PHARMACOLOGICAL PAIN MANAGEMENT IN CANINES

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GOALS: THE GOAL OF THIS LESSON IS TO PRESENT A SYNOPSIS OF DIAGNOSIS AND TREATMENT OF PAIN IN CANINES

OBJECTIVES:

1. IDENTIFY ETIOLOGY AND EPIDEMIOLOGY OF PAIN IN CANINES
2. RECOGNIZE DIAGNOSITIC STRATEGIES TO CORRECTLY CATEGORIZE PAIN IN CANINES
3. RECOMMEND BOTH PHARMACOLOGICAL AND NONPHARMACOLOGICAL PAIN MANAGEMENT EXPEDIENTS IN CANINES
4. DESCRIBE THE PHARMACIST'S ROLE IN OPTIMAL CANINE PAIN TREATMENT PLANS

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Introduction

Pain is defined as a deleterious effect on several organ systems in which the body's stress response is amplified to traumatic injury, metabolomic, and endocrine derangements. As such, pain will often hinder the healing and recovery process. Saint Augustine once stated that "the greatest evil is physical pain". This has been an accepted philosophy by many healthcare professionals including veterinary specialists. Consequently, obtaining a pain score has frequently been considered the 'fourth vital sign', following temperature, pulse, and respiration. Successful pain management is an indispensable component in veterinary medicine as it reduces morbidity, alleviates pain, expedites patient recovery, and enhances the patient's quality of life.

Analogous to the human species, canines experience pain in much the same manner as their human counterparts. As it is often considered a human right and medical necessity to manage pain in humans, this ideology is frequently extrapolated to veterinary patients as well. This objective requires a fully integrated approach that utilizes a continuum of care that incorporates pain anticipation by employing pain scales, recognition and systematic assessment, early intervention both pharmacological and non-pharmacological, an individualized assessment of response, and follow-up measures to provide optimal pain management treatment modalities. Multidisciplinary teams including the veterinarian, specialist, pharmacist, and pet owner are encouraged to maximize recognition, assessment, treatment, and prevention of pain in canines. The pet owner is often considered the most integral part of the team as they have the greatest exposure to the dog and are able to assess the patient's deviations from normal, everyday behavior. Assuaging pain is both a professional obligation as well as a key contributor to improved quality of life.

BACKGROUND

Identifying factors of pain are comparable in both humans and canines. In veterinary patients, aversive sensory and emotional experience is connected with actual or potential tissue damage. Potential causes of pain include but are not limited to trauma, major or minor surgery, and acute or chronic inflammatory conditions. Pain is considered the endpoint of nociceptive input and only appears in a conscious animal. Pain is a multidimensional occurrence as it employs the autonomic pathways in which emotion and memory are involved.

Two types of pain have been identified; acute and chronic pain. Proper identification and management of both types of pain can ultimately result in life preservation. Acute pain includes both nociceptive and inflammatory responses that is a result of trauma, surgery, and/or medical conditions or diseases. Acute pain often has a specific and treatable cause that lasts less than six months once inflammatory and healing processes are concluded. Identification and management of acute pain is imperative as undermanaged and incomplete resolution of acute pain can transition into the complex phenomenon known as chronic pain, which can last up to a lifetime. Chronic pain is defined as persistent pain that continues beyond the allotted acute pain recovery period. Insufficient recognition and management of chronic pain can result in premature euthanasia. In dogs, chronic pain is dominated by the underdiagnosed disorder of degenerative joint disease (DJD). DJD is ubiquitously found in dogs of all ages and inevitably progresses over time.

Pain management therapy often concentrates on the underlying cause of pain rather than the arbitrary labels on duration of pain. Causes of pain include nociceptive, inflammatory and pathological pain. Nociceptive pain arises when peripheral neural receptors are stimulated by a noxious stimulus such as surgical incisions, trauma, hot or cold exposure, etc. Hyperalgesia is defined as an exaggerated response to noxious stimulus. Whereas allodynia consists of a painful response to non-noxious stimuli. Examples of allodynia would be light touch or pressure which is an expansion of the painful field beyond its original boundaries. As such, pain is protracted beyond the expected time of inflammation and healing. Inflammatory pain surfaces with the gradual activation of the immune system in response to injury or infection. Lastly, pathological pain (also known as maladaptive pain) results when pain is magnified and sustained by molecular, cellular and microanatomic changes, collectively defined as peripheral and central hypersensitization. Pathological pain can occur within a matter of minutes to certain acute pain triggers such as nerve injury, severe tissue trauma, or presence of pre-existing inflammation.

PRESENTATION OF PAIN IN CANINES

The communication gap between humans and their best friend, the dog, makes accurate pain assessment challenging and difficult to measure. As to be expected, the canine patient cannot communicate about their character of pain, location or length of pain, and ultimately whether pain even exists. During pain assessment, veterinary professionals must rely on the pet owner's pain narrative, their own clinical observations and experience, and various parameters that have been documented to evaluate pain in dogs.

From an evolutionary perspective, dogs exhibit a survival mechanism in which they hide their painful symptoms. In addition to pain assessment's subjective nature and bias, this survival mechanism has a compounded effect to make it even more challenging to accurately diagnosis pain, as it manifestations itself in many different forms. There is not a universal method in which dogs present their pain, which results in an arduous diagnosis of pain. Canines may either maintain normal behavior, have loss of normal behavior, or develop new behaviors while experiencing pain.

Pet owners are the greatest source and reference in determining the canine patient's pain level. Often owners will witness diminished function and mobility in their dog which is indicative of progressive disability. Potential signs for pet owner's to be on the lookout for when evaluating their dog's pain is if they are hesitant to do their usually daily tasks (such as reluctance to eat and/or drink, being touched or handled, uneasiness to rest, GI disturbances, decreased grooming, changes in urination and defecation habits, etc). In addition, decreased activity may be evident (such as reduced tendency to walk, climb stairs, jump in the car, engage in play, difficulty to stand, limping, stiffness, increased panting, restlessness and so on). Behavioral anomalies often accompany the more obvious indicators, however they are frequently overlooked and attributed to other health issues. Therefore, pet owners and veterinary practitioners must be vigilant of recognizing behavioral changes that are indicative of pain during the assessment process. Evident behavioral symptoms of pain include but are not limited to whimpering vocalization, quiet withdrawal, antisocial, uncharacteristic aggression, ears flat against head, and increased licking to painful/sensitive areas which can lead to skin redness and exacerbated hot spots.

An acronym that encapsulates the main traits displayed in canine pain is BEST friend:

B-behavioral changes
E-eating less
S-skin redness, scabs
T- tarry stool, diarrhea vomiting
FRIEND

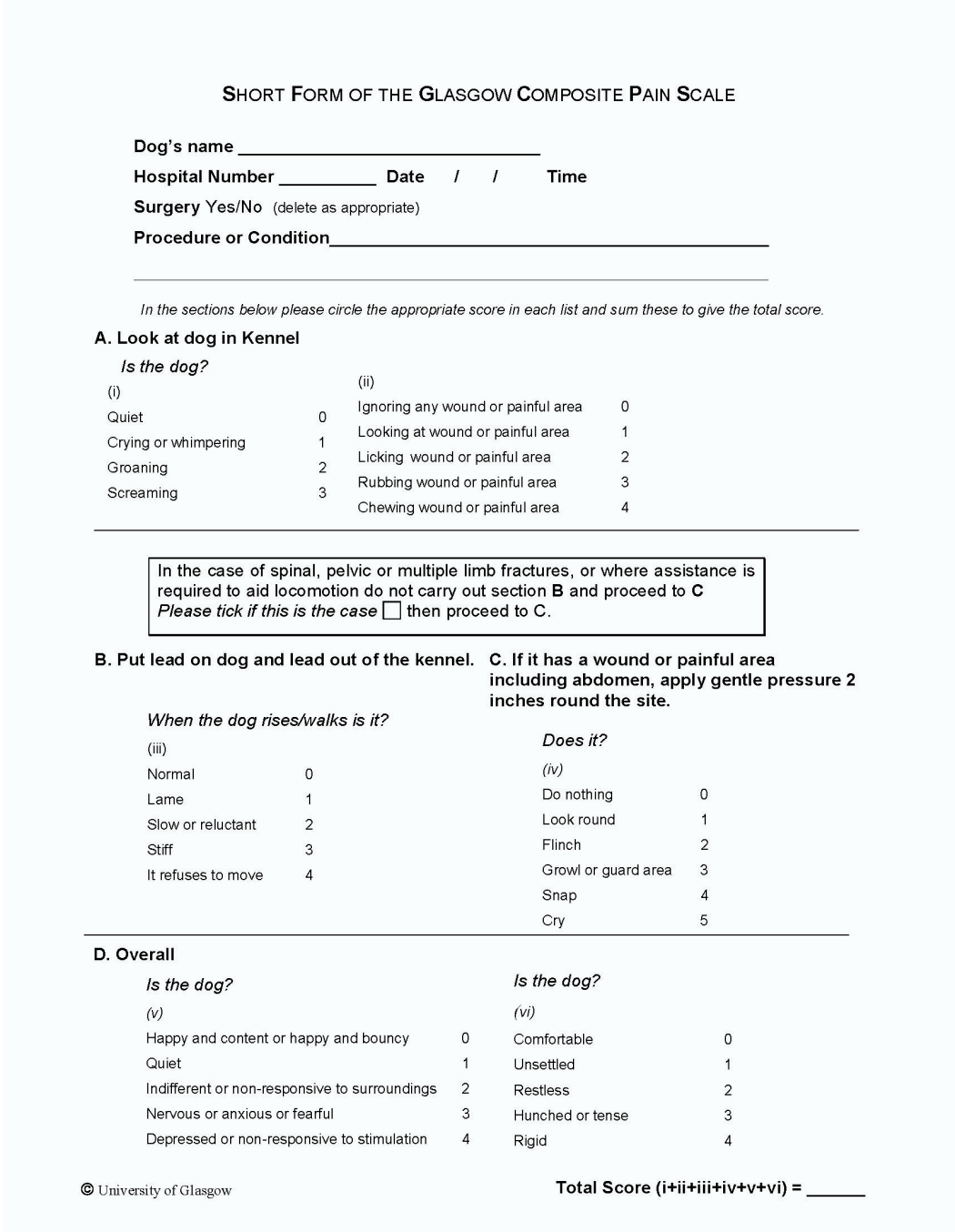
PAIN ASSESSMENT- SCALES AND RECORDING

Canine pain scoring scales and management guidelines have been established for utilization by pet owners and veterinary professionals to facilitate the diagnosis process. With the employment of pain scales, it is imperative that pet owners and veterinary specialists are cognizant of any variations in animal behavior (physically, mentally, emotionally, etc). Pain scales are multifaceted as they can be utilized for continual monitoring of pain levels in hospitalized patients, in-clinic examinations, acute pain exacerbations, and chronic pain management. Despite the potential for various personnel caring for and assessing the patient's pain, standardized pain recording formats allow for a less biased and subjective critique. Obstacles faced that can significantly affect and alter pain parameters and thus create an inaccurate pain score are trauma, surgery, anesthesia, pharmacologic intervention and stress when being handled by unfamiliar individuals and in unfamiliar settings.

Standard practice upon pain evaluation in a veterinary setting commences with a questionnaire supplied to the pet owner to assess their animal's pain based on a multitude of factors. In addition, veterinary staff will obtain a patient history from the owner which helps decipher abnormal pain patterns that have arisen compared to the patient's baseline. To facilitate the diagnosis, owners should be versed in acknowledging any problematic indicators that are associated with pain.

The Guidelines Task Force advises utilizing pain scoring tools both for acute and chronic pain. Numerous pain recording scales exist for canines and there is currently no prevailing standard method for assessment. It is important to note that pain scales are not interchangeable. Uniformity should be enforced by employing the same pain scale every time the patient is evaluated to minimize variability between recordings. Subjectivity and bias by different pain scale assessors can be minimized by encouraging the same veterinary specialist to evaluate the patient throughout the duration of the dog's assessment period. Implementation of the aforementioned strategies result in a more effective treatment plan which ultimately leads to optimal patient care.

Image 1: Pain scale and recording format 1 example



SHORT FORM OF THE GLASGOW COMPOSITE PAIN SCALE

Dog's name _____

Hospital Number _____ **Date** / / **Time**

Surgery Yes/No (delete as appropriate)

Procedure or Condition_____

In the sections below please circle the appropriate score in each list and sum these to give the total score.

A. Look at dog in Kennel

Is the dog?

(i)		(ii)	
Quiet	0	Ignoring any wound or painful area	0
Crying or whimpering	1	Looking at wound or painful area	1
Groaning	2	Licking wound or painful area	2
Screaming	3	Rubbing wound or painful area	3
		Chewing wound or painful area	4

In the case of spinal, pelvic or multiple limb fractures, or where assistance is required to aid locomotion do not carry out section **B** and proceed to **C**
Please tick if this is the case ☐ then proceed to C.

B. Put lead on dog and lead out of the kennel.

When the dog rises/walks is it?

(iii)	
Normal	0
Lame	1
Slow or reluctant	2
Stiff	3
It refuses to move	4

C. If it has a wound or painful area including abdomen, apply gentle pressure 2 inches round the site.

Does it?

(iv)	
Do nothing	0
Look round	1
Flinch	2
Growl or guard area	3
Snap	4
Cry	5

D. Overall

Is the dog? (v)		*Is the dog?* (vi)	
Happy and content or happy and bouncy	0	Comfortable	0
Quiet	1	Unsettled	1
Indifferent or non-responsive to surroundings	2	Restless	2
Nervous or anxious or fearful	3	Hunched or tense	3
Depressed or non-responsive to stimulation	4	Rigid	4

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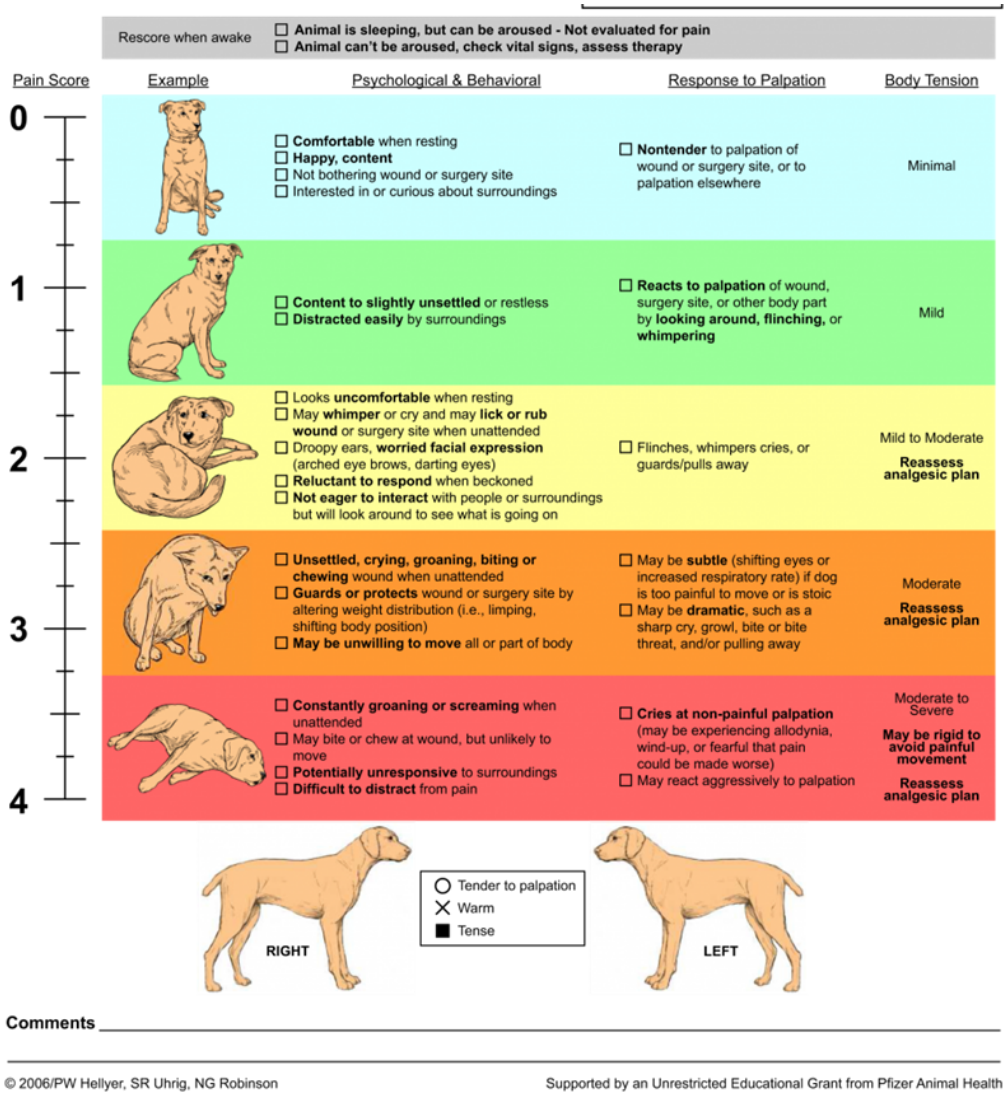
Total Score (i+ii+iii+iv+v+vi) = _____

GLASGOW COMPOSITE MEASURE PAIN SCALE–SHORT FORM

Image 2: Pain scale and recording format 2 example



Rescore when awake	☐ Animal is sleeping, but can be aroused - Not evaluated for pain ☐ Animal can't be aroused, check vital signs, assess therapy		

Pain Score	Example	Psychological & Behavioral	Response to Palpation	Body Tension
0		☐ **Comfortable** when resting ☐ **Happy, content** ☐ Not bothering wound or surgery site ☐ Interested in or curious about surroundings	☐ **Nontender** to palpation of wound or surgery site, or to palpation elsewhere	Minimal
1		☐ **Content to slightly unsettled** or restless ☐ **Distracted easily** by surroundings	☐ **Reacts to palpation** of wound, surgery site, or other body part by **looking around, flinching,** or **whimpering**	Mild
2		☐ Looks **uncomfortable** when resting ☐ May **whimper** or cry and may **lick or rub wound** or surgery site when unattended ☐ Droopy ears, **worried facial expression** (arched eye brows, darting eyes) ☐ **Reluctant to respond** when beckoned ☐ **Not eager to interact** with people or surroundings but will look around to see what is going on	☐ Flinches, whimpers cries, or guards/pulls away	Mild to Moderate **Reassess analgesic plan**
3		☐ **Unsettled, crying, groaning, biting or chewing** wound when unattended ☐ **Guards or protects** wound or surgery site by altering weight distribution (i.e., limping, shifting body position) ☐ **May be unwilling to move** all or part of body	☐ May be **subtle** (shifting eyes or increased respiratory rate) if dog is too painful to move or is stoic ☐ May be **dramatic**, such as a sharp cry, growl, bite or bite threat, and/or pulling away	Moderate **Reassess analgesic plan**
4		☐ **Constantly groaning or screaming** when unattended ☐ May bite or chew at wound, but unlikely to move ☐ **Potentially unresponsive** to surroundings ☐ **Difficult to distract** from pain	☐ **Cries at non-painful palpation** (may be experiencing allodynia, wind-up, or fearful that pain could be made worse) ☐ May react aggressively to palpation	Moderate to Severe **May be rigid to avoid painful movement** **Reassess analgesic plan**

Comments _____

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Image 3: Pain management continuum of care approach

Figure 1: PLATTER approach to pain management

PLan	Every case should start with a patient-specific pain assessment and treatment plan
Anticipate	The patient's pain management needs should be anticipated whenever possible so that either preventive analgesia can be provided or, in the case of pre-existing pain, it can be treated as soon as possible
TreaT	Appropriate treatment should be provided that is commensurate with the type, severity and duration of pain that is expected
Evaluate	The efficacy and appropriateness of treatment should be evaluated; in many cases, using either a client questionnaire or an in-clinic scoring system
Return	Arguably the most important step, this action takes us back to the patient – where the treatment is either modified or discontinued based on an evaluation of the patient's response

PHARMACOLOGICAL PAIN MANAGEMENT GUIDELINES

Once our canine companion's pain score has been established and an accurate diagnosis has been assigned, pharmacological interventions are introduced. Successful pain management commonly involves a combination of both pharmacological and nonpharmacological strategies. Regarding pharmacological tactics, an integrative and multimodal approach utilizing several classes of pain-modifying medications is often implemented to provide synergistic pain modulating effects thus reducing the reliance on one single agent. The rationale behind this methodology is that it targets multiple pain pathways which results in a potentiation of analgesic effects. In addition, lower doses of each individual drug are often tolerated thereby diminishing side effect potentials. Medication allocation should take into account the canine patient's anticipated level of pain as well as the individual's patient needs. Anticipatory and prophylactic analgesia is more effective than analgesia administered once pain has already surfaced. This preventive analgesic distribution allows for both a dose and anesthetic sparing effect.

DIFFERENCES BETWEEN HUMAN VERSUS CANINE PROCESSESSING OF NSAIDS AND APAP

Numerous overlaps and similarities exist between the human and canine central nervous system. Consequently, many individuals are under the false pretense that human approved over-the-counter (OTC) analgesics can be extrapolated for use in their canine companion. While there are many commonalities between human and veterinary pain medications, ultimately dogs are not to be considered and treated as small people. Consultation with a veterinary healthcare professional is warranted before any medication is administered and dosed to dogs.

The primary reason dogs cannot tolerate human OTC pain relievers is due to the fact that they have a reduced ability to break down NSAIDs (non-steroidal anti-inflammatory drugs) and Tylenol (APAP). As such, toxic adverse effects often arise following administration. The primary adverse effects observed from non-approved NSAIDs in dogs are gastrointestinal (GI) perforations, liver and kidney damage and toxicity, and seldomly even death. The most common APAP adverse drug reactions (ADRs) are dose dependent liver toxicity which can result in liver failure and red blood cell damage which interferes with oxygen delivery to organs. Due to the aforementioned issues, it is imperative that designated FDA approved canine pain relievers are exclusively reserved for administration in this species.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are extensively utilized in both humans and animals for mild/moderate pain and discomfort as they are analgesics that contain an anti-inflammatory component. Additionally, NSAIDs are employed as pain modulators, inflammatory reducers, blood clot preventers, and antipyretics. This class of drugs thwarts a specific enzyme in the body called cyclooxygenase (COX), which manufactures prostaglandins. COX is present in most bodily tissues with primary residence in the gastrointestinal tract and kidneys. Prostaglandins are a group of lipids that congregate at the site of injury, tissue damage, and/or infection. This coalescence of prostaglandins contributes to the induction and potentiation of pain, inflammation, and fever in the body. Contrarily, prostaglandins also have protective effects in the body. Prostaglandins protect the lining of the stomach and intestines, help provide blood flow to the kidneys, and sustain platelet function.

Table 1: Common Over-the-Counter Pain Relievers for People

Active Ingredient	Some Common Brand Names
Aspirin	ASCRIPTIN, BAYER, BUFFERIN, ECOTRIN
Ibuprofen	ADVIL, MOTRIN
Naproxen sodium	ALEVE, MIDOL EXTENDED RELIEF, NAPROSYN
Acetaminophen (**not** an NSAID)	TYLENOL

Table 2: FDA-Approved Nonsteroidal Anti-Inflammatory Drugs for Dogs

Active Ingredient	Brand Names
Carprofen	Marketed under multiple trade names
Deracoxib	DERAMAXX, DOXIDYL*
Firocoxib	PREVICOX
Grapiprant	GALLIPRANT
Meloxicam	Marketed under multiple trade names
Robenacoxib	ONSIOR (for a maximum of 3 days)

Image 4: COX and prostaglandin relationship

The majority of NSAIDs block COX, which results in the assembly of fewer prostaglandins (Image 5). The remaining NSAIDs interfere with the activity of specific prostaglandins (Image 6).

Image 5: Effect of NSAIDs

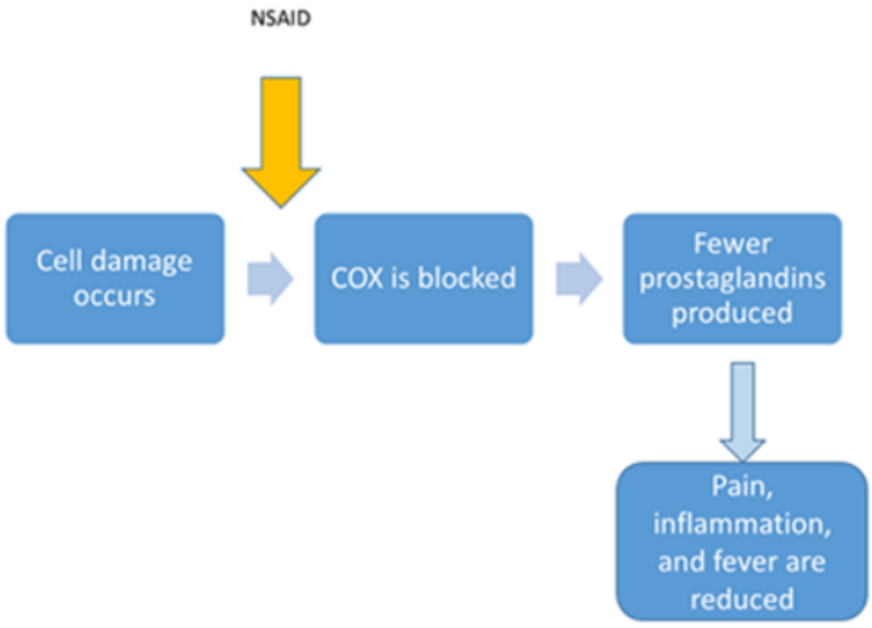
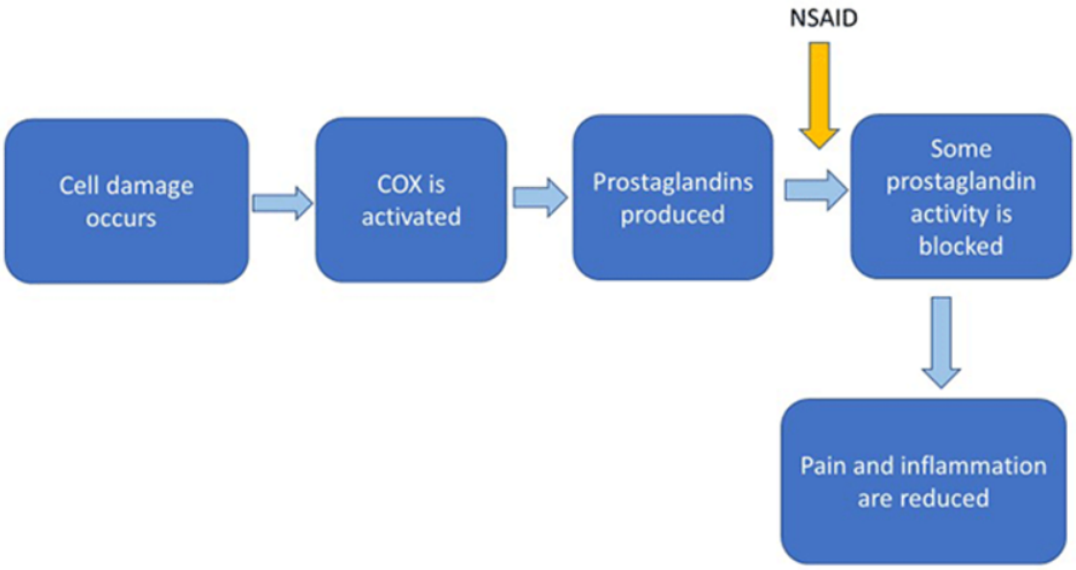


Image 6: Effect of NSAIDs



While the benefits of NSAIDs are numerous, they do not go without potential repercussions evident in their extensive side effect profile. An overview of the ADRs witnessed in dogs administered NSAIDs include; potential for liver, kidney, stomach and/or GI issues, behavioral changes, loss of appetite, skin redness, scabs, tarry stool/diarrhea, vomiting, lethargy, and prolonged blood clotting time. However, it should be noted that there is strong evidence for continued use of NSAIDs in canine pain management as their safety and efficacy profile for long-term administration is overall considered advantageous as the benefits outweigh the risks in the majority of pain cases. Evidence has suggested that there is not a correlation between higher risk for NSAID-induced ADRs with prolongation of treatment. As such, long-term use of NSAIDs is often acceptable and encouraged by veterinary professionals to optimize pain relief. To increase drug compliance and avoid premature cessation of NSAIDs, dog owners should be informed that NSAID treatment may take several weeks before clinical improvement is observed. Avoidance of combining drugs (such as multiple NSAIDs or NSAID and a steroid) needs to be addressed to circumvent ADRs particularly in the digestive tract.

Caution should be employed in canine patients that are dehydrated, undergoing anesthesia, or are diagnosed with kidney disease when contemplating NSAID use. Under normal circumstances, prostaglandins encourage the arteries supplying the kidneys to open, thus allowing for adequate blood flow to this vital organ. However, once NSAIDs are introduced, prostaglandin production is inhibited and blood flow to the kidneys is reduced, potentially contributing to kidney damage and in extreme cases, kidney failure. As such, veterinary specialists should proceed with caution in canine's that exhibit any kidney abnormalities. If NSAIDs administration is obligatory, IV fluids should be delivered to maintain kidney blood flow, thus decreasing the potential of kidney complications. In addition, it is paramount that during anesthesia renal parameters are continually monitored and a normotensive state maintained with concomitant NSAID employment.

Image 7: Ways to minimize risks associated with NSAIDs

❖ Obtain a complete medication history Avoid or use extreme caution with concurrent or recent use of NSAIDs and/or corticosteroids (including some nutritional supplements that may contain aspirin or other cyclooxygenase-inhibiting mechanisms). Practitioners should observe the following additional precautions due to potential drug interactions:
– Avoid with furosemide and use caution with angiotensin-converting enzyme inhibitors.
– Avoid with potentially nephrotoxic drugs (eg, aminoglycosides, cisplatin).
– Caution with use of additional multiple highly protein-bound drugs (eg, phenobarbital, digoxin, ciclosporin [cyclosporine], cefovecin, chemotherapy agents).

❖ Be discriminating in patient selection Be cautious or avoid NSAIDs in patients with the following existing/anticipated conditions:
– Low-flow states such as dehydration, hypovolemia, congestive heart failure and hypotension. In such cases, IV fluid support and blood pressure monitoring should be available for anesthetized animals.
– Renal, cardiac or hepatic dysfunction.

❖ Provide verbal and written client instructions to avoid the medications described above and to discontinue and alert the hospital at the first sign of an adverse event (see below).

❖ Recognize the earliest signs of adverse events and withdraw NSAID treatment immediately if those events occur, especially in the case of any GI signs in dogs and cats with diminished appetites.

❖ Perform laboratory monitoring The frequency will depend on the risk factor of the patient:
– Ideally within the first month of initiating therapy then 6 monthly thereafter in low-risk patients.
– For at-risk patients, monitor every 2–4 months depending on risk factor assessment.

❖ Utilize a balanced, integrated analgesic approach as part of NSAID-sparing strategies.

❖ Consider washout periods Clinically relevant washout periods remain controversial and largely undefined. Based on pharmacokinetics, practitioners who wish to err on the side of caution may want to withhold meloxicam for 5 days and other NSAIDs or short-acting corticosteroids for 7 days prior to initiating treatment with another NSAID. In the case of long-acting corticosteroids, a longer washout period needs to be considered. Aspirin should not be administered because there are safer alternatives. If a course of treatment with aspirin has been started in a dog, the recommended washout period before starting an approved veterinary NSAID is up to 10 days.

❖ Use gastroprotectants to either treat suspected gastropathy or prevent its occurrence, especially if no washout period occurs. Proton pump inhibitors, H2 antagonists, misoprostol (the drug of choice in humans) and sucralfate can be helpful.

❖ Dose optimization Base dosage on lean body weight. Although there is no definitive evidence that NSAID dose reduction lowers the risk of adverse events, some clinicians recommend titrating to the lowest effective dose.

Two reactions involving the liver are witnessed with NSAID use; dose dependent toxicity and dose independent toxicity. In dose dependent toxicity, the higher the dose of NSAID, the greater the likelihood of liver toxicity. Thus, there is a direct correlation between dose and liver damage potential. In dose independent toxicity, liver ADRs are apparent regardless of the dose administered. This is an unpredictable abnormal canine sensitivity to NSAIDs and usually surfaces within the first three weeks of medication initiation. Caution needs to be emphasized in canine patients that already possess liver disease.

The most common side effect observed with NSAIDs is GI abnormalities. In extreme cases, ulcers and life-threatening internal bleeding may occur with continued NSAID use. The predominant risk factors for NSAID induced GI perforations are improper dosing, frequent administration, simultaneous use with other NSAIDs or corticosteroids, anorexia, and an existing predisposition to GI abnormalities prior to NSAID use. To lessen and potentially eradicate GI lesions, studies have indicated that NSAIDS that spare COX-1 have GI protecting effects.

Image 8 : Approved NSAIDs in canines and dosing

Drug	Indication	Species, Dose[b], Route[c]	Frequency
Ketoprofen[d]	Surgical and chronic pain	Dogs: 2·0 mg/kg, IV,SC,IM 1·0 mg/kg PO Cats: as for dogs	 Once postoperative Once per day for up to 3 additional days
Meloxicam[d]	Surgical pain/acute musculoskeletal	Dogs: 0·2 mg/kg IV, SC 0·1 mg/kg PO Cats: 0·3 mg/kg SC Or, Up to 0·2 mg/kg SC 0·05 mg/kg PO	 Once Once per day One dose only; do not follow-up with any additional dosing. Once Once per day for up to 4 additional days
	Chronic pain	Dogs: 0·2 mg/kg PO 0·1 mg/kg PO Cats: 0·1 mg/kg PO 0·05 mg/kg PO	 Once on Day 1 Once per day to follow; use the lowest effective dose Once on Day 1 Once per day to follow; use the lowest effective dose
Cimicoxib[d]	Surgical pain	Dogs: 2 mg/kg PO	 Once daily for 4 to 8 days
	Chronic pain	Dogs: 2 mg/kg PO	 Once daily; use lowest effective dose
Mavacoxib[d]	Chronic pain	Dogs: 2 mg/kg PO	 Dose on day 0, day 14 then once per month for up to 5 further treatments
Robenacoxib[d]	Surgical pain	Dogs: 2 mg/kg SC Cats: 2 mg/kg SC 1 mg/kg PO	 Once Once daily for up to 3 days Once daily for up to 3 days
	Acute musculoskeletal pain	Cats: 1 mg/kg PO	 Once daily for up to 6 days
	Chronic pain	Dogs: 1 mg/kg PO	 Once daily. Can be adjusted to lowest effective dose
Carprofen[d]	Surgical pain	Dogs: 4 or 4·4 mg/kg SC, IV, PO 2 or 2·2 mg/kg SC, IV, PO Cats: 2 to 4 mg/kg SC, IV	 Once per day for up to 4 days Every 12h for up to 4 days One dose only; do not follow-up with any additional dosing.
	Chronic pain	Dogs: 4 or 4·4 mg/kg PO 2 or 2·2 mg/kg PO	 Once daily; use lowest effective dose Every 12h; use lowest effective dose
Etodolac[d]	Chronic pain	Dogs: 10–15 mg/kg SC, PO	 Once daily; use lowest effective dose
Deracoxib[d]	Surgical pain	Dogs: 3–4 mg/kg PO	 Once daily for up to 7 days
	Chronic pain	Dogs: 1–2 mg/kg PO	 Once daily; use lowest effective dose
	Dental pain	Dogs: 1–2 mg/kg PO	 Once daily for up to 3 days
Firocoxib[d]	Surgical pain	Dogs: 5 mg/kg PO	 Once daily for up to 3 days
	Chronic pain	Dogs: 5 mg/kg PO	 Once daily; use lowest effective dose

Aspirin (acetylsalicylic acid) is a NSAIDs that is prescribed less frequently in veterinary medicine for canines. Aspirin interrupts the assembly of prostaglandins throughout the body by targeting COX-1 and COX-2. The main difference between aspirin and other NSAIDs, is that aspirin also acts as an anti-coagulant. Due to these anti-coagulation properties, increased bleeding may be apparent. To circumvent GI bleeding, coated aspirin and simultaneous food consumption upon administration is advised. Aspirin is typically approved for short term use in our canine companions. The mainstay for aspirin utilization is for canine patients that exhibit osteoarthritis, clotting disorders, and musculoskeletal inflammation.

Opioids

Opioids are a widely utilized drug class in veterinary medicine that is reserved for more severe pain such as extreme surgical pain, advanced cancer cases, progressed DJD, major acute trauma, fractured bones, etc. Given the ubiquitous nature of these products, it is incumbent that veterinary specialists have a sound knowledge of opioids. Opioids primary mechanism of action is inhibitory, as it closes the N-type voltage-operated calcium channels while simultaneously opening calcium-dependent inwardly-correcting potassium channels. This results in hyperpolarization and a reduction in neuronal excitability in the central nervous system, thus producing analgesic effects. Opioids are classified based on the type of opioid receptor they interact with and thus produce their effects on. Three opioid receptors exist- mu, delta, and kappa (δ, κ and μ).

Opioids are utilized for their analgesic effects throughout the pre, intra, and post-operative periods. The employment of opioids throughout surgical procedures results in expedited post-operative recovery outcomes. Opioids are frequently administered in combination with other drug classes as a routine pre-operative procedure to optimize analgesia. Opioid and α-2 adrenergic agonist simultaneous administration produce synergistic effects, permitting a lower dose utilization of each individual product without interfering with overall sedation or analgesic optimization. Opioid requirements for canines are widely variable and thus frequent evaluations should be conducted to determine ongoing opioid needs. Canines exhibit a robust first pass metabolism and highly variable pharmacokinetic profile of opioids resulting in specific dosing requirements to yield appropriate drug concentrations in the body. As such, periodic re-administration of parenteral opioids may be warranted as well as altering the constant or variable rate of infusion to ensure the accurate opioid dose is delivered and desired analgesic therapeutic effects are maintained. Side effects of opioids observed in canine use include; nausea, vomiting, constipation, restlessness, behavioral changes, reduced blood pressure and heart rate, slowed breathing, somnolence, and seizures. Additionally, it is imperative to asses (prior to discharge from the veterinary setting) if drug diversion by the canine patient's owner is improbable, in order to ensure the dog is receiving proper pain management at home.

Image 9: Commonly used opioid analgesics in canines

Opioid	Route of administration	Duration (hours unless otherwise indicated)	Dose range (mg kg^{-1} unless otherwise indicated)	Infusion rate (IV)	Main side effects and considerations	Brand name
Morphine[1]	IM (SC, slow IV)	~4 (dog) 6–8 (cat)	0.1–1 (dogs) 0.1–0.2 (cats)	0.1–0.5 mg kg^{-1} hr^{-1}	Vomiting, possible histamine release (esp IV)	
Methadone	IM (SC, slow IV)	~4 (dog and cat)	0.5–1 (dogs) 0.3–0.6 (cats)	--	Licensed doses are higher than those commonly used	Comfortan® (Dechra Veterinary Products)
Pethidine	IM (SC in cats)	~1 (dog) 1–1.5 (cat)	3.5–5 (dogs) 5–10 (cats)	--	Possible histamine release (esp IV)	Pethidine (Dechra Limited)
Fentanyl[2]	IV (IM)	20 min following a single dose	2–10 µg kg^{-1}	0.1–0.7 µg kg^{-1} min^{-1} (dogs) 0.1–0.5 µg kg^{-1} min^{-1} (cats)	Bradycardia respiratory depression	Fentadon® (Dechra Veterinary Products)
Alfentanil[1]	IV	5 min following a single dose	5–50 µg kg^{-1} (most commonly 5–10 µg kg^{-1})	1–2 µg kg^{-1} min^{-1}	bradycardia, cardiac arrest* respiratory depression	Rapifen® (Janssen-Cilag Ltd)
Remifentanil[1]	Only given by IV infusion	only given by infusion	--	0.1–0.5 µg kg^{-1} min^{-1}	bradycardia, respiratory depression	Ultiva® (Abbott)
Buprenorphine	IM (SC, IV) Oral transmucosal in cats	? ~ 6	10–20 µg kg^{-1}	–	–	Vetergesic® (Alstoe Limited)
Butorphanol	IM (SC, IV)	¾–1	0.2–0.8	–	–	Torbugesic® (FortDodge), Dolorex® (MSD)

α-2 Adrenergic agonists

α-2 Adrenergic induce reliable, dose-dependent sedation, pain modification, and muscle relaxation in dogs. This drug class stimulates presynaptic α-2 receptors in the central nervous system, stimulating inhibitory neurons which result in a reduction in sympathetic output. α-2 agonists are located on opioid receptors, and thus are often used as an adjunct to injectable and inhalational anesthetics which results in a synergistic, drug-sparing anesthetic effect. The combination of these agents simultaneously allows for low or even micro doses of alpha-2 agonists to be administered, which results in less side effects. Side effects seen with this drug class primarily involve the cardiovascular system (AV block, sinus arrhythmia, and sinoatrial block), decreased respiratory rate, peripheral venous desaturation, vomiting, increased urine output, and transient hyperglycemia. Medetomidine is a highly selective alpha-2 agonist that is approved for use in canines and utilized for sedation and analgesic medical procedures. Medetomidine dose in canines is 5-20 mcg/kg IM.

Local anesthetics

The International Veterinary Academy of Pain Management encourages the use of local anesthetics during every surgical procedure due to their safety and efficacy. Local anesthetics are used preemptively, postoperatively, and as an adjunct to general anesthesia. This class of drugs ceases the creation and proliferation of nerve impulses, which inhibits peripheral nerve conduction. This is achieved by reversibly binding and thus blocking the voltage-gated sodium channels in the nerve membrane. Local anesthetics provide predictable anesthetics and often evade the utilization of general anesthesia which produces depressant effects on the patient. Unlike general anesthesia, local anesthetics are the only drug class that allow for the patient to remain fully conscious while entirely inhibiting pain perception and thus providing complete analgesia. Furthermore, local anesthetics express antimicrobial and immunomodulating properties, which subsequently reduce postoperative maladaptive pain. Local anesthetics can be applied directly at the incision site or at a specific nerve to provide analgesia to a greater area. The most common local anesthetics seen in veterinary medicine are Lidocaine, Mepivacaine, and Bupivacaine.

Local anesthetics are generally well tolerated and considered safe in dogs. ADRs for local anesthetics are largely reserved for very high doses or inadvertent IV administration. Albeit rare, side effects may include dizziness, headaches, blurred vision, twitching muscles, continuing numbness, weakness or pins and needles, bruising, redness, itching, or swelling at the injection site.

Table 3: General dosing information for commonly used local anesthetic agents

AGENT	MAXIMUM TOTAL INFILTRATION DOSE, MG/KG		ONSET, MIN	DURATION, HR	TOXIC DOSE, MG/KG
	DOG	CAT			
Lidocaine 2%	5	2.5	5–10	1–2	10
Mepivacaine 1%–2%	5	2.5	5–10	2–3	30
Bupivacaine 0.5%	2	1	10	3–6	4

Table provided courtesy of Dr. Stephen A. Greene, Washington State University, Pullman, Wash.

Ketamine

Ketamine is a medication that is administered to induce and maintain dissociative anesthesia, which produces pain relief, sedation, and amnesia. Ketamine's mechanism of action is via its N-methyl-D-aspartate receptor antagonist actions which results in pain modulating effects. Studies support ketamine's ability to prevent pain, anti-hyperalgesia and anti-allodynic clinical effects in canines via constant rate infusion (CRI) at approximately 10mcg/kg/min.

The International Veterinary Academy of Pain Management has encouraged the use of ketamine during trans-operative pain management. The administration of ketamine via a multimodal approach permits anesthetic-sparing effects, diminishes exaggerated and maladaptive pain states, enhances analgesic effects of other drugs, and improves anesthetic cardiovascular and respiratory parameters. While rare, side effects that could be seen with ketamine include elevated heart rate, high blood pressure, respiratory issues, muscle tremors, spastic bodily movements, erratic recovery, vocalization, and seizures.

Tramadol

Tramadol is an analgesic comparable to opioids and is classified as a synthetic opioid. Its primary function is to alter the transmission and perception of pain via the central nervous system. Additionally, tramadol increases the levels of norepinephrine and serotonin in the dog's brain which enhances its pain-relieving attributes. In contrast to humans, tramadol in dogs has a very short half-life (1.7 hrs versus 7 hrs in humans) and minute amounts of the opioid metabolite O-desmethyltramadol (M1) are produced. The typical dosing of tramadol in canines for pain is 0.45-1.8mg/lbs po q8-12hrs. Overdose of tramadol in dogs typically follow the same adverse effects seen in opioids with the addition of serotonergic and noradrenergic components. Tramadol is typically well tolerated, but adverse reactions to be cognizant of include; vomiting, nausea, loss of appetite, constipation, diarrhea, drowsiness, anxiety, dizziness, and tremors.

Gabapentin

Gabapentin is administered to canines for both its analgesic as well as its anticonvulsant properties. Gabapentin binds to the α2δ subunit of the voltage gated calcium channels to increase GABA and antagonize AMPA in the brain, which leads to a decrease in the release of excitatory neurotransmitters. Neuropathic pain, specifically hyperalgesia and allodynia, is the primary indication for gabapentin use. This product is also utilized in patient's diagnosed with chronic arthritic pain and malignancy pain. The primary adverse effects witnessed in gabapentin administered to dogs are; somnolence, ataxia, and diarrhea. Gabapentin is often combined with other pain modifying medications to optimize pain relief while simultaneously allowing for a lower dosage of each individual drug, consequently decreasing the overall side effect profile. The accepted dose for gabapentin in dogs is quite variable at 10-30mg/kg po up to three times daily prn.

Amantadine

A relatively new and 'off label' product of interest in pain reform is Amantadine. Amantadine is marketed as an antiviral medication and inadvertently was discovered to simultaneously exhibit chronic pain (specifically degenerative joint disease) modulating effects. This drug exerts a pain-modifying effect by antagonizing the N-methyl-D-aspartate receptor on the postsynaptic side of the cleft. By doing so, this mechanism blocks the transmission of noxious stimuli from those receptors resulting in a decrease in the propensity of pain impulses that are transmitted throughout the central nervous system and processed in the brain. Amantadine is often paired with other pain medications such as NSAIDs, opioids, or gabapentin to procedure synergistic properties and consequently reduced dosage requirements. Due to the novelty of this drug in its off-label pain relieving use, side effects are not well established. Potential side effects appear to affect the GI system primarily resulting in soft stools, diarrhea, gassiness, and vomiting. The primary acceptable dose of amantadine in canines for analgesia is 3-5mg/kg po q12-24h.

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are considered a first-line therapy and very effective drug class in the treatment of selective neuropathic pain conditions in humans. In canines, albeit off label, amitriptyline is prescribed for separation anxiety, pruritus, and neuropathic musculoskeletal pain. Potential side effects seen upon amitriptyline administration include; drowsiness/sedation, constipation, dry mouth, and urinary retention. Less commonly, dogs may exhibit hyperexcitability, irregular heart rhythms, seizures, decreased blood cell counts, vomiting, diarrhea, and endocrine issues. The dose used for neuropathic pain in dogs for amitriptyline is 1-2mg/kg po q12-24h.

Maropitant

Maropitant is indicated in canines to treat vomiting and motion sickness. As can be expected, vomiting can contribute to the postsurgical sequela and exacerbation of pain. Inadvertently, mild pain control is a secondary effect observed with this central antiemetic medication. It is hypothesized that the pain curbing effects of this drug is due to the blockade of substance-P binding to the neurokinin-1 receptor, which is involved in pain processing. Potential side effects evident with maropitant include; lethargy, decreased appetite, diarrhea, allergic reactions, uncoordinated walking, and convulsions. The dose prescribed in dogs 7 months of age and older is 2mg/kg po once daily until resolution of symptoms.

Bisphosphonates

Bisphosphonates are a drug class that hinder the loss of bone density, thus providing pain relief in canines diagnosed with osteosarcoma. These medications exhibit anti-osteoclast activity, which prevent osteoclast cells from replicating and thus result in bone strengthening and rebuilding. Bisphosphonates are used as adjuvant therapy for the management of osteosarcoma. The combination of bisphophonates, chemotherapy and/or radiation is most prevalent in osteosarcoma canine patients. The most common bisphosphates dispensed to dogs are oral alendronate and intravenous pamidronate and zolendronate. The primary adverse drug reactions seen with this drug class include GI abnormalities (nausea, vomiting, diarrhea, appetite alterations) and kidney toxicity. With bisphosphonates kidney toxicity propensity, urine and blood tests should be obtained prior to initiation of therapy as well as periodically during treatment to ensure kidney markers are within normal limits.

Corticosteroids

While corticosteroids do not demonstrate primary analgesic tendencies, their ability to display anti-inflammatory properties makes them a valuable contributor to canine pain therapy and management. This drug class is produced in the adrenal glands which results in steroid hormones. However, numerous prescribed corticosteroids are synthetic and are considered much more potent and longer lasting than their naturally occurring counterparts. Examples of synthetic corticosteroids used in veterinary medicine include prednisone, prednisolone, dexamethasone, triamcinolone, and methylprednisolone.

Corticosteroid administration is copious, as it can be applied to dog's eye and skin for pain relief as a topical cream, taken orally which is indicated for systemic inflammatory issues including bone and joint pain, or as a steroid injection into the joints and/or muscles. While an abundance of side effects often accompanies corticosteroid use, their benefits outweigh the risks in most cases. Short-term side effects evident with their use include; increased thirst and urination, increased hunger, panting, loss of energy, behavioral changes, development or worsening of infections, and vomiting or nauseous. Long-term side effects include; urinary tract infections, poor wound healing, development of obesity due to increased hunger, muscle weakness secondary to protein catabolism, development of calcinosis cutis, stomach ulcers, immune suppression, high blood sugar, swollen liver, osteoporosis, alopecia, increased susceptibility to fungal infections, development of demodectic mange, and predisposition to diabetes mellitus.

Polysulfated glycosaminoglycans

Polysulfated glycosaminoglycan (PSGAG) is an FDA approved arthritis medication in canines that is prescribed to prevent joint degeneration and to protect the cartilage in joints thus providing pain relief. While the exact mechanism of action of PSGAG is not fully understood, it is hypothesized that PSGAG interferes with PGE2 and catabolic enzymes including but not limited to stromelysin, elastase, and metalloproteases. In addition, this drug catalyzes the synthesis of hyaluronic acid, proteoglycan, and collagen. PSGAG dosing is 2mg/lbs IM twice weekly for up to 4 weeks. Potential side effects are rare but include vomiting, diarrhea, lack of appetite, bleeding, atypical bruising, or sleepiness.

Nutraceuticals and other oral supplements

A nutraceutical is defined as any substance that is a food or has food components and provides medical or health benefits. These products may contain isolated nutrients, dietary supplements, or herbal products. It is estimated that up to 33% of small animal owners distribute nutraceuticals to their pets. The primary use of nutritional supplements in canines is to alleviate osteoarthritis and inflammatory symptoms thereby relieving their discomfort and improving mobility. While a wide spectrum of these agents exists, the most common ones exhibiting anti-inflammatory characteristics and thus provide pain relief in dogs include; omega-3 fatty acids, microlactin, glucosamine/chondroitin, hyaluronic acid, methylsulfonylmethane, Perna canaliculus extracts, olive oil, tart cherry extract, modified milk protein, manganese, vitamin C and B, Yucca, herbs, and avocado and soybean unsaponifiables.

The Task Force encourages caution when employing nutraceuticals as they are not subject to the same rigorous testing and quality assurance as their prescription drug counterparts. As such, it is imperative to ensure that companion owners utilize veterinary resources and consult with veterinary professionals before commencing a nutraceutical supplement regimen.

Non-traditional and contemporary pain mediating therapies

Numerous clinical studies have been conducted to investigate cannabis' effect on canines. While approval has still not been granted for animals for this widely used human product, studies have indicated seizure and chronic pain benefits in dogs. Due to the novelty of cannabis use in small animals, much is still needed to be determined before prescribing can commence. Dogs have different endocannabinoid receptors than humans, therefore react different and dosage requirements need to be significantly adjusted. Overdose and toxicity have frequently occurred in dogs by accidental consumption of cannabis. Side effects include; dribbling urine, dizziness, low blood pressure, dilated pupils, easily startled, disorientation, increased vocalization, lack of coordination, and hyperactivity. In severe cases, tremors, seizures, and coma may result.

While research is lacking for cannabidiol (CBD) use in dogs, anecdotal studies suggest pain, inflammation, seizure, and anxiety benefits can be observed with its use. Preliminary indications for CBD's potential administration in the veterinary realm include but are not limited to; arthritis, pyritis, cancer, anxiety, epilepsy, bone healing, IBS, degenerative, myelopathy, and relieving pain. Analogous to cannabis, the safety and efficacy profile on CBD is lacking. As such, it is advised to consult with veterinary specialists before considering this product to evade any potential ADRs. The principal side effects observed are; dry mouth, low blood pressure, and drowsiness.

Antihistamines

While antihistamines are not used to contribute to the eradication or minimization of pain, this drug class can evade pain if used properly. According to experts, approximately 20% of all dogs will develop allergies over their lifetime. Repercussions of untreated allergies can lead to serious skin and ear infections which inadvertently result in pain. Unmanaged allergies can frequently result in hot spots (also known as moist dermatitis) and is a painful condition which is characterized by bright red, moist, pustule and swollen skin which often transitions to a skin infection. The most common antihistamines administered to dogs are Diphenhydramine, Cetirizine, Loratadine, Clemastine, and Hydroxyzine. It is advised to concurrently administer omega-3 fatty acids to significantly reduce skin itch and inflammation due to allergies.

CLIENT EDUCATION

Prior to the canine patient's discharge from the veterinary establishment, it is crucial that client education is provided. This necessary instructional overview is a fundamental component that facilitates the recovery period, as the pet owner is able to manage the patient's pain at home. In order to expedite the healing process, direct participation of the owner is warranted to provide a continuum of care thus contributing to the pet's quality of life.

Ideally, veterinary staff will provide the client with both written and verbal pain management instructions in order to facilitate the comprehension and thus implementation of the treatment plan. In addition, all major ADRs should be discussed to allow the owner to be cognizant of when to contact the veterinarian. To optimize the dog's drug compliance and administration success, a hands-on demonstration of how to administer the medications while simultaneously handling the pet should be performed. A client information sheet should be provided for each drug the canine is prescribed.

Veterinary healthcare professionals should confirm their client understands:

1. The medication's indication
2. Duration of treatment
3. Administration specifics of drug (frequency, given with food, shaking of liquid, dose, etc.)
4. Storage requirements
5. Drug interactions
6. Side effect profile
7. Toxicity and allergic reactions responses
8. Missed dosage instructions/unsuccessful administration
9. Follow-up instructions

NON-PHARMACEUTICAL APPROACHES

Non-pharmacological approaches to managing canine pain rely on non-medication therapies. Evidence-based data and empirical evidence has validated the significance of non-pharmacological remedies in the pain management realm. The employment of non-pharmacological approaches allows for less reliance on analgesics which in turn decreases potential ADRs, drug dependence, and veterinary healthcare costs. The conjunction of both pharmaceutical and nonpharmaceutical entities enables a synergistic multimodal pain management methodology that expedites the attainment of pain relief in dogs. Numerous non-pharmacological pain management strategies exist that contribute to the alleviation of pain and will be explored.

Image 10: Example of client information sheet

What YOU Should Know About Your Pet's Pain Medication

What are NSAIDs?

Nonsteroidal anti-inflammatory drugs, NSAIDs, are prescribed as pain, inflammation and fever relievers. NSAIDs are most commonly used for the symptomatic relief of arthritic pain in geriatric pets. Aspirin and ibuprofen are well-recognized human NSAIDs. The Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) has approved specific NSAIDs for use in pets with osteoarthritis. Ask your veterinarian which pain reliever is right for your pet.

What are the benefits of NSAIDs?

A decade ago, few drugs were available to treat pets in pain. Today, veterinarian-prescribed NSAIDs offer relief to pets, helping control symptoms such as, inflammation, swelling, stiffness and joint pain. In addition to providing pain control, veterinarians also believe that NSAIDs help pets heal better and faster.

Are NSAIDs safe?

The FDA considers NSAIDs to be "safe and effective when used according to the label and when pet owners are informed about common NSAID adverse reactions." According to the American Veterinary Medical Association (AVMA), the NSAIDs available today are much safer than they have ever been in the past and cause far fewer side effects. The FDA also notes that "duration of use makes a difference in the safety" of NSAIDs as the risk of side effects can increase the longer a pet is given an NSAID.

What are the side effects of NSAIDs?

The following is a list of side effects, some more common than others, to watch for while giving NSAIDs to your pet:

- Change in appetite
- Vomiting
- Change in bowel movements, such as diarrhea or black, tarry, or bloody stools
- Change in behavior, such as activity levels, aggression or lack of coordination
- Seizures
- Yellowing of gums, skin or whites of the eyes (jaundice)
- Change in drinking habits — frequency or amount consumed
- Change in urination habits — frequency, color or smell
- Change in skin — redness, scabs or scratching
- Lethargy and/or depression

More serious side effects include gastrointestinal bleeding, ulcers, perforations, and in rare cases, kidney and liver damage, and death.

Consistent, open communication with your veterinarian and close monitoring of your pet can make NSAIDs a beneficial and cost-effective treatment option.

What should you do before your pet uses NSAIDs?

Ask your veterinarian about the benefits, risks and side effects of any medication, including NSAIDs. An informed pet owner is the best defense against serious side effects from NSAIDs.

Tell your veterinarian about your pet's symptoms and current medications, including prescriptions, over-the-counter drugs, vitamins, herbal supplements and flea control products. Giving NSAIDs in combination with any other medications/ supplements could seriously harm your pet.

All pets should receive thorough history and physical examinations, as well as appropriate blood and urine testing, before initiation of NSAID therapy. Ask your veterinarian about the testing protocols that are best for your pet.

What should you do while your pet is using NSAIDs?

Drugs used to control pain in pets, such as NSAIDs, should be given only when necessary and in the smallest effective dose. If your pet's condition seems to improve, you should discuss continued use of NSAIDs with your veterinarian.

Never give NSAIDs to a pet or increase the dose or frequency without your veterinarian's instructions. Because each pet responds to NSAIDs differently, no one medication is considered more effective or safe than another.

Blood and urine testing should be performed on a regular basis during the use of NSAIDs.

Watch for any NSAIDs side effects in your pet. If you suspect an adverse reaction, stop the use of the drug and contact your veterinarian immediately.

For more information from the FDA, visit *http://www.fda.gov/fdac/features/2006/506_nsaid.html*

AAHA AMERICAN ANIMAL HOSPITAL ASSOCIATION
Healthy Practices. Healthier Pets.

The American Animal Hospital Association is an international organization of 6,000 companion animal veterinary care teams, comprised of more than 36,000 veterinary professionals. Established in 1933, AAHA is the only organization that accredits veterinary practices throughout the U.S. and Canada for dedication to high standards of veterinary care. More than 3,000 AAHA-accredited practices pass regular reviews of AAHA's stringent accreditation process that covers patient care, client service and medical protocols. For pet care information or referral to an AAHA practice, visit *www.healthypet.com*.

Weight optimization

Weight optimization can be achieved by the owner regulating the dog's diet, as well as implementing a regimented exercise routine. Overweight dogs have a surplus of adipose tissue compared to their leaner counterparts, resulting in the secretion of cytokines which contributes to a surplus of inflammatory markers in the body. The disease state most affected by an elevated body mass index (BMI) and cytokine level in canines is DJD. Studies have indicated that even a mere 6% weight loss can produce an advantageous effect on the clinical outcomes of DJD in canines. Weight optimization can delay the emergence and severity of DJD in canines, thus prophylactic diet and exercise regimens are strongly encouraged for at risk patients. Owners of dogs diagnosed with DJD should implement a nutrition management program to achieve a leaner body goal for their companion. Specifically formulated diets are advantageous in preventing or attenuating DJD in dogs. DJD canine patients ideally need to consume diets rich in omega-3 fatty acids. Foods that contain a high concentration of omega-3 fatty acids include salmon, cod liver oil, sardines, anchovies, and oysters**.**

Acupuncture

Acupuncture is another non-medication reliant veterinary approach that is encouraged by The Guidelines Task Force, as it provides a compelling and safe means of pain management in canine patients. Acupuncture originated in China and is an alternative form of pain relief therapy that involves the penetration of microneedles into the skin at targeted problem areas. Acupuncture relies on the mechanism of stimulating nerves in local tissues which releases neuropeptides resulting in vasodilating and increased circulation at concentrated areas. In addition, acupuncture produces analgesic tendencies as endogenous endorphins and enkephalins are released from the brain, spinal cord, and peripheral nerves which aids in the alleviation of both acute and chronic pain. This process allows for increased blood flow and oxygenation of tissues, facilitated healing, and analgesia effects. The advantages of acupuncture are multifold including its noninvasive, often pleasant technique, increase in blood circulation to areas of concentrated pain, pain relief, negligible side effects, and reduction of additional pain treatment modalities. Acupuncture is primarily used in dogs that exhibit arthritis and joint disorders, chronic back pain, and granulomas.

Physical rehabilitation

Physical rehabilitation is an integral component of long-term pain treatment that is often utilized in musculoskeletal injury, postsurgical recovery, DJD, and conformational abnormalities in canines. The justification of physical rehabilitation is the restoration of musculoskeletal strength and function, endurance and proprioception, and simultaneous reduction of pain and inflammation. Benefits of physical rehabilitation in canines include reduction or eradication of pain, conservation of physical abilities, avoidance of surgery, improved mobility, injury recovery, and prevention of falls. Physical therapy is multimodal as it involves the coalescence of various techniques to facilitate recovery and analgesic effects including; exercise and manual therapy/manipulation, joint mobilizations, stretching, massage, myofascial release, heat and cold treatments, neuromuscular electrical stimulation, transcutaneous electrical nerve simulations, cryotherapy (with or without compression), and therapeutic ultrasound.

Thermal modification

Both heat and cold therapies are utilized in pain management. Heat therapy displays primary benefits in chronic pain, whereas cold compression is chiefly allocated for acute pain. Heat therapy promotes increased circulation and blood flow to designated areas which in turn creates a soothing and relaxed effect on muscles and expedites the healing process of damaged tissues.

Whereas, cold compression is employed in acute injury (including post-surgical procedures) as it demonstrates benefits in reducing pain and inflammation and aids in the recovery of affected muscles. Cold therapy reduces blood flow and nerve activity to a particular area which subsequently results in pain relief.

Environmental modifications

Environmental modifications are frequently overlooked when addressing canine pain. Upon being admitted to an unfamiliar setting (such as a veterinary clinic or hospital), inevitable stress ensues and interferes with typical behaviors witnessed in dogs such as eating, grooming, sleeping, elimination, etc. As such, there is a strong correlation between the exacerbation of pain and stress. As observed in humans, fear, anxiety, stress and distress lead to hyperalgesia in animals as well. Approaches to mitigate hyperalgesia induced by the aforementioned factors include environmental modifications such as supplying bedding, blankets or clothing from home with familiar scents, providing food from home, allowing visitation of dog owners, separating in-patients from one another, using species-specific synthetic pheromones, gentle and proper handling, and calming sounds/music. Environmental modifications can also be extrapolated to the home setting. In canine patients with DJD, carpets, non-slippery surfaces, stair limitations, and ramps will improve their mobility and accessibly to rooms in addition to averting potential injuries.

Chiropractic care and Massage therapy

Chiropractic care in dogs is increasingly being offered as a supplement to pain management in veterinary clinics in order to improve mobility, reduce pain, and enhance their overall quality of life. This treatment modality concentrations primarily on the realigning of the musculoskeletal system (bones, muscles, and connective tissue) with great emphasis on the spine. The benefits of chiropractic manipulation include; increased blood flow, release of pressure and tension, improved oxygen flow, increased mobility, and analgesia.

Chiropractic care is beneficial in canine patients that exhibit arthritis, chronic pain conditions, degenerative disc disease, GI issues, tissue trauma, hip dysplasia, mobility issues, nerve abnormalities, and stiffness/tension. Massages rely on mechanical pressure on muscles which produces several benefits in the body to assist in the alleviation of pain. Massages are often encouraged alongside chiropractic care to produce an advantageous synergistic pain effect in dogs. The dynamic combination of both chiropractic and massage therapies allows for both the skeletal and muscle systems to undergo increased analgesia concurrently. This is accomplished by improved nervous system functioning, reduced inflammation, increased blood flow and circulation, and improved flexibility and range of motion. Independent of chiropractic utilization, massages are still considered beneficial as they aid in the facilitation of pain relief. Massages are regarded as valuable in pain mitigation as damaged muscles, tendons, and joints are relaxed by an increase in blood circulation which enables the interruption of the pain cycle by the release of endogenous endorphins throughout the dog's body. A handful of massage types exist ; deep tissue, myofascial, and neuromuscular massage. Massage tactics are indicated in dogs that have been diagnosed with fibromyalgia, myofascial pain syndrome, radiating pain, strains and sprains, tendonitis, and injury.

TENS therapy

A transcutaneous electrical nerve stimulator (TENS) is a non-invasive technique that affixes electrical current devices along specific skin areas to stimulate targeted nerves and thus generate analgesic properties. TENS relies on selective stimulation of a large diameter non-noxious afferents to decrease noxious central transmission and sensitization at a segmented level in the central nervous system. TENS is utilized in both the management of acute and chronic pain as it modifies nociceptive, neuropathic, and musculoskeletal pain.

Image 11: Summary of interventions for dogs (pharmacological and non-pharmacological)

Table 5 Summary of appropriate interventions for pain in dogs and cats

	Approved NSAIDs	Other analgesic drugs	Opioid premed ± tranquilizer/sedative	Local and/or regional anesthetic	Chondroprotectants (GAGs)	Acupuncture	Therapeutic joint diets	Therapeutic exercise	Weight management	Lifestyle/environmental change	Optimal surgical technique	Patient warming perioperative	Other non-pharma interventions	Comments/details
DJD dog	X	X		X (1)	X	X	X	X	X	X			X	
DJD cat (with CKD)	X (2)	X		X (1)	X	X	X	X	X	X			X	
Soft tissue abdominal surgery	X	X (3)	X	X		X					X	X	X	
Dental surgery	X	X (3)	X	X		X					X	X	X	
Orthopedic procedure	X	X	X	X	X (4)	X	X (4)	X (4)	X (4)	X (4)	X	X	X	
Hospital procedures:														
IV catheterization			X (5)	X (8)							X (6)		X	Consider local anesthetic cream
Urinary catheterization	X		X (9)	X (10)							X (6)	X	X	
Bone marrow aspiration	X		X (9)	X							X (6)	X	X	Consider general anesthesia
Radiography (painful and/or arthritic patient)			X (9)										X	
Anal sac expression			X (9)											
Ear cleaning	X (7)		X (7)	X (7)									X	Consider general anesthesia for deep ear cleaning
Thoracocentesis and/or abdominocentesis	X		X (9)	X							X (6)		X	

Notes:
1 Local or regional analgesia may be useful in localization of pain and short term relief of significant DJD pain
2 See discussion on pages 256–258 concerning the use of non-steroidal anti-inflammatory drugs (NSAIDs) in cats
3 The addition of other analgesic drugs will depend on patient characteristics and extent of the procedure
4 These interventions will be helpful pre- and postoperatively for the relief and/or prevention of postoperative and chronic pain
5 Ideally premedications should precede other preparations for general anesthesia such as placement of an IV catheter
6 These are invasive procedures and should be treated as such to optimize patient care and minimize trauma/tissue damage and post-procedural pain
7 The level of intervention will be tailored to the invasiveness of the procedure. Deep ear cleaning will require more significant intervention than superficial cleaning in most cases
8 In non-emergency settings (eg, routine pre-surgical application)
9 Chemical restraint in lieu of manual restraint when patient is fractious, distressed or otherwise intolerant of the procedure
10 Sterile lidocaine lubricant; caution in cases of urethral or bladder mucosal damage
GAGs = glycosaminoglycans, CKD = chronic kidney disease, DJD = degenerative joint disease

HOSPICE AND PALLIATIVE CARE

In the unfortunate event pharmacological and nonpharmacological therapies have been unsuccessful, hospice and palliative care is explored. While hospice and palliative care are often used interchangeably, there are distinct differences. Palliative care focuses on pain control and enhanced quality of life as its paramount features. Palliative care allows for the best quality of life during the remainder of the canine patient's life.Dogs will proceed with this option if they have been unresponsive to curative treatments. Both pain medication and nonpharmacological therapies are utilized during palliative care. Routine quality of life (QOL) assessments are executed to determine end-of-life decisions.

Hospice care is recommended for canines when their life expectancy is less than 6 months and focus has shifted to the management and amelioration of the dying process. Hospice care is designated for the terminally ill dogs who predominately require compassionate comfort during the end of their life. The goals of hospice care are to provide canines with a dignified death that is as pain-free and humane as possible. Once all options have been deemed futile, euthanasia is a humane alternative which alleviates the animal of their pain and suffering.

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CE Quiz

1.Ketamine can be administered in dogs for pain management via:

a. IV
b. IM
c. SC
d. PO
e. All of the above

2.Chronic pain in canines is defined as pain that lasts longer than 12 months?

a. True
b. False (lasts longer than 6 months)

3.Which receptor do opioids not interact with to produce analgesic effects:

a. Omega (Ω)
b. Mu (δ)
c. Delta (κ)
d .kappa (μ)

4.In canines that exhibit DJD, a diet rich in what component is advantageous in pain relief:

a. Folate
b. Niacin
c. Omega-3 fatty acids
d.Omega-6 fatty acids

5.What is the dose of Tramadol in canines for alleviation of pain:

a. 0.45-1.8mg/lbs po q8-12hrs
b. 45-62mg/lbs po q24hrs
c. 0.002-0.02mg/lbs po q12-24hrs
d. 110-135mg/lbs po q6-8hrs

6.In the dog pain management continuum of care approach, the R in the acronym PLATTER stands for:

a. Recover
b. Response
c. Reduce
d. Return

7.Combining a NSAID and steroid produces a synergistic analgesic effect with a minimal side effect profile in canines:

a. True
b. False (combination results in increased risk of GI ADRs such as ulcers and thus should not be used concurrently).

8.Aside from its 'off label' pain modulating effects, what is the primary indication for Amantadine:

a. Antibiotic
b. Antiviral
c. Anti-depressant
d. Diuretic

9.Does tramadol in canines have a longer or shorter half-life than humans:

a. Longer
b. Shorter

10.What is not a potential side effect of NSAIDs:

a. Liver toxicity
b. Kidney toxicity
c. GI ulcers
d. Increased appetite

Answer Sheet

NOVEMBER 2021

This activity is a **FREE** service to members of the Kentucky Pharmacists Association. The fee for non-members is $30. Mail completed forms to: KPERF, 96 C Michael Davenport Blvd., Frankfort, KY 40601. Credit will be applied to your CPE Monitor Profile.

Title: PHARMACOLOGICAL PAIN MANAGEMENT IN CANINES

Name: _____

Email: _____

NABP eProfile ID #: _____

Birthdate (MM/DD): _____

Completion Date: _____

Please circle: Pharmacist or Technician

UNIVERSAL ACTIVITY #: 0143-0000-21-011-H01-P&T | **CONTACT HOUR**: 3 | **EXPIRES**: 12/08/2024

PLEASE CIRCLE THE APPROPRIATE ANSWERS:

1. A B C D E	2. A B	3. A B C D	4. A B C D	5. A B C D
6. A B C D	7. A B	8. A B C D	9. A B	10. A B C D

INFORMATION PRESENTED IN THE ACTIVITY:

MET MY EDUCATIONAL NEEDS __ YES __ NO
FIGURES AND TABLES WERE USEFUL __ YES __ NO
ACHIEVED THE STATED OBJECTIVES __ YES __ NO
POSTTEST WAS APPROPRIATE __ YES __ NO
WAS WELL WRITTEN __ YES __ NO
IS RELEVANT TO MY PRACTICE __ YES __ NO
COMMERCIAL BIAS WAS PRESENT __ YES __ NO IF YES, PLEASE EXPLAIN ON A SEPARATE SHEET
UNMET OBJECTIVES: _____

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