Using of Analgesic medication in veterinary practice

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Introduction

Pain has been defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

+ Pain is always subjective and therefore difficult to impossible to measure.

+ Pain is always unpleasant.

+ When untreated or under-treated, pain can have a significant detrimental impact on the health of the painful individual.

+ When pain is expected or present, it should be assessed and treated appropriately.

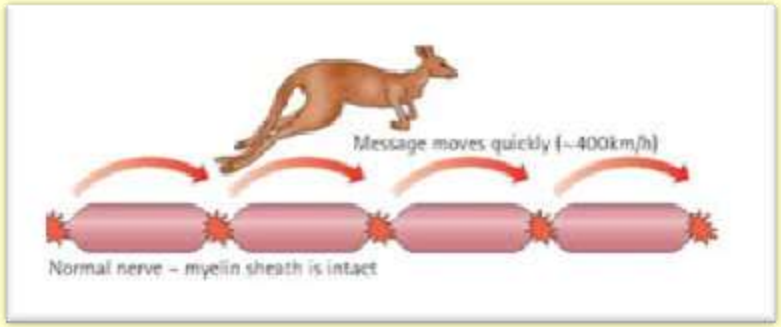
Nociceptors

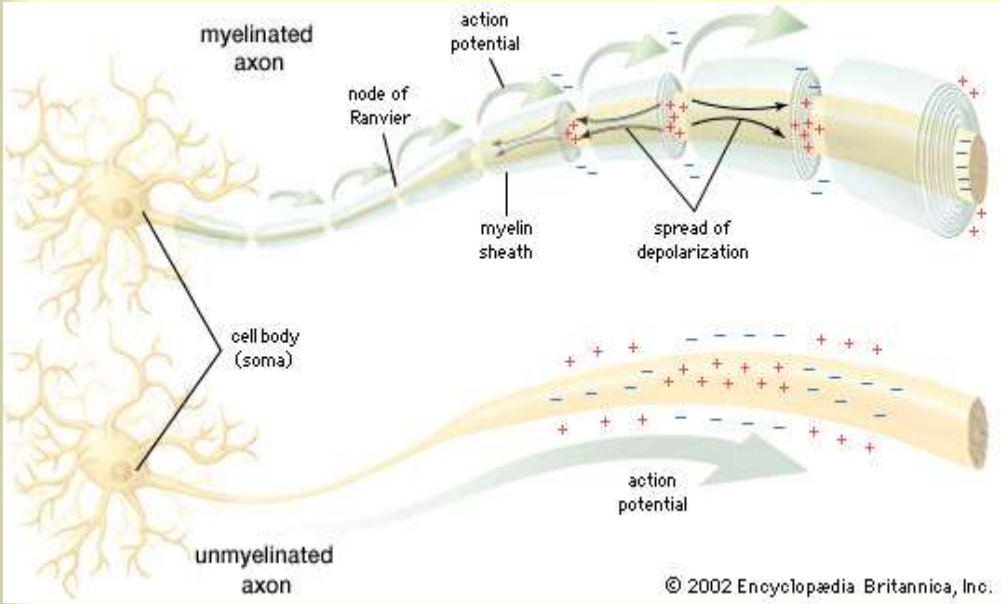
❖ five pain receptors (Nociceptors) are present in the body (mainly skin, viscera and Musculoskeletal system)

1. **Thermal nociceptors** are activated by noxious heat or cold at various temperatures.
2. **Mechanical nociceptors** respond to excess pressure or mechanical deformation.
3. **Chemical nociceptors** have TRP (Transient receptor potential channels) channels that respond to a wide variety of chemicals to allow for cationic inflow to the neurons .
4. **silent or sleeping nociceptors** their response comes only on the onset of inflammation to the surrounding tissue.
5. **Polymodal nociceptors** perform a combined functions of the four previous receptors.

Conducting neurons

A-Delta fibres	C- fibres
myelinated	unmyelinated
fast (first) pain -conduct at 5-35m/sec	Slow (second) pain – conduct at 0.5-2.0m/sec
Associated with Sharp, brief, prinking pain	Associated with dull,burning, aching, prolonged pain
Well localised	More diffuse
Elicited by mechanical or thermal stimuli	Elicited mainly by chemical stimuli or persisting mechanical or thermal stimuli





Pathophysiology of pain

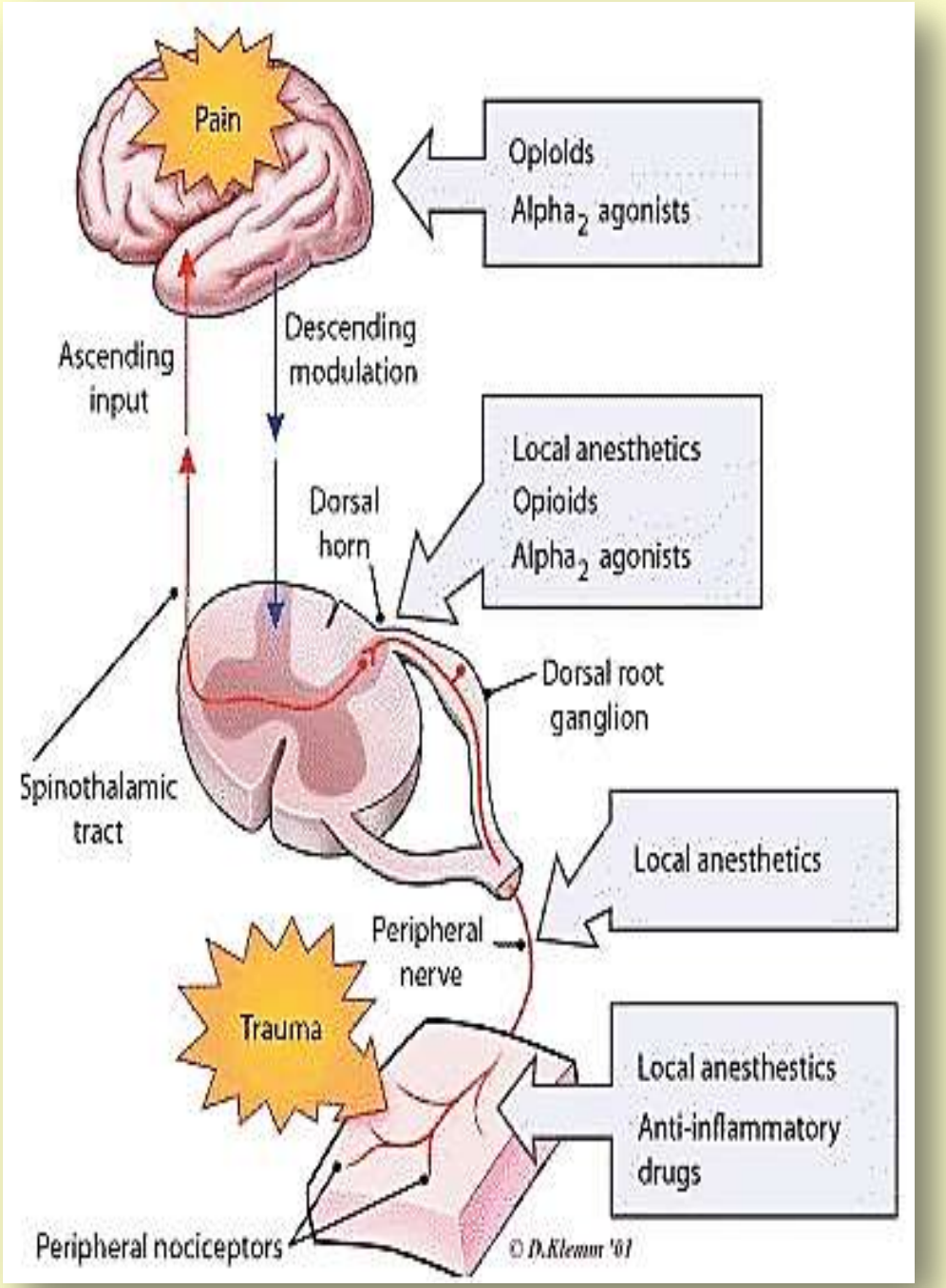
Initiation- the noxious stimuli is applied to the site of pain.

Transduction - the transfer of a nociceptive signal from the site of injury into a neural impulse.

Transmission -occurs along the afferent A-delta and C fibers of neurons to the dorsal horn of the spinal cord

Perception - occurs once the transmitted signals reach higher centers in the CNS.

Modulation -the process of altering pain transmission. Both inhibitory and excitatory mechanisms modulate pain impulse transmission in the CNS and PNS.



Classification of pain

Pain is classified according to:

1- Duration: Acute (Transient puncture) vs. chronic (cancer, osteoarthritis).

2- Nature: Nociceptive (Inflammation) vs. Neuropathic (Diabetes).

3- Type: Psychological (mental shock) vs. Physical (Trauma).

4- Origin: Somatic (Muscular twitching) vs. Visceral (smooth muscle spasm).

5- Severity: mild (laceration)vs. moderate (injury) vs. severe (Amputation).

Clinical Signs of pain in farm animals

Birds-reluctance to move; ruffled feathers; inappetance; aggression; lack of grooming; overgrooming; feather picking; vocalization; weight loss .

Cattle - may grunt or bellow; reluctance to move; inappetence or decreased appetite; decreased milk production; teeth grinding; painful facial expression; hunched appearance .

Cats - reluctance to move; inappetence; attempts to hide; lack of grooming; may growl; abnormal postures; tachycardic; may tremble .

Dogs - may be reluctant to move; inappetence; may growl or bite;; tachycardic; shift positions frequently; may tremble; may vocalize .

Goats, llamas, sheep-may grunt or bleat; teeth grinding; reluctance to move; inappetence or decreased appetite; painful facial expression; hunched appearance; recumbency; loss of social behavior .

Horses-may attempt to run from pain; painful expression; may roll (often violently); may grunt; flared nostrils; tachycardic; tachypneic .

Swine-decreased appetite; recumbency; aggression; vocalization; loss of social behavior .

Opioids

- **drugs that bind to all or part of a subtype of opioid receptors (Mu, Kappa and Delta). An opioid may be synthetic, semisynthetic, or naturally occurring. The drug may be an agonist, partial agonist or an antagonist.**

	Receptor Types		
Effects	**μ**	**κ**	**δ**
Analgesia			
Supraspinal	+	+	+
Spinal	+	+	+
Sedation	+	+	0
↓Respiration	+	0	0
↓GI transit	+	0	0
Diuresis	0	+	0
NT Release			
↓Acetylcholine	+	0	0
↓Dopamine	+	0	+
Hormone Release			
Prolactin	+	0	0
Growth hormone	+	0	+
↓Vasopressin	0	+	0
Euphoria	+	0	0
Dysphoria	0	+	0
Miosis (dogs)	+	+	0
Vasodilatation	+	0	0
Bradycardia	+	0	0

Opioids	Elimination $t_{1/2}$ in Humans (hours)	Relative Analgesic Activity (Morphine = 1)
Tramadol	6.3–8.8	<0.5
Nalbuphine	5	0.5–1.0
Morphine	3.7	1
Butorphanol	2.1–8.8	4–7
Hydromorphone	2.6	5
Oxymorphone	1.3	10
Alfentanil	1.5–2	7.5–25
Buprenorphine	37	30
Fentanyl	4	75–125
Sufentanil	2.5	375–1,250

	Receptor Types		
Drugs	μ	κ	δ
Tramadol	+	0	0
Methadone	+ + +	0	0
Morphine	+ + +	+	0
Etorphine	+ + +	+ + +	+ + +
Fentanyl	+ + +	0	0
Sufentanil	+ + +	+	+
Butorphanol	P	+ + +	0
Buprenorphine	P	− −	0
Nalbuphine	− −	+ +	0
Naloxone	− − −	− −	−
Diprenorphine	− − −	− − −	− −

Corticosteroids

- used to decrease inflammation and to prevent or treat immune-mediated responses.
- they used to manage chronic inflammation.
- Inhibit phospholipases pathway, consequently, inflammatory cascade.

Side effects of Glucocorticoids

1- Suppression of endogenous glucocorticoid synthesis.

2- Suppression of the response to infection or injury.

3- GIT disturbances- perforations.

4- Cataract, glaucoma.

5- Fluid and electrolyte disturbances.

Corticosteroid	Anti-Inflammatory Potency	Sodium-Retaining Potency
Short-acting (≤12 hours)*		
Hydrocortisone	1	1
Cortisone	0.8	0.8
Fludrocortisone	10	125
Intermediate-acting (12–36 hours)*		
Prednisone	4	0.8
Prednisolone	5	0.8
Methylprednisolone	5	0.5
Triamcinolone	5	0
Long-acting (36–72 hours)*		
Paramethasone	10	0
Betamethasone	25	0
Dexamethasone	25	0
Flumethasone	30	0

Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

- **commonly used in both large and small animal patients as a primary means of managing chronic pain and as adjunctive therapy for acute pain.**
- **Mechanism of action - inhibition of cyclooxygenases (COX) - enzymes that catalyze the production of prostaglandins.**

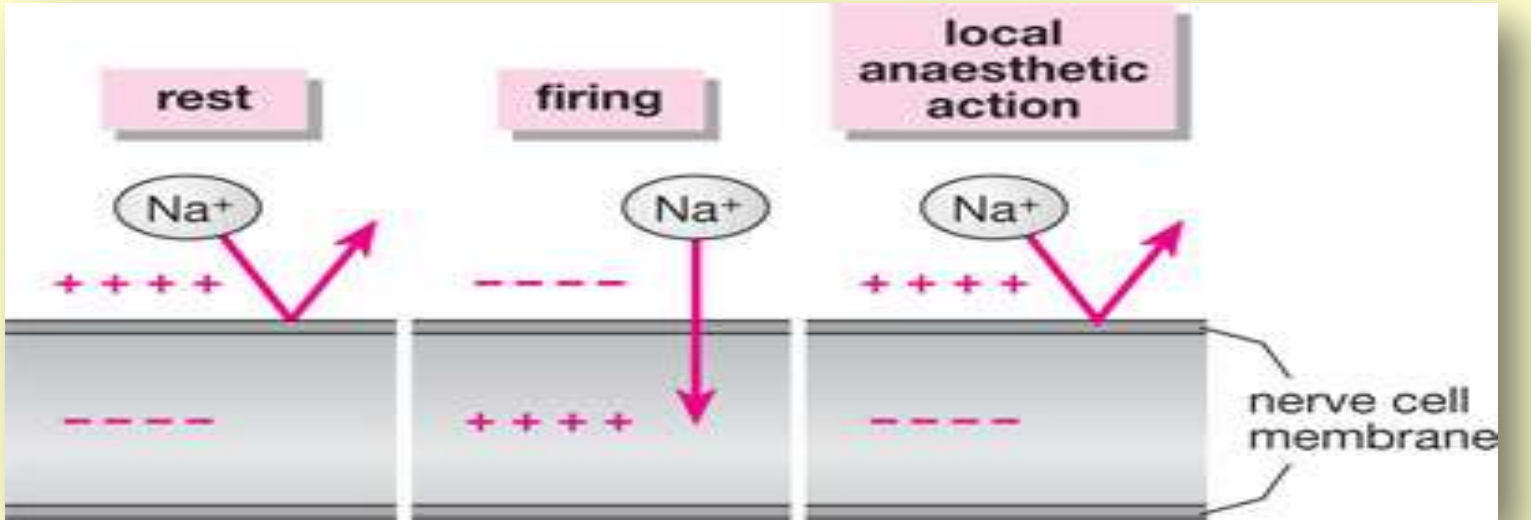
Group	Examples	Therapeutic uses
Salicylate Derivatives	Acetyl Salicylic Acid (Aspirin®) and related salicylate products.	Mild to moderate pain, anti-clot, antipyretic and for rheumatoid arathritis.
Fenamates Derivatives	Meclofenamate (Meclomen®) and mefenamic acid (Ponstel®).And Diclofenac (Voltaren®)	Mild to moderate pain, rheumatoid arthritisand osteoarthritis, ankylosing spondolytis.
Acetic Acid Derivatives	Indomethacin (Indocin®)	Rheumatoid arthritis, moderate to sever osteoarthritis, ankylosing spondolytis, gouty arthritis.
Enolic acid Derivatives	Piroxicam (Feledin®) and Meloxicam (Mobic®) Phenylbutazone Diperone (Metalgene)	Mild to moderate pain, Rheumatoid arthritis and osteoarthritis Antipyretic.
Propionic Acid Derivatives	Ibuprofen (Advil®), fenoprofen (Nalfon®), ketoprofen (Orudis®), and naproxen (Naprosyn®).	Long term management of mild to moderate pain, rheumatoid arthritis and osteoarthritis
Paraaminophenol Derivatives	Para-acetoaminophin (Paracetmol®)	Antipyretic.
Selective COX-2 inhibitors	Celecoxib (Celebrex®) and rofecoxib (Vioxx®)	Acute\long term treatment of rheumatic arthritis, osteoarthritis and management of acute pain

NSAIDs Adverse Effects

- Nausea
- Gastrointestinal distress, ulceration, bleeding
- Vomiting
- CNS stimulation
- Headache
- Vertigo
- Mental confusion
- Hypersensitivity reactions (rash, fever)
- Hepatic damage (elevated serum enzymes)

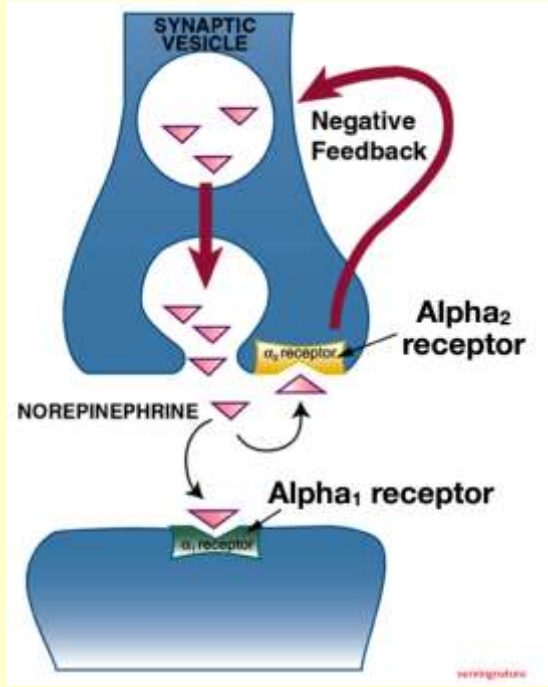
Local Anesthetics

- Local anesthetics provide pain relief by blocking pain stimuli from reaching the central nervous system (brain and spinal cord).
- inhibit of nerve impulse transmission by blocking sodium conduction through nerve membrane ion channels.
- Local anesthetics commonly used for pain management in veterinary medicine - Lidocaine, Procaine, Bupivacaine.
- local anesthetics must contact nerves for activity, they are administered at the desired site of action.
- inadvertent overdosage or accidental IV injection can manifest as toxicity -seizures, hypotension, cardiovascular collapse, cardiac arrest.



Alpha-2 Adrenergic Agonists

- The veterinary use of α2-adrenergic agonists was first reported in the late 1960s and revolutionized sedation and anesthesia particularly with large animals.(xylazine-ketamine cocktail).
- Alpha-2-adrenergic agonists produce profound sedation, provide chemical restraint, and produce analgesia.
- Administration of alpha-2 agonists can be parenteral; intramuscular, and intravenous, as well as transdermal and neuroaxial.
- Commonly used alpha-2 agonists in veterinary medicine include Xylazine, Detomidine, and Medetomidine.
- Antagonists are available-atipamezole, yohimbine, and tolazoline.



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