Management of Pain in Veterinary Patients

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EXPECTED LEARNING OUTCOME

1. To understand postoperative pain and its pathophysiology
2. To understand the consequences of untreated pain
3. To highlight some practical approaches to assessment of pain
4. To gain an in-depth understanding of pain management options
5. Critically assess the holistic approach to pain management post-spay

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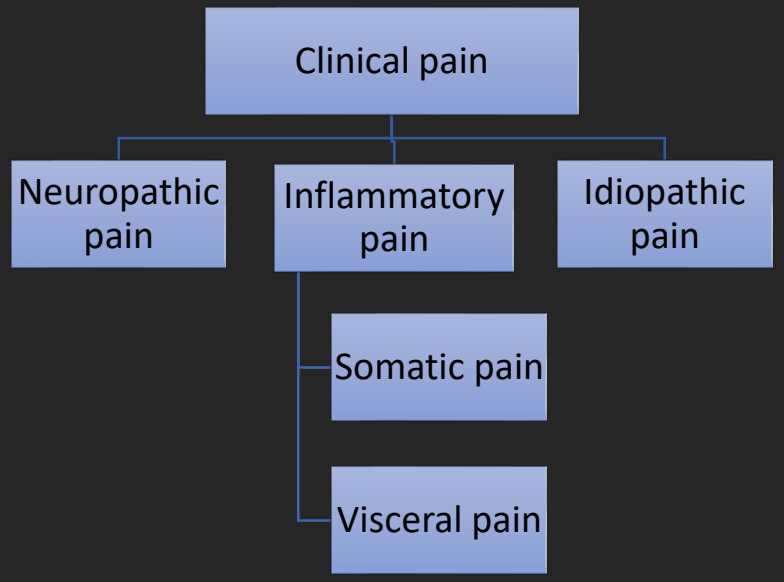
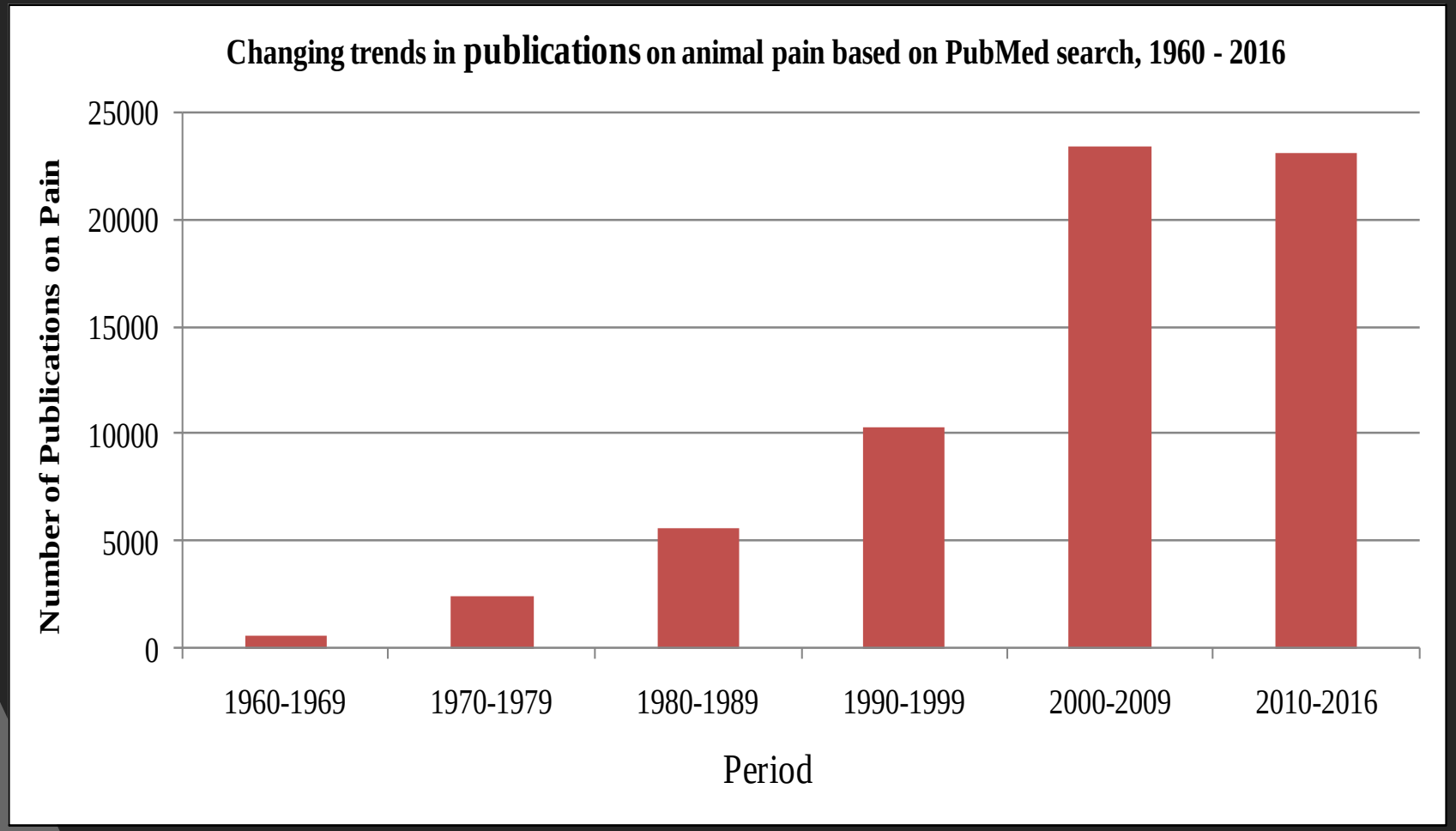
Classification of pain

1. Physiological Pain: Serves to protect the body by warning of contact with tissue damaging stimuli. Therefore serves to minimize damage
2. Clinical Pain: Produced by peripheral tissue injury or damage to the central nervous system



Importance of pain - Trends in pain research



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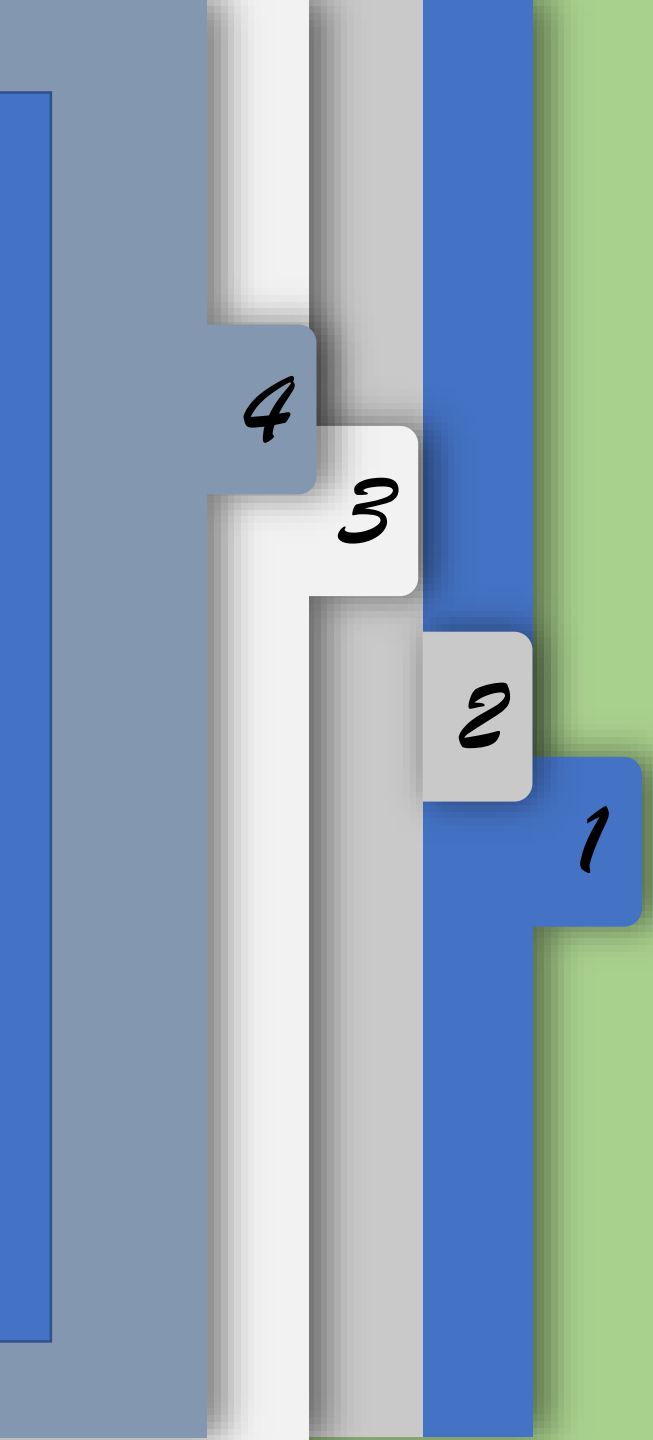

Consequences of untreated pain

1. Stress response (*Hormonal, Metabolic, Immunologic*)
2. Maladaptive physiological responses
3. Delayed Wound healing
4. Maladaptive behaviours
5. Patient Suffering

Gwendolyn and Carrol, 1996; Gaynor, 1999; Mwangi et al., 2019

Challenges in management of pain

Arise from:

- ⇨Many different species reacting differently to noxious stimuli
- ⇨A wide variety of clinical signs manifested
- ⇨Different responses to treatment of pain
- ⇨Different individual requirements for analgesia
- ⇨Availability of drugs
- ⇨Economic constraints

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Assessment of pain

Based on:

1) Anthropomorphism
2) Unprovoked behavior
3) Behavioral responses to external stimuli
4) Clinical signs
5) Laboratory evaluation

Pain Scoring tools

- Scoring tools, such as pain scales based on behavioural changes, are very useful to record changes in pain over time or after intervention.
- Few pain scales are validated to assess acute pain in companion animals.

Table 1. Acute pain scales validated in companion animals

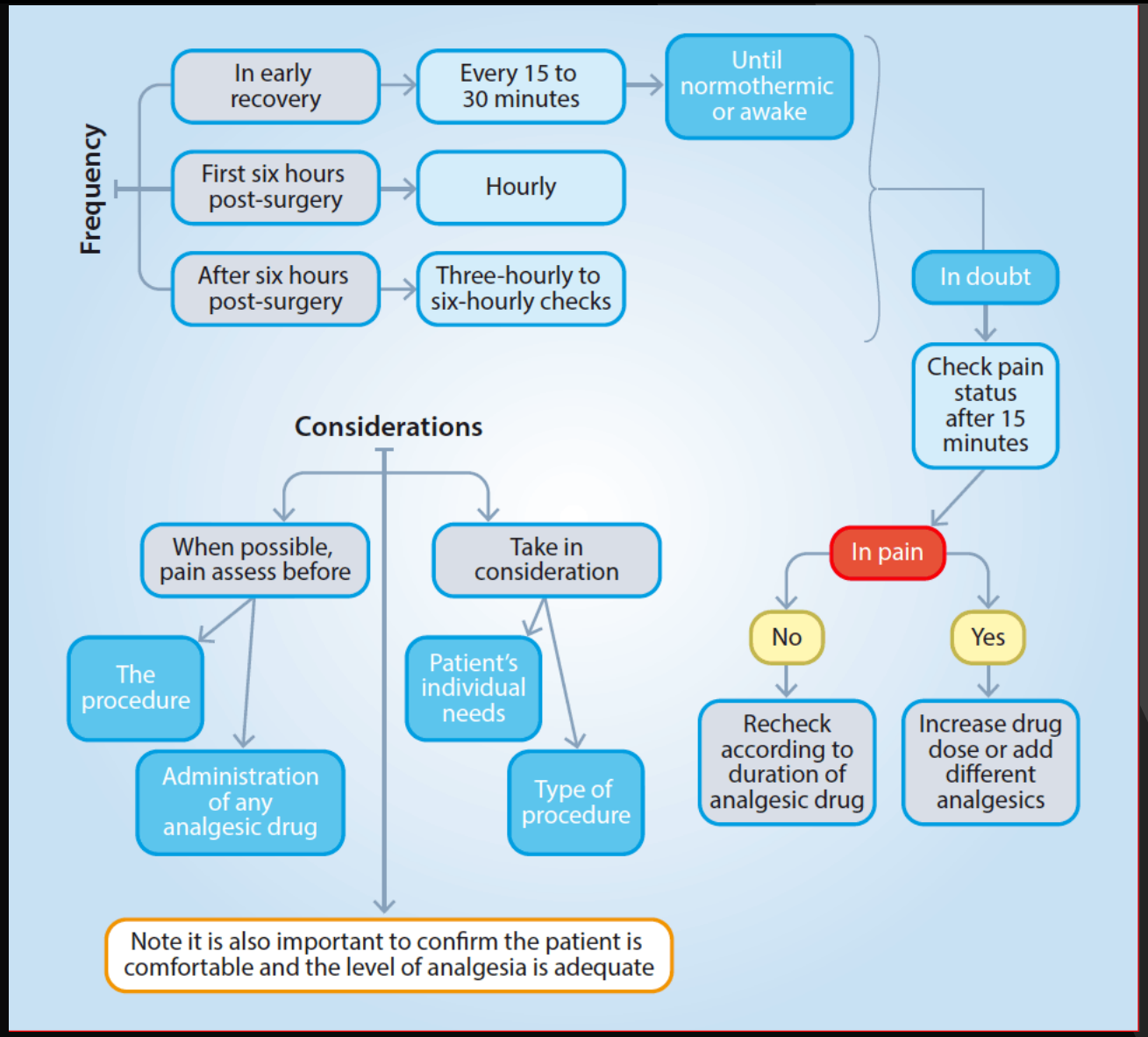
Cats	Dogs
• The UNESP-Botucatu Multidimensional Composite Pain Scale – only within the context of post-ovariohysterectomy (Brondani et al, 2013) • The Glasgow Composite Measure Pain Scale (Calvo et al, 2014)	The short form of the Glasgow Composite Measure Pain Scale (Morton et al, 2005)

Short form of the Glasgow composite pain scale

Observation	*Score*	*Patient criteria*
Comfort	0	Happy and content or happy and bouncy
	1	Quiet
	2	Indifferent or non-responsive to surroundings
	3	Nervous or anxious or fearful
	4	Depressed or non-responsive to stimulation
Vocalization	0	Quiet
	1	Crying or whimpering
	2	Groaning
	3	Screaming
Posture	0	Comfortable
	1	Unsettled
	2	Restless
	3	Hunched or tense
	4	Rigid
Attention to the wound	0	Ignoring the wound
	1	Looking at the wound
	2	Licking the wound
	3	Rubbing the wound
	4	Chewing the wound
Response to touch (applying gentle pressure 2 inches round the site)	0	Do nothing
	1	Look round
	2	Flinch
	3	Growl or guard area
	4	Snap
	5	Cry
Mobility (put lead on dog and lead out of the kennel) When the dog rises/walks is it?	0	Normal
	1	Lame
	2	Slow or reluctant
	3	Stiff
	4	It refuses to move

- Minimum Score: 0
- Maximum Score: 24
- Point of rescue or intervention analgesia: ≥ 5/20 (if animal cannot be walked out) or ≥ 6/24 if animal can be walked out of the kennel.

Frequency of pain assessments and considerations



Management of pain

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Pharmacological mgmt. - opioids

- Opioids bind to opioid receptors in the central and peripheral nervous systems inhibiting release of excitatory neurotransmitters from afferent fibres in the spinal cord, thereby inhibiting synaptic transmission of painful stimuli.

- Opioids are usually divided in four groups: full agonists (morphine, methadone, fentanyl and its derivatives, pethidine [meperidine], etc); agonist-antagonists (butorphanol and nalbuphine), partial agonists (buprenorphine), and antagonists (naloxone, nalmefene and naltrexone) that are in general devoid of agonist activity.

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Table 2. Suggested doses and dosing frequencies of opioid analgesic drugs in cats and dogs

Opioid analgesic	Dogs	Cats	Receptor	Receptor action	Route of administration	Duration of action	Comments
Methadone	0.1mg/kg to 0.4mg/kg	0.1mg/kg to 0.4mg/kg	Mu	Full agonist	SC/IM/IV	2 to 6 hours	Has N-methyl-D-aspartate receptor antagonist properties
Morphine	0.3mg/kg to 0.5mg/kg	0.1mg/kg to 0.3mg/kg	Mu	Full agonist	IM/IV	2 to 6 hours	Caution with IV administration due to histamine release
Buprenorphine	0.01mg/kg to 0.02mg/kg	0.02mg/kg to 0.04mg/kg	Mu	Partial agonist	SC/IM/IV (oral transmucosal in cats)	4 to 8 hours	Moderate pain
Butorphanol	0.2mg/kg to 0.4mg/kg	0.2mg/kg to 0.4mg/kg	Mu and kappa	Mu antagonist, kappa agonist	SC/IM/IV	1 to 2 hours	Mild to moderate pain
Pethidine	3mg/kg to 5mg/kg	5mg/kg to 10mg/kg	Mu	Full agonist	SC/IM	90 minutes	• Do not administer IV due to histamine release • Mild pain
Fentanyl	0.002mg/kg to 0.005mg/kg (bolus) Constant rate infusion (CRI) 0.003mg/kg/hr to 0.006mg/kg/hr	0.001mg/kg to 0.003mg/kg CRI 0.002mg/kg/hr to 0.003mg/kg/hr	Mu	Full agonist	IV (bolus) IV (CRI)	20 to 40 minutes Can cause accumulation after prolonged CRI	Can be used as an initial loading dose previous to CRI Can be used for significant minimum alveolar concentration reduction during anaesthesia
Tramadol	2mg/kg to 5mg/kg	2mg/kg to 4mg/kg	Mu	Agonist	By mouth	8 hours	Mild to moderate pain as an adjunctive
Naloxone (antagonist)	0.01mg/kg to 0.02mg/kg	0.01mg/kg to 0.02mg/kg		Antagonist	IV		Reversal of both agonist and agonist/antagonist opioids

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Table 3. Factors to consider when choosing the most appropriate opioid	
Duration of action	Long acting opioids, such as methadone or buprenorphine, are primarily used for the postoperative management of pain to avoid frequent redosing
Level of pain	Pain assess the patient to decide whether it is experiencing mild, moderate or severe pain
Other analgesic drugs administered	Administering local anaesthetics at the time of surgery might allow the use of opioids of lower efficacy, such as buprenorphine instead of methadone

Side effects - opioids

Most common side effects, usually associated with excessive doses, include;

- vomiting (pre-medication),
- dysphoria,
- nausea,
- panting,
- bradycardia,
- histamine release (morphine and pethidine [meperidine] especially when given IV),
- urinary incontinence / retention
- respiratory depression.
- Less commonly, inappetance, restlessness, constipation, and hypothermia or hyperthermia (usually after hydromorphone in cats) can be observed.

Any of these adverse effects are readily reversed with careful titration of naloxone

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Pharmacological mgmt. - NSAIDs

- NSAIDs influence the expression of arachidonic acid derivatives in the body. This relates largely to the production of prostaglandins catalysed by the enzyme cyclooxygenase (COX 1 and 2).
- NSAIDs are drugs that exert antipyretic, anti-inflammatory and analgesic effects
- In a few patients NSAIDs may cause adverse effects: related to the gastrointestinal tract and, less frequently, the renal system.
- Adverse effects appear commonly in conjunction with hypovolaemia, hypotension or co-treatment with drugs influencing kidney function, and these clinical scenarios should be corrected or stabilized prior to NSAID use.

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Table 4. NSAIDs used in the perioperative period in dogs and cats

Drug	Indication	Species	Dose/route/frequency
Meloxicam	Surgical pain/acute musculoskeletal	Dogs	• 0.2mg/kg SC, IV as first loading dose • 0.1mg/kg by mouth (PO) once daily
		Cats	• 0.2mg/kg SC once • 0.05mg/kg PO once per day for up to 4 additional days
Carprofen	Surgical pain	Dogs	• 4mg/kg SC, IV, PO once per day for up to 4 days • 2mg/kg SC, IV, PO every 12 hours for up to 4 days
		Cats	2mg/kg to 4mg/kg SC, IV – one dose only; DO NOT follow up with additional dosing
Firocoxib	Surgical pain	Dogs	5mg/kg PO once daily for up to 3 days
Paracetamol	Perioperative adjunctive analgesia	Dogs	10mg/kg IV, PO every 12 hours
		Cats	DO NOT USE

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Figure 3: Nine ways to minimize the risks of 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.

Pharmacological mgmt. – Local anaesthetics

- Local anaesthetics are the main drugs used for locoregional anaesthesia and analgesia (Lemke and Dawson, 2000).
- Evidence shows local anaesthetics not only have antinociceptive, but also immune-modulating antimicrobial and tissue-healing effects (Johnson et al, 2008; Cassuto et al, 2006).

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- Lidocaine can be used IV as a bolus or as a CRI in dogs to provide antiarrhythmic, inhalant-anaesthetic sparing, anti-inflammatory effects and systemic analgesia. It can be combined with methadone (or morphine) and/or ketamine in a CRI for postoperative analgesia.

Pharmacological mgmt. – Local anaesthetics

- A pilot study on the analgesic effects of IV lidocaine in dogs undergoing intraocular surgery (Smith et al, 2004) demonstrated a bolus of 1mg/kg, followed by a CRI of 0.02mg/kg/min produced comparable postoperative analgesia to morphine 0.15mg/kg IV bolus followed by a CRI of 0.1mg/kg/hr.

- Conflicting results in cats CAUTION!!!!

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Pharmacological mgmt. – Local anaesthetics

- Evidence on prolonged postoperative analgesia when local analgesics are used for wound infusion either by infiltration or use of wound catheters (Huuskonen et al., 2012; Kushnir et al., 2017)

- Currently undertaking a systematic review on benefits (Analgesics and anaesthetics sparing) of local anaesthetics during spay and castration in dogs and cats.

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Table 6. Potency and duration of most commonly used local anaesthetics

Short duration local anaesthetic (LA) – low potency	Intermediate duration LA – intermediate potency	Long duration LA – high potency
● Procaine 0.5% to 1% Slow onset of action Duration: 60 to 90 minutes Maximum recommended dose: 12mg/kg in dogs and 6mg/kg in cats Relative potency: 1	● Lidocaine 1% to 2% Fast onset (1 to 4 minutes) Duration: 120 to 240 minutes Maximum recommended dose: 6mg/kg in dogs and 2mg/kg in cats Relative potency: 2 ● Mepivacaine 1.5% Rapid onset Duration: 90 to 150 minutes Maximum recommended dose: 4mg/kg in dogs and 2mg/kg in cats Relative potency: 2	● Bupivacaine 0.25% to 0.75% Intermediate onset (10 to 20 minutes) Duration: 180 to 360 minutes Maximum recommended dose: 2mg/kg in dogs and 1.5mg/kg in cats Relative potency: 8 ● Ropivacaine 0.75% Intermediate onset Duration: 180 to 300 minutes Maximum recommended dose: 2mg/kg in dogs and 1mg/kg in cats Relative potency: 4

Pharmacological mgmt. – Adjuncts

Table 5. Adjunctive analgesic drugs in dogs and cats

Drug	Dose	Comments
Ketamine	• Dogs: 0.2mg/kg to 1mg/kg IV bolus followed by 0.002mg/kg/min (0.12mg/kg/hr) to 0.01mg/kg/min (0.6mg/kg/hr) • Cats: 0.2mg/kg to 1mg/kg IV bolus followed by 0.002mg/kg/min (0.12mg/kg/hr) to 0.01mg/kg/min (0.6mg/kg/hr)	Higher infusion rates are during surgery and tapered in the recovery period
Gabapentin	• Dogs: starting dose 10mg/kg by mouth (PO) every 8 to 12 hours • Cats: starting dose 5mg/kg PO every 12 hours	Dose can be altered according to the response. Treatment may be required for several weeks – gradual withdrawal recommended. Main side effect of this drug is sedation
Medetomidine	• Dogs: 0.001mg/kg to 0.005mg/kg IV or IM followed by constant rate infusion (CRI) 0.001mg/kg/hr to 0.005mg/kg/hr IV • Cats: 0.001mg/kg to 0.005mg/kg IV or IM followed by a CRI 0.001mg/kg/hr to 0.005mg/kg/hr IV	In conscious or anaesthetised dogs, where sedative and cardiopulmonary effects can be tolerated, low doses of medetomidine can be administered, either as a bolus or CRI

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Non-pharmacological pain management post-surgery

- Acupuncture
- Cold therapy: decrease acute inflammatory pain
- Physiotherapy
- Good nursing care or recovering the patient in a comfortable and warm environment
- Nutritional support
- Allowing interaction with owners (companion animals)

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Techniques of pain management

Conclusion

- Veterinarians need to recognize pain and familiarize themselves with practical pain assessment tools in order to manage pain effectively.

- Multimodal drug therapy, pre-emptive analgesia are some techniques that can be adopted in a clinical setup

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