RETHINKING OA AND PAIN MANAGEMENT IN VETERINARY MEDICINE

Conny Mosley

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Thank you

TRUE NORTH
VETERINARY DIAGNOSTICS

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Disclaimer

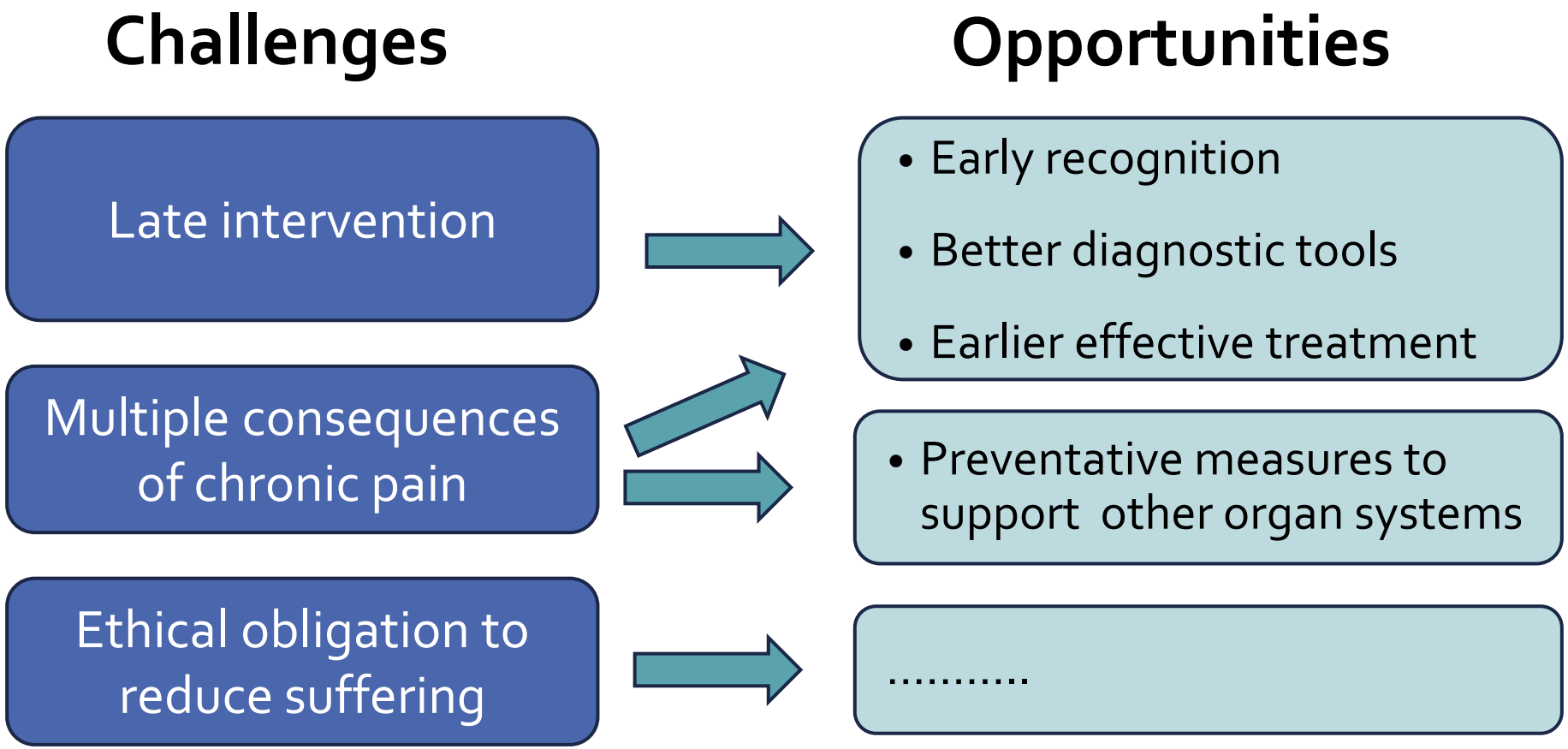
Veterinary Consultant for Pain & Internal Medicine for Elanco Canada

Director- Canadian Association of Veterinary Cannabinoid Medicine

Founding Member of Canadian One Health Pain Initiative

Agenda:

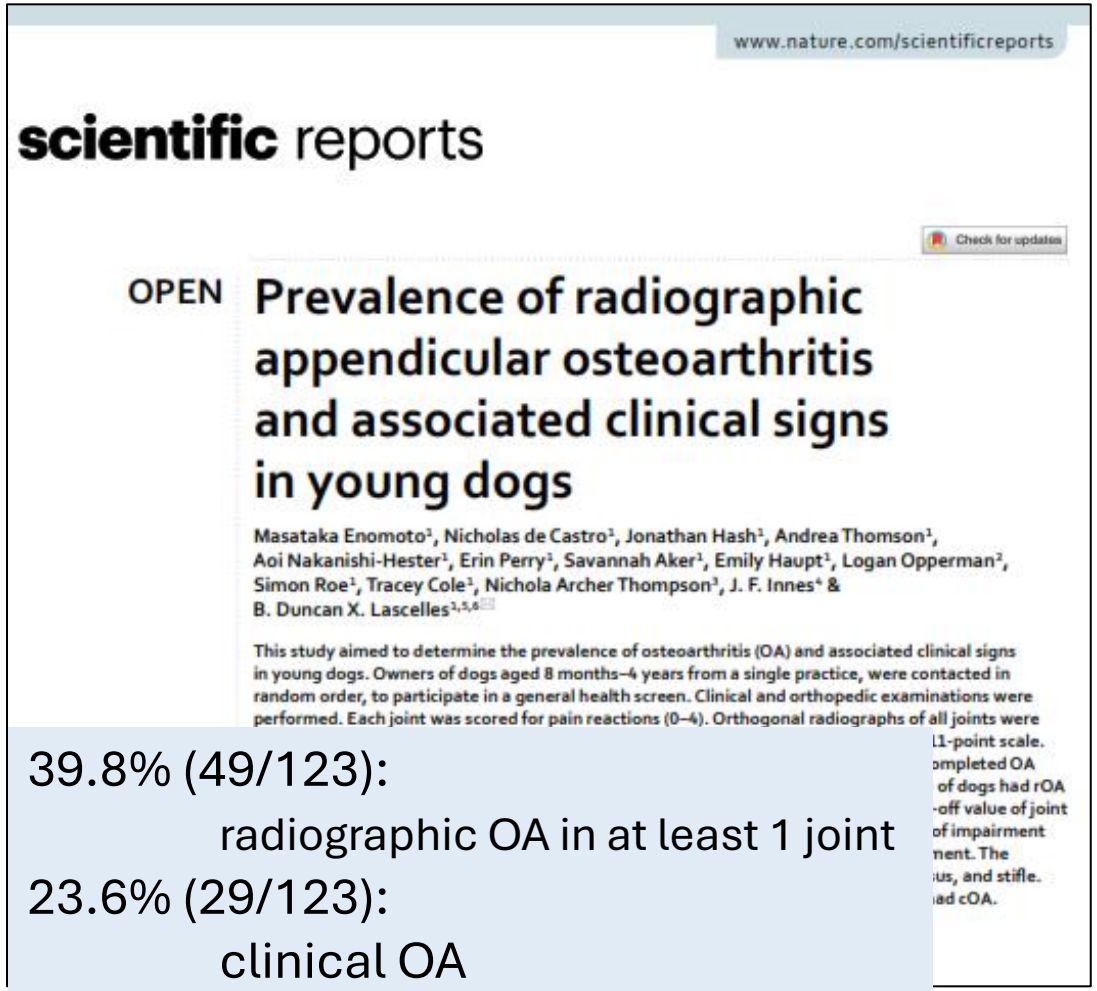
Current thoughts on State of Affair – Pain and OA



Current Situation

- High prevalence of orthopedic developmental disease in young dogs
- High prevalence of OA and pain in all age stages
- Lack of recognition of early signs of discomfort
- Reluctance of effective treatment or preventative measures
- Inability to reverse the disease progression

OA Prevalence



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Prevalence of radiographic appendicular osteoarthritis and associated clinical signs in young dogs

Masataka Enomoto[1], Nicholas de Castro[1], Jonathan Hash[1], Andrea Thomson[1], Aoi Nakanishi-Hester[1], Erin Perry[1], Savannah Aker[1], Emily Haupt[1], Logan Opperman[2], Simon Roe[1], Tracey Cole[1], Nichola Archer Thompson[3], J. F. Innes[4] & B. Duncan X. Lascelles[1,5,6]

This study aimed to determine the prevalence of osteoarthritis (OA) and associated clinical signs in young dogs. Owners of dogs aged 8 months–4 years from a single practice, were contacted in random order, to participate in a general health screen. Clinical and orthopedic examinations were performed. Each joint was scored for pain reactions (0–4). Orthogonal radiographs of all joints were

39.8% (49/123):
radiographic OA in at least 1 joint
23.6% (29/123):
clinical OA

BSAVA

ORIGINAL ARTICLE

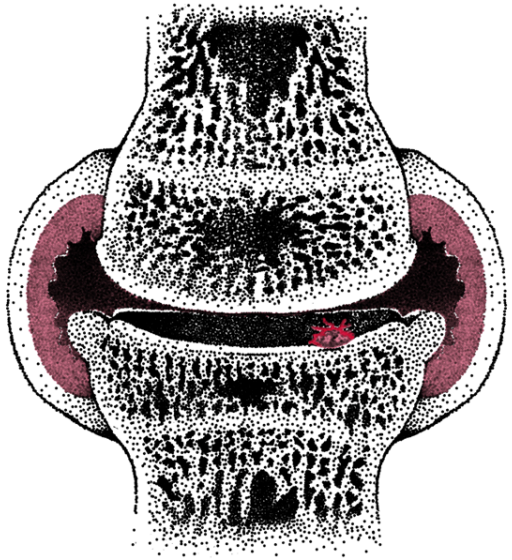
Identification of canine osteoarthritis using an owner-reported questionnaire and treatment monitoring using functional mobility tests

A. Wright[1,*], D. M. Amodie[*], N. Cernicchiaro[†], B. D. X. Lascelles[‡], A. M. Pavlock[§], C. Roberts[¶] and D. J. Bartram[*]

Key findings from this study revealed that client responses to the OA completed checklist assisted in identifying 188 (38%) previously undiagnosed cases of OA, confirmed by physical or radiographic examination, from 500 previously undiagnosed dogs attending non-acute healthcare visits, or specifically presented because of stiffness or lameness. The proposed checklist represented a starting point for discussion with owners and further veterinary investigation. We report prevalence (38%) at almost double that of previous, widely cited prevalence estimates of 20% for OA in the canine population (Johnston 1997). In addition, less than half (n=60, 47.2%) of the enrolled dogs presented for stiffness or lameness, irrespective of the fact that all enrolled dogs were previously undiagnosed cases of OA. This indicates that OA is considerably underdiagnosed in dogs, and far more prevalent in the canine population than previous estimates suggest, likely due to signs going unrecognised by owners and veterinarians.

Spotting the “off”

The Consequences of Chronic Pain



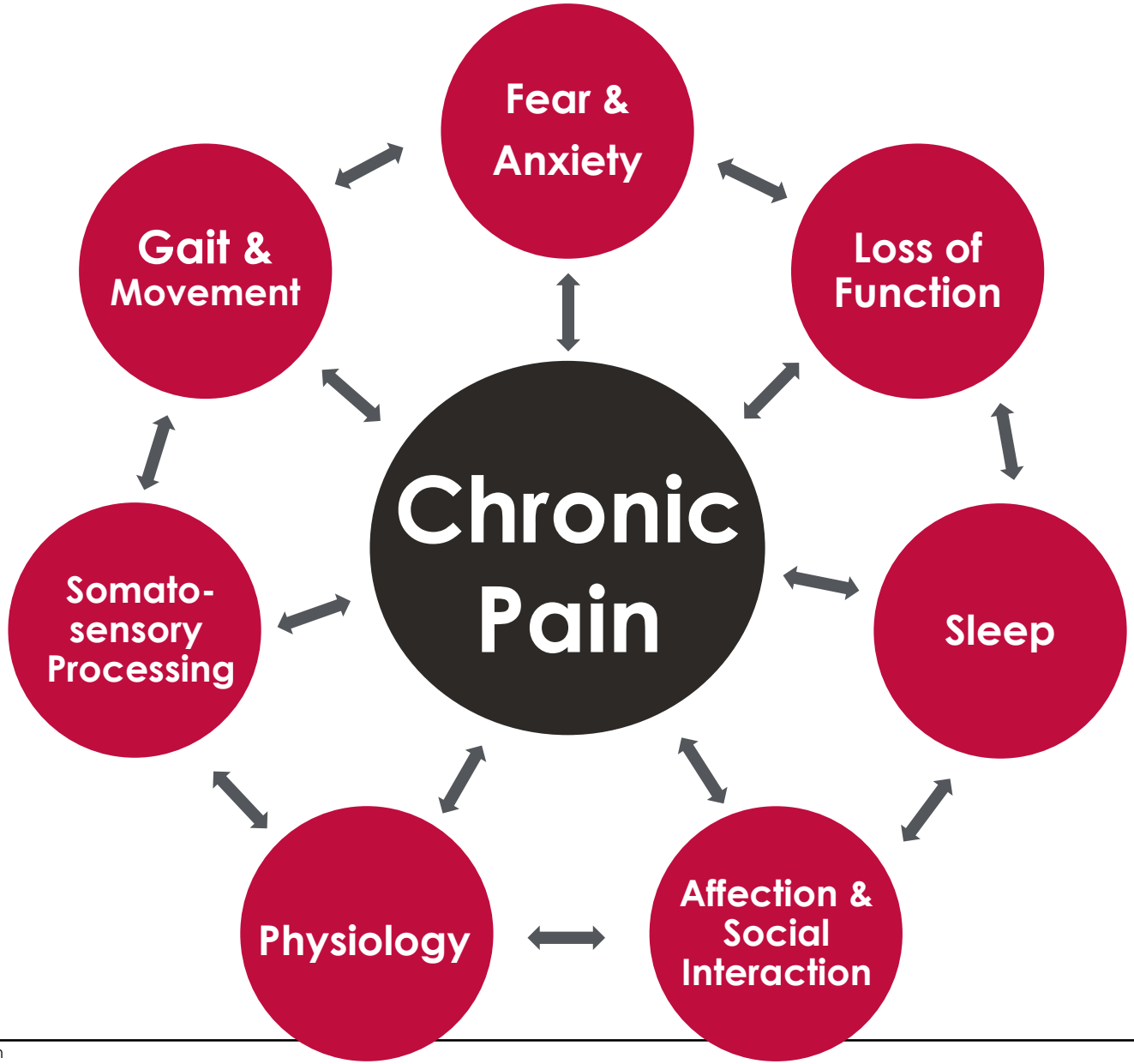
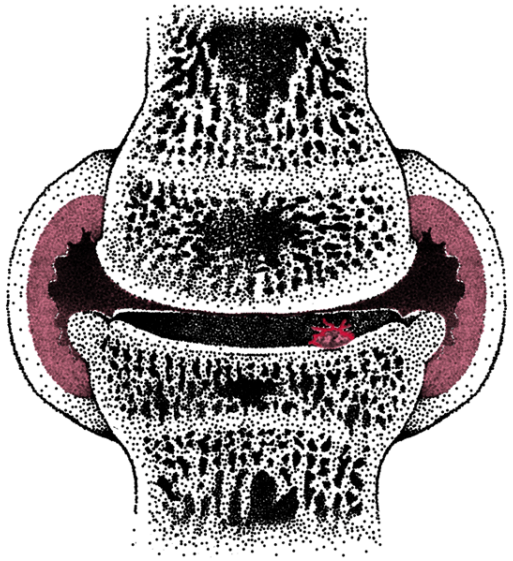
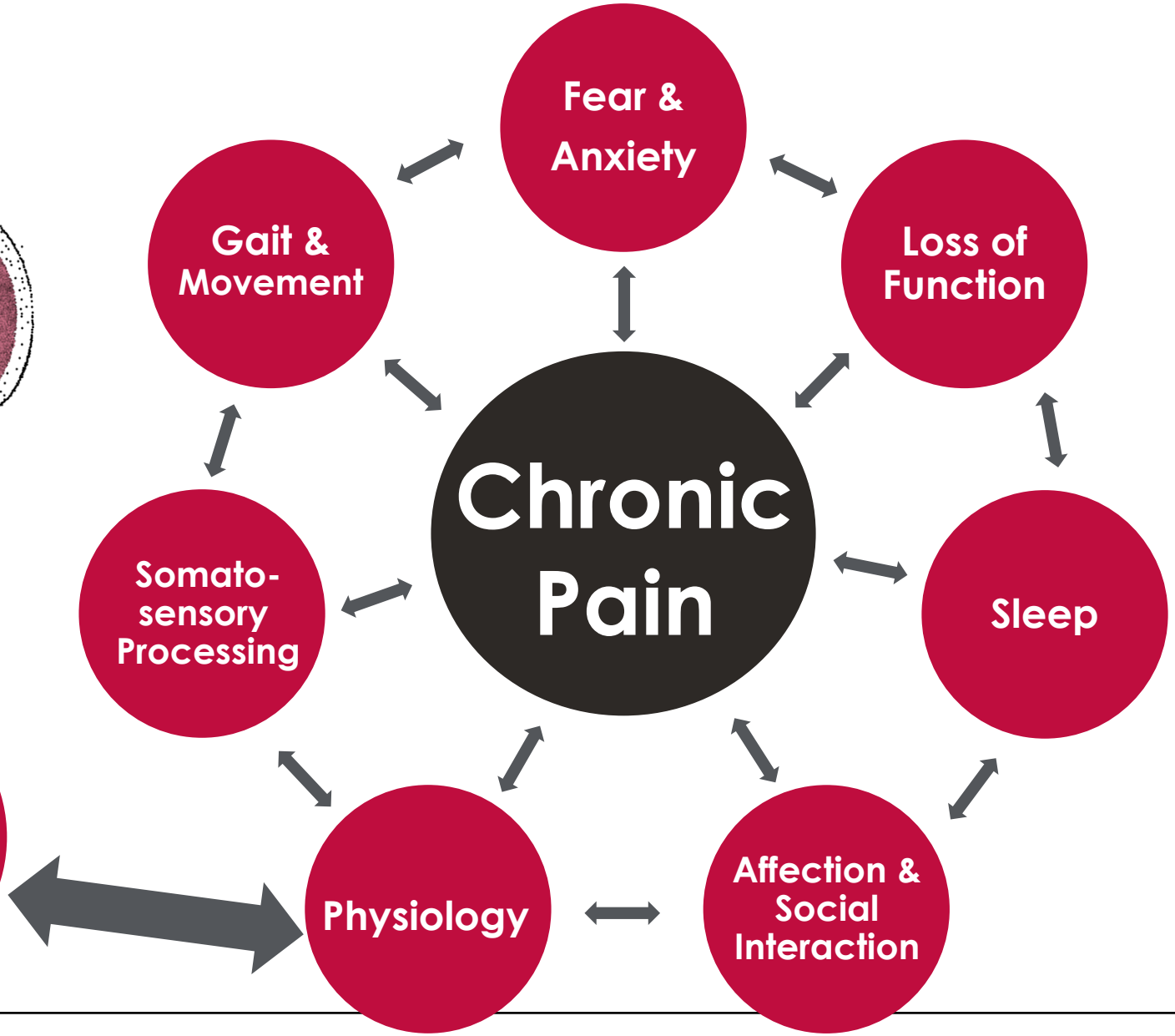


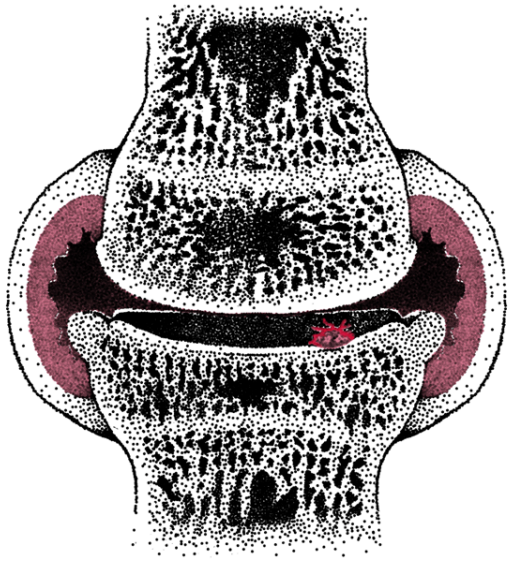
Image: Adapted from Enomoto, Lascelles and Capon

The Consequences of Chronic Pain





The Consequences of Chronic Pain



Fear & Anxiety

Gait & Movement

Loss of Function

Somato-sensory Processing

Chronic Pain

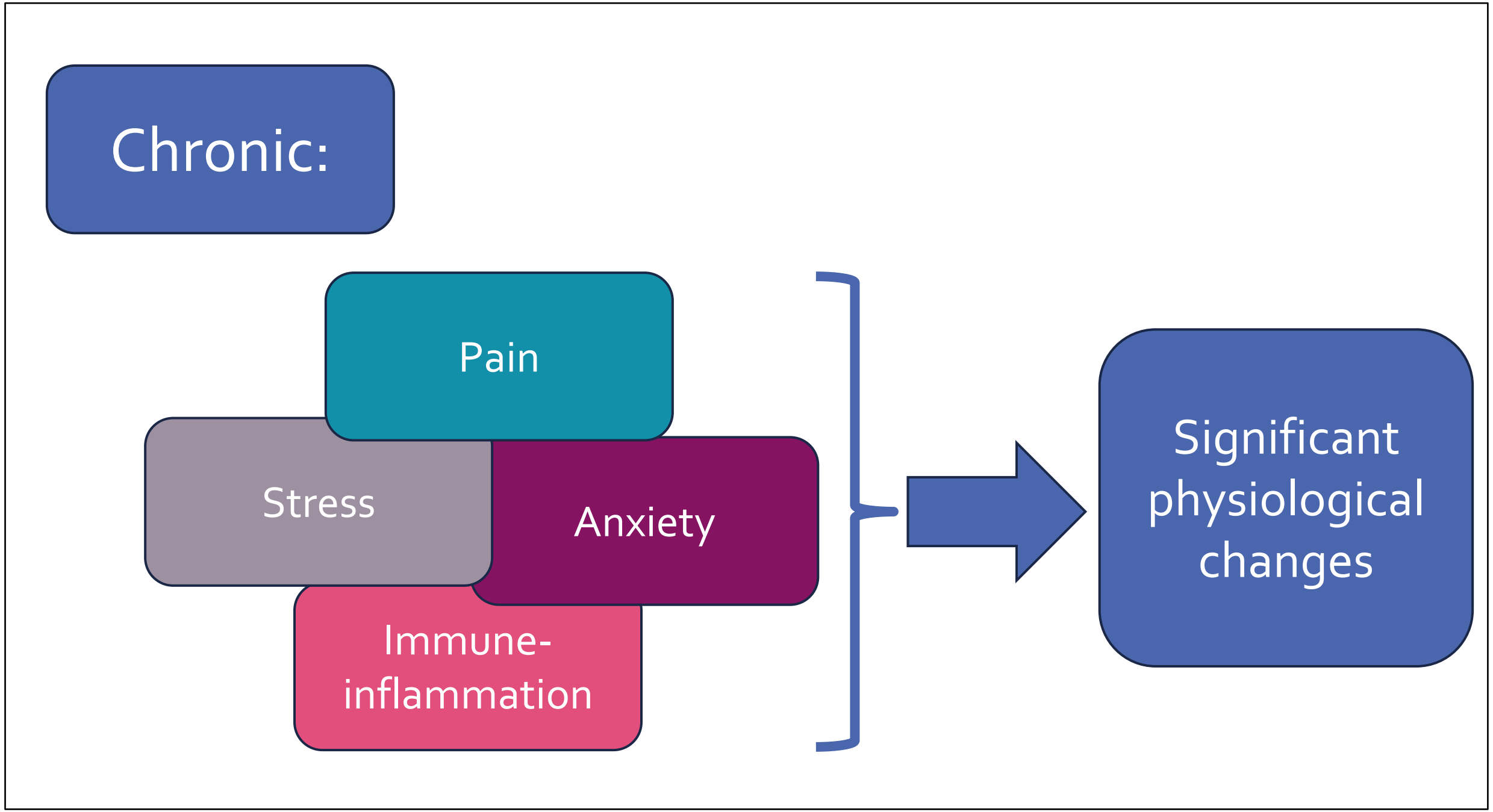
Sleep

Other Organ Disease

Physiology

Affection & Social Interaction

Human Animal Bond & Multiple Effects on Human Health

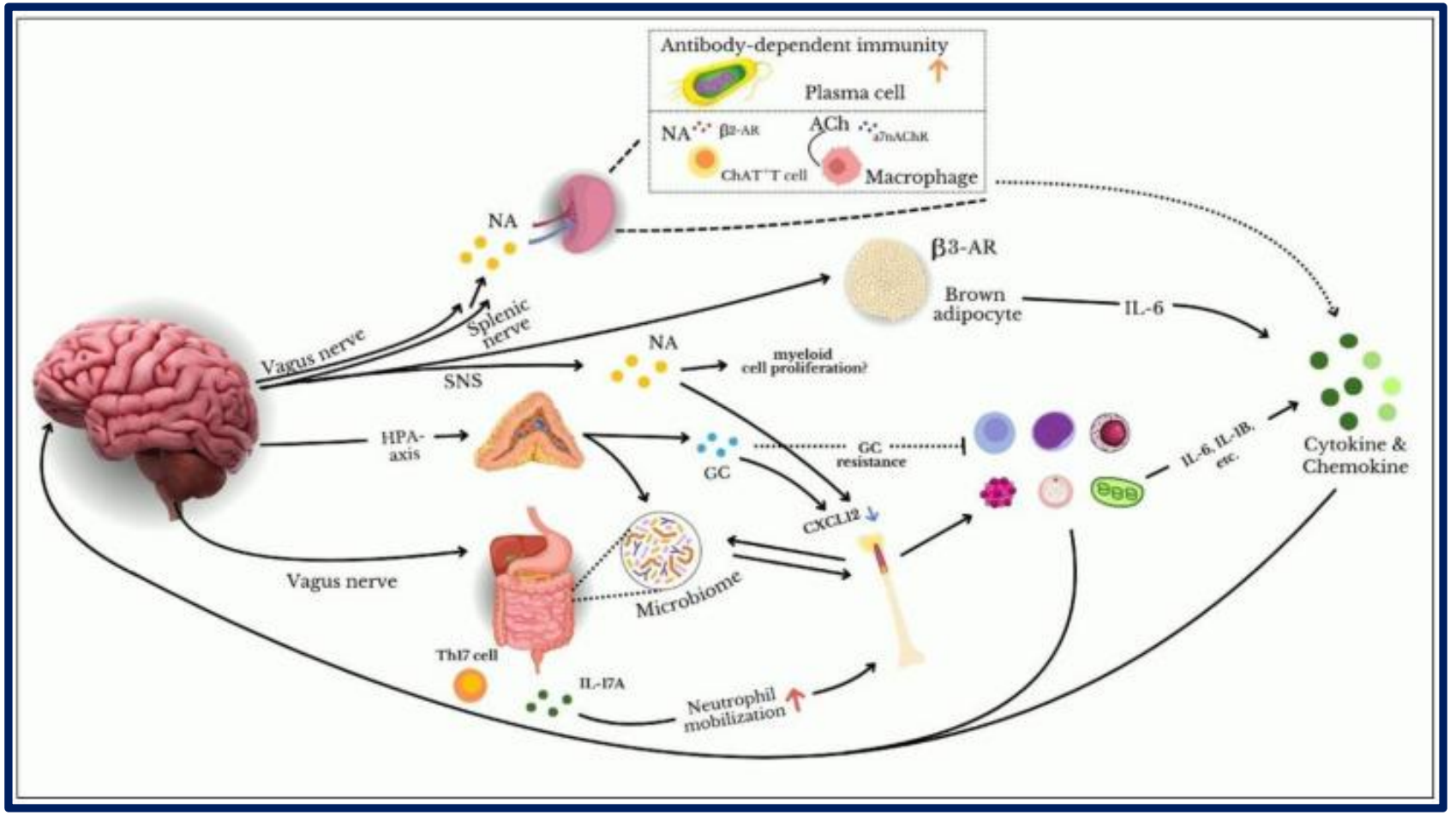

Chronic:
Pain
Stress
Anxiety
Immune-inflammation
Significant physiological changes

Role of Immune System in Stress and Pain

- Immune cells are integral to both physiological and pathological pain
  - The immune system play crucial role in both causing and resolving pain
  - Innate immune cells like macrophages, neutrophils, and mast cells release inflammatory mediators
  - Neuroimmune axis an emerging aspect of pain development

Aakanksha Jain, Sara Hakim, Clifford J. Woolf, Immune drivers of physiological and pathological pain. J Exp Med 6 May 2024; 221 (5): e20221687.

Pathways Connecting Stress to Immune Function



Alotiby A. Immunology of Stress: A Review Article. J Clin Med. 2024 Oct 25;13(21):6394.

Leaky Gut & Inflammation

- Gut microbiome essential for maintaining intestinal homeostasis and systemic health
- Impaired intestinal permeability in conjunction with different bacteria/toxins can enter bloodstream, potentially causing systemic endotoxemia and chronic low-grade inflammation

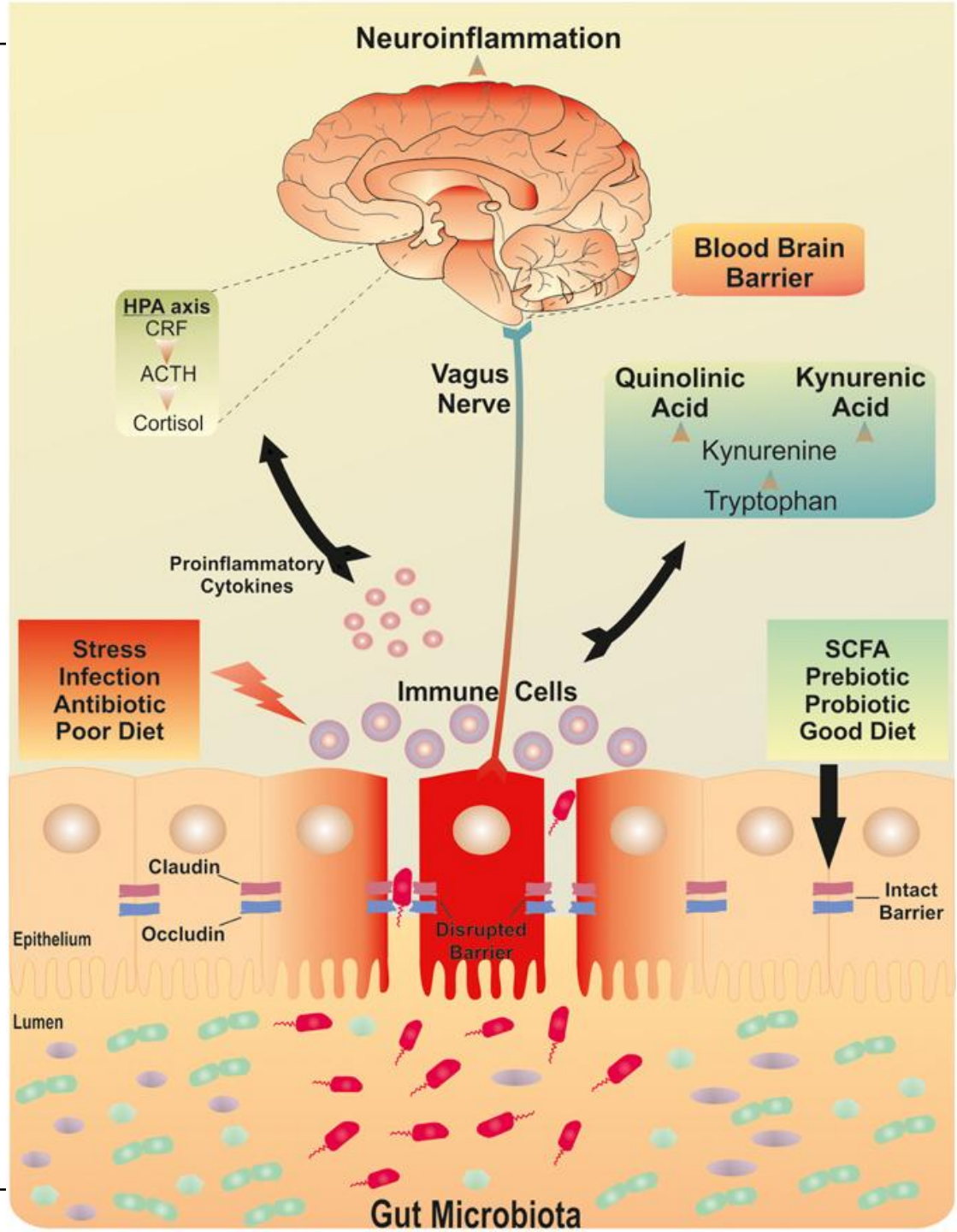
▸ AIMS Public Health. 2023 Aug 22;10(3):710–738. doi: 10.3934/publichealth.2023049

Possible relationship between the gut leaky syndrome and musculoskeletal injuries: the important role of gut microbiota as indirect modulator

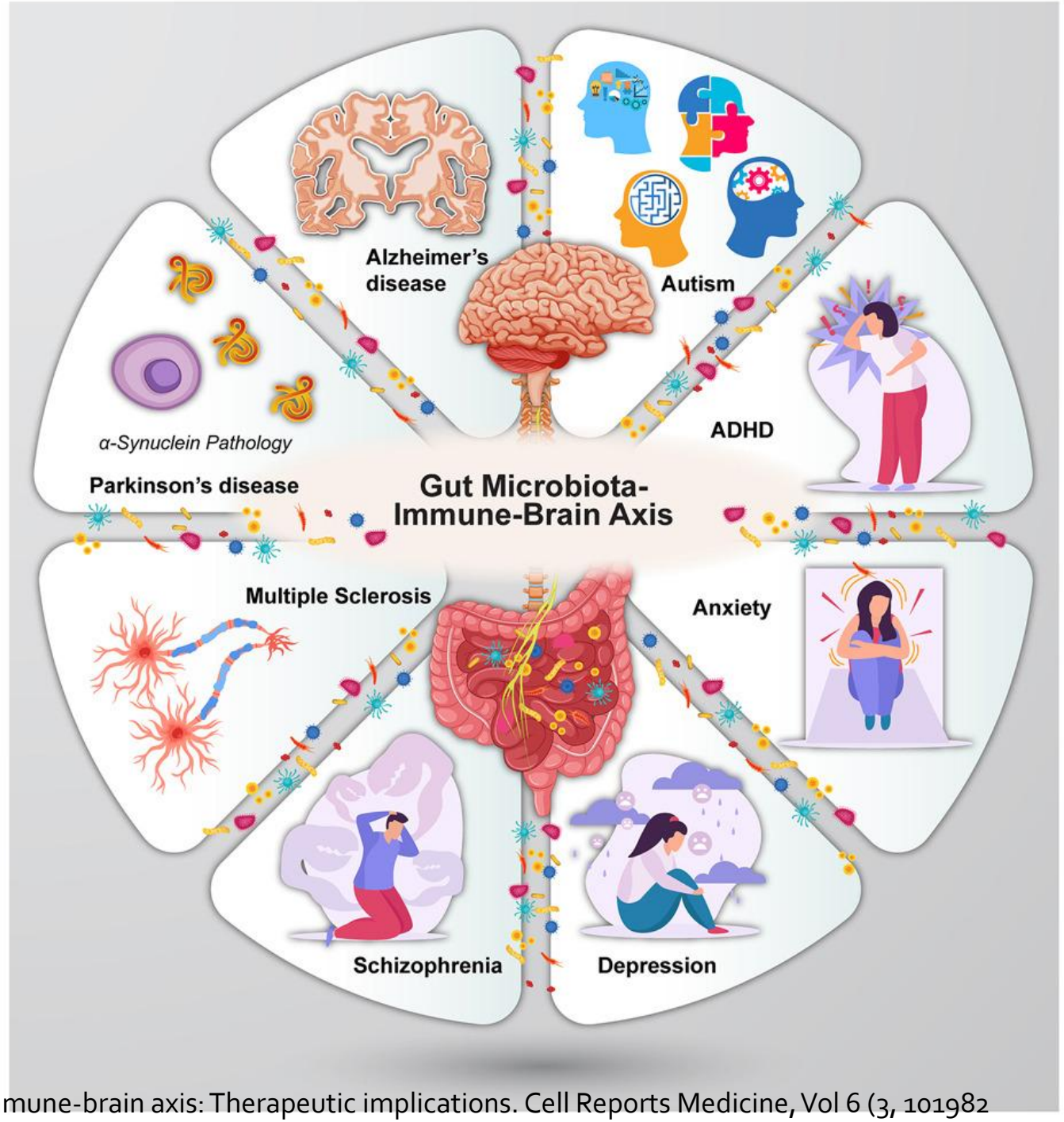
Jesús Álvarez-Herms [1,2,*], Adriana González [1], Francisco Corbi [3], Iñaki Odriozola [4], Adrian Odriozola [1]

Brain-Gut-Microbiota Axis

- Signaling pathways between the gut microbiota, intestinal barrier and brain
- A dysfunctional intestinal barrier or "leaky gut" permits a proinflammatory state with implications for neuroinflammation



Kelly Jr et al. Breaking down the barriers: the gut microbiome, intestinal permeability and stress-related psychiatric disorders. Front Cell Neurosci. 2015 Oct 14;9:392



O'Riordan, K. . The gut microbiota-immune-brain axis: Therapeutic implications. Cell Reports Medicine, Vol 6 (3, 101982

Function of the BBB

Highly Selective Gatekeeper

1. Protection
   - Defense against toxins and pathogens
   - Regulation of ion and neurotransmitter levels
   - Control of macromolecule movement
2. Nutrient Supply
   - Facilitating the transport of essential molecules
   - Specific transport systems
3. Homeostasis
   - Maintaining a stable micro-environment for neuronal function
   - Regulating inflammation

Physiology of a healthy BBB

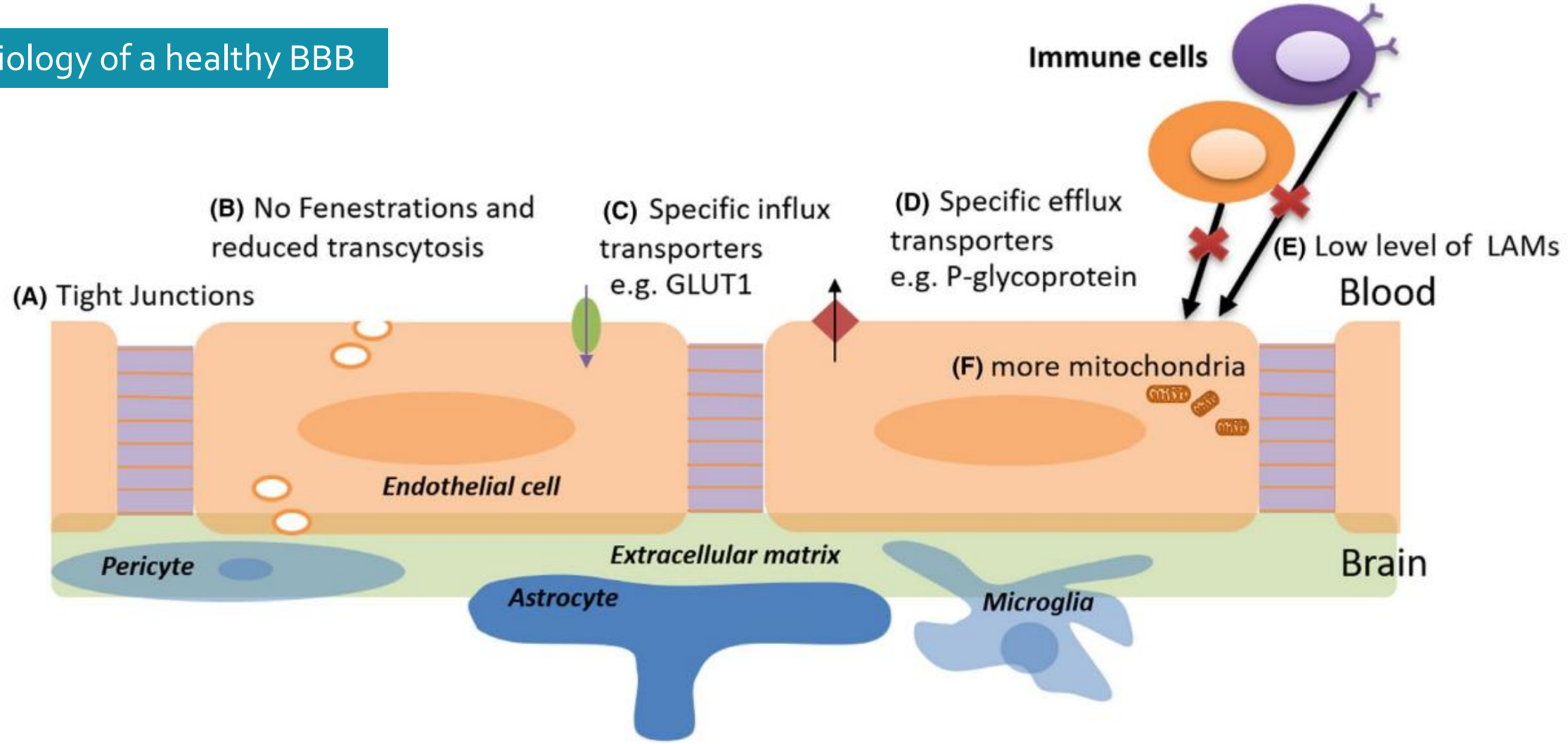
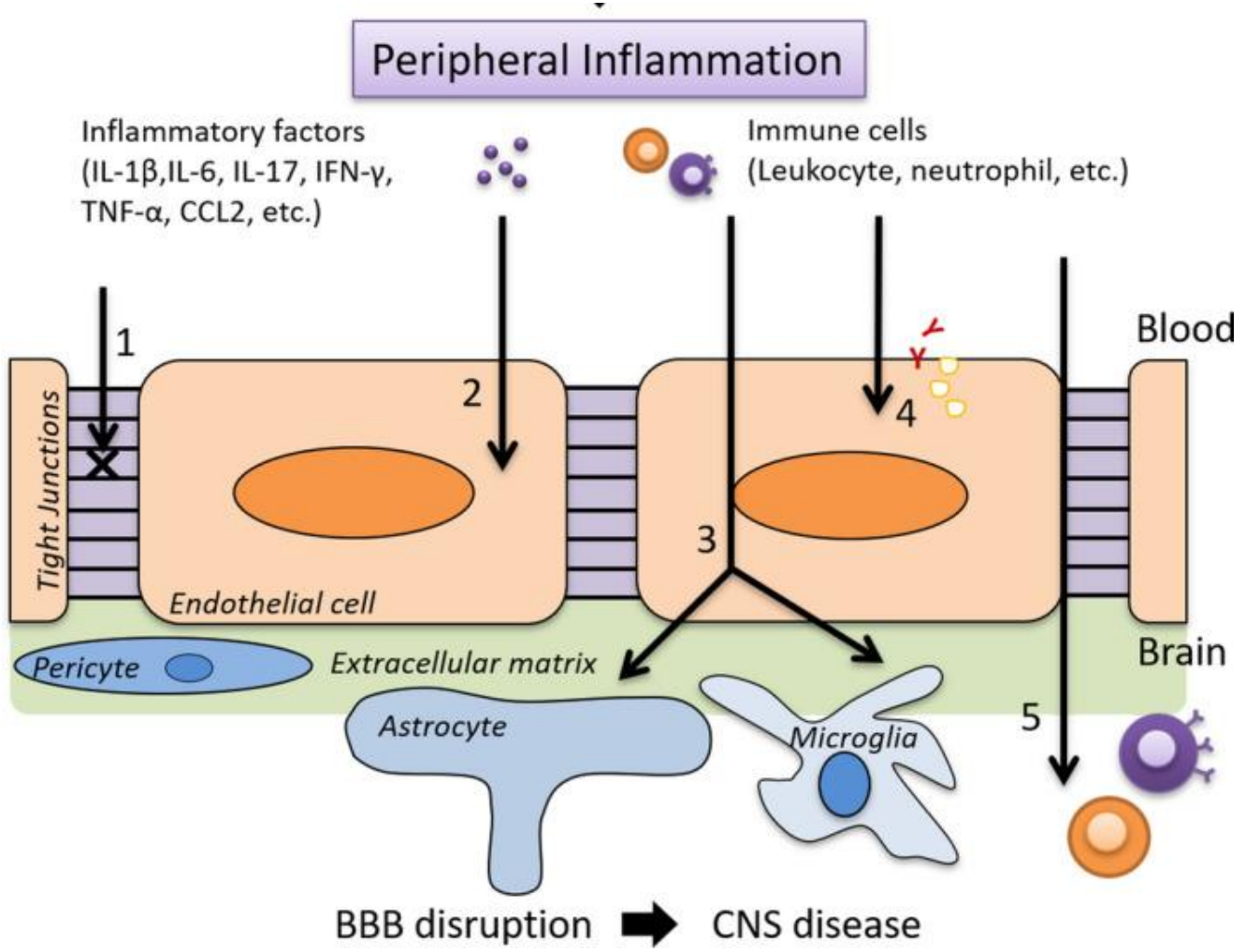


FIGURE 1 Schematic diagram of the physiological characteristics of the BBB. GLUT1, glucose transporter 1; LAMs, leukocyte adhesion molecules

Immune Cells
Inflammatory Factors



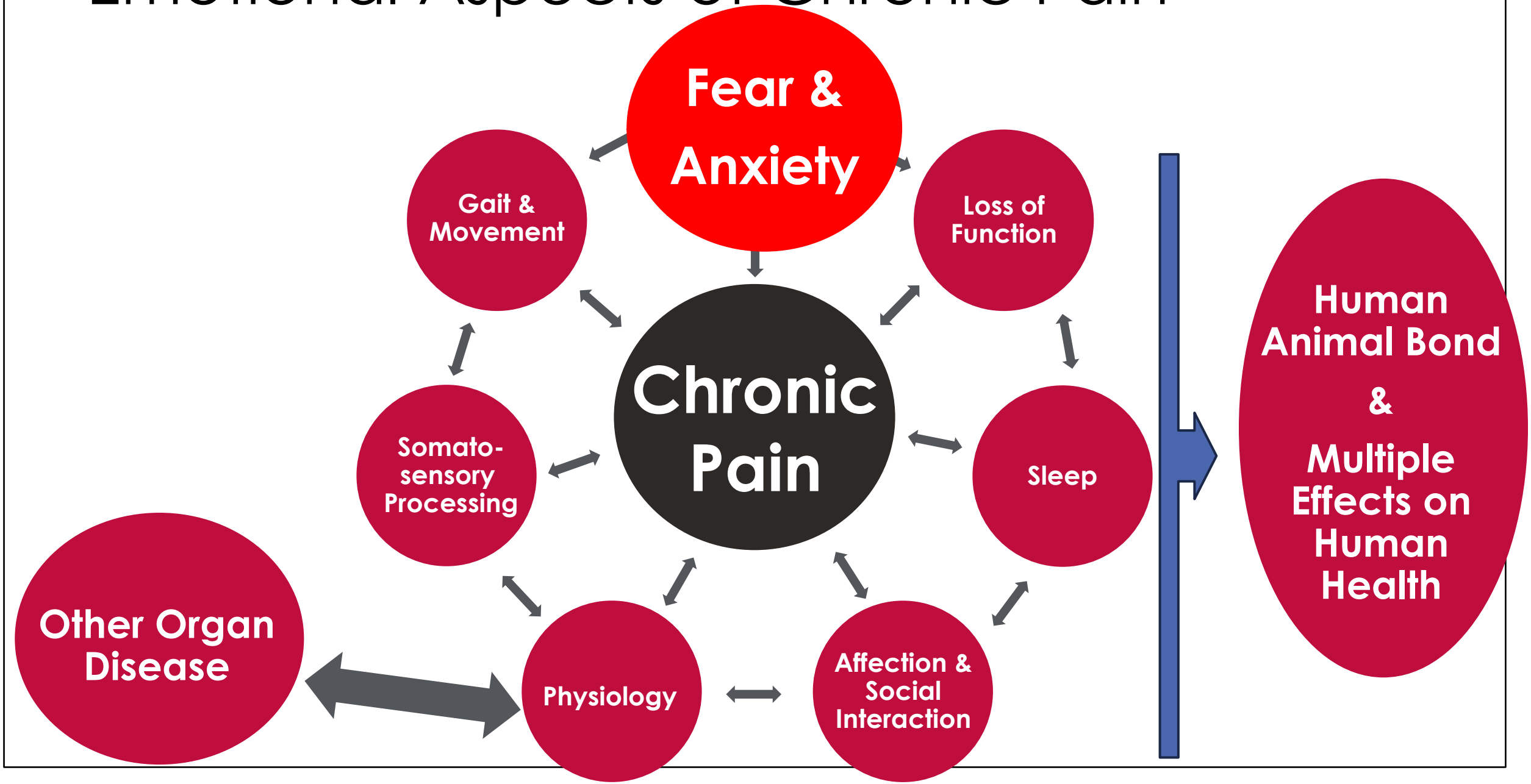
Pathophysiology of a leaky BBB

Huang X et al. Peripheral inflammation and blood-brain barrier disruption: effects and mechanisms. CNS Neurosci Ther. 2021

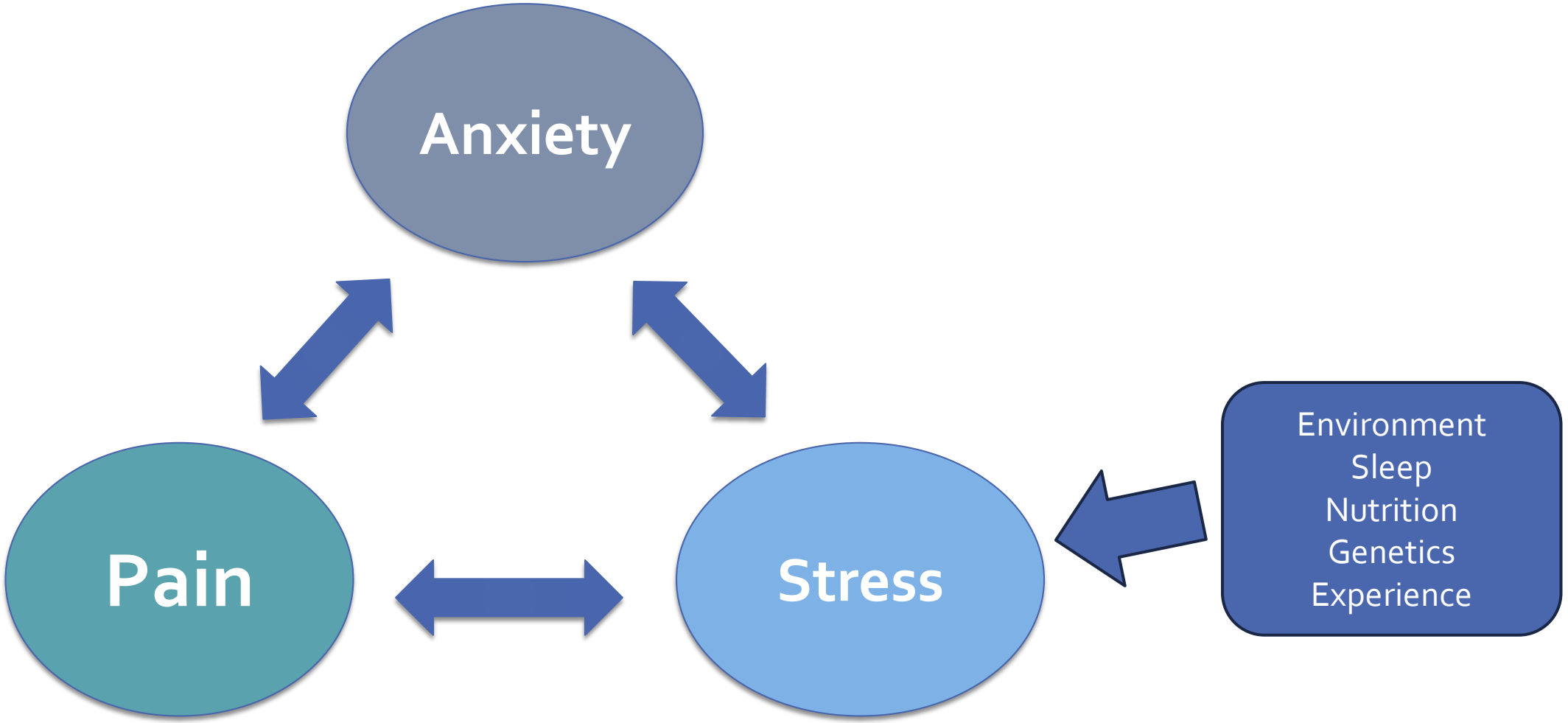
Consequences of Chronic Pain/Inflammation/Stress

- Immune system activation on various levels of the pain pathway
  - Intricate connection between pain neurons and immune cells
- Chronicity has impact on all organs, including CNS
- Early and effective treatment is underutilized and important
- Fine balance between intervention and endogenous immune response

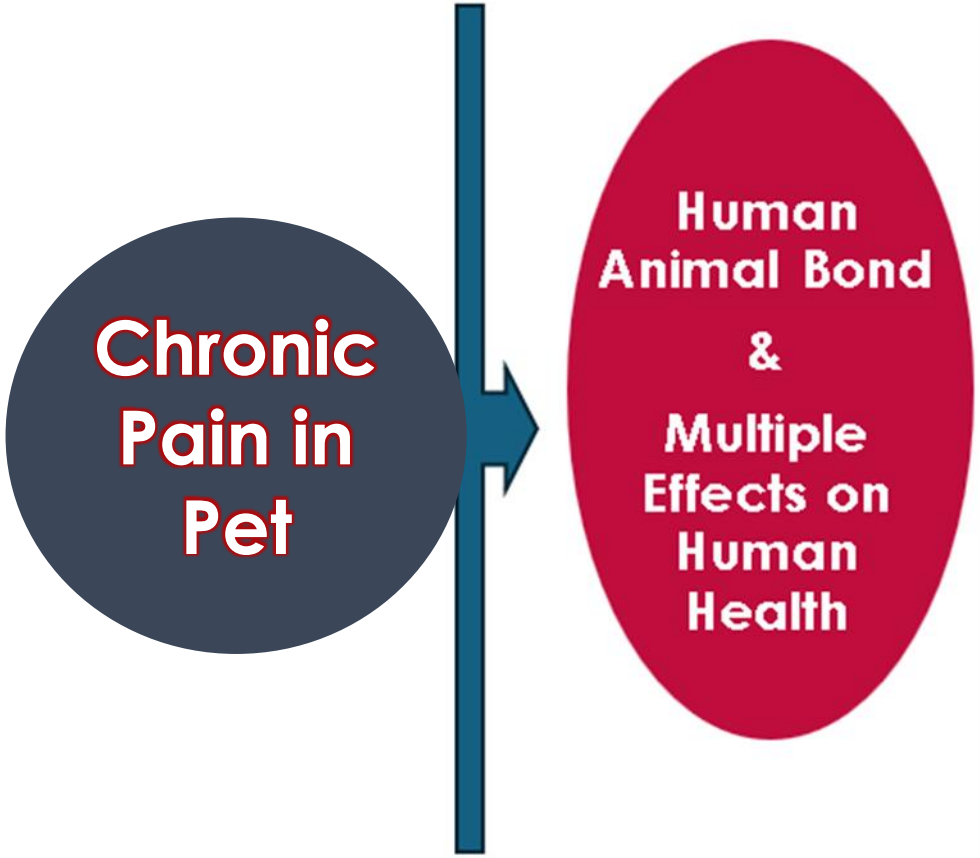
Emotional Aspects of Chronic Pain



Emotional Aspects of Pain Perception & Analgesia



Effects on Human Health



animals

MDPI

Review

A Conceptual Framework for the Co-Construction of Human–Dog Dyadic Relationship

Laurie Martin, Colombe Otis, Bertrand Lussier and Eric Troncy *

GREPAQ (Groupe de Recherche en Pharmacologie Animale du Québec), Faculty of Veterinary Medicine, Université de Montréal, Saint-Hyacinthe, QC J2S 2M2, Canada; laurie.martin.4@umontreal.ca (L.M.); colombe.otis@umontreal.ca (C.O.); bertrand.lussier@umontreal.ca (B.L.)
* Correspondence: eric.troncy@umontreal.ca

- Negative effects on owner-dog relationship (guilt, helplessness, worry) and health (psychosomatic, physical)

Critical Look at Procedures

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OPEN

Declawing in Cat is associated with neuroplastic sensitization and long-term painful afflictions

Mathieu LaChance[1,2], Colombe Otis[1,2], Tristan Juette[2], Jérôme R. E. del Castillo[1,2], Aliénor Delsart[1,2], Maxim Moreau[1,3], Beatriz P. Monteiro[1], Aude Castel[1,2], Bertrand Lussier[1,2,3], Johanne Martel-Pelletier[1,2,3], Jean-Pierre Pelletier[1,2,3] & Eric Troncy[1,2,3]✉

Call for Action

Call to action: the case for a worldwide ban on declawing

This study provides robust evidence that declawing has chronic, deleterious effects on feline welfare and supports universal ban of this convenience-based surgery. Onychectomy-induced axonopathy exacerbates the neuropathic component of OA pain, leading to biomechanical dysfunction, maladaptive neuroplasticity, and impaired quality of life. Given that declawing is performed for owner convenience rather than as a medical necessity, these findings strongly support legislative efforts to ban the procedure.

Veterinary professionals must take an active role in educating cat owners about the severe long-term consequences of declawing and advocate for alternative strategies such as behavioral training, nail trimming, and the use of scratching posts. Indeed, other procedures such as flexor tenotomy/tendonectomy should be avoided as they alter the expression of natural feline behavior and could generate chronic pain similarly to declawing. Additionally, regulatory bodies should incorporate scientific evidence into policy decisions to protect feline welfare. As veterinary medicine continues to evolve toward evidence-based practice, it is imperative to recognize declawing not as a routine procedure, but as an ethically unacceptable intervention with lasting negative consequences for cats.

In conclusion, this study reinforces the urgent need to prohibit declawing and shift toward compassionate, welfare-focused veterinary care that prioritizes the well-being of feline patients.

Back to OA

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This study aimed to determine the prevalence of osteoarthritis (OA) and associated clinical signs in young dogs. Owners of dogs aged 8 months–4 years from a single practice, were contacted in random order, to participate in a general health screen. Clinical and orthopedic examinations were performed. Each joint was scored for pain reactions (0–4). Orthogonal radiographs of all joints were made under sedation. Each joint was scored for radiographic OA (rOA) severity on an 11-point scale. Clinical OA (cOA) was defined as an overlap of rOA and joint pain in ≥ 1 joint. Owners completed OA questionnaires. The owners of 123 dogs agreed to participate. Overall, 39.8% (49/123) of dogs had rOA in ≥ 1 joint, and 16.3% (20/123) or 23.6% (29/123) dogs had cOA, depending on the cut-off value of joint pain; moderate (2), or mild (1), respectively. Owners of dogs with cOA observed signs of impairment in approximately 30% of cases. Only 2 dogs with cOA were receiving OA pain management. The most commonly affected joints in descending order of frequency were elbow, hip, tarsus, and stifle. Radiographically visible OA is common in young dogs, and 40–60% of dogs with rOA had cOA. However, OA-pain appears underdiagnosed and undertreated in young dogs.

Current Situation

- High prevalence of orthopedic developmental disease in young dogs
- High prevalence of OA and pain in all age stages
- Lack of recognition of early signs of discomfort
- Reluctance of effective treatment or preventative measures
- Inability to reverse the disease progression

Opportunities:

- Early recognition
- Better diagnostic tools
- Better owner education
- Earlier effective treatment

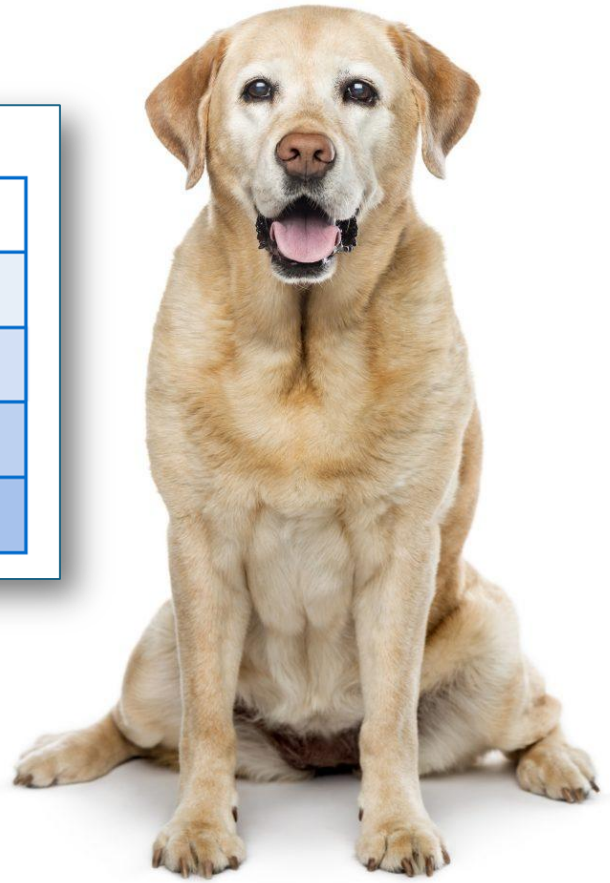
When, Where and What…

COAST
Stage 2

COAST
Canine OsteoArthritis Staging Tool

COAST Stage		
Pre-clinical	0	Clinically normal. No OA risk factors.
	1	Clinically normal, but OA risk factors present.
Clinical	2	Mild OA
	3	Moderate OA
	4	Severe OA

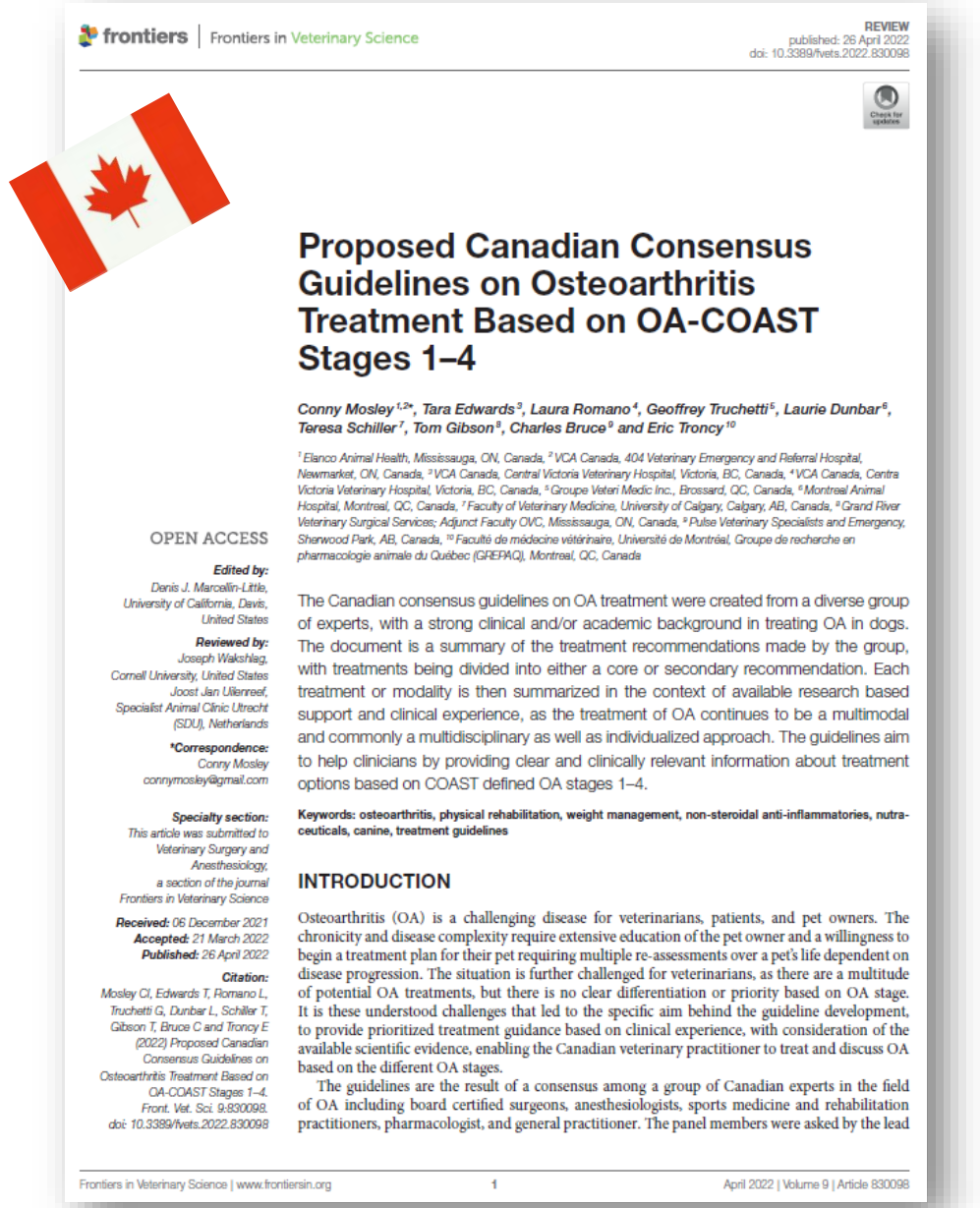
COAST
Stage 4



Understanding Pain Progression

Understanding OA Progression

Treatment based on Stage of OA



frontiers | Frontiers in Veterinary Science

REVIEW
published: 26 April 2022
doi: 10.3389/fvets.2022.830098

Proposed Canadian Consensus Guidelines on Osteoarthritis Treatment Based on OA-COAST Stages 1–4

Conny Mosley[1,2], Tara Edwards[3], Laura Romano[4], Geoffrey Truchetti[5], Laurie Dunbar[6], Teresa Schiller[7], Tom Gibson[8], Charles Bruce[9] and Eric Troncy[10]*

[1] Elanco Animal Health, Mississauga, ON, Canada, [2] VCA Canada, 404 Veterinary Emergency and Referral Hospital, Newmarket, ON, Canada, [3] VCA Canada, Central Victoria Veterinary Hospital, Victoria, BC, Canada, [4] VCA Canada, Centra Victoria Veterinary Hospital, Victoria, BC, Canada, [5] Groupe Veteri Medic Inc., Brossard, QC, Canada, [6] Montreal Animal Hospital, Montreal, QC, Canada, [7] Faculty of Veterinary Medicine, University of Calgary, Calgary, AB, Canada, [8] Grand River Veterinary Surgical Services; Adjunct Faculty OVC, Mississauga, ON, Canada, [9] Pulse Veterinary Specialists and Emergency, Sherwood Park, AB, Canada, [10] Faculté de médecine vétérinaire, Université de Montréal, Groupe de recherche en pharmacologie animale du Québec (GREPAQ), Montreal, QC, Canada

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Mosley CI, Edwards T, Romano L, Truchetti G, Dunbar L, Schiller T, Gibson T, Bruce C and Troncy E (2022) Proposed Canadian Consensus Guidelines on Osteoarthritis Treatment Based on OA-COAST Stages 1–4. Front. Vet. Sci. 9:830098. doi: 10.3389/fvets.2022.830098

The Canadian consensus guidelines on OA treatment were created from a diverse group of experts, with a strong clinical and/or academic background in treating OA in dogs. The document is a summary of the treatment recommendations made by the group, with treatments being divided into either a core or secondary recommendation. Each treatment or modality is then summarized in the context of available research based support and clinical experience, as the treatment of OA continues to be a multimodal and commonly a multidisciplinary as well as individualized approach. The guidelines aim to help clinicians by providing clear and clinically relevant information about treatment options based on COAST defined OA stages 1–4.

Keywords: osteoarthritis, physical rehabilitation, weight management, non-steroidal anti-inflammatories, nutraceuticals, canine, treatment guidelines

INTRODUCTION

Osteoarthritis (OA) is a challenging disease for veterinarians, patients, and pet owners. The chronicity and disease complexity require extensive education of the pet owner and a willingness to begin a treatment plan for their pet requiring multiple re-assessments over a pet's life dependent on disease progression. The situation is further challenged for veterinarians, as there are a multitude of potential OA treatments, but there is no clear differentiation or priority based on OA stage. It is these understood challenges that led to the specific aim behind the guideline development, to provide prioritized treatment guidance based on clinical experience, with consideration of the available scientific evidence, enabling the Canadian veterinary practitioner to treat and discuss OA based on the different OA stages.

The guidelines are the result of a consensus among a group of Canadian experts in the field of OA including board certified surgeons, anesthesiologists, sports medicine and rehabilitation practitioners, pharmacologist, and general practitioner. The panel members were asked by the lead

Goals for Early OA Stages

Recognition of Risk Factors (1)

Prevention Education

Recognition of EARLY OA Stages (2)

Appropriate EARLY Treatment

GOALS:

- Strengthen musculature
- Maintain healthy weight
- Slow down OA progression
- Reduce inflammation
- Decrease risk of pain sensitization

1. Mosley C, Edwards T, Romano L, et al. Proposed Canadian consensus guidelines on osteoarthritis treatment based on OA-COAST stages 1–4. Front Vet Sci. 2022;9:446.

Recognizing Signs and Risk Factors for OA

- Lack of association between 'compensation' and discomfort
  - Opportunity to intervene earlier to avoid compensatory problems
    - Muscle , spine, behaviour
- Lack of education on risk factors
  - Opportunity for breed specific education and preventative exercises
  - Promoting fitness (as simple as appropriate warm-ups for sporting dogs)

Preventative approach in vet med

Compensatory Adaptations

https://www.istockphoto.com/

Early Detection

Images: Google doodle image search

Goals for Early OA Stages

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Early Intervention

Goals:

- Strengthen musculature
- Maintain healthy weight

- Reduce inflammation
- Decrease risk of pain sensitization

- Slow down OA progression

Opportunities:

- Rehab consultation and exercises
- Risk adverse activity
- Joint health diet

- Appropriate and effective treatment to reduce flare ups & joint inflammation at early stages

- Unclear AND all of the above

ACADEMIA
NUTRITION & DIETETICS

Systematic Review
Published: 2025-06-12
https://doi.org/10.20935/AcadNutr7676

Role of functional foods and nutraceuticals in nutrition and health

Sanket Shirodkar[1,*], Fida Khanchey[1], Nilesh Babre[1]

Academic Editor: Carlo Pedrolli

Abstract

Functional foods and nutraceuticals have garnered attention for their potential role in promoting health and preventing disease. With increasing global interest in diet-based interventions, there is a need to evaluate their efficacy in managing chronic diseases such as cardiovascular diseases, diabetes, and obesity. Functional foods provide health benefits beyond essential nutrition, whereas nutraceuticals include bioactive compounds in concentrated medicinal forms. This systematic review explores their classification, mechanism of action, health benefits, and regulatory aspects. The studies included were pulled up from PubMed, Scopus, and Web of Science. The findings suggest that functional foods and nutraceuticals play a role in the prevention of cardiovascular disease, cancer, metabolic disorders, and neurodegenerative conditions. However, challenges such as bioavailability, genetic variability, and regional regulatory differences persist. Standardized regulations and personalized nutrition strategies are essential for optimizing their efficacy.

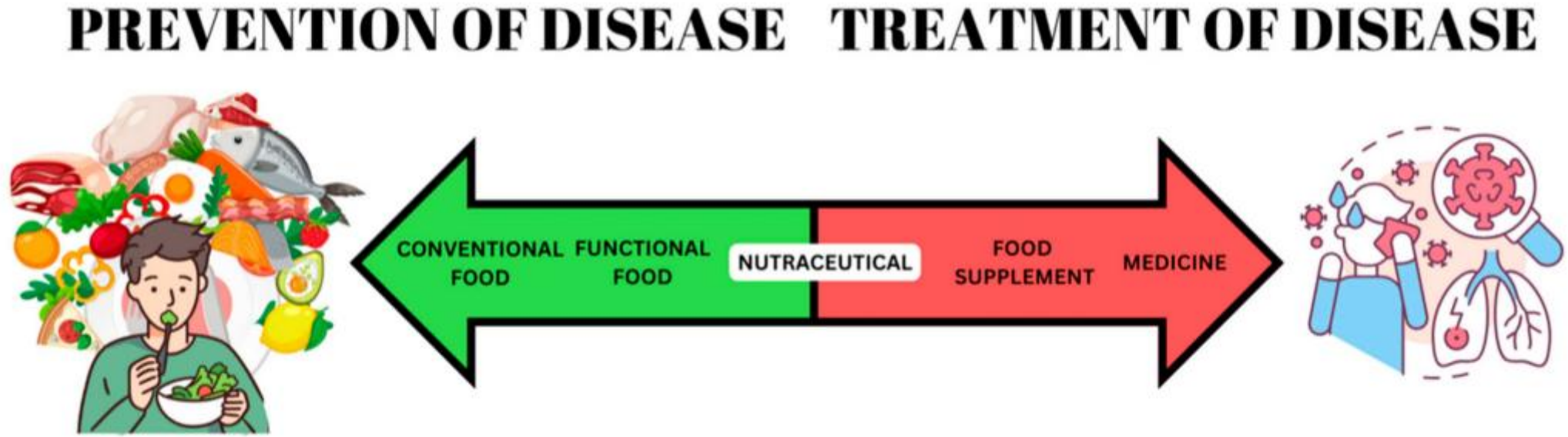


Figure 4 • Functional food–nutraceutical interface.

Nutraceuticals:

Number 1 goal of supplements/nutraceuticals is to **support and strengthen the endogenous system** to aid its ability to prevent disease and support its own healing mechanisms

Efficacy

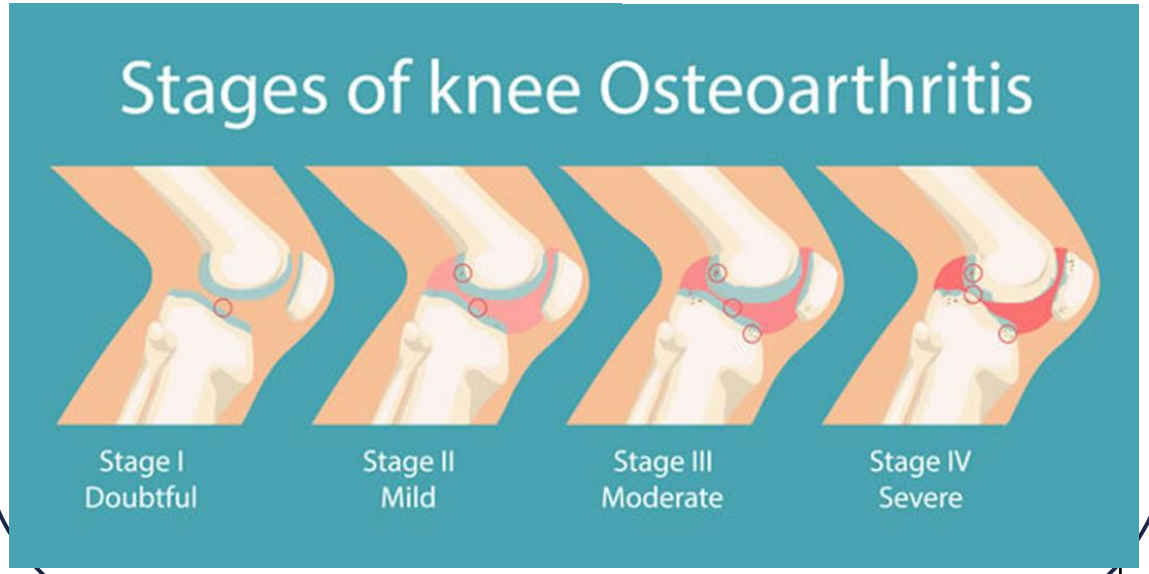
Question:
Are we assessing the 'correct' efficacy outcome measures?

Symptom relief

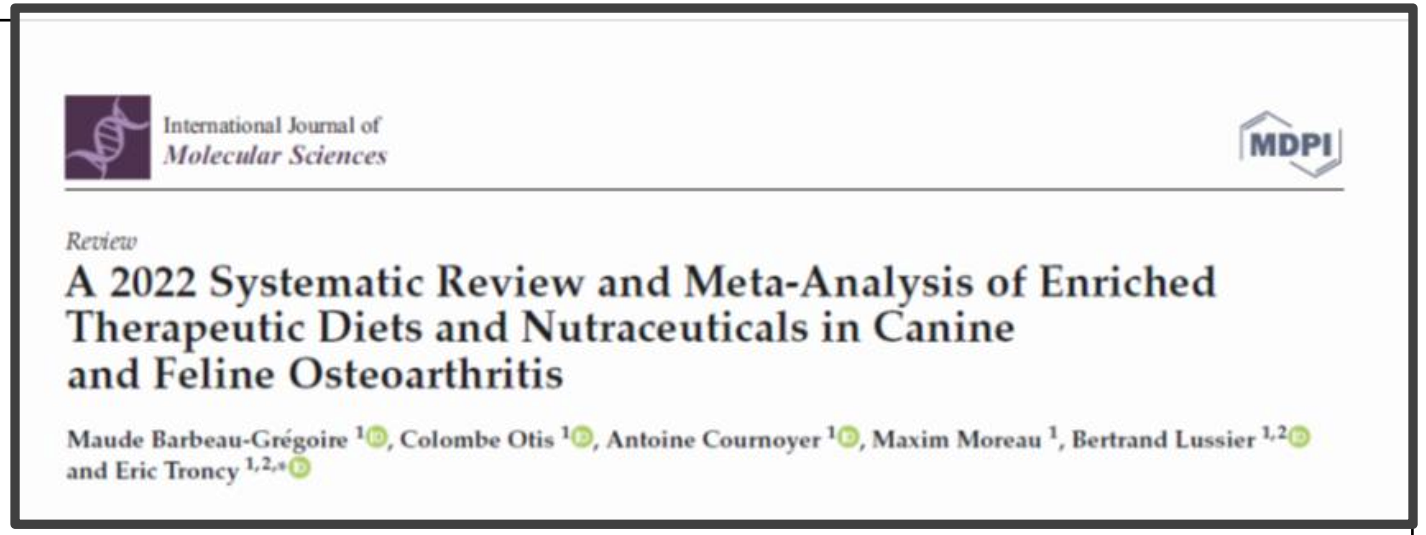
versus

Self healing support

Progression prevention



Conclusion:



International Journal of *Molecular Sciences*

MDPI

Review

A 2022 Systematic Review and Meta-Analysis of Enriched Therapeutic Diets and Nutraceuticals in Canine and Feline Osteoarthritis

Maude Barbeau-Grégoire [1], Colombe Otis [1], Antoine Cournoyer [1], Maxim Moreau [1], Bertrand Lussier [1,2] and Eric Troncy [1,2,*]

- **Evidence for efficacy was:**
- Good for:
  - Omega'3s
- Less for:
  - Cannabinoids (but promising)
- Weak for:
  - Collagen based products
- Absent for:
  - Chondroitin and glucosamine (worse than the placebo)

Question:

What to consider when choosing a product

1. Do we have research to back up the claims and MOA?
   Safety research?
   Efficacy research? In-vivo or in-vitro?

2. What is our pharmacokinetic understanding?
   Is dosing established and adequate in product?

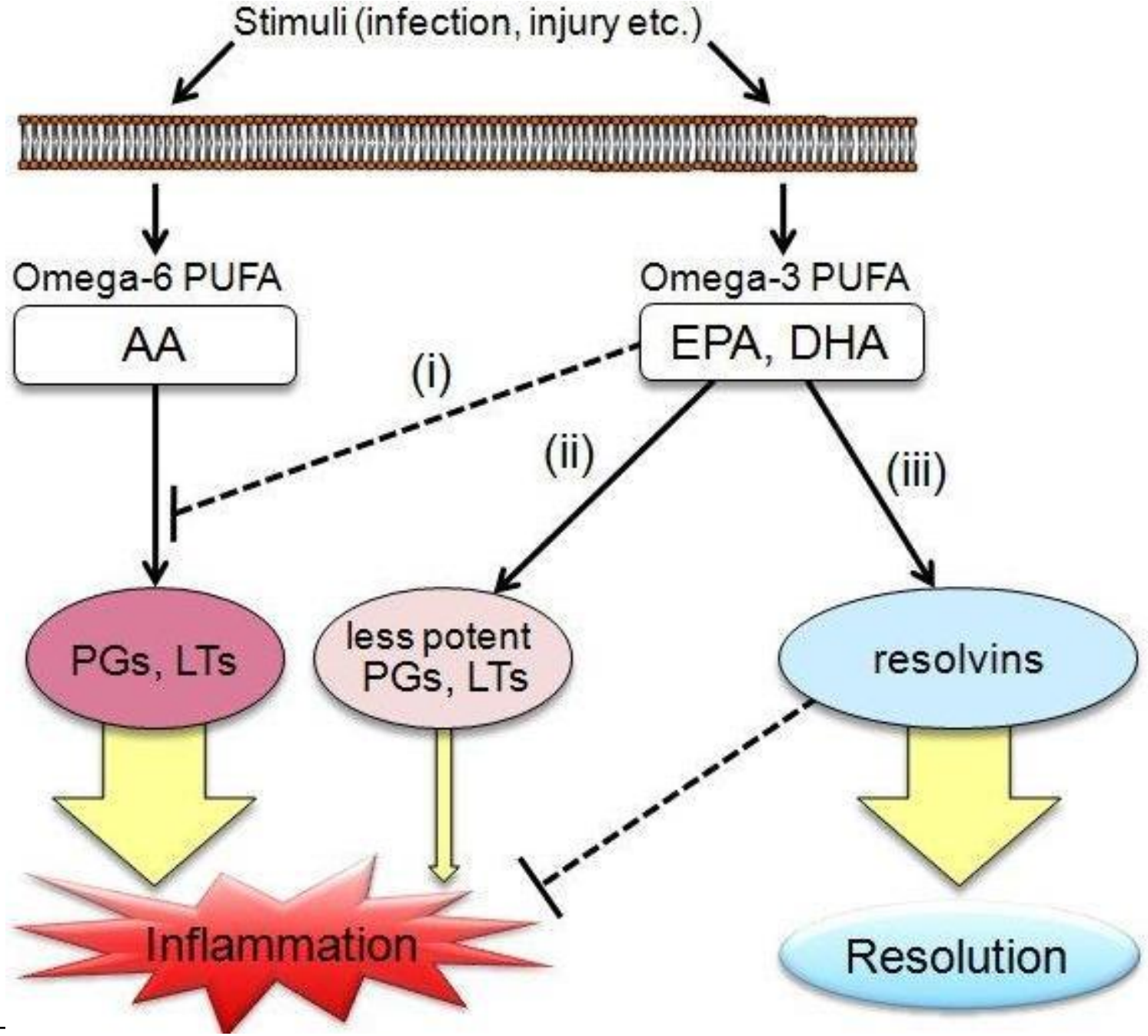
Omega'3s FA

Dosing:
80-100mg/kg/day: dogs
50mg/kg/day: cats

- Omega'3s FA should be specified as EPA/DHA
  - Marine based !
  - Plant-based:
    - The precursor of EPA/DHA in plants (flaxseed, soy oil, nuts) is ALA (alpha-linolenic acid)
    - The conversion rate of ALA to EPA is significantly less than from fish/marine based oil and a full conversion from ALA to DHA does not occur, only to its precursor docosapentaenoic acid (DPA)

EPA/DHA

Specialized Pro-resolving Mediators (SPMs)



Product Considerations

- Case example: 28kg dog with OA and skin issues

Description | Features | **Ingredients** | Shipping & Returns

Fish oil, natural smoked meat flavour, rosemary extract, ascorbyl palmitate. Guaranteed Analysis: Serving Size: 1 tsp (5 mL) Crude fat: min 94% Moisture: max 0.1% Vitamin E: min 15 IU/kg EPA omega-3 fatty acid: min 720 mg DHA omega-3 fatty acid: min 450 mg

Per serving: 1tsp (5mls):
750mg EPA and 450mg DHA = 1200mg/5mls total = 240mg/ml

Dose: 100mg/kg = 2800mg
2800mg : 240mg/ml = 11mls

NZ Green-Lipped Mussel Extract

- ***Perna Canaliculas***
- Chondro-modulatory and anti-inflammatory properties
  - Contains glycosaminoglycans (chondroitin sulfate)
  - Amino acid (glutamine)
  - Omega-3 fatty acids (including DHA, EPA)
  - Eicosatetraenoic acid
- Prebiotic activity in the intestinal microbiome
- Proteins & peptides: anti-microbial, anti-inflammatory, anti-oxidant, bio-adhesive and anti-hypertensive properties
- Increases plasma concentrations of DHA/EPA

Table 1. Table summarizing studies evaluating the effects of Greenshell™ mussel (GSM; *Perna canaliculus*) extracts in cats, dogs, and horses.

Animal	Study Type	*N*	Supplement/Diet	Dosage	Duration (Day)	Measurements	Results	Reference
Cat	Randomized, controlled trial, double blinded, naturally occurring DJD	40	Dry expanded diet incorporating EPA, DHA, GSM extract, and glucosamine/chondroitin sulfate	4 mg/kg/day	70	Subjective owner assessments; semi-objective veterinary assessments; objective active monitoring	Diet supplementation improved objective measures of mobility in cats with DJD associated pain	Lascelles et al. 2010 [17]
Dog	Randomized control trial, double blinded, placebo controlled, naturally occurring DJD	31	Powdered GSM extract was incorporated into test diet	0.3% DM	42	Semi-objective veterinary assessments	Reduced arthritis score, joint pain and joint swelling scores. No change in joint crepitus or range of joint movement	Bui and Bierer 2003 [23]
	Randomized, controlled trial, double blinded, naturally occurring DJD	96	Powdered GSM extract plus standard diet (18–30 mg/kg/day), semi-moist treatment incorporating GSM extract (18–30 mg/kg/day) and dry main meal with GSM (0.3% DM)	18–30 mg/kg/day or 0.3% DM	42	Semi-objective veterinary assessments	Incorporation of GSM mussel extract reduced arthritic score, joint pain and swelling scores irrespective of the experimental diet form provided	Bierer and Bui 2002 [24]
	Randomized, controlled trial, placebo controlled, naturally occurring DJD	70	Powdered GSM extract mixed into the animal's normal diet (chondrotin sulphate also evaluated)	11 mg/kg/day	84	Subjective owner assessments; semi-objective veterinary assessments	No effect observed	Dobenecker et al. 2002 [18]
	Not randomized controlled trial. Naturally occurring osteoarthritis	85	Dry expanded diet incorporating GSM extract	0.3% DM	50	Semi-objective veterinary assessments	Reduced arthritic score, improved mobility, improved manipulation (pain, swelling, crepitus, movement range)	Servet et al. 2006 [25]
	Double blinded, naturally occurring OA	30	Balanced diet incorporating GSM extract (Medi-Cal/Royal Canin, St. Charles, MO, USA)	Not Stated	90	Subjective owner assessments; objective assessments.	OA symptoms were reduced by balanced diet and further reduced by the inclusion of GSM extract in the diet.	Rialland et al. 2013 [20]
	Randomized, controlled trial, placebo controlled, naturally occurring DJD	81	Oral tablets containing GSM extract	22–37 mg/kg/day	56 *	Subjective owner assessments; semi-objective veterinary assessments	Improved clinical symptoms	Pollard et al. 2006 [26]
	Randomized, double controlled trial, placebo controlled, double blinded, naturally occurring OA	45	Oral capsules containing GSM extract (Lyproflex®; VMD, Arendonk, Belgium)	20–49 mg/kg/day	56	Subjective owner assessments; semi-objective veterinary assessments; objective assessments	Chronic orthopedic pain alleviated. However, GSM extract less effective than carprofen	Hielm-Björkman et al. 2013 [27]

Question:

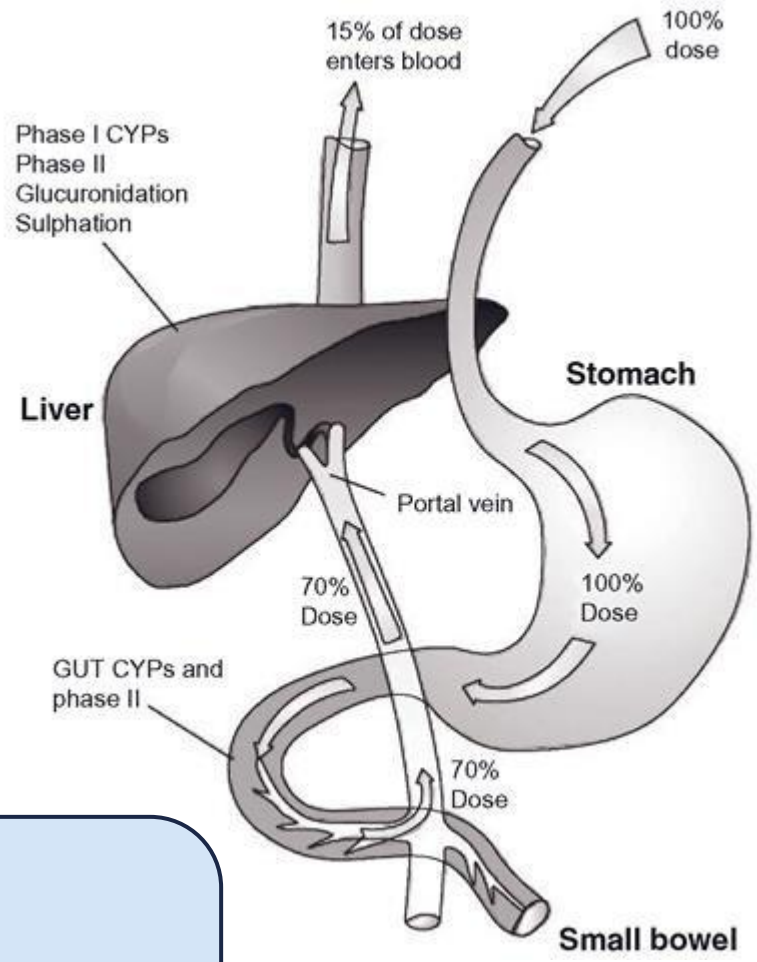
More is Less
or
Less is More

Could some products be underdosed to reach adequate therapeutic levels?

What is our pharmacokinetic understanding?
Safety research? Efficacy research?

Question:

What is our pharmacokinetic understanding?



First Pass Effect

Reduced bioavailability for many orally administered drugs in dogs and cats

Polysulfated Glycosaminoglycan - Adequan

Open Veterinary Journal, (2025), Vol. 15(9): 4007-4023
Review Article
DOI: *10.5455/OVJ.2025.v15.i9.6*

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Submitted: 07/04/2025 Revised: 10/08/2025 Accepted: 25/08/2025 Published: 30/09/2025

Polysulfated glycosaminoglycan as a treatment for osteoarthritis in veterinary medicine: Summary of the pharmacological, laboratory, and clinical data

Gary W. White*

GCT Consulting Services, Inc., Sallisaw, USA

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- Extracted from the seed of *Biota orientalis* plant
  - Antioxidant and anti-inflammatory properties
    - High conc of non-methylene-interrupted fatty acids (NMIFA)
    - - Reduce inflammatory mediators in macrophages and microglial cells
    - - Reduce PGE_2 and COX_2, replace AA
    - - Reduce synovial PGE_2 and GAG
    - - Reduce IL1
    - - Inhibition of MAPKs
    - Increase in chondrocyte numbers
    - Inhibition of osteophyte growth

In vitro

- Non-inferior to Carprofen in clinical OA trial

AUSTRALIAN VETERINARY JOURNAL
AUSTRALIA'S PREMIER VETERINARY SCIENCE TEXT

ORIGINAL ARTICLE

A randomised controlled masked clinical trial of two treatments for osteoarthritis in dogs

T Whittem, L Richards, J Alexander, C Beck, C Knight, M Milne, M Rockman, R Saunders
... See all authors

First published: 26 April 2021 | https://doi.org/10.1111/avj.13066

Epiitalis®

- *Biota orientalis*

frontiers | Frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 01 June 2022
doi: 10.3389/fvets.2022.858391

Examining the Effects of the Oral Supplement *Biota orientalis* in the Osteochondral Fragment-Exercise Model of Osteoarthritis in the Horse

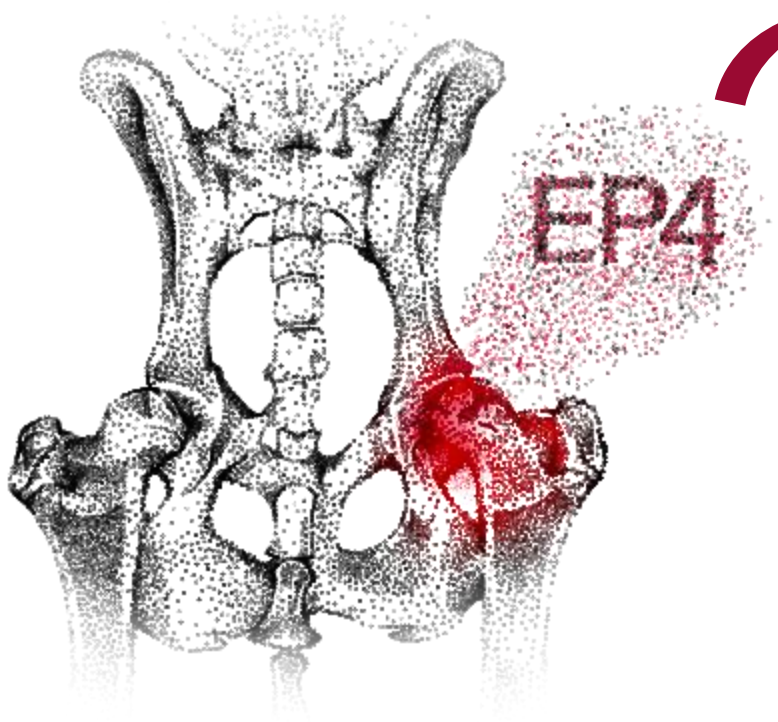
*Kathryn A. Seabaugh[1], Myra F. Barrett[1], Sangeeta Rao[2], C. Wayne McIlwraith[1] and David D. Frisbie[1]**

[1] Orthopaedic Research Center, C. Wayne McIlwraith Translational Medicine Institute, Colorado State University, Fort Collins, CO, United States, [2] Department of Clinical Sciences, Colorado State University, Fort Collins, CO, United States

Results:

Compared to placebo a significant decrease was found in synovial fluid prostaglandin E2 concentration and white blood cell counts in horses treated with BO. There was a significant reduction in radiographic scores for subchondral lysis of the radial carpal bone, osteophyte formation, subchondral sclerosis of the radial carpal bone, and total radiographic score for the horses treated with BO. There was no significant difference between treatment groups in clinical lameness findings, MRI findings, macroscopic grading or histologic grading. This study suggests a significant anti-inflammatory effect from oral BO that should be further investigated in clinical OA.

Receptors and their roles in Osteoarthritis



- Peripheral & Central Sensitization
- Progression of OA

EP4 Receptor

Bone Research

www.nature.com/boneres

ARTICLE OPEN

PGE2 activates EP4 in subchondral bone osteoclasts to regulate osteoarthritis

Wenhao Jiang[1,2], Yunyun Jin[2], Shiwei Zhang[2], Yi Ding[2], Konglin Huo[2], Junjie Yang[2], Lei Zhao[2], Baoning Nian[2], Tao P. Zhong[2], Weiqiang Lu[2], Hankun Zhang[2], Xu Cao[3], Karan Mehul Shah[4], Ning Wang[4], Mingyao Liu[2] and Jian Luo[1,2]

In summary, our study identifies a novel mechanism by which PGE2, acting on subchondral bone osteoclasts, mediates OA pathogenesis. We provide evidence to suggest that these actions of PGE2 on osteoclasts occur via the EP4 receptor. Furthermore, targeting PGE2/EP4 in osteoclasts remarkably attenuates subchondral bone angiogenesis and sensory neuron innervation, thus reducing pain sensitivity. Finally, we also identified HL-43 as a potent EP4 antagonist, which, similar to *EP4* deletion, reduced OA progression, osteophyte formation, and pain sensitivity and improved subchondral bone microarchitecture and is therefore a novel candidate for OA treatment.

Jiang W. et al. Bone Res. 2022 Mar 9;10(1):27

cells

MDPI

Article

Inhibition of PGE2 in Subchondral Bone Attenuates Osteoarthritis

Qi Sun [1], Yuanzhen Zhang [1], Yilan Ding [2,3], Wenqing Xie [2,3], Hengzhen Li [2,3], Shaohua Li [1], Yusheng Li [2,3,*] and Ming Cai [1,*]

[1] Department of Orthopaedics, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, Shanghai 200072, China
[2] Department of Orthopedics, Xiangya Hospital, Central South University, Changsha 410008, China
[3] National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha 410008, China
* Correspondence: liyusheng@csu.edu.cn (Y.L.); cmdoctor@tongji.edu.cn (M.C.); Tel.: +86-13975889696 (Y.L.); +86-13816147208 (M.C.); Fax: +86-073184327332 (Y.L.); +86-010-59367999 (M.C.)

Abstract: Aberrant subchondral bone architecture is a crucial driver of the pathological progression of osteoarthritis, coupled with increased sensory innervation. The sensory PGE2/EP4 pathway is involved in the regulation of bone mass accrual by the induction of differentiation of mesenchymal stromal cells. This study aimed to clarify whether the sensory PGE2/EP4 pathway induces aberrant structural alteration of subchondral bone in osteoarthritis. Destabilization of the medial meniscus (DMM) using a mouse model was combined with three approaches: the treatment of celecoxib, capsaicin, and sensory nerve-specific prostaglandin E2 receptor 4 (EP4)-knockout mice. Cartilage degeneration, subchondral bone architecture, PGE2 levels, distribution of sensory nerves, the number of osteoprogenitors, and pain-related behavior in DMM mice were assessed. Serum and tissue PGE2 levels and subchondral bone architecture in a human sample were measured. Increased PGE2 is closely related to subchondral bone's abnormal microstructure in humans and mice. Elevated PGE2 concentration in subchondral bone that is mainly derived from osteoblasts occurs in early-stage osteoarthritis, preceding articular cartilage degeneration in mice. The decreased PGE2 levels by the celecoxib or sensory denervation by capsaicin attenuate the aberrant alteration of subchondral bone architecture, joint degeneration, and pain. Selective EP4 receptor knockout of the sensory nerve attenuates the aberrant formation of subchondral bone and facilitates the prevention of cartilage degeneration in DMM mice. Excessive PGE2 in subchondral bone caused a pathological alteration to subchondral bone in osteoarthritis and maintaining the physiological level of PGE2 could potentially be used as an osteoarthritis treatment.

Keywords: subchondral bone; PGE2; osteoarthritis; bone remodeling; sensory nerve; COX2

check for updates

Citation: Sun, Q.; Zhang, Y.; Ding, Y.; Xie, W.; Li, H.; Li, S.; Li, Y.; Cai, M. Inhibition of PGE2 in Subchondral Bone Attenuates Osteoarthritis. *Cells* **2022**, *11*, 2760. https://doi.org/10.3390/cells11172760

Academic Editors: Irene Gutiérrez-Cañas and Alexander E. Kalyuzhny

Received: 26 July 2022
Accepted: 30 August 2022

frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 24 October 2024
DOI 10.3389/fvets.2024.1461628

Check for updates

Core Multimodal Treatment for 4 months

Galliprant®
2 mg/kg once daily

Fish Oil
100 mg/kg/day for the first week, then up to 200 mg/kg/day as tolerated

Exercise
gradual increase in leash exercise up to 30 minutes, twice daily

Response to treatment with grapiprant as part of a standard multimodal regimen in young dogs with appendicular joint osteoarthritis associated pain

Masataka Enomoto[1], Jonathan Hash[1], Tracey Cole[1], Maria D. Porcel Sanchez[1], Andrea Thomson[1], Erin Perry[1], Savannah Aker[1], Aoi Nakanishi-Hester[1], Emily Haupt[1], Logan Opperman[2], Simon Roe[1], Nichola Archer Thompson[3], John F. Innes[4] and Benedict Duncan Xavier Lascelles[1,5,6]*

Integrative Approaches to Treatment and Prevention

- Modalities:
  - Specific muscle strengthening and maintaining exercises
  - Manual therapies to avoid myofascial complications
- Household and lifestyle adjustments
  - Raised food bowls
  - Flooring
  - Fitness plan
- Nutrition:
  - Optimize weight with optimal nutrition

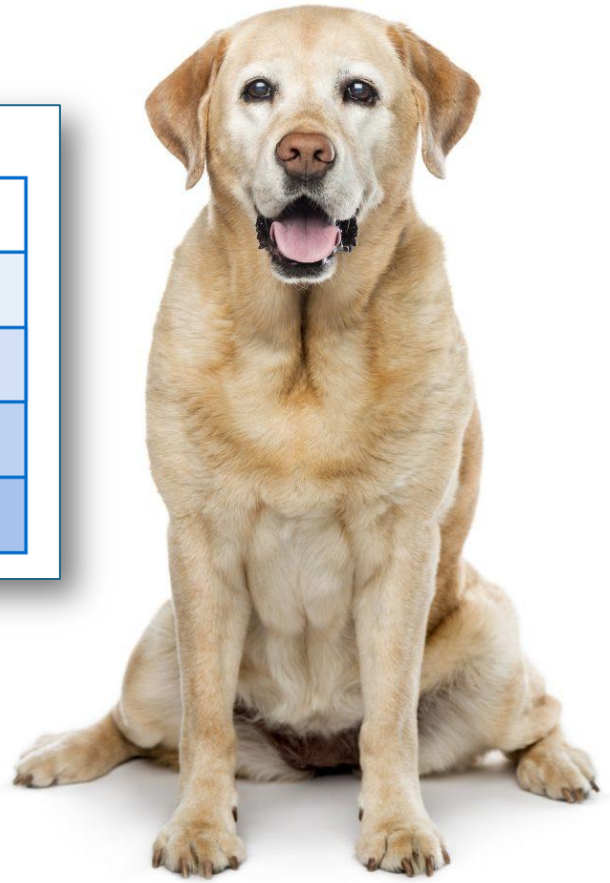
When, Where and What…

COAST
Stage 2

COAST
Canine OsteoArthritis Staging Tool

COAST Stage		
Pre-clinical	0	Clinically normal. No OA risk factors.
	1	Clinically normal, but OA risk factors present.
Clinical	2	Mild OA
	3	Moderate OA
	4	Severe OA

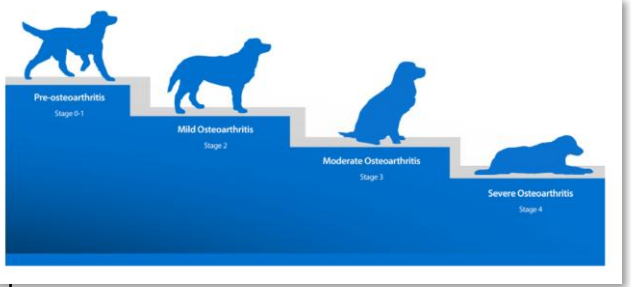
COAST
Stage 4



https://www.dreamstime.com/stock-image-young-labrador-retriever-4-months-old-image23770831

COAST

Canine OsteoArthritis Staging Tool



NAME _____ DATE _____

Grade The Dog

Enter results of the pet owner assessments (CMI and their opinion of overall degree of their dog's discomfort) as well as the results of the orthopedic examination. Severity increases from left to right. Hover over the radio button for additional information whenever available.

PET OWNER ASSESSMENTS	Clinical Metrology Instrument (CMI)	0 or Very Low Score Not clinically affected	Low Score Mildly affected	Medium Score Moderately affected	High Score Severely affected
	Example provided for LOAD score conversion	0	MILD <10	MODERATE 11-20	SEVERE TO EXTREME 21+
	Degree of Dog's Discomfort	None	Low Level	Moderate Level	Unbearable
EVALUATION BY VETERINARIAN	Effect on Static Posture	Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal
	Effect on Motion	Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal

Grade The Joint

Select side and most severely affected joint

RIGHT | LEFT | SHOULDER | ELBOW | CARPUS | HIP | STIFLE | HOCK

EVALUATION BY VETERINARIAN	Pain upon Manipulation	None	Mild	Moderate	Severe
	Passive Range of Movement	Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal
	Radiography	No radiographic signs of OA	Mildly Abnormal	Moderately Abnormal	Severely Abnormal

Disease Severity

Highest grade equates to COAST stage

DOG GRADE JOINT GRADE

Re-evaluate if disparity of 2 or more grades between dog and joint results

PRE-CLINICAL	MILD	MODERATE	SEVERE
0-1	2	3	4

COAST Stage of Canine Osteoarthritis

PM-CA-22-0060

Cachon T, et al ; COAST Development Group. Face validity of a proposed tool for staging canine osteoarthritis: Canine OsteoArthritis Staging Tool (COAST). VetJ.2018 May;235:1-8

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COAST
Canine OsteoArthritis Staging Tool

NAME _____ DATE _____

Grade The Dog

Enter results of the pet owner assessments (CMI and their opinion of overall degree of their dog's discomfort) as well as the results of the orthopedic examination. Severity increases from left to right. Hover over the radio button for additional information whenever available.

PET OWNER ASSESSMENTS

Clinical Metrology Instrument (CMI)	0 or Very Low Score Not clinically affected ○	Low Score Mildly affected ○	Medium Score Moderately affected ○	High Score Severely affected ○
Example provided for LOAD score conversion	0	MILD <10	MODERATE 11-20	SEVERE TO EXTREME 21+
Degree of Dog's Discomfort	None ○	Low Level ○	Moderate Level ○	Unbearable ○

EVALUATION BY VETERINARIAN

Effect on Static Posture	Normal ○	Mildly Abnormal ○	Moderately Abnormal ○	Severely Abnormal ○
Effect on Motion	Normal ○	Mildly Abnormal ○	Moderately Abnormal ○	Severely Abnormal ○

Grade The Joint

Select side and most severely affected joint

RIGHT | LEFT | SHOULDER | ELBOW | CARPUS | HIP | STIFLE | HOCK

EVALUATION BY VETERINARIAN

Pain upon Manipulation	None ○	Mild ○	Moderate ○	Severe ○
Passive Range of Movement	Normal ○	Mildly Abnormal ○	Moderately Abnormal ○	Severely Abnormal ○
Radiography	No radiographic signs of OA ○	Mildly Abnormal ○	Moderately Abnormal ○	Severely Abnormal ○

Disease Severity

Highest grade equates to COAST stage

Cachon T, et al ; COAST Development Group. Face validity of a proposed tool for staging canine osteoarthritis: Canine OsteoArthritis Staging Tool (COAST). VetJ.2018 May;235:1-8

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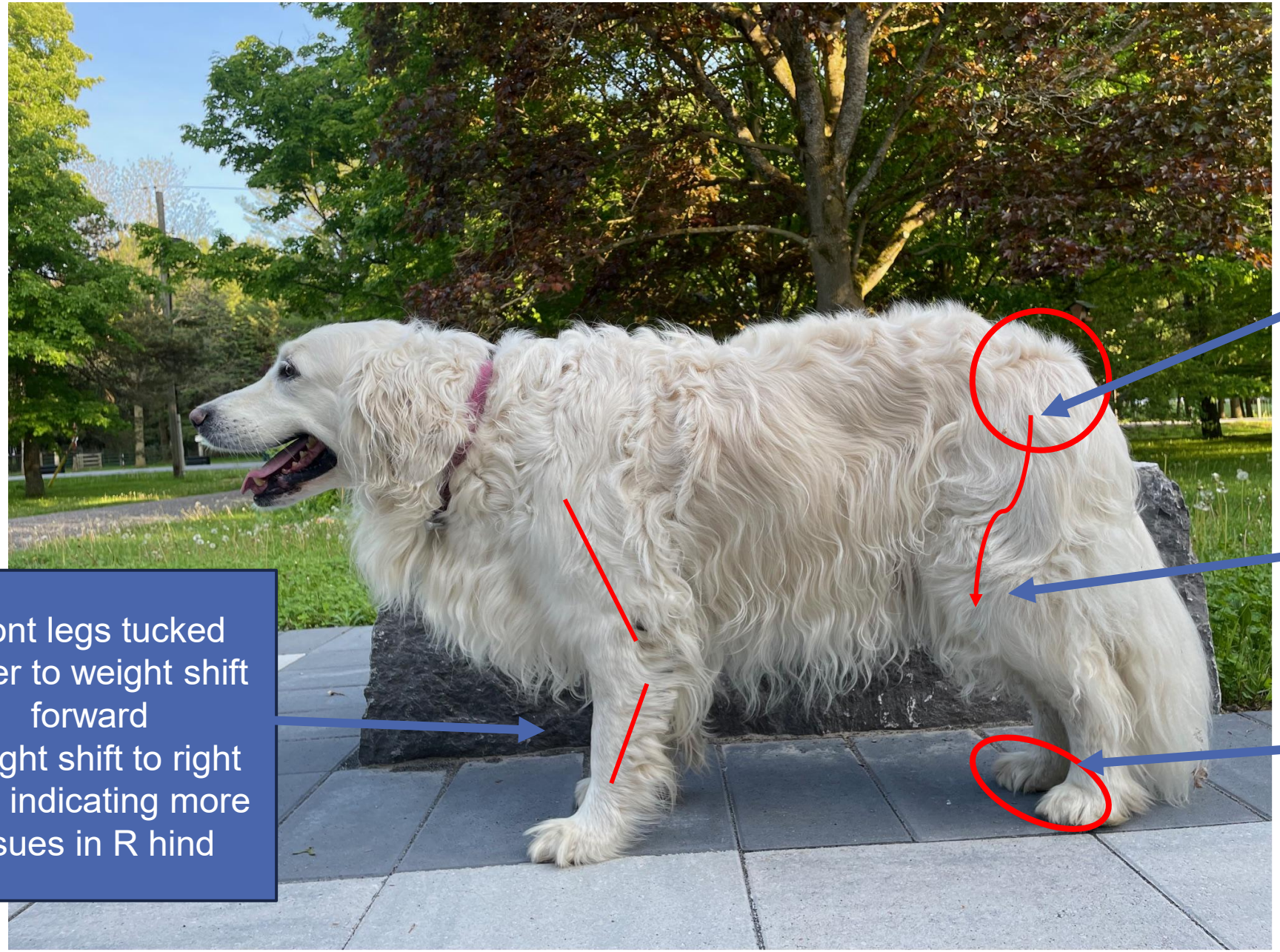

HIPS are the primary issue

Knees rotated in to open up hips

Stance tucked under and in to avoid pressure on hip joint

Front legs tucked under to weight shift forward
Weight shift to right front indicating more issues in R hind

Orthopedic Exam

EnCORE Videos

EnCORE videos by Duncan Lascelles

Ep 1 Intro

Elanco Canada

Ep 1: https://vimeo.com/502816620/555a55f6a6 Ep 2: https://vimeo.com/503172163/ce6435b5be Ep 3:...

Ep 2 Observation

Elanco Canada

Ep 1: https://vimeo.com/502816620/555a55f6a6 Ep 2: https://vimeo.com/503172163/ce6435b5be Ep 3:...

Ep 3 Overall Assessment

Elanco Canada

Ep 1: https://vimeo.com/502816620/555a55f6a6 Ep 2: https://vimeo.com/503172163/ce6435b5be Ep 3:...

EP 5 Detailed Assessment - Hin…

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Ep 1: https://vimeo.com/502816620/555a55f6a6 Ep 2: https://vimeo.com/503172163/ce6435b5be Ep 3:...

Ep 6 Wrap-Up

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Ep 7 Tools

Elanco Canada

Ep 1: https://vimeo.com/502816620/555a55f6a6 Ep 2: https://vimeo.com/503172163/ce6435b5be Ep 3:...

Muscle Evaluation

- Atrophy
- Painful/tight areas
- Trigger Points

ISSUE 6

pawsitivity™

Helping dogs and cats lead active, pain-free lives.

Click here to view Dr. Romano perform a quick muscle exam. Easy to implement into your exams. >

It's not just the joint that hurts. Recognizing Myofascial Pain Syndrome as a source of pain.

Dr. Laura Romano, DVM, DACVSMR

Goals for LATE OA Stages

Strengthen/Maintain Mobility

Appropriate Pain Control

Improve QoL

1. Mosley C, Edwards T, Romano L, et al. Proposed Canadian consensus guidelines on osteoarthritis treatment based on OA-COAST stages 1–4. Front Vet Sci. 2022;9:446.

Treatment Opportunities in Later Stage OA

Goals:

- Strengthen and maintain musculature
- Maintain healthy weight

- Reduce PAIN and inflammation
- Treat peripheral and central pain sensitization

- Provide a good QoL

Opportunities:

- Rehabilitation service and exercises
- Encourage adequate activities
- Joint health diet

- Appropriate and effective pain management for musculoskeletal system
- Support other organ systems

- Lifestyle adjustments

Rehabilitation!

- Important for joint, spine, muscle and cognitive support
  - Effected joints
  - All systems that compensate for the effected limb
- Supporting tools and appropriate monitoring

Pain - Important to Effectively Treat!

- **Pharmaceuticals:**
  - NSAIDs
  - Pregabalin
  - Cannabinoids
  - Ketamine
  - Anti-NGF
  - Amantadine

- **Joint injections:**
  - HA
  - Steroids
  - PRP
  - Stemcells

- **Rehabilitation:**
  - Exercises & UWT
  - Acupuncture
  - Manual Therapies:
    - Massages
    - Osteopathy
    - Chiropractic
  - PEMF
  - Laser

- **Supplements:**
  - TCVM or Western botanical medicine
  - Chondroprotective agents
- **NUTRITION**

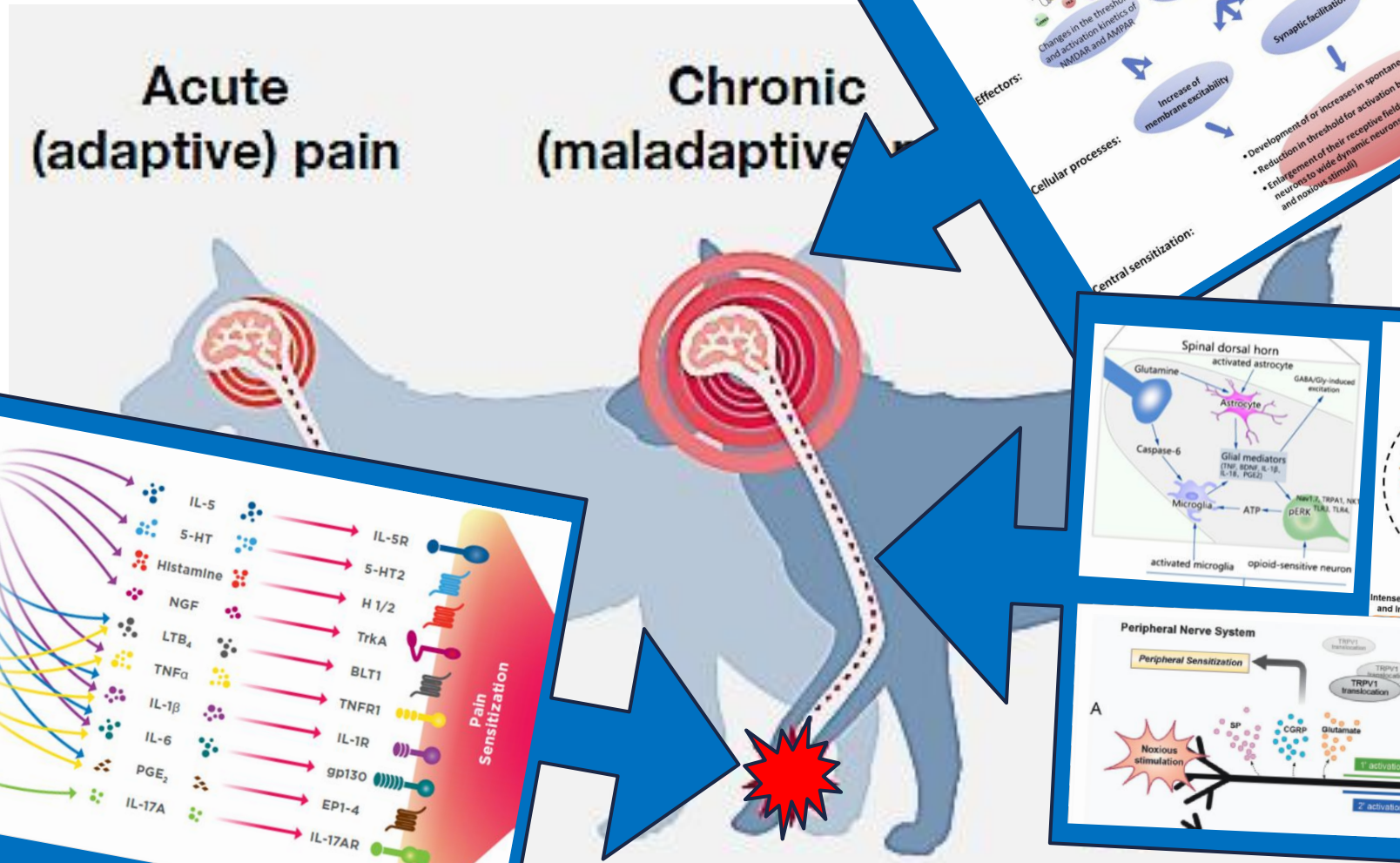
Pain Management Tools

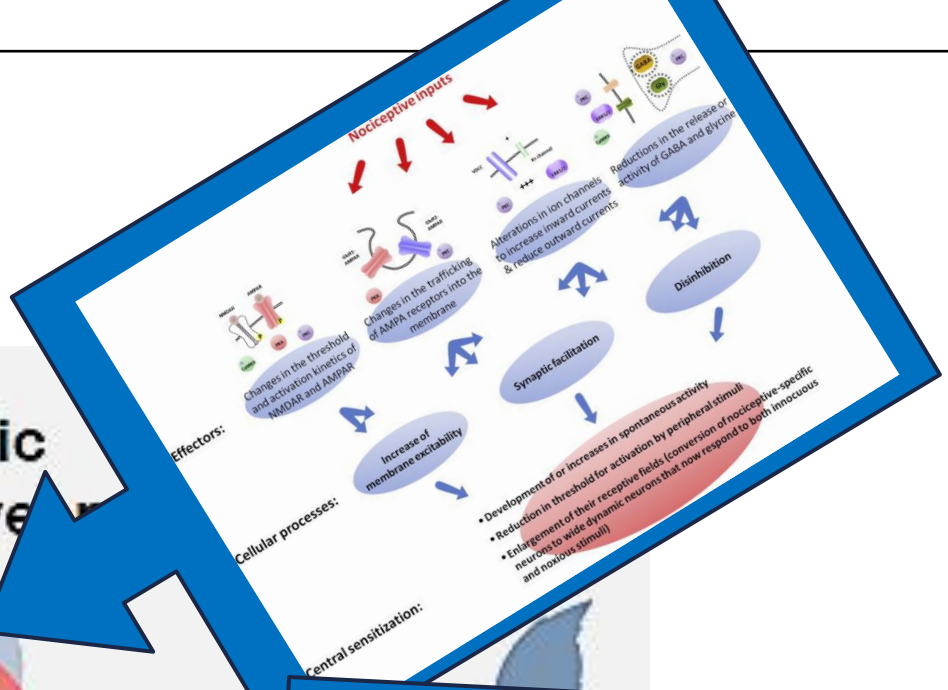
- Recognize individual pain perception and pain pathway upregulation

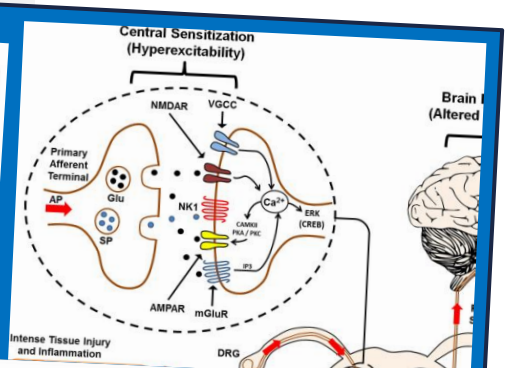
→ Treat accordingly based on response

- Assess treatment efficacy critically
  - Video observations
  - Pain Journal

Understanding Pain







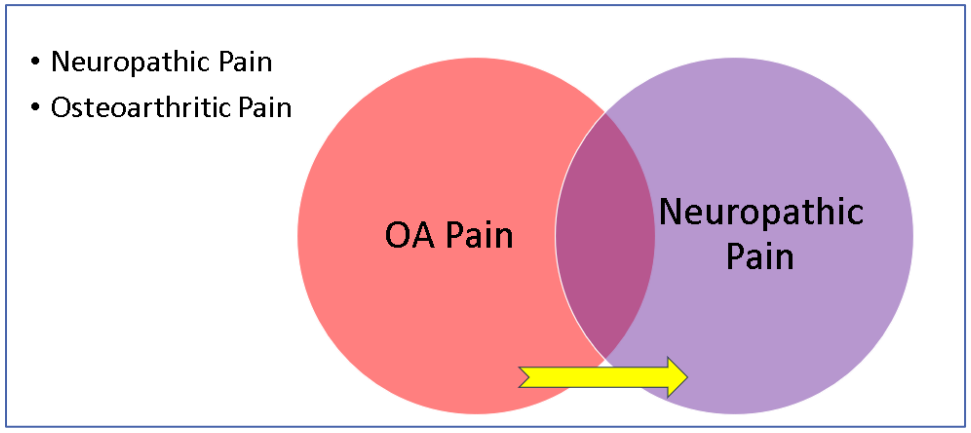
Gabapentinoids

- Gabapentin has little evidence in vet med and is widely used extra-label based on anectodical clinical opinions

- Its anxiolytic role is most useful, including for pain management
- Inability to assess analgesic potential or true inability to provide analgesia

When NOT to use Gabapentin:

- Single agent for acute pain!
- First line or sole treatment for chronic pain.
- First line or sole treatment for seizures.



Gabapentin Canine OA

BSAVA Congress

Tramadol and gabapentin improve peak vertical force in osteoarthritic dogs already receiving non-steroidal anti-inflammatory drugs

James Miles, Jimmy Bøjesen, Philip Christensen, Emilie Andersen-Ranberg, Anne Vitger, Helle Harding Poulsen, Lise Nikolic Nielsen

Department of Veterinary Clinical Sciences, University of Copenhagen, Copenhagen, Denmark

OBJECTIVES

Osteoarthritis is a common, disabling condition of older dogs. The response to non-steroidal anti-inflammatories may be insufficient to maintain a good quality of life. Limited data exist regarding the effect of adjunctive analgesics in these patients despite widespread usage.

METHODS

Twenty-four osteoarthritic dogs were prospectively recruited to a randomised, observer-blinded, crossover study. In addition to non-steroidal anti-inflammatory treatment, patients received either tramadol (3–5 mg/kg) or gabapentin (8–12 mg/kg) thrice daily for 4 weeks, with a one-week washout between treatments. Using a Tekscan pressure-sensitive walkway, peak vertical force for the worst-affected limb was used as the outcome measure. Haematology, biochemistry and urinalysis were performed before and after each treatment period.

RESULTS

Eighteen dogs completed the trial. Both tramadol and gabapentin significantly ($p < 0.01$) increased peak vertical force (mean 6.7% and 6.4%, respectively). No carryover or period effects of treatment were seen ($p > 0.05$). No statistically significant difference was found between treatments, but more dogs achieved an increase of >5% in peak vertical force with gabapentin than with tramadol (61% vs 50%). No significant changes to selected paraclinical parameters were observed. One or more side effects (typically transient and dose-dependent) occurred in up to 70% of dogs with both treatments.

STATEMENT (CONCLUSIONS)

Both tramadol and gabapentin can improve weight bearing in osteoarthritic dogs, and both appear safe for short-term use in older patients, but the incidence of side effects appears high compared to previous reports, and may outweigh the benefits in some patients. Owner counselling is recommended before and during use of these medications.

Gabapentin - Feline OA

Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats

Alonso G. P. Guedes MV, PhD
Julie M. Meadows DVM
Bruno H. Pypendop DrMedVet, DrVetSci
Eric G. Johnson DVM
Bianca Zaffarano DVM

From the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, University of Minne-

OBJECTIVE
To evaluate effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life (QOL) in osteoarthritic geriatric cats.

DESIGN
Blinded, placebo-controlled, randomized crossover-design study.

ANIMALS
20 osteoarthritic cats (≥ 10 years old).

Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats

OBJECTIVE

To evaluate effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life (QOL) in osteoarthritic geriatric cats.

DESIGN

Blinded, placebo-controlled, randomized crossover-design study.

ANIMALS

20 osteoarthritic cats (≥ 10 years old).

PROCEDURES

Cats received gabapentin (10 mg/kg [4.5 mg/lb]) or placebo treatment, PO, every 12 hours for 2 weeks, followed by the alternate treatment (with no washout period). Activity was assessed with a collar-mounted accelerometer. A client-specific outcome measure (CSOM) questionnaire was used weekly to collect owner assessments of 3 selected activities in which their cats had impaired mobility; QOL ratings (worse, the same, or improved) following crossover to each treatment and for the overall study period were collected at the end of the investigation. Activity counts, CSOM and QOL data, and deterioration in impaired activities (ie, decrease of ≥ 2 points in CSOM scores) associated with treatment crossover were assessed statistically. Adverse events were recorded.

RESULTS

Gabapentin administration was associated with significantly lower mean daily activity counts (48,333 vs 39,038 counts/d) and significantly greater odds (approx 3-fold change) of CSOM ratings indicating improvement in impaired activities, compared with results for the placebo treatment. A greater proportion of cats had deterioration in impaired activities after the crossover from gabapentin to placebo than when the opposite occurred, but the proportion of cats with worsened QOL did not differ between sequences. Adverse events were noted for 10 cats (9 that completed the study) during gabapentin treatment (sedation, ataxia, weakness, and muscle tremors) and 1 cat during placebo treatment (lethargy).

CONCLUSIONS AND CLINICAL RELEVANCE

Gabapentin treatment was associated with improvement in owner-identified impaired activities of osteoarthritic cats. Activity levels were lower than those during placebo treatment, and sedation was the most common adverse effect. (*J Am Vet Med Assoc* 2018;253:579–585)

Gabapentin in Feline OA

- Gabapentin in geriatric cats with osteoarthritis
  - 10 mg/kg Q 12 hours for 2 weeks, compared with placebo
  - Compared to the placebo, gabapentin resulted in:
    - Improvement with owner-identified impaired activities, but overall activity levels measured by the accelerometer were decreased
    - Quality of life scores were not significantly different
  - Reported side effects with gabapentin included sedation and hindlimb weakness in this cat population

Guedes AGP, et al (2018) Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats. JAVMA. 253(5): 579-85.

Gabapentinoids

Gabapentin

- MOA
  - Blocks VGCa^{2+} channels
  - Some serotonin effects
  - Increase in GABA
- PK:
  - TID necessary
- Side effects
  - Sedation, ataxia
    - 'Drunken sailor walk'

Pregabalin

- Same MOA
- Superior PK
  - ↑ Bioavailability
  - ↑ Duration (BID dosing, 3-5mg/kg)
  - ↓ Side effects

Pharmacokinetics of single-dose oral pregabalin administration in normal dogs. Veronica Salazar, VAA, 2009

Ketamine

- Dr. Lindsey Fry
  - Informative IVAPM lecture available on youtube:

https://www.youtube.com/watch?v=D_3d2UbIDQo

MOA:
- Blocking NMDA receptor: reducing windup
- Resetting central neuromodulation at microglia level and descending pathway

Ketamine CRI:
- Place catheter
- Bolus 0.25-0.5mg /kg (depending on case, more fractious or more palliative cases will receive lower dose). Give slowly over 1-3min
- CRI: 2-10mcg/kg/min for 2-6h (length and dose is depending on case).
- Some will start with 2mcg/kg/min and increase slowly overtime (ie double) every 20-30min, but can increase faster at subsequent visits if well tolerated.
- Side effects to look for: tachycardia, agitation

Ketamine administered SQ:
- 0.5mg/kg SQ every 4 weeks
- Decrease dose for giant breeds or very palliative cases to evaluate initial response. Once monthly may have to be reduced to every 2 weeks in some individual cases.

Anti-NGF

- Innovation for pain management
- Still a lot to learn about role of NGF in physiology and pathophysiology

Received: 1 September 2021 | Revised: 25 March 2022 | Accepted: 14 May 2022
DOI: 10.1002/jor.25382

RESEARCH ARTICLE

Journal of Orthopaedic Research®

Nerve growth factor receptors in equine synovial membranes vary with osteoarthritic disease severity

Anna Kendall | Stina Ekman | Eva Skiöldebrand

Vet Comp Orthop Traumatol 2025; 38(04): A1-A35
DOI: 10.1055/s-0045-1810284

PODIUM ABSTRACTS

A Randomized, Double-Blinded, Noninferiority Trial Evaluating the Efficacy of Bedinvetmab (Librela), a Fully Canine Anti-Nerve Growth Factor Monoclonal Antibody, Compared to Grapiprant for Osteoarthritis Pain in Dogs using Force Plate Gait Analysis

Authors

Author Affiliations

M. Enomoto, L. Buslinger, C. Thonen-Fleck, R. Tomacheuski, E. Kawecki-Wright, S. Aker, A. Maney, M. Edel, J. F. Innes, B. D. X. Lascelles,

Acetaminophen

- MOA: Not fully understood
  - Anti-pyretic:
    - central COX - inhibition
  - Analgesic mechanisms:
    - TRPV1-mediated anti-nociception
    - Anandamide reuptake inhibition
    - Other mechanisms?

Comparison of the effects on lameness of orally administered acetaminophen-codeine and carprofen in dogs with experimentally induced synovitis

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Stephanie A. Kleine DVM, PhD
Megan M. Norton MS
Gabriella S. Sandberg BS
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Received September 3, 2019.
Accepted December 30, 2019.

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Address correspondence to Dr. Budsberg (Budsberg@uga.edu).

OBJECTIVE
To compare the ability of acetaminophen-codeine (AC; 15.5 to 18.5 mg/kg and 1.6 to 2.0 mg/kg, respectively) or carprofen (4.2 to 4.5 mg/kg) administered PO to attenuate experimentally induced lameness in dogs.

ANIMALS
7 purpose-bred dogs.

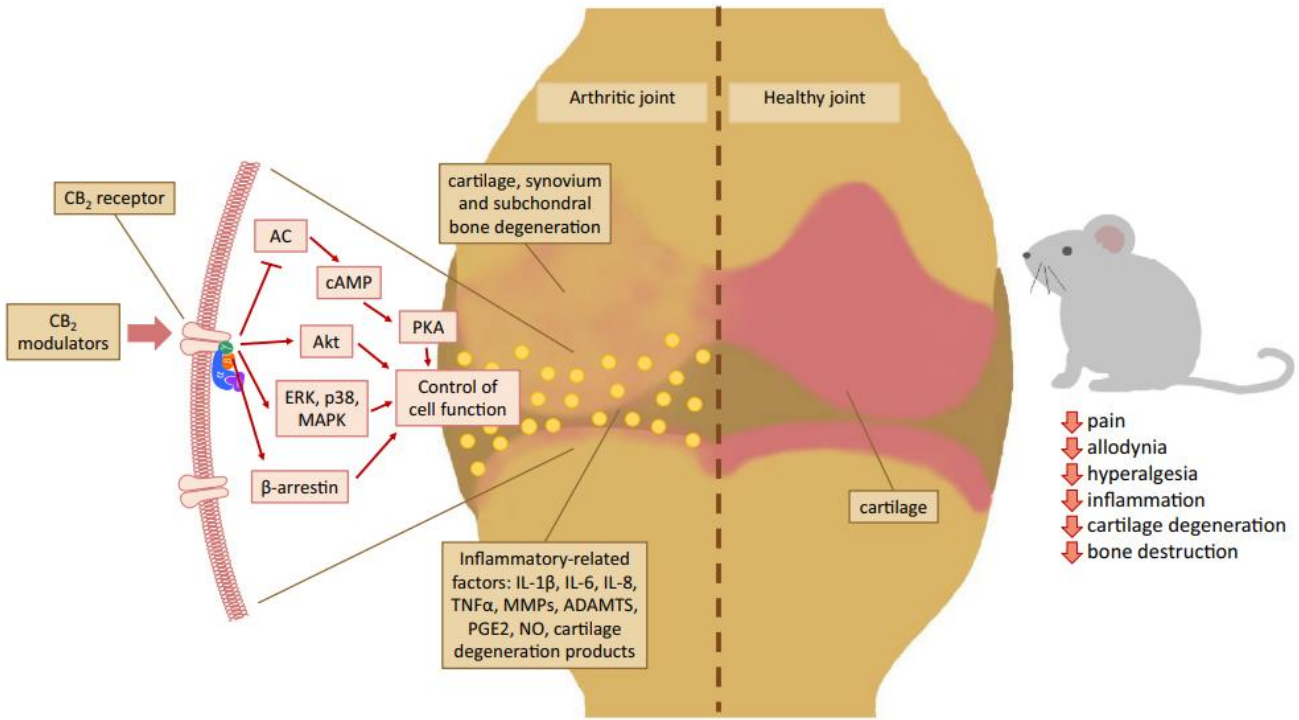
PROCEDURES
A blinded crossover study was performed. Dogs were randomly assigned to receive AC or carprofen treatment first and then the alternate treatment a minimum of 21 days later. Synovitis was induced in 1 stifle joint during each treatment by intra-articular injection of sodium urate (SU). Ground reaction forces were assessed, and clinical lameness was scored at baseline (before lameness induction) and 3, 6, 9, 12, 24, 36, and 48 hours after SU injection. Plasma concentrations of acetaminophen, carprofen, codeine, and morphine were measured at various points. Data were compared between and within treatments by repeated-measures ANOVA.

RESULTS
During AC treatment, dogs had significantly higher lameness scores than during carprofen treatment at 3, 6, and 9 hours after SU injection. Peak vertical force and vertical impulse during AC treatment were significantly lower than values during carprofen treatment at 3, 6, and 9 hours. Plasma concentrations of carprofen (R)- and (S)-enantiomers ranged from 2.5 to 19.2 µg/mL and 4.6 to 25.0 µg/mL, respectively, over a 24-hour period. Plasma acetaminophen concentrations ranged from 0.14 to 4.6 µg/mL and codeine concentrations from 7.0 to 26.8 ng/mL, whereas plasma morphine concentrations ranged from 4.0 to 58.6 ng/mL.

CONCLUSIONS AND CLINICAL RELEVANCE
Carprofen as administered was more effective than AC at attenuating SU-induced lameness in dogs. (*Am J Vet Res* 2020;81:627–634)

Cannabinoids

Graphic abstract



Pharmacological Reports (2021) 73:681–699
https://doi.org/10.1007/s43440-021-00270-y

REVIEW

Cannabinoid-based therapy as a future for joint degeneration. Focus on the role of CB_2 receptor in the arthritis progression and pain: an updated review

Marta Bryk[1] · Katarzyna Starowicz[1]

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Cannabinoid receptor type 2 is upregulated in synovium following joint injury and mediates anti-inflammatory effects in synovial fibroblasts and macrophages

P. Rzeczycki, C. Rasner, L. Lammlin, L. Junginger, S. Goldman, R. Bergman, S. Redding, A.J. Knights, M. Elliott, T. Maerz*

Orthopaedic Research Laboratories, Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA

ELSEVIER

Biomedicine & Pharmacotherapy
Volume 186, May 2025, 118040

The emerging role of endocannabinoid system modulation in human fibroblast-like synoviocytes: Exploring new biomarkers and potential therapeutic targets

Jakub Chwastek [a c], Marta Kędziora [a], Małgorzata Borczyk [b], Michał Korostyński [b], Fabiana Piscitelli [d], Vincenzo Di Marzo [d e], Katarzyna Starowicz [a]

Valastro et al. BMC Veterinary Research (2017) 13:309
DOI 10.1186/s12917-017-1245-7

BMC Veterinary Research

RESEARCH ARTICLE Open Access

Characterization of endocannabinoids and related acylethanolamides in the synovial fluid of dogs with osteoarthritis: a pilot study

Carmela Valastro*, Debora Campanile[1], Mariarosaria Marinaro[2], Delia Franchini[1], Fabiana Piscitelli[3], Roberta Verde[3], Vincenzo Di Marzo[3] and Antonio Di Bello[1]

Cannabinoids

Cannabis and Cannabinoid Research
Volume 8, Number 6, 2023
© Mary Ann Liebert, Inc.
DOI: 10.1089/can.2021.0244

Open camera or QR reader and scan code to access this article and other resources online.

ORIGINAL RESEARCH

Therapeutic Effects of Non-Euphorigenic Cannabis Extracts in Osteoarthritis

Vengadeshprabhu Karuppagounder,[1,2,†] Juliet Chung,[1,2,†] Ahmed Abdeen,[1,2] Amy Thompson,[1,2] Andreas Bouboukas,[1,2] William J. Pinamont,[1,2] Natalie K. Yoshioka,[1,2] Diana E. Sepulveda,[3,4] Wesley M. Raup-Konsavage,[3] Nicholas M. Graziane,[3,4] Kent E. Vrana,[3] Reyad A. Elbarbary,[1,2,5,*] and Fadia Kamal[1–3,*]

mice. CBD oil and CBG oil treatments significantly reduced synovitis in DMM mice. Only CBG oil reduced cartilage degeneration, chondrocyte loss, and matrix metalloproteinase 13 expression, with a significant increase in the number of anabolic chondrocytes. Subchondral bone remodeling found in vehicle-treated DMM mice was not ameliorated by either CBD or CBG oil.

Conclusions: Our results show evidence for the therapeutic efficacy of CBD oil and CBG oil, where both oils ameliorate pain and inflammation, and improve gait and locomotor activity in OA mice, representing clinical pain and function. Importantly, only CBG oil is chondroprotective, which may provide superior efficacy in future studies in OA patients.

Keywords: osteoarthritis; therapeutics; pain; DMOAD; cannabinoids

CBG

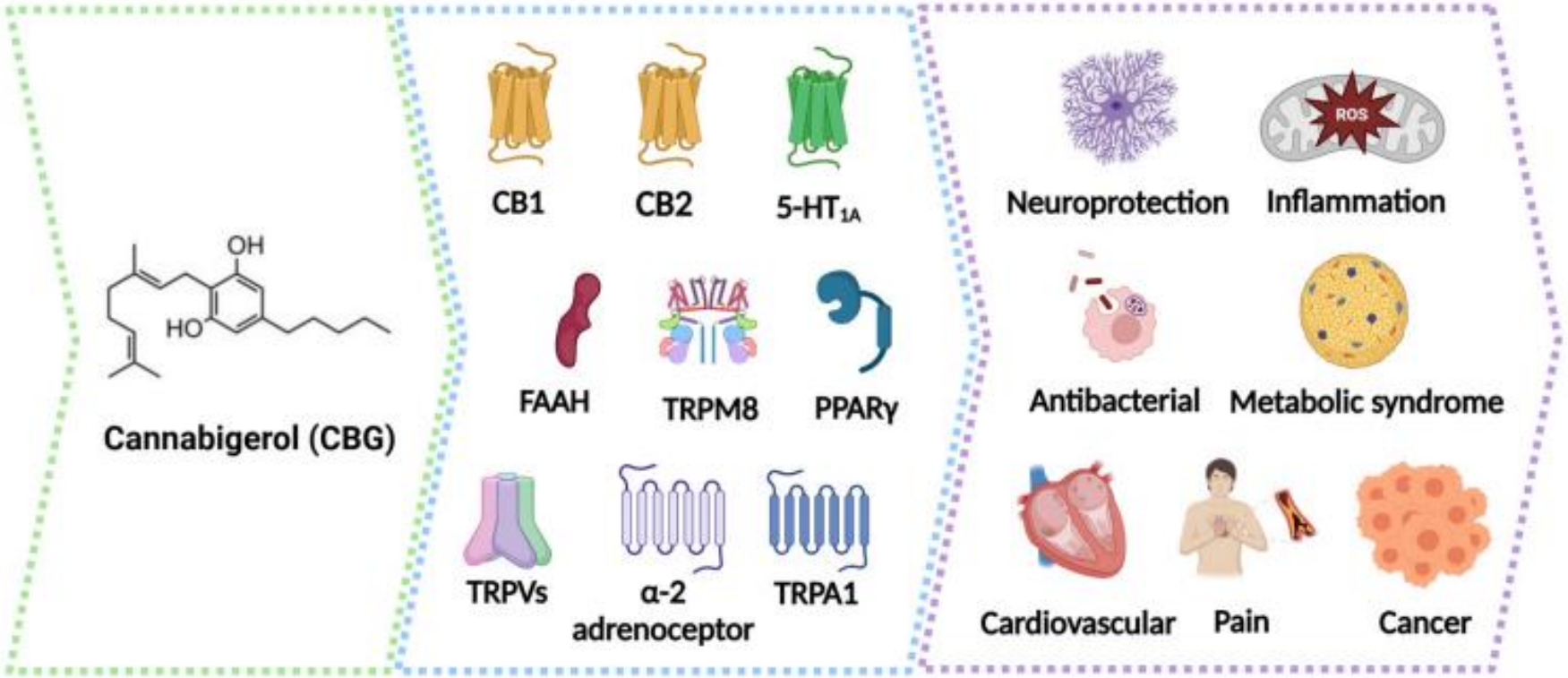
molecules

MDPI

Review

Cannabigerol (CBG): A Comprehensive Review of Its Molecular Mechanisms and Therapeutic Potential

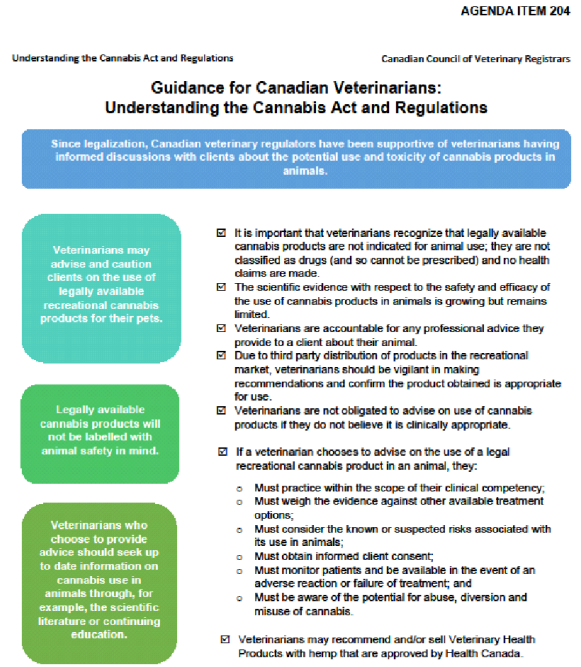
Shijia Li [1,†], Weini Li [2,†], Naseeb Kaur Malhi [3], Junwei Huang [1], Quanqi Li [1], Ziwei Zhou [1], Ruiheng Wang [2], Jiangling Peng [1,*], Tong Yin [4,*] and Honggen Wang [5]



Pharmacodynamic properties of CBG at related receptors

CCVR Guidance

- **"If a veterinarian chooses to advise on the use of a legal recreational cannabis product in an animal, they:**
  - Must practice within the scope of their clinical competency;
  - Must weigh the evidence against other available treatment options;
  - Must consider the known or suspected risks associated with its use in animals;
  - Must obtain informed client consent;
  - Must monitor patients and be available in the event of an adverse reaction or failure of treatment;
  - Must be aware of the potential for abuse, diversion and misuse of cannabis."



AGENDA ITEM 204

Understanding the Cannabis Act and Regulations — Canadian Council of Veterinary Registrars

Guidance for Canadian Veterinarians:
Understanding the Cannabis Act and Regulations

Since legalization, Canadian veterinary regulators have been supportive of veterinarians having informed discussions with clients about the potential use and toxicity of cannabis products in animals.

Veterinarians may advise and caution clients on the use of legally available recreational cannabis products for their pets.

Legally available cannabis products will not be labelled with animal safety in mind.

Veterinarians who choose to provide advice should seek up to date information on cannabis use in animals through, for example, the scientific literature or continuing education.

- ☑ It is important that veterinarians recognize that legally available cannabis products are not indicated for animal use; they are not classified as drugs (and so cannot be prescribed) and no health claims are made.
- ☑ The scientific evidence with respect to the safety and efficacy of the use of cannabis products in animals is growing but remains limited.
- ☑ Veterinarians are accountable for any professional advice they provide to a client about their animal.
- ☑ Due to third party distribution of products in the recreational market, veterinarians should be vigilant in making recommendations and confirm the product obtained is appropriate for use.
- ☑ Veterinarians are not obligated to advise on use of cannabis products if they do not believe it is clinically appropriate.
- ☑ If a veterinarian chooses to advise on the use of a legal recreational cannabis product in an animal, they:
  - Must practice within the scope of their clinical competency;
  - Must weigh the evidence against other available treatment options;
  - Must consider the known or suspected risks associated with its use in animals;
  - Must obtain informed client consent;
  - Must monitor patients and be available in the event of an adverse reaction or failure of treatment; and
  - Must be aware of the potential for abuse, diversion and misuse of cannabis.
- ☑ Veterinarians may recommend and/or sell Veterinary Health Products with hemp that are approved by Health Canada.

CCVR Guidance - in a Nutshell

- May advise/caution on legal products
- Must stay within competency
- Must obtain informed consent
- Must monitor and document
- Not obligated to advise

Documentation & Medical Records

"Client inquired about Cannabinoids for "Fluffy". We discussed this option at length with reviewing current studies, legality, risk and benefits specifically for Fluffy. With this information Ms. Smith would like to pursue this treatment avenue. I recommended XPRODUCT based on Fluffy's disease and product composition. Ms Smith will order the product from OCS, send a photo to confirm, and we will reconnect about specific dosing and administration tips, starting at 0.5mg/kg BID"

Tip: NOT IN PRESCRIPTION SECTION

Safety and Efficacy of the Therapeutic Use of Cannabis-Based Products in the Treatment of Dogs: An Integrative Review

Diego Fontana de Andrade,[1,*] João Lourenço Hasckel Gewehr,[2] and Erik Amazonas de Almeida[3]

Table 3. Main Findings of Efficacy Studies of Cannabis-Based Products in the Treatment of Dogs

Product description	Medical conditions	Route of administration	Dosage regimen	Experimental design	No. of participants	Main results	References
Cannabis extract containing CBD, THC, CBC, and CBG incorporated in an oily matrix (olive oil)	Osteoarthritis	Oral	2 mg of CBD/kg of body weight, every 12 h, for 4 weeks	Randomized, double-blinded (veterinarian and tutor), crossover and placebo-controlled	16	↓ pain and ↑ dogs' activity	Gamble et al.[16]
Purified Cannabis extract containing CBD	Intractable idiopathic epilepsy	Oral	2.5 mg/kg of body weight, twice a day, for 12 weeks	Randomized, double-blinded (veterinarian and tutor), placebo-controlled	16	↓ frequency of seizures, but no difference was observed in the proportion of respondents between the test and placebo groups	McGrath et al.[18]
Purified Cannabis extract containing CBD incorporated into an oily matrix (MCT)	Osteoarthritis	Oral transmucosal	2 mg/kg of body weight, every 12 h, for 12 weeks	Randomized, placebo-controlled	21	↓ pain perception and improvement in the animals' quality of life	Brioschi et al.[22]
Chewable treat formulated with purified Cannabis extract containing CBD	Anxiety	Oral	0.7 mg/kg of body weight, twice a day, for 7 days	Randomized, placebo-controlled	16	There was no evidence of anxiolytic effect associated with the administration of CBD	Morris et al.[19]
Isolated CBD incorporated into an oily matrix (vegetable oil)	Osteoarthritis	Oral	0.5 or 1.2 mg/kg of body weight once a day for 6 weeks	Randomized, double-blinded (veterinarian and tutor), placebo controlled	16	Improvement in the animals' quality of life (only to the test group treated with the highest dose)	Verrico et al.[20]
Purified Cannabis extract containing CBD	Aggressive behavior	Oral	Approximately 1.25 mg/kg body weight once daily for 45 days	Randomized, blinded (dog behavior observers), placebo controlled	24	There was no evidence of reduction in animals' aggressive behavior	Corsetti et al.[21]
Purified Cannabis extract containing CBD	Osteoarthritis	Oral	2.5 mg/kg of body weight, every 12 h, for 6 weeks	Randomized, double-blinded, crossover and placebo-controlled	23	There were no differences between groups on activity count, clinical metrology instrument, and objective gait analysis	Mejia et al.[25]

Pharmacokinetic Data

Pharmacokinetic and Safety Evaluation of Various Oral Doses of a Novel 1:20 THC:CBD *Cannabis* Herbal Extract in Dogs

Alan Chicoine[1], Kate Illing[1], Stephanie Vuong[2], K. Romany Pinto[3], Jane Alcorn[2] and Kevin Cosford[3]*

[1] Department of Veterinary Biomedical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, SK, Canada, [2] College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK, Canada, [3] Department of Small Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon. SK. Canada

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 04 September 2020
doi: 10.3389/fvets.2020.00505

Pharmacokinetics of Cannabidiol, Cannabidiolic Acid, Δ9-Tetrahydrocannabinol, Tetrahydrocannabinolic Acid and Related Metabolites in Canine Serum After Dosing With Three Oral Forms of Hemp Extract

Joseph J. Wakshlag[1], Wayne S. Schwark[2], Kelly A. Deabold[3], Bryce N. Talsma[3], Stephen Cital[4], Alex Lyubimov[5], Asif Iqbal[5] and Alexander Zakharov[5]*

OPEN ACCESS

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 11 February 2020
doi: 10.3389/fvets.2020.00051

Preliminary Investigation of the Safety of Escalating Cannabinoid Doses in Healthy Dogs

Dana Vaughn, Justyna Kulpa and Lina Paulionis*

Canopy Animal Health, Canopy Growth Corporation, Toronto, ON, Canada

"CBD Products"

Hemp Oil Hemp Seed Oil	Oil derived from hemp seeds, contain large % of FA, other nutrients. Does NOT contain any cannabinoids or terpenes
CBD Oil	A very broad term to describe oil-based product containing CBD
Full Spectrum Oil	A cannabis extract that contains all of cannabinoids, terpenes, and flavonoids found in the parent plant, ideally in similar ratio to that found in raw material
Broad Spectrum Oil	Does not include ALL ingredients, otherwise similar to full spectrum oil

https://www.cavcm.com/post/the-hype-about-hemp-products

CAVCM 2025 OCS Product List

ONTARIO CANNABIS STORE

Company	Product	CBD mg/ml (listed as range provided)		THC mg/ml	CBD:THC Ratio Estimate	Total (known) Cannabinoids (mg/mL)	$$$	Terpenes/Terpenoids Present		Carrier Oil	Extraction Method
Axea	THC-Free Daytime CBD Isolate Oil	49.5	55	0	49.5:0 to 55:0	49.5-55	30mL $44.95	N	ocs.ca - CBD isolate	MCT	ND
Blissed	Breathe High CBD Oil	24	30	0-2	24:0 to 15:1	24-32	20mL $24.95	Y	Blissed website - Caryophyllene, Guaiol, Bisabolol (confirmed by email) Ocs.ca – terpenes removed	MCT	CO2
COVE	CBD Cannabis Oil	17	23	0-3	17:0 to 8:1	17-26	20mL $49.95	Y	Cove website & ocs.ca - Myrcene, Beta-Caryophyllene	MCT	CO2
Divvy	CBD 75 Oil	67.1	90.7	0-4	67:0 to 17:1	67-95	30mL $54.95	N	ocs.ca - terpenes removed	MCT	C02
Dosecann	CBD 100 Oil	98	105	0-3.3	98:0 to 30:1	98-108	30mL $74.95	N	Dosecann website – product unavailable Ocs.ca Terpenes Removed	MCT	ND
Dosecann	CBD Orange Oil	50	53	0-2	50:0 to 27:1	50-55	30mL $39.95	N	Dosecann website – product unavailable Ocs.ca Terpenes Removed. "Natural orange flavour"	MCT	ND
Dosecann	CBD Oil	26	26	1	26:1	27	30mL $19.95	N	Dosecann website – unflavoured Ocs.ca – terpenes removed	MCT	CO2
Dosecann	CBD Omega Lemon Lavender Oil	24.7	24.7	0	25:0	25	30mL $29.95	?	Dosecann website - product unavailable	Ahiflower Seed Oil	ND
Edison Cannabis Co	CBD Oil	10	11	0-1	10:0 to 11:1	10-12	25mL $19.95	?	Edison website – not disclosed Edison phone - waiting for a response Ocs.ca Beta-Caryophyllene	Sunflower Oil	Ethanol

https://www.cavcm.com/product-list-ocs

CBD Dominant Products

MEDIPHARM LABS

CBD25 Regular Formula Oil

Blend

THC
0 - 57 mg

CBD
655.5 - 769.5 mg

30 ml

$36.45 Taxes Included

MEDIPHARM LABS

CBD50 Plus Formula Oil

Blend

THC
0 - 71.25 mg

CBD
1368 - 1539 mg

30 ml

$62.50 Taxes Included

MEDIPHARM LABS

CBD 100 Ultra Formula Oil

Blend

THC
0 - 142.5 mg

CBD
2707.5 - 2999.2 mg

30 ml

$88.30 Taxes Included

MEDIPHARM LABS

CBN:CBD 1:2 Relax Formula

Blend

THC
0 - 57 mg

CBD
510 - 630 mg

30 ml

$44.90 Taxes Included

MEDIPHARM LABS

CBG:CBD 1:2 Advanced Formula Oil

Blend

THC
0 - 28.5 mg

CBD
484.5 - 655.5 mg

30 ml

$45.50 Taxes Included

Product Selection

Pain:

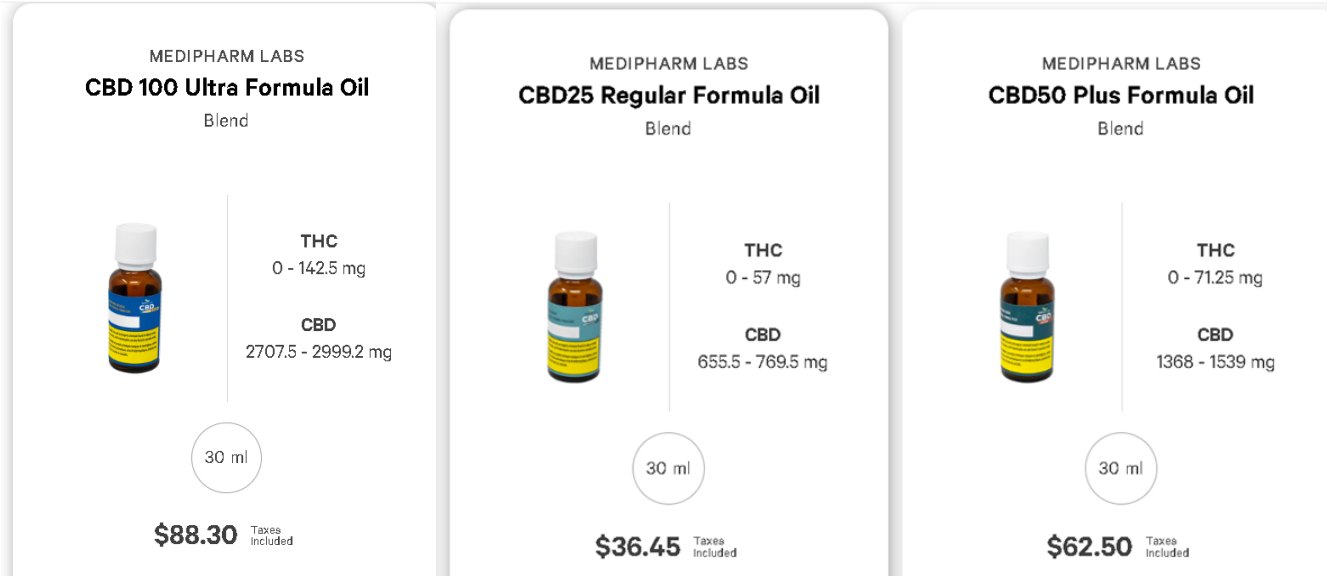
Full spectrum: CBD:THC- 20:1,

+ CBG, CBDA

Terpenes:

beta-caryophyllene

myrcene



CBD dominant Product

- Medipharm CBD50 Plus
  - 50: 1 CBD: THC product
  - Full spectrum
  - Terpenes: may vary

No full COA available

		25:1				
Medipharm Labs	CBD 50 Plus Formula Oil	48:0 to 24:1	48-56	30mL $59.95	Y	Medipharm Labs website – not disclosed ocs.ca - terpenes vary Other source - Guaiol, Terpineio, Borneol, Linalool, Cedrene, Frenchyl, Myrcene

Calculation

*1ml MCT Oil = ~0.94g
So, 1ml = ~1g

Published dosing range:
0.5-2mg/kg BID

MEDIPHARM LABS

CBD50 Plus Formula Oil

00628639000866

$59.95 / bottle

Taxes Included

THC ?
0.00 - 57.00 mg
0.00 - 2.00 mg/g

CBD ?
1368.00 - 1539.00 mg
48.00 - 54.00 mg/g

PLANT TYPE ?
Blend

- Dosing:
  - 0.2mg/kg BID
  - > **0.2mg/kg x 30kg = 6mg**
  - Product:
    - CBD 52.8mg/ml + THC 1.3mg/ml =54.1mg/ml total cannabinoids
  - > **6mg : 54.1mg/ml = 0.11ml**

  - **Plan: 1 week 0.1mls BID > increase to 0.2mls (0.4mg/kg) for another week**
  - **Continue to 1-2mg/kg**
    - **Adjust dose/product choice based on response**

Product Selection

Seizures:

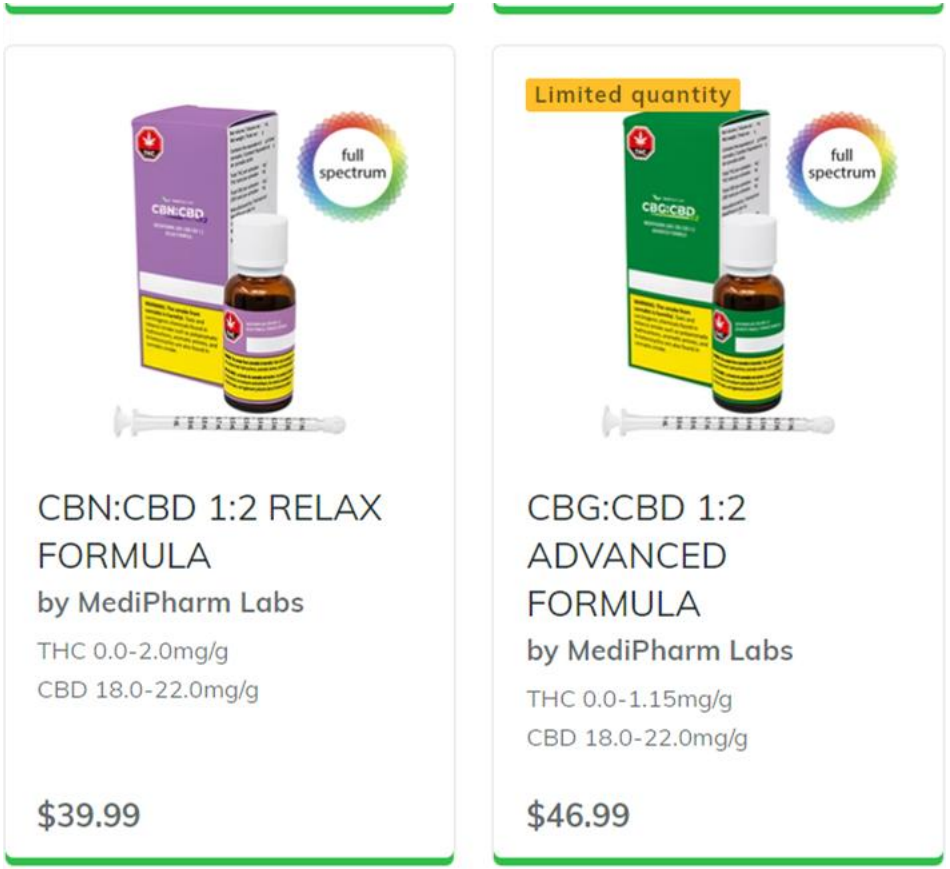
CBD/CBN

Terpenes: linalool

(full spectrum vs. isolates)

Canine Cognitive Dysfunction:

CBD/CBG



CBD Dominant Products

CBN:CBD 1:2 RELAX FORMULA

by MediPharm Labs

THC 0.0-2.0mg/g

CBD 18.0-22.0mg/g

$39.99

Limited quantity

CBG:CBD 1:2 ADVANCED FORMULA

by MediPharm Labs

THC 0.0-1.15mg/g

CBD 18.0-22.0mg/g

$46.99

High-CBG, High-CBD. With 10mg/ml of CBG and 20mg/ml of CBD (300 mg of CBG and 600 mg of CBD per 30ml bottle), MediPharm Labs' CBG:CBD 1:2 is pharma-quality oil made using quality cannabis extract. The advanced formula is produced at MediPharm Labs using strict manufacturing standards to bring you the highest quality and purity. This high-quality formulated oil has a subtle cannabis flavour. The pharmaceutical-grade coconut/palm-based MCT carrier oil has been carefully chosen for its eco-conscious practices from plantations.

Produced in	Ontario
Producer	MediPharm Labs
Type	Blend
THC	0.0-1.15mg/g
CBD	18.0-22.0mg/g
Method of consumption	INGEST
Extraction process	CO2
Carrier oil(s)	MCT
Packaging material	Glass

Ufeelu Brand

PRICE DROP

UFEELU

Rest Drops

Blend

THC
0 mg

CBD
855 - 945 mg

30 ml

$39.30 Taxes Included ~~$46.60~~

UFEELU

Calm Drops

Blend

THC
0 mg

CBD
855 - 945 mg

30 ml

$40.15 Taxes Included

UFEELU

Dream Drops

Blend

THC
0 mg

CBD
570 - 630 mg

30 ml

$50.00 Taxes Included

UFEELU

Relief Drops

Blend

THC
0 mg

CBD
855 - 945 mg

30 ml

$52.05 Taxes Included

UFEELU

Focus Drops

Blend

THC
0 mg

CBD
570 - 630 mg

30 ml

$56.95 Taxes Included

CBD Dominant Products - BC

CBD OIL 30

by Pure Sunfarms

THC 0.0-1.6mg/g

CBD 27.0-33.0mg/g

$31.99

CLEAR CBD 100 OIL

by Floresense

THC 2.0-8.0mg/g

CBD 95.0-106.0mg/g

~~$34.99~~

$31.99

CBD OIL 2500 (CARMAGNOLA)

by LoFi

THC 1.0-3.0mg/g

CBD 48.0-52.0mg/g

$42.99

MAX STRENGTH CBD 200 DROPS

by Glacial Gold

THC 0.0-3.0mg/g

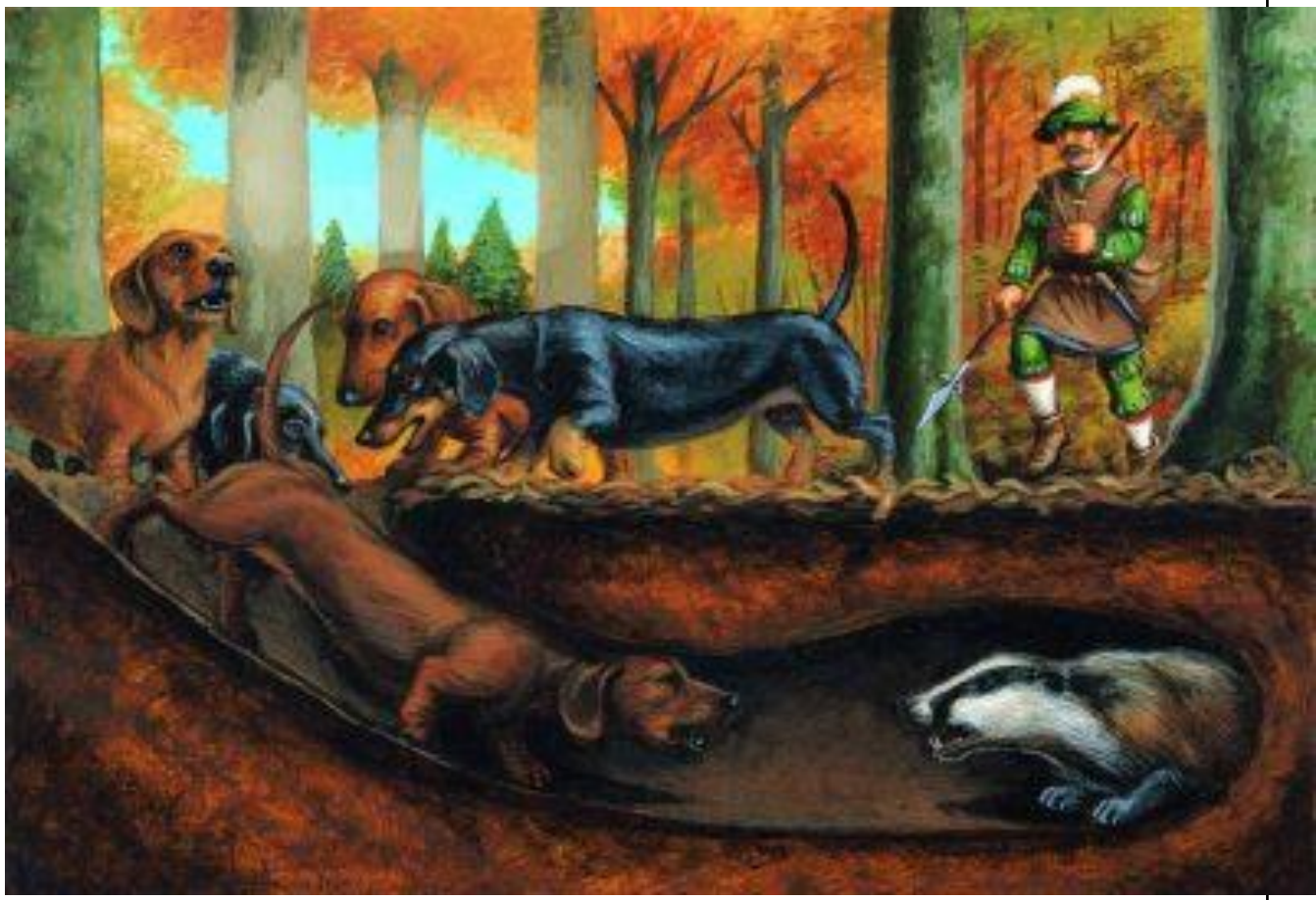
CBD 190.0-210.0mg/g

$46.99

Our Role to Effectively Prevent and Treat Suffering

- Prevention requires recognition of problems
  - Orthopedic developmental abnormalities at alarming incidence
  - Obesity and lack of appropriate exercise
  - Public awareness of breed disposition and risk factors
  - Recognition of early signs and commitment to treatment
- Effective treatment
  - Based on stage of disease (dental, orthopedic, skin)

Our Role in Genetic Science
Breeding Standards



Our Role in Genetic Science Breeding Standards

Images: Google doodle image search

Opportunities?

- How to…
  - Raise public awareness of unethical breeding
    - Better understanding of disease related risk factor and preventative measures
  - Take legislative steps for animal welfare

Other Ethical Dilemmas Related to Pain

- Ineffective Pain Management- Examples:
  - Postoperative Gabapentin instead of NSAID
  - Supplements only for chronic pain (ie.glucosamines)

Shift in Focus

- Focus on Preventative Medicine
- Focus on Early Treatment
- Focus on Recognizing the Signs of Pain
- Focus on Collaboration
- Focus on Research that help answer the right Questions

CANADIAN ONE HEALTH PAIN INITIATIVE

Thank you

TRUE NORTH
VETERINARY DIAGNOSTICS

True North Veterinary Diagnostics Inc. offers services in veterinary diagnostic hematology, chemistry, urinalysis, endocrinology, cytology, histopathology, microbiology, serology, necropsy and immunohistochemistry to veterinarians throughout British Columbia, and beyond. We look forward to serving you and your patients.

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