Opioids
- ▶ Supplements
- ▶ PSGAGs
- ▶ Rehabilitative techniques and modalities
- ▶ Complementary medicine
- ▶ Anti nerve growth factor monoclonal antibody injections

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- ▶ Complementary medicine
- ▶ **INTERVENTIONAL PAIN MANAGEMENT techniques**

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INTERVENTIONAL PAIN MANAGEMENT (IPM): WHAT IS IT ?

- A comprehensive approach to analgesia
- Involves performing minimally invasive procedures
- To modify pain
- "neuromodulatory"
 - To treat chronic pain
 - To diagnose chronic forms of pain
 - To prognosticate

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INTERVENTIONAL PAIN MANAGEMENT TECHNIQUES

- Epidural injections
- Peripheral nerve blocks
- Intra and periaricular infiltrations
- "Soft tissue" injection
- Peripheral nerve and spinal stimulation
- Toxin application
- Radiofrequency modulation
- Cryoanalgesia
- Acupuncture and acupuncture injections
- Infusion therapies
 - Systemic and local

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"NEUROLYTIC PROCEDURES"

- Chemical neurolytic:
 - Phenol
 - Glycerol
 - alcohol
- Surgical neurectomy

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ISSUES WITH NEURODESTRUCTIVE INTERVENTIONS

- Nerve regrowth with pain recurrence
- Spontaneous nerve firing (glycerol)
- Prolonged motor palsy
- Autonomic (ex: Bowel or bladder) dysfunction
- Permanence

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Away from destruction of nerves Towards "changing" nerve signaling

NEURODESTRUCTIVE TO NEUROMODULATORY

KNORROVA H ET AL 2021

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NOCICEPTION

Ivalos IH et al 2019

- Transduction
- Transmission
- Modulation
- Projection
- Perception

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▶ Thermal
 ▶ Mechanical
 ▶ Chemical

- TRPV
- TRPM8
- K2P
- ASIC
- Piezo
- VoltGNa
- TRPA1
- TRKA

- Influx of Na or Ca
- Increase in IC Ca
- Reduction in potassium flow

MECHANISMS OF TRANSDUCTION & TRANSMISSION

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The later stages of inflammation have been shown to have an increased role for peripheral opioid antinociception

Peripheral opioids and alpha two agents prevent vesicular release of noradrenaline and substance P.

Opioid placement peripherally does not have the adverse effects of systemic opioid analgesia

Use of peripherally acting opioid agonists for the prolonged treatment of inflammatory pain has **not** been shown to induce tolerance

*Labuz et al 2006, van Ingen et al 2010, Zollner et al 2008

PERIPHERAL NOCICEPTOR BASED ANALGESIA

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▶ Propagation of action potential
 ▶ Na and K voltage gated channels

Inflammatory mediators

▶ Relay into dendrites and out of axon (nerve terminal release)
 ▶ Ca voltage gated channels

TRANSMISSION

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▶ Opioid reduction (Marolf V et al 2021)
 ▶ MAC reduction (Synder CJ et al 2013)
 ▶ Post op QOL (Caniglia A et al 2012)
 ▶ Return to function (Campoy L et al 2013)

THE EFFECTIVENESS OF PERIPHERAL NERVE BLOCKS (TARGETING THE NA CHANNELS)

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The dorsal horn cells have different "modes" of operation based on the balance of:

*Sensory input

*Interneuron "gate" control

AND

**"higher center" (descending) control

vs

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- Mode 1: normal pain input
 - Depolarization of peripheral neurons causes normal Excitatory transmitter release in dorsal horn
 - Output of dorsal horn interneurons is proportional to stimulus received
- Mode 2: normal pain suppression
 - Output of the dorsal horn interneurons is partially inhibited by
 - A beta fiber activity slowing C fiber activity
 - Descending pathways suppress or slow transmission
 - Medications which modify incoming A fiber signals and interneurons in the dorsal horn

Dorsal horn normal function modes

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- Mode III: normal input, enhanced output
 - Consistent activity in peripheral nerve fibers results in
 - Substance P dumping
 - Phosphorylation
 - Voltage gated Na and Ca channel opening
 - Calcium influx
 - Excessive gene induction and expression
- Mode IV: subnormal input, grossly enhanced output
 - Sprouting processes
 - Activation of glial cells
 - Cell death of overexcited inhibitory neurons

Dorsal horn pathological function modes

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Dorsal horn "modes"

Mode 1 - Normal

Mode 2 - Suppressed

Mode 3 - Sensitized

Mode 4 - Reorganized

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Chronic pain's new definition

- Chronic pain results when the Dorsal horn cannot "return" to "normal function" modes I and II
- Chronic pain is the result of the body's inability to restore its physiological functions to normal or pre-pain homeostasis levels

Loeser & Melzack 1999

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Diagnosics

- ▶ Radiology
- ▶ Needle scope
- ▶ Ultrasound
- ▶ CT
- ▶ Thermal imaging
- ▶ Sensory mapping
- ▶ Pain biotrace
- ▶ Activity monitor
- ▶ Meridian mapping

Treatment

- ▶ Echolocation
- ▶ Neurostim location
- ▶ Fluoroscopy
- ▶ CT
- ▶ +/- MRI

MODALITIES WHICH HAVE AIDED SUCCESS OF IPM

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- ▶ Osteoarthritis
- ▶ Degenerative disc disease
- ▶ Acral lick granuloma
- ▶ Spinal pain
- ▶ Post fracture or osteotomy pain
- ▶ Lumbosacral disease
- ▶ Cancer
- ▶ Chronic pancreatitis
- ▶ Chest pain
- ▶ Glaucoma
- ▶ Dental disease

DIFFICULT PAIN ISSUES: CHALLENGES WITHIN SMALL ANIMAL MEDICINE

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- ▶ Ropivacaine 0.5%
- ▶ Lidocaine 2%
 - ▶ 3 day duration improved attitude
- ▶ Ropivacaine 0.5%
- ▶ Methylpred acetate 0.5mg/kg
- ▶ Buprenorphine 1mcg/kg
 - ▶ 16 day duration improvement
- ▶ Owners elect to enucleate

Retrolubar and peribulbar regional techniques in cats: a preliminary study in cadavers

Yusef Shiba-Benjamin*, Peter J. Pincus*, David J. Mapp*, Philip H. Kass* & Erik B. Whisen*

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- ▶ 3 month history of "odd gait", "bunny hopping"
- ▶ Worse on RH
- ▶ Rads obtained
- ▶ Owners desire non surgical approach
- ▶ Nonsteroidal anti-inflammatories irritate GI



ANGEL 1.2 YEAR M MALINOIS

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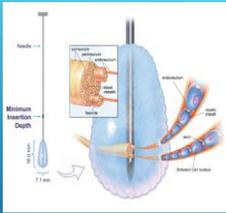
Initial reduction in inflammation

- ▶ Arthrocentesis
- ▶ Lidocaine/dexamethasone injections
 - ▶ +/- sterile amica
- ▶ trigger points
- ▶ acupoints

Alves JC et al. 2018. Evaluation of the effect of mesotherapy in the management of back pain in police working dog

Schneider C. Traumeel - an emerging option to nonsteroidal anti-inflammatory drugs in the management of acute musculoskeletal injuries

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CRYOANALGESIA

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OTERO PE AND DA PORTELA EDS. MANUAL OF SMALL ANIMAL REGIONAL ANESTHESIA

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- ▶ Fabie M et al. 2013. A randomized controlled trial of the efficacy of autologous platelet therapy for the treatment of osteoarthritis in dogs
- ▶ Cuerdo B et al. 2020. Objective Comparison between Platelet Rich Plasma Alone and in Combination with Physical Therapy in Dogs with Osteoarthritis Caused by Hip Dysplasia
- ▶ Alves C et al. 2021. Platelet-rich plasma therapy in dogs with bilateral hip osteoarthritis



Continued anti-inflammatory and regenerative

- ▶ Intraarticular PRP
- ▶ Cryoanalgesia
- ▶ Physical rehab
 - ▶ Photobiomodulation
 - ▶ Therapeutic exercise
 - ▶ Core strengthening
 - ▶ Hip extension
 - ▶ Underwater treadmill
 - ▶ Therapeutic ultrasound

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- ▶ 11 mos later
 - ▶ Rare lameness
 - ▶ Active lifestyle
- ▶ Second IA platelet injection planned for end of summer
- ▶ Occasional acetaminophen dosing



ANGEL 1.2 YEAR M MALINOIS

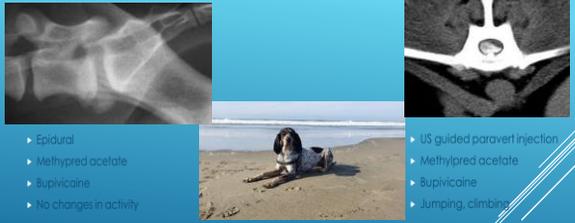
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Adako J et al. 2022

ULTRASONOGRAPHIC IMAGING PROTOCOL AND SONOANATOMY OF THE LUMBAR SPINE IN HEALTHY DOGS

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- ▶ Epidural
- ▶ Methylpred acetate
- ▶ Bupivacaine
- ▶ No changes in activity

- ▶ US guided paravert injection
- ▶ Methylpred acetate
- ▶ Bupivacaine
- ▶ Jumping, climbing

WOLF JL ET AL 2021. ULTRASOUND GUIDED PARAVERTEBRAL PERINEURAL CORTICOSTEROID INJECTION FOR SIGNS OF REFRACTORY CERVICAL PAIN ASSOCIATED WITH FORAMINAL INTERVERTEBRAL DISK PROTRUSION IN FOUR DOGS

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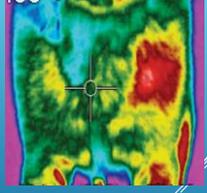


- ▶ 2 month duration LF lameness
- ▶ Worsens with exercise and in pm after rest
- ▶ Otherwise healthy
- ▶ Fails to respond to rest, exer modification and nsaid. adequan
- ▶ Protective/caution
- ▶ Treadmill running 3 X/week
- ▶ Pain on shoulder and elbow extension

APOLLO, 2 YEAR OLD MC PIT CROSS

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- ▶ Peritendinous injection:
 - ▶ 80% improvement in 3 days
- ▶ Home ex program
 - ▶ Side stepping up and down hill
 - ▶ wobble board balance
 - ▶ Enrichment feeding
 - ▶ Shake
 - ▶ Digging
 - ▶ Crawling
 - ▶ Reduced treadmill duration and distance for 1 month



21 DAY POST FRONTAL THERMOGRAPHY

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VELMA 8 YR FS DLH

- ▶ Denistry performed
- ▶ R cephalic IV catheter placed
- ▶ 2 weeks post began licking at site of catheter
- ▶ Otherwise healthy cat
- ▶ H/O FLUID early in life
- ▶ Owner moves from NYC to region

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- ▶ GP: antibiotics, cytopoint, apoquel, prednisone: non responsive
- ▶ Dermatologist:
 - ▶ Fungal culture negative
 - ▶ Bacterial C and S negative
 - ▶ Biopsy: lymphoplasmacytic funiculosis
 - ▶ Mycobacterial stain negative
- ▶ Non responsive to methylpred, dexamethasone, Gabapentin, amitriptyline, fluoxetine, amantadine, tramadol, buprenorphine, topical
- ▶ Bandage non responsive
- ▶ Life in E Collar

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- ▶ Radial nerve blockade
- ▶ Distal brachium
 - ▶ Lidocaine
 - ▶ Bupivacaine
 - ▶ Dexamethasone
- ▶ 1 month non focus



GOODARD L. 2012

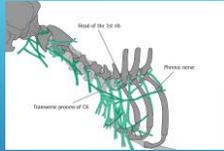


OFERO PE ET AL. 2021

PALLIATIVE LOCOREGIONAL BLOCKADE

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- ▶ Proximal Paracervical brachial plexus blockade
 - ▶ Bupivacaine
 - ▶ Buprenorphine
 - ▶ Midazolam
 - ▶ Methylprednisolone acetate
 - ▶ Sarapin
- ▶ No return to lesion for 8 months



Head of the 1st rib
Plexus nerve
Transverse process of C1

Sarapin/P Bloc: An injectable source of the volatile salts of Pitcher Plant (Sarraceniaceae) with 0.75% w/v Benzyl Alcohol as a preservative.

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- ▶ Pehora C et al. 2017. Dexamethasone as an adjuvant to peripheral nerve block
- ▶ Edinoff AN et al. 2021. Adjuvant Drugs for Peripheral Nerve Blocks: The Role of Alpha-2 Agonists, Dexamethasone, Midazolam, and Non-steroidal Anti-inflammatory Drugs
- ▶ Prabhakar A et al. 2019. Adjuvants in clinical regional anesthesia practice: A comprehensive review
- ▶ Prasad GVK et al. 2020. Review of adjuvants to local anesthetics in peripheral nerve blocks: Current and future trends

PALLIATIVE LOCOREGIONAL SUBSTANCE EVIDENCE

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Local Anesthetic Peripheral Nerve Block Adjuvants for Prolongation of Analgesia: A Systematic Qualitative Review

Meghan A. Kirksey^{1,2}, Stephen C. Haskins^{1,2}, Jennifer Cheng¹, Spencer S. Liu^{1,2*}

Sixty one novel clinical trials and meta-analyses

analgesic duration data for the following adjuvants: buprenorphine (6), morphine (6), fentanyl (10), epinephrine (3), clonidine (7), dexmedetomidine (7), dexamethasone (7), tramadol (8), and magnesium (4)

perineural buprenorphine, clonidine, dexamethasone, dexmedetomidine, and magnesium most consistently demonstrated prolongation of peripheral nerve blocks

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<https://www.nysora.com/topics/pharmacology/analgesic-adjuvants-peripheral-nervous-system/>

TABLE 3. Best analgesic adjuvants in the peripheral nervous system by route of administration.

Route	Agent and Dose
Perineuronal/perineural	Dexamethasone 4–10 mg; buprenorphine 0.3 mg; clonidine 1–2 µg/kg; tramadol 200 mg
IVRA	Dexmedetomidine 0.5 µg/kg; magnesium 1.5 g
Intra-articular	Clonidine 150 µg; morphine 5 mg
Local infiltration	Ketamine 3 mg/mL

NYSORA

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- ▶ Palliative RUMM block q. 4 months for 11 months
 - ▶ Grade 3/5 to 1/5 (increased weightbearing) lameness
 - ▶ Reduction in gabapentin
- ▶ Month 11, severe lameness return
- ▶ Bier block performed
 - ▶ Lidocaine
 - ▶ Buprenorphine
 - ▶ Midazolam
 - ▶ Dexmedetomidine
- ▶ increased play, longer activity periods




NONAMI 6 YEAR OLD INTACT MASTIFF

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- ▶ Month 11, severe lameness return
- ▶ Bier block performed
 - ▶ Lidocaine
 - ▶ Buprenorphine
 - ▶ Midazolam
 - ▶ Dexmedetomidine
- ▶ Increased play, longer activity periods

Wallo A 1999
KELMER G ET AL 2016 REGIONAL LIMB PERFUSION IN HORSES
EMANI SA ET AL 2021 BIER BLOCK AS A SUCCESSFUL MANAGEMENT OF A PATIENT WITH
INTRACTABLE COMPLEX REGIONAL PAIN SYNDROME (CRPS) TYPE 1: A CASE REPORT

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- ▶ 1 month prior T1 T2 DDL
- ▶ Lengthy "deroofing"
- ▶ Fluoro guided facet injection
 - ▶ Dexmedetomidine
 - ▶ Buprenorphine
 - ▶ Triamcinolone
- ▶ Removal of body brace
- ▶ Rest for one week
- ▶ Gentle neck excursions "heads of the shoulder"
- ▶ Enrichment feeding
- ▶ Oclal
 - ▶ Pregabalin
 - ▶ Clonidine
- ▶ No further painful episodes

FINN 5 YR MC FRENCHIE CROSS

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THANK YOU FOR YOUR ATTENTION

Questions, comments: Andrea.looney@amcny.org

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