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GUIDELINES FOR RECOGNITION, ASSESSMENT AND TREATMENT OF PAIN

WSAVA Global Pain Council members and co-authors of this document:

Karol Mathews DVM DVSc DACVECC (Canada)

Peter W Kronen Dr Vet Med, DVM DECVAA (Switzerland)

Duncan Lascelles BSc BVSc PhD DSAS DECVS DACVS MRCVS (USA)

Andrea Nolan MVB DVA PhD DECVAA DECVPT MRCVS (UK)

Sheilah Robertson BVMS (Hons) PhD DACVAA DECVAA DECAWBM (WSEL) DACAW MRCVS (USA)

Paulo VM Steagall MV MS PhD DACVAA (Brazil/Canada)

Bonnie Wright DVM DACVAA (USA)

Kazuto Yamashita DVM MS PhD DJCVS (Japan)

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INTRODUCTION

The ability to experience pain is universally shared by all mammals, including companion animals, and as members of the veterinary healthcare team it is our moral and ethical duty to mitigate this suffering to the best of our ability. This begins by evaluating for pain at every patient contact. However, and despite advances in the recognition and treatment of pain, there remains a gap between its occurrence and its successful management; the inability to accurately diagnose pain and limitations in, and/or comfort with, the analgesic modalities available remain root causes. Both would benefit from the development, broad dissemination, and adoption of pain assessment and management guidelines.

The World Small Animal Veterinary Association (WSAVA) is an 'association of associations' with 91 current members representing over 145,000 small animal veterinarians globally. As such, it is the global voice of the small animal veterinary healthcare team and has a long-standing and successful history of developing global guidelines on the recognition, diagnosis, and/or treatment of common small animal ailments having a global relevance. To date, these have included hepatic, gastrointestinal, and renal diseases; vaccine guidelines; and nutritional recommendations. Standardization efforts are one of the WSAVA's core activities, which also include animal welfare, continuing education, and the World Congress; the pain assessment and management guidelines have unique relevance to all.

Based on this background, the Global Pain Council (GPC) was established and charged with the task of developing pain assessment and treatment guidelines having universal relevance, taking into account regional differences in attitude, education and available analgesic modalities. These guidelines will be used to enshrine pain assessment as the 4$_{th}$ vital sign and be the foundation for further continuing education efforts based on regional variations to ensure both clinical relevance and the impetus for advancement.

GPC Vision: An empowered, motivated, and globally unified veterinary profession that effectively recognizes and minimizes pain prevalence and impact.

GPC Mission: To raise global awareness and provide a call to action based upon an understanding that all animals are sentient and can therefore feel pain and suffer from it. Through the identification of regionally specific resources for recognizing and treating pain, and targeted education, the Global Pain Council strives to elevate the level of confidence and competence in applying pain treatments.

Use of this document

This document is designed to provide the user with easy-to-implement, core fundamentals on the successful recognition and treatment of pain in the day-to-day small animal clinical practice setting. While not intended to be an exhaustive treatise on the subject matter, the text does provide an extensive reference list and there is additional material on the WSAVA website (www.wsava.org) designed to provide resources for those wanting to further their knowledge of this subject matter based on the current literature.

There are no geographic limitations to the occurrence of pain, nor to the ability to diagnose it. The only limiting factors are awareness, education, and a commitment to include pain assessment in every physical examination. As such, the pain assessment guidelines herein should be easily implemented regardless of practice setting and/or location.

In contrast, there are real regional differences in the availability of the various classes of analgesics, specific analgesic products, and the regulatory environment that governs their use. This represents a significant hurdle to the ideal management of pain in various regions of the world, irrespective of the ability to diagnose. In the treatment section of these guidelines, these issues are taken into account by the provision of 'tiered' management guidelines beginning with comprehensive pain management modalities that represent the current 'state of the art' followed by alternative protocols that may be considered where regulatory restrictions on analgesic products prevent ideal case management. Owing to space limitations, tiered management cannot be listed for all situations, but the analgesics available can be selected from the recommended management. It should also be recognized that in some situations, whether due to a etiology or available analgesics, euthanasia may be the only moral or ethical (hence viable) treatment option available. Humane methods are presented.

Sections are given on the various product and procedure modalities including pharmacology, mechanism of action, indications, contraindications, dosing, and practical clinical notes to help guide the reader in tailoring the therapeutic protocol to the needs of the individual patient.

Recognize this document as providing guidelines only, with each situation unique and requiring the individual assessment and therapeutic recommendations that only a licensed veterinarian can provide. There are a number of statements that are the collective opinion of the authors, based on their cumulative experience with pain management gained within their respective fields but not yet

evidenced via published data. It is the view of the group that providing this guidance is important in areas where to date there is little published work to underpin clinical pain treatment in dogs and cats.

The contents should also be put into context of the following pain assessment and management tenets:

- Pain is an illness, experienced by all mammals, and can be recognized and effectively managed in most cases
- Pain assessment should accompany every patient assessment
- Treat predictable pain – pain associated with surgery is 100% predictable
- Pain assessment is key to determining the degree and duration of pain treatment but should not replace the adage of treating predictable pain
- Perioperative pain extends beyond 24 hours and should be managed accordingly
- Practice preventive (preemptive) pain management – initiate appropriate treatment before a procedure to prevent the onset of pain, and continue this to prevent occurrence of pain for the duration of time commonly recommended for the problem or which the patient requires
- Response to appropriate treatment is the gold standard to measure the presence and degree of pain.

We can't always know that our patient does hurt, but we can do our best to ensure that it doesn't hurt

SECTION 1: INTRODUCTION TO PAIN, ITS RECOGNITION AND ASSESSMENT

1. UNDERSTANDING PAIN

Pain is a complex multi-dimensional experience involving sensory and affective (emotional) components. In other words, 'pain is not just about how it feels, but how it makes you feel', and it is those unpleasant feelings that cause the suffering we associate with pain. The official definition of pain by the International Association for the Study of Pain (IASP) is: "an unpleasant sensory and emotional experience, associated with actual or potential tissue damage, or described in terms of such damage".[1] Pain is a uniquely individual experience in humans and animals, which makes it hard to appreciate how individuals feel. In non-verbal patients, including animals, we use behavioural signs and knowledge of likely causes of pain to guide its management. The conscious experience of pain defies precise anatomical, physiological and or pharmacological definition; furthermore, it is a subjective emotion that can be experienced even in the absence of obvious external noxious stimulation, and which can be modified by behavioural experiences including fear, memory and stress.

At its simplest, pain is classified as either acute or chronic. The distinction between acute and chronic pain is not clear, although traditionally an arbitrary interval of time from onset of pain has been used – e.g. pain of more than 3 months' duration can be considered to be chronic.

Acute pain is generally associated with tissue damage or the threat of this and serves the vital purpose of rapidly altering the animal's behaviour in order to avoid or minimize damage, and to optimize the conditions in which healing can take place, stopping when healing is complete. Acute pain varies in its severity from mild-to-moderate to severe-to-excruciating. It is evoked by a specific disease or injury; it serves a biological purpose during healing and it is self-limiting. Examples of acute pain include that associated with a cut/wound, elective surgical procedures, or acute onset disease e.g. acute pancreatitis. In contrast, chronic pain persists beyond the expected course of an acute disease process, has no biological purpose and no clear end-point and in people, as well as having an effect on physical wellbeing, it can have a significant impact upon the psychology of the sufferer.

Chronic pain is generally described in human medicine as pain that persists beyond the normal time of healing, or as persistent pain caused by conditions where healing has not occurred or which remit and then recur. Thus acute and chronic pain are different clinical entities, and chronic pain may be considered as a disease state.

The therapeutic approaches to pain management should reflect these different profiles. The therapy of acute pain is aimed at treating the underlying cause and interrupting the nociceptive signals at a range of levels throughout the nervous system, while treatment approaches to chronic pain must rely on a multidisciplinary approach and holistic management of the patient's quality of life.

Many dogs and cats suffer from long-term chronic disease and illness which are accompanied by chronic pain. During the lifetime of the animal acute exacerbations of the pain may occur (breakthrough pain), or new sources of acute pain may occur independently which may impact on the management of the underlying chronic pain state ('acute on chronic pain'). For these animals aggressive pain management is required to restore the animal's comfort.

2. PHYSIOLOGY AND PATHOPHYSIOLOGY OF PAIN

Pain is a subjective emotion, which can be experienced even in the absence of obvious external noxious stimulation, and which can be enhanced or abolished by a wide range of behavioural experiences including fear and memory. Adaptive 'physiological' pain announces the presence of a potentially harmful stimulus and thus has an essential protective function. In contrast, maladaptive pain represents malfunction of neurological transmission and serves no physiological purpose, leading to chronic syndromes in which pain itself may become the primary disease. Conscious perception of pain represents the final product of a complex neurological information-processing system, resulting from the interplay of facilitatory and inhibitory pathways throughout the periphery and central nervous systems. Several distinct types of pain exist, classified as nociceptive, inflammatory and neuropathic.[2] Cancer pain often displays characteristics of both inflammatory and neuropathic pain.

The conscious experience of acute pain resulting from a noxious stimulus is mediated by a high-threshold nociceptive sensory system. The basic neuroanatomy of this system is reviewed elsewhere.[3] Nociceptors represent the free endings of primary sensory neurons, with their cell bodies located in the dorsal root and trigeminal ganglia. The primary afferent nerve fibres which carry information from these free nerve endings to their central location consist of two main types: unmyelinated C-fibres and myelinated A-delta fibres. Following tissue trauma, changes in the properties of nociceptors occur such that large-diameter Aβ fibres, normally not associated with nociception, may also transmit 'pain information'. Unmyelinated C-fibres are activated by intense mechanical, chemical and thermal stimuli contributing to the 'slow burn' sensation of pain. The Aδ fibres conduct impulses more quickly and contribute to the rapid 'stab' of the acute pain response and function primarily as a warning, is protective, resulting in rapid withdrawal from the stimulus. Delay of withdrawal results in C-fibre activation, the intensity of which is dependent on injury. There is also a population of so-called 'silent' nociceptors, which may become active during inflammation or tissue damage such as occurs in inflammatory bowel disease and cystitis, for example.

Primary afferent fibres carrying sensory information from nociceptors synapse in the dorsal horn of the spinal cord. The fibres of 'nociceptive' responsive cells of the spinal cord project to various higher centres involved in pain transmission, both ipsilaterally and contralaterally to their site of origin. Several spinal-brainstem-spinal pathways are activated simultaneously when a noxious stimulus occurs, providing widespread positive and negative feedback loops by which information relating to noxious stimulation can be amplified or diminished (descending inhibitory pathways). The cerebral cortex is the seat of conscious experience of pain. The cerebral cortex exerts top-down control and can modulate the sensation of pain. Central pain associated with a cortical or subcortical lesion can result in severe pain, which is not associated with any detectable pathology in the body.

Pain is considered to consist of three key components: a sensory-discriminatory component (temporal, spatial, thermal/mechanical), an affective component (subjective and emotional, describing associated fear, tension and autonomic responses), and an evaluative component, describing the magnitude of the quality (e.g. stabbing/ pounding; mild/severe). Undoubtedly, an animal's pain experience is similarly composed, although our tendency is to focus on pain intensity alone.

Clinical pain

The nociceptive sensory system is an inherently plastic system and when tissue injury or inflammation occurs, the sensitivity of an injured region is enhanced so that both noxious and normally innocuous stimuli are perceived as painful. The clinical hallmarks of sensitization of the nociceptive system are hyperalgesia and allodynia. Hyperalgesia is an exaggerated and prolonged response to a noxious stimulus, while allodynia is a pain response to a low-intensity, normally innocuous stimulus such as light touch to the skin or gentle pressure. Hyperalgesia and allodynia are a consequence of peripheral and central sensitization. Peripheral sensitization is the result of changes in the environment bathing nociceptor terminals as a result of tissue injury or inflammation. Chemical mediators are released by damaged cells which either directly activate nociceptors, or sensitize the nerve terminals. This results in long-lasting changes in the functional properties of peripheral nociceptors. Trauma and inflammation can also sensitize nociceptor transmission in the spinal cord to produce central sensitization. This requires a brief but intense period of nociceptor stimulation (e.g. a surgical incision, intense input following tissue trauma, or following nerve injury). As a result, the response threshold of the central neurons falls, their responses to subsequent stimulation are amplified and their receptive fields enlarge to recruit additional previously 'sleeping' afferent fibres into nociceptive transmission.

Inflammatory pain is usually responsible for acute postoperative pain, until the wound has healed. It has a rapid onset and, in general, its intensity and duration are related directly to the severity and duration of tissue damage. The changes in the nociceptive system are generally reversible and normal sensitivity of the system should be restored as tissue heals. However, if the noxious insult was severe, or if a focus of ongoing inflammation persists, then pain will persist as is the case in dogs with chronic inflammatory diseases such as arthritis, otitis, gingivitis, dermatitis and back pain.

Neuropathic pain is defined as pain caused or initiated by a primary lesion, injury or dysfunction in the peripheral nervous system or central nervous system. There follows a plethora of changes in the peripheral nervous system, spinal cord, brainstem and brain as damaged nerves fire spontaneously and develop hyper-responsivity to both inflammatory and normally innocuous stimuli.[4] In humans, neuropathic pain is commonly manifested in, for example, post-amputation phantom limb pain and post-herpetic

neuropathy; furthermore, it has been suggested that neuropathic pain is the major cause of long-term post surgical pain in humans.[5] It is surprising, therefore, that neuropathic pain is not described in animals more commonly; however, this may be due to lack of awareness of the potential for neuropathic pain and its recognition. Prevention of neuropathic pain is frequently accomplished by appropriate selection and duration of administration of analgesic(s).

Post-surgical pain: persistent pain after surgery remains a problem in humans, particularly following major surgery, with a minority of these patients experiencing severe chronic pain, often neuropathic in nature. The risk of persistent post-surgical pain in dogs and cats has not been quantified; however, it is likely to occur. Veterinarians should be aware of the potential for chronic pain to exist.

Breakthrough pain (BTP) may occur with all painful conditions (e.g. arthritis). It is defined as an abrupt, short-lived, and intense pain that 'breaks through' the analgesia that controls pain. The analgesic protocol should be re-assessed by careful examination and observation to ensure there is no new underlying problem causing pain. Veterinarians may be unaware of the occurrence of BTP in patients with persistent pain unless specific questions are asked of the client.

Chronic pain: there is no direct link between the duration or intensity of injury which transforms acute transient pain into chronic pain. However, as with neuropathic pain, appropriate management of acute pain is essential to prevent establishment of chronic pain. As noted, the pain information processing systems display plasticity, driven by peripheral and central sensitization. This plasticity can be reversible, as is commonly the case in acute inflammatory pain; or it can be long-lasting which is associated with changes expressed in the phenotype of the nociceptive cells and their expression of proteins involved in pain processing.

3. RECOGNITION AND ASSESSMENT OF ACUTE PAIN IN CATS

Acute pain is the result of a traumatic, surgical, medical or infectious event that begins abruptly and should be relatively brief. This pain can usually be alleviated by the correct choice of analgesic drugs, most commonly opioids and non-steroidal anti-inflammatory drugs (NSAIDs). For successful relief of pain, one must first look for it and recognize it. It is recommended that assessment of pain is incorporated into Temperature, Pulse and Respiration (TPR) examinations, making pain the 4th vital sign we monitor. Cats that have been injured or undergone surgery should be monitored closely and pain must be treated promptly to prevent it from escalating. Treatment must be continued until the acute inflammatory response abates. The degree of trauma dictates the intensity and duration of the inflammatory response but treatment may be required for several days. Feral cats require preemptive administration of analgesics based on the severity of the proposed surgical procedure rather than based on their behaviour; in addition, interactive pain assessment is not possible in this population.[6]

Neuroendocrine assays measuring ®–ενδορπην, catecholamines and cortisol concentrations in plasma have been correlated with acute pain in cats; however, these are also influenced by other factors such as anxiety, stress, fear and drugs.[7] Objective measurements such as heart rate, pupil size and respiratory rate have not been consistently correlated with signs of pain in cats – therefore we depend on subjective evaluation based on behaviour.[8] A multidimensional composite pain scale (UNESP-Botucatu) for assessing postoperative pain in cats has been validated and can be applied in the clinical setting as a useful tool.[8a]

Pain assessment and recognition

Take into consideration the type, anatomical location and duration of surgery, the environment, individual variation, age, and health status. The cat should be observed from a distance then, if possible, the caregiver should interact with the cat and palpate the painful area to fully assess the cat's pain. A good knowledge of the cat's normal behaviour is very helpful as changes in behaviour (absence of normal behaviours such as grooming and climbing into the litter box) and presence of new behaviours (a previously friendly cat becoming aggressive, hiding or trying to escape) may provide helpful clues. Some cats may not display clear overt behaviour indicative of pain, especially in the presence of human beings, other animals or in stressful situations. Cats should not be awakened to check their pain status; rest and sleep are good signs of comfort but one should ensure the cat is resting or sleeping in a normal posture (relaxed, curled up). In some cases cats will remain very still because they are afraid or it is too painful to move, and some cats feign sleep when stressed.[9]

Facial expressions and postures: these can be altered in cats experiencing pain: furrowed brow, orbital squeezing (squinted eyes) and a hanging head (head down) can be indicators of pain. Following abdominal surgery a hunched position and/or a tense abdomen is indicative of pain. Abnormal gait or shifting of weight and sitting or lying in abnormal positions may reflect discomfort and protection of an injured area. Comfortable cats should display normal facial expressions, postures and movement after successful analgesic therapy. Figure 1 provides examples of normal postures and facial expressions and those that may be indicative of pain.

Behavioural changes associated with acute pain in cats: reduced activity, loss of appetite, quietness, hiding, hissing and growling (vocalization), excessive licking of a specific area of the body (usually involving surgical wounds), guarding behaviour, cessation of grooming, tail flicking and aggression may be observed. Cats in severe pain are usually depressed, immobile and silent. They will appear tense and distant from their environment.[10]

Dysphoria versus pain: thrashing, restlessness and continuous activity can be signs of severe pain in cats. However, these can also be related to dysphoria. Dysphoria is usually restricted to the early postoperative period (20–30 min) and/or associated

FIG 1. Illustrations of normal postures and facial expressions and those that may be indicative of pain. (A) A cat with a normal posture – the cat's head is up, the cat is alert and the eyes are open. (B) A cat resting after surgery in a normal relaxed and curled up position. (C) This cat is 'flat out' and tense after surgery – also note the facial expression. (D) and (E) These cats have had abdominal surgery; the hunched posture and low hung head are suggestive of pain. Note also that the eyes are either held shut or half closed and appear "slanted" or "squinted" compared to the cat in Figure 1A.

with poor anaesthetic recoveries after inhalant anaesthesia and/or ketamine administration and/or after high doses of opioids. Hyperthermia associated with the administration of hydromorphone and some other opioids may lead to anxiety and signs of agitation in cats.

4. RECOGNITION AND ASSESSMENT OF ACUTE PAIN IN DOGS

Acute pain occurs commonly in dogs as a result of a trauma, surgery, medical problems, infections or inflammatory disease. The severity of pain can range from very mild to very severe. The duration of pain can be expected to be from a few hours to several days. It is generally well managed by the use of analgesic drugs. The effective management of pain relies on the ability of the veterinarian, animal health technician and veterinary nurse to recognize pain, and assess and measure it in a reliable manner. When the dog is discharged home, owners should be given guidance on signs of pain and how to treat it.

Objective measurements including heart rate, arterial blood pressure and plasma cortisol and catecholamine levels have been associated with acute pain in dogs;[11] however, they are unreliable as stress, fear and anaesthetic drugs affect them. Thus, evaluation of pain in dogs is primarily subjective and based on behavioural signs.

Pain recognition

Behavioural expression of pain is species-specific and is influenced by age, breed, individual temperament and the presence of additional stressors such as anxiety or fear. Debilitating disease can dramatically reduce the range of behavioural indicators of pain that the animal would normally show e.g. dogs may not vocalize and may be reluctant to move to prevent worsening pain. Therefore, when assessing a dog for pain a range of factors should be considered, including the type, anatomical location and duration of surgery, the medical problem, or extent of injury. It is helpful to know the dog's normal behaviour; however, this is not always practical and strangers, other dogs, and many analgesic and other drugs (e.g. sedatives) may inhibit the dog's normal behavioural repertoire.

Behavioural signs of pain in dogs include:

- change in posture or body position (Figures 2 and 3)
- change in demeanour (Figure 4)

• vocalization
• altered reaction to touch
• altered interaction with people (e.g. reduced interaction, aggression)
• altered mobility (e.g. lameness, reluctance to move)
• reduction in appetite.

Pain assessment protocol

The most important step in managing acute pain well is to actively assess the dog for signs of pain on a regular basis, and use the outcomes of these assessments (through observation and interaction) along with knowledge of the disease/surgical status and history of the animal to make a judgement on the pain state of the dog. It is recommended that carers adopt a specific protocol and approach every dog in a consistent manner to assess them for pain. Dysphoria should be considered where panting, nausea, vomiting or vocalization occurs immediately following opioid administration.

• Observe the dog in its kennel/bed and consider its demeanor and posture
• Approach the dog and interact with it, calling its name, and consider its response
• Touch the dog (around a wound/damaged tissue as appropriate), and consider its response (normal, aggressive, flinching etc.).

Where a dog is judged to be in pain, treatment should be given immediately to provide relief. Dogs should be assessed continuously to ensure that treatment has been effective, and thereafter on a 2–4 hourly basis.

Pain measurement tools: these should possess the key properties of validity, reliability and sensitivity to change. Pain is an abstract construct so there is no gold standard for measurement and as the goal is to measure the affective component of pain (i.e. how it makes the dog feel), this is a real challenge. This is further compounded by the use of an observer to rate the dog's pain. Few of the scales available for use in dogs have been fully validated. Simple uni-dimensional scales, including the Numerical Rating Scale (NRS), the Visual Analogue Scale (VAS) and the Simple Descriptive Scale (SDS) (Figure 5), have been used.[12,13] These scales require the user to record a subjective score for pain intensity. When using these scales, the observer's judgment can be affected by factors such as age,
gender, personal health and clinical experience, thus introducing a degree of inter-observer variability and limiting the reliability of the scale. However, when used consistently, these are effective as part of a protocol to evaluate pain as described above. Of the three types of scales described (and there are others in this category), the NRS (0 to 10) is recommended for use due to its enhanced sensitivity over the SDS and increased reliability over the VAS.

Composite scales include the Glasgow Composite Measure Pain Scale and its short form (CMPS-SF),[14,15] and the French Association for Animal Anaesthesia and Analgesia pain scoring system, the 4A-Vet.[15] The CMPS-SF, validated for use in measuring acute pain, is a clinical decision-making tool when used in conjunction with clinical judgement. Intervention level scores have been described (i.e. the score at which analgesia should be administered), thus it can be used to indicate the need for analgesic treatment. The instrument is available to download online.[16] The 4A-Vet, which is also available online,[17] is available for use in cats and dogs, although evidence for its validity and reliability have not yet been demonstrated. The Colorado State University (CSU) acute pain scale for the dog[18] combines aspects of the numerical rating scale along with composite behavioural observation, and it has been shown to increase awareness of behavioural changes associated with pain. The University of Melbourne Pain Scale combines physiologic data and behavioural responses.[19] Japanese Society of Study for Animal Pain (JSSAP) Canine Acute Pain Scale (written in Japanese) is a numerical rating scale combined with behavioural observation and can be downloaded from the website.[20] All of the composite scales above are easy to use and include interactive components and behavioural categories.

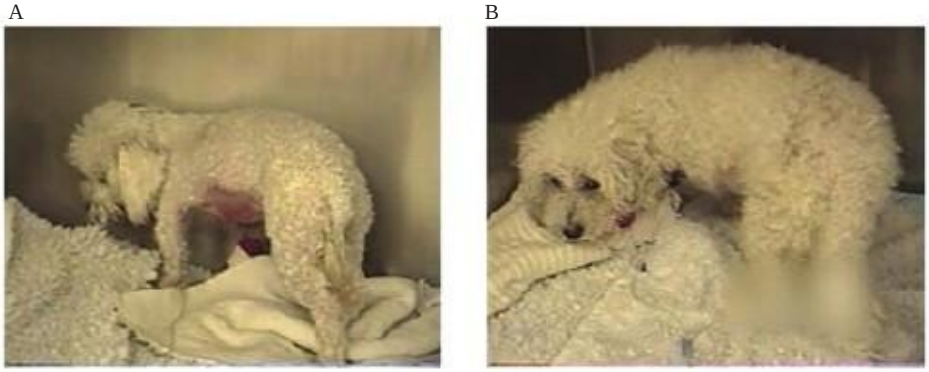


Fig 2. (A) Post-laparotomy (B) severe dermatitis

Fig 3. Gastroesophageal pain

A

B

Fig 4. (A) Pancreatitis, painful (B) pancreatitis, pain free

i) Simple Descriptive Scale (SDS)

No pain, Mild pain, Moderate pain, Severe Pain

Categories may be assigned numbers for data collection purposes; however, they are not numerical values.

ii) Numerical Rating Scale (NRS)

0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10.

0: no pain; 10, maximum pain possible

iii) Visual Analogue Scale (VAS)

|------------------------x--|

No pain maximum pain possible

Using the scales: The observer makes an assessment of the amount of pain a dog is experiencing based on their observation of and interaction with the dog, and their clinical judgement. A category (SDS) or number (NRS) is selected, or a mark made on the line (VAS) to reflect that judgement.

Fig 5. Uni-dimensional scales that have been described for use in dogs

5. RECOGNITION AND ASSESSMENT OF CHRONIC PAIN IN CATS

Chronic pain is of long duration, and is commonly associated with chronic diseases e.g. degenerative joint disease (DJD), stomatitis and intervertebral disk disease. It may also be present in the absence of ongoing clinical disease, persisting beyond the expected course of an acute disease process – such as neuropathic pain following onychectomy, limb or tail amputation. As cats live longer there has been an increased recognition of chronic pain associated with certain conditions, which has a negative impact on quality of life (QoL). In recent years, treatment options for some cancers in companion animals have become a viable alternative to euthanasia, and managing chronic pain and the impact of aggressive treatment protocols has become a challenging and important welfare issue.

Pain recognition is the keystone of effective pain measurement and management. The behavioural changes associated with chronic pain may develop gradually and may be subtle, making them most easily detected by someone very familiar with the animal (usually the owner).

Owner assessments are the mainstay of the assessment of chronic pain, but how these tools should be constructed optimally for cats is not fully understood. Many of the tools for measuring chronic pain in humans measure its impact on the patient's QoL, which includes physical and psychological aspects. Very little work has been performed in cats, but there are some studies assessing QoL or health-related quality of life (HRQoL) in cats being treated with antiviral agents,[21] and cats with cardiac disease,[22,23] cancer[24] and diabetes mellitus.[25] There is a growing understanding of behaviours that may be associated with the chronic pain of musculoskeletal disease in cats.[26,27] Recently, progress has been made in developing an owner-directed instrument for the assessment of chronic musculoskeletal pain in cats,[28,29,30] and also in understanding what owners consider to be important for their cat's QoL.[31] At the present time, there are no validated instruments available. However, we recommend that behaviours are assessed in these broad categories:

- General mobility (e.g. ease of movement, fluidity of movement)
- Performing activities (e.g. playing, hunting, jumping, using a litter-box)
- Eating, drinking
- Grooming (e.g. scratching)
- Resting, observing, relaxing (how well these activities can be enjoyed by the cat)
- Social activities involving people and other pets
- Temperament.

Each of these should be assessed and 'scored' in some manner (e.g. using either a descriptive, numerical rating or visual analogue scale). Re-evaluation over time will help determine the impact of pain, and the extent of pain relief.

6. RECOGNITION AND ASSESSMENT OF CHRONIC PAIN IN DOGS

Chronic pain is of long duration and is commonly associated with chronic diseases. It may also be present in the absence of ongoing clinical disease, persisting beyond the expected course of an acute disease process. As dogs live longer there has been an increase in the
incidence of painful chronic conditions such as osteoarthritis (OA) and in recent years the treatment of cancer in companion animals has become a viable alternative to euthanasia. For many chronic conditions, chronic pain is a challenge as is the impact of aggressive treatment protocols. Treatment options for chronic pain are complex, and response to treatment is subject to much individual variation. Accordingly the veterinarian must monitor health status effectively on an ongoing basis in order to tailor treatment to the individual.

Chronic pain recognition

Pain recognition is the keystone of effective pain management. The behavioural changes associated with chronic pain may develop gradually and may be subtle, so that they can only be detected by someone very familiar with the animal (usually the owner). In people, chronic pain has both a physical and a psychological impact which adversely affect the patient's QoL. As a consequence many of the tools for measuring human chronic pain measure its impact on the patient's QoL. At present, a few tools have been described to evaluate chronic pain in dogs and these have provided information about the range of alterations in the demeanour, mood and behaviour of dogs as a consequence of chronic pain. Broadly these can be categorized as follows:

- Vitality and mobility – how energetic, happy, active/ lethargic, contented, playful is the dog; ease of lying, sitting, jumping up, tolerance to exercise
- Mood and demeanour including states of alertness, anxiety, whether it is for example withdrawn, sad, dull, confident, its playfulness and sociability
- Levels of distress (e.g. vocalization [moaning, groaning], demeanour [e.g. depressed] and response to other dogs and humans)
- Indicators of pain (e.g. comfort levels, stiffness, lameness).

Chronic pain measurement

Owner assessments are the mainstay of the assessment of chronic pain in dogs. Functional assessment, QoL and HRQoL tools have been developed and used.[32,33] QoL measures used in veterinary medicine vary from simple scales tied to certain descriptors of behaviours[34] to broad, unconstrained assessments.[35-37] Questionnaires have been developed to assess HRQoL in dogs with DJD, cardiac disease,[38] cancer,[39,40] chronic pain,[41,42] spinal cord injuries[43,44] and atopic dermatitis,[45] while some are less specific.[46,47]

Several instruments focused mainly on functional assessment (Clinical Metrology Instruments, CMIs) have been developed for canine OA and have undergone a variable degree of validation.[13,35,48-52] Such questionnaires typically include a semi-objective rating of disease parameters such as 'lameness' and 'pain' on either a discontinuous ordinal scale or a visual analogue scale.

At the present time, the most fully validated instruments available are:

- GUVQuest[41,42]
- Canine Brief Pain Inventory[53]
- Helsinki Chronic Pain Index (available on request to author)
- Texas VAS Instrument (available on request to author)
- Liverpool Osteoarthritis in Dogs (available on request to author)
- JSSAP Canine Chronic Pain Index (can be downloaded from the JSSAP website)[20].

GUVQuest is an owner-based questionnaire developed using psychometric principles for assessing the impact of chronic pain on the HRQoL of dogs, and is validated in dogs with chronic joint disease and cancer. The Canine Brief Pain Inventory (CBPI) has been used to evaluate improvements in pain scores in dogs with OA and in dogs with osteosarcoma. The Helsinki Chronic Pain Index (HCPI) is also an owner-based questionnaire and has been used for assessing chronic pain in dogs with OA and, along with the CBPI, has been evaluated for content validity, reliability[48,51] and responsiveness.[35,51] The CMI from Texas A&M[13] has been investigated for validity and reliability but not responsiveness. The Liverpool Osteoarthritis in Dogs ('LOAD') CMI has been validated in dogs with chronic elbow OA, and has been shown to be reliable with satisfactory responsiveness.[49] Recently, its validity for both forelimb and hind limb OA was demonstratred.[54] The JSSAP Canine Chronic Pain Index is an owner-based questionnaire written in Japanese and has been used for assessing chronic pain in dogs with OA.

Out of this work some key messages have emerged:

- Owner information is a key resource when assessing chronic pain
- Owners may need prompting and close questioning to report changes in their dog's behaviours as they may not associate these changes with chronic pain
- There is an evidence base for the behaviours that alter in association with chronic pain (see above); these should be the basis of exploration with owners
- Changes in dogs' behaviours may be subtle, and take place gradually. Veterinarians need to ensure that when questioning the owner they prompt owners to reflect over a period of time (months)
- The veterinarian may find it useful to identify behaviours from the owner that can be used as marker behaviours to help determine response to treatment.

Recognizing chronic pain – osteoarthritis as an example

Evaluating the canine OA patient consists of a combination of a veterinary assessment or examination, and the owner's assessment. The overall assessment of the negative impact of OA on the patient involves an evaluation of four broad categories:

- Mobility (the quality of moving freely)
- Activity (the ability to perform specific activities)
- Pain (adverse sensory and emotional experience)
- Affective effects (mood, feelings).

These are all interconnected. Careful assessment of these four categories and their adverse effects will guide the prioritization of treatment
strategies. To fully assess these four categories, the clinician needs to gather data on:

- Body balance, muscle mass, muscle health
- Ease of movement and mobility
- Gait and limb use
- Joint-associated pain and mobility
- Other factors affecting mobility (such as neurological disease, patella luxation, cruciate ligament insufficiency, systemic medical disease)

• Ability to perform specific activities
• Level of engagement, happiness.

Such a complete assessment will involve input from both the veterinarian (physical and orthopaedic examination) and the owner (owner completed QoL, HRQoL and Functional Assessments) and forms a baseline for future assessment.

7. ASSESSING RESPONSE TO TREATMENT OF PAIN IN CATS AND DOGS

Assessing the response to pain treatment/intervention strategies is a fundamental aspect of effective pain management. Too often dogs and cats are given one-off doses of analgesic drugs without effective follow-up. Methods of assessing pain in dogs and cats, both acute and chronic, are described in other sections.

Key principles of assessing response to treatment:

• Adopt a rigorous protocol for assessing pain severity. Whether this is based on one of the currently available instruments for assessing pain or on a locally developed approach, it is critical to interact with the animal, and use a knowledge of normal behaviours and behaviours indicative of pain to assess the dog or cat
• Adopt the above protocol/approach for all animals in your care
• Involve the owner in assessing pain and response to treatment through effective open questioning techniques
• Undertake a baseline assessment of the level of pain at the initial consultation
• Repeat assessments on a regular basis and, in particular, at an appropriate time after treatment. The interval between repeat assessments will depend on the nature of the pain (acute/chronic), the intensity of the pain and the success of therapy.

Acute pain

Dogs and cats should be assessed on a regular basis following surgery, in the early recovery period every 15–30 minutes (depending on the surgical procedure) and on an hourly basis thereafter for the first 6–8 hours after surgery. Thereafter, if pain is well controlled, 3–6 hourly assessment is recommended. The exact time interval depends on the severity of the surgery, the type of drugs used to manage pain and other factors relating to the animal's physical status. If in doubt about pain status re-assess the animal in 15 minutes.

Chronic pain

Dogs and cats should be assessed on a regular basis guided by the evidence below:

• Owners are a key information source for animals with chronic pain
• Owners may need prompting and close questioning to report changes in their cat's or dog's behaviour as they may not associate these changes with chronic pain
• Changes in cat's and dogs' behaviour may be subtle, and take place gradually. When questioning owners, prompt them to reflect over a period of time (months).

There is an evidence base for the key domains of behaviour that alter in association with chronic pain (see Sections 5 and 6). This should be the basis of exploration with owners at initial presentation and on subsequent re-evaluation of progress.

8. NEUROPATHIC PAIN

Neuropathic pain[55] (defined as pain caused or intiated by a primary lesion or dysfunction in the peripheral or central nervous system) is associated with nerve root and plexus avulsion injuries and central nervous system pathology. Any chronic pain condition can subsequently develop a neuropathic component due to the continual nociceptive barrage and subsequent changes in the functioning of the nervous system.[56] Behavioural patterns described by owners such as repeated chewing, biting or scratching at the same site, spontaneous crying and adverse reaction to touch where no pathology is visible may be indicators of neuropathic pain. Excessive sensitivity (hypersensitivity) on examination suggests a neuropathic component to pain, and a poor response to standard (NSAID, opioid) analgesics may also suggest the presence of neuropathic pain. Should neuropathic pain be suspected, both the causal condition, and the neuropathic pain state itself should be addressed. Physical examination for identifying neuropathic pain should include testing for the following:[57,58]

• Hyperalgesia is considered to exist when the animal responds adversely, and more aggressively, to a noxious stimulus (e.g. pin prick) either directly on the area of the body from which the pain originates (primary) or in an uninjured adjacent area (secondary)

• Allodynia (pain elicited from non-injured tissues by non-noxious stimuli – tactile allodynia [Aβ stimulus]) is considered to exist when the animal responds adversely to light touch applied to normal (non-injured) tissues distant from the area of primary hyperalgesia or hyposensitivity.

9. PERCEIVED LEVEL OF PAIN ASSOCIATED WITH VARIOUS CONDITIONS

The designation of conditions into categories below is intented to serve only as a guide. Pain may vary according to the patient and the condition. Each patient should be assessed individually.

Severe-to-excrutiating	
Central nervous system infarction/tumours	Meningitis
Fracture repair where extensive soft tissue injury exists	Spinal surgery
Ear canal ablation	Burn injury
Articular or pathological fractures	Limb amputation
Necrotizing pancreatitis or cholecystitis	Thrombosis/ischaemia
Bone cancer	Hypertrophic osteodystrophy
Aortic saddle thrombosis	
Neuropathic pain (nerve entrapment/inflammation, acute intervertebral disc herniation)	
Inflammation (extensive e.g. peritonitis, fascitis – especially streptococcal, cellulitis)	
Moderate-to-severe (varies with degree of illness or injury)	
Immune-mediated arthritis	Panosteitis
Capsular pain due to organomegaly	Hollow organ distension
Traumatic diaphragmatic rupture	Pleuritis
Trauma (i.e. orthopaedic, extensive soft tissue, head)	Frostbite
Ureteral/urethral/biliary obstruction	
Glaucoma	
Uveitis	Corneal abrasion/ulceration
Early or resolving stages of soft tissue injuries/inflammation/disease	
Mesenteric, gastric, testicular or other torsions	
Mucositis	Intervertebral disc disease
Mastitis	Peritonitis with septic abdomen
Extensive resection and reconstruction for mass removal and corrective orthopaedic surgery (osteotomies; cruciate surgery; open arthrotomies)	Oral cancer Dystocia
Moderate	
Soft tissue injuries (i.e. less severe than above)	Urethral obstruction
Ovariohysterectomy	Cystitis
Diagnostic arthroscopy and laparoscopy	Osteoarthritis
Mild-to-moderate	
Dental disease	Otitis
Superficial lacerations	Mild cystitis
Chest drains	Abscess lancing
Castration	

Data from K Mathews.[59]

10. COMMON PAIN MISCONCEPTIONS

'Opioids cause respiratory depression in dogs and cats'

False. This misconception has arisen from the fact that humans are very sensitive to the respiratory depressant effects of opioids. However,
this is not the case in dogs and cats and opioids have a wide safety margin in healthy patients. In sick animals, opioid drugs should be titrated to effect to minimize the risk of respiratory compromise. For this to occur, the patient must be markedly mentally depressed.

'Non-steroidal anti-inflammatory drugs are toxic in dogs and cats'

False. As most pain is associated with inflammation NSAIDs are the mainstay of analgesia for both acute and chronic pain in dogs and cats, and are widely and safely used in many animals around the world. The analgesic benefits far outweigh the potential risks. However, it is essential that the individual patient is screened for potential risk factors prior to administration and monitored during treatment. Many of the NSAIDs licensed for use in humans have a narrow safety margin in animals and should be used with caution. Where approved drugs are available, they should be used preferentially.

'If I alleviate pain, the animal will move and disrupt its suture line/fracture repair'

False. The use of pain to control movement following surgery is unethical. Where activity needs to be controlled, other means should be adopted (e.g. cage confinement, controlled leash walking). Controlled walking exercise is essential for postoperative orthopaedic

repair to ensure appropriate 'stress' for bone healing and to maintain muscle mass to support the limb. Non-use results in bone and muscle atrophy. Without analgesic administration, movement may be too painful. Non-treated pain associated with abdominal or thoracic incisions prevents normal ventilation/oxygenation.

'Newborn and infant animals don't feel pain'
False. Animals of all ages feel pain.

'Analgesics mask signs of patient deterioration'
False. Appropriate pain relief eliminates pain as a potential cause for signs of patient deterioration (e.g. tachycardia).

'Anaesthetics are analgesics and therefore prevent pain'
False. The majority of anaesthetics (inhalant, propofol, barbiturates) block conscious perception of pain but are not analgesic as nociception is still occurring during the unconscious state. The pain generated during the anaesthetic state will be experienced upon awakening. Ketamine, however, has anti-hyperalgesic and some analgesic properties.

SECTION 2: PAIN MANAGEMENT

11. GENERAL APPROACHES TO THE TREATMENT OF PAIN

Pain is a complex phenomenon, which is different in every individual and involves both a sensory (nociception) and affective (emotional) component. Decades of research into pain management indicate that pain is best managed early and aggressively; it is harder to combat pain once it is well established than it is to manage pain before it becomes severe. Clearly this is not always possible but when it is, prevention should be the focus of the analgesic plan. In the treatment of all pain, the aim is to abolish it or, at the very least, to reduce it to a minimum.

The term preemptive analgesia has been used to describe the treatment of pain using analgesic drugs given in advance of the pain stimulus occurring; the underlying theory behind such an approach is based on the premise that by reducing the magnitude of nociceptive input to the spinal cord, peripheral and central sensitization are reduced and thereby perioperative pain and hyperalgesia are reduced. However, this is a somewhat restricted view of the events which trigger postoperative and acute inflammatory pain. The focus of what is termed preventive analgesia is to reduce the impact of the total peripheral nociceptive barrage associated with noxious pre-, intra- and postoperative or traumatic stimuli.[60] Drugs with a demonstrated preventive effect in humans include the NSAIDs, local anaesthetics and N-methyl-D-aspartate (NMDA) antagonists (e.g. ketamine). These drugs not only reduce the severity of acute post-surgical pain, but in some cases also reduce the incidence of chronic (persistent) postoperative pain.

Analgesic drugs all have the potential to cause side effects. When pain is moderate or severe, the veterinarian should consider combining drugs that act at different sites in the pain pathway to provide optimal analgesia; multimodal analgesia (sometimes referred to as balanced analgesia) is the name given to this approach to treating pain. Combining different classes of analgesic drugs allows the veterinarian to optimize the management of pain, while limiting the occurrence of side effects. Drugs most commonly used in multimodal analgesia include opioids, NSAIDs, local anaesthetics, NMDA antagonists and alpha$_2$ adrenoceptor agonists.

The choice of drug(s) used to treat pain will depend on the underlying cause of pain and the severity and duration of pain. Alleviation of chronic pain will require drugs or drug preparations with a long duration of action, and possibly a range of adjunct therapies. Knowledge of the pharmacology of analgesic drugs in each species is required to optimise drug choice. Factors including age, breed and physical status may influence drug pharmacology and consequently the efficacy and dosing regimen of analgesic drugs. For example, when compared to 'adults', drugs in very young animals (puppies and kittens less than 12 weeks of age) and geriatric animals (>75% life expectancy) often have a different pharmacokinetic profile which may alter the effective dose and dosing interval. It is unwise to extrapolate pharmacokinetic data from one species to another; this is particularly true between the dog and the cat.

For the management of acute pain or acute exacerbations of chronic pain, in particular severe pain, drugs should be titrated to effect, and a multimodal approach used. Dosing intervals are influenced by the severity of pain, patient factors and the combination of drugs used, and should be modified according to patient response.

Acute pain

Acute pain is initiated by a traumatic, surgical or infectious event and begins abruptly and should last a predictable length of time, correlating with the severity of the insult.

Perioperative pain

There are four key time-points when the choice of analgesic strategy will influence a patient's postoperative pain status; these are the preoperative; intraoperative; immediate postoperative ('in hospital'); and later postoperative periods ('at home'). The most important

time periods to consider are the preoperative and intraoperative periods – time periods when postoperative pain can be prevented, or very much reduced, via the concept of preventive[61-63] and multimodal[64-66] analgesia. To prevent re-initiation of pain, treatment should continue until the inflammatory response is minimal.

An effective perioperative pain management regimen would normally incorporate drugs from several different classes. Pain relief can also be provided by non-drug therapies. Although the scientific evidence supporting these therapies is largely lacking in veterinary medicine, several modalities are often used including local hypothermia (cold therapy) and hyperthermia; passive range-of-motion exercises; massage; therapeutic exercise; hydrotherapy; ultrasound and electrical stimulation. Surgical technique can have an important impact on perioperative pain.[67] Gentle tissue handling and techniques that minimize trauma (e.g. small incisions; arthoscopy, laparoscopy) should be employed whenever possible.[68] The site of surgery also impacts on pain; after intrathoracic and intra-abdominal procedures, movements that place tension on the incision (such as deep breathing and coughing) increase the intensity of pain. The face, mouth and anal/perianal area appear to be highly sensitive sites and surgery in these areas is likely to be associated with significant pain. Where inflammation is present, such as metritis or pyometra, the degree of pain experienced during and after ovariohysterectomy may be greater than that associated with the routine procedure which might warrant more frequent or higher dosing of analgesics over a longer period of time.

Chronic pain

This is pain of long duration. In humans, chronic pain is often accompanied by fear, anxiety, depression and anger, which can exacerbate pain and its negative impact on the patient's QoL. It is estimated that at least 30% of pet dogs and cats that are seen by veterinarians can be classified as 'senior' and this population is likely to have a high prevalence of chronic pain. However, chronic pain is often not diagnosed as it is often mistaken for 'getting old'. Veterinarians treating animals with chronic disease should consider the potential for accompanying chronic pain, even in the absence of immediately obvious signs. The changes in behaviour that accompany chronic pain may be insidious in onset and subtle.[42]

The approach to treatment depends on the underlying cause of pain, its duration at presentation and how well it has been managed previously. Chronic disease may not be static and acute exacerbations of previously well-controlled pain can occur and these can be especially challenging to treat. A multimodal approach (combination therapy) is likely to be most effective[69] and owner education is essential. The mainstays of treatment of chronic pain are the NSAIDs; however, adjunct drug therapies, physical and other approaches (e.g. acupuncture, surgery) may play an important role in management. There is a wide range of NSAIDs licensed for long-term use in dogs; they are most commonly given orally and long-acting injectable preparations are available. In cats, the only NSAID currently approved for long-term use is meloxicam.

Although many non-drug therapies are suggested to be effective for the management of chronic pain, there is little evidence behind their efficacy, and almost nothing known about potential side effects. In addition, drug side effects, disease progression or co-morbidities can be mistaken for worsening pain, leading to additional treatments that are at best non-efficacious, or at worst detrimental. One example is the dog with chronic OA which then develops neurological disease and is prescribed additional drugs in an attempt to alleviate what is thought to be only pain-related difficulty in mobility. In all chronic pain cases, non-drug treatments should be used alongside drug treatments, and there should be regular evaluation to detect beneficial and unwanted effects, and regular reassessment of the patient's pain.

12. OPIOIDS

What they are

Opioids are drugs that have opiate-like activities and are the cornerstone of effective pain treatment. They vary in their receptor specificity, potency and efficacy, resulting in different clinical effects. 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. They have high efficacy and are remarkably safe.[70] However, butorphanol and nalbuphine exhibit a ceiling effect where increasing dosages above those recommended will not confer further analgesia, only side effects. Most opioids are controlled substances with the benefit of reversibility. Individual variability after opioid administration may be observed due to differences in pharmacokinetic-pharmacodynamic effects, gender, age and genotype, among others. With the exception of remifentanil, these drugs are metabolized by the liver into active and/or inactive metabolites. Tramadol is considered to be an opioid. Dogs, unlike cats and humans, cannot form appreciable quantities of the active metabolite[71] and potential analgesia may be due to the serotonin re-uptake inhibition.

How they work

Opioids bind to opioid receptors (μ, |, ™ and nociceptin, and their subtypes) 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. Postsynaptically, enhanced K_+ efflux causes neuronal hyperpolarization of spinal cord projection neurons and inhibits ascending nociceptive pathways. Opioids do not interfere with motor function.[72]

Indications

Opioids produce analgesia, euphoria, mydriasis (cats) or miosis (dogs), sedation or excitement, and several other physiological effects depending on the animal species. Opioids are efficacious analgesic drugs for treatment of moderate to severe pain. Their analgesic effects depend on the dose, route of administration, delivery system and species to which the drug is given.[73] Opioids are widely used in the perioperative setting as part of multimodal and/or preemptive or preventive analgesic protocols as well as for inhalant anaesthetics sparing-effects. They are also widely administered in emergency and critical care patients (i.e. pancreatitis, burns, traumas, meningitis). Epidural administration of morphine is used for postoperative analgesia in the clinical setting. Opioids do not cause excitement ("morphine-mania") in cats if appropriate doses and intervals are used. Using the IV route, sedation normally occurs in dogs. Intravenous and intramuscular administration is preferred;[74] however, buprenorphine given by the oral transmucosal route has been demonstrated to produce effective antinociception in cats.

Side effects

Most common side effects, usually associated with excessive doses, include vomiting (pre-medication), dysphoria, nausea, panting, bradycardia, and histamine release (morphine and pethidine [meperidine] especially when given IV), urinary incontinence / retention and 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 (see Table 1).

Contraindications

The clinician must balance the pros and cons of opioid administration as some adverse effects may be clinically irrelevant when pain management is a priority.

Drug interactions

Opioids are combined with benzodiazepines, alpha$_2$ adrenoceptor agonists or acepromazine (neuroleptanalgesia) in order to improve sedation while minimizing side effects. Opioids may have a synergistic effect when combined with NSAIDs and local anaesthetics as

Table 1. Suggested doses (mg/kg) and dosing frequencies of opioid analgesic drugs in cats and dogs

Opioid analgesic	Dog (mg/kg)	Cat (mg/kg)	Route of administration	Comments
Morphine*	0·3–1 q 2–4h	0·2–0·4 q 4–6h	IM	Cautious use with IV administration due to histamine release
Pethidine (meperidine)	3–5 q 1–2h	3–10 q 1–2h	IM	Do not administer IV due to histamine release
Methadone*	0·5–1 q 3–4h	0·3–0·6 q 4h	IM, IV (dogs)	Has NMDA receptor antagonist properties
Oxymorphone	0·05–0.2 q 4h	0·03–0·1 q 4–6h	IM, IV	
Hydromorphone*	0·05–0.2 q 2–6h	0·025–0·1 q 4–6h	IM, IV	
Tramadol	4–6 q 6–8h	2–4 q 6–8h	IM, IV, PO	May cause hyperthermia in cats Weak affinity for opioid receptors Noradrenaline (norepinephrine) and serotonin re-uptake inhibitor
Fentanyl*‡	Bolus 2–5 μg/kg + CRI 3–6 μg/kg/h	Bolus 1–3 μg/kg + CRI 2–3 μg/kg/h	IV	Doses may be increased for inhalant anaesthetic-sparing effect or for maximum analgesia
Alfentanil‡	Bolus 20–50 μg/kg + CRI 30–60 μg/kg/h	Bolus 10–30 μg/kg + CRI 20–30 μg/kg/h	IV	Doses may be increased for inhalant anaesthetic-sparing effect or for maximum analgesia
Sufentanil‡	Bolus 0·2–0·5 μg/kg + CRI 0·3–0·6 μg/kg/h	Bolus 0·1–0·3 μg/kg + CRI 0·2–0·3 μg/kg/h	IV	Doses may be increased for inhalant anaesthetic-sparing effect or for maximum analgesia
Remifentanil	6–12 μg/kg/h	4–6 μg/kg/h	IV	Doses may be increased for inhalant anaesthetic-sparing effect or for maximum analgesia. It does not require a bolus Limited analgesic efficacy in most cases of moderate or severe pain.
Butorphanol	0·2–0·4 q 1–2h	0·2–0·4 q 1–2h	IM, IV	Limited analgesic efficacy in moderate or severe pain
Pentazocine	1–2 q 2–4h	1–2 q 2–4h	IM, IV	Limited analgesic efficacy in moderate or severe pain Can be given oral transmucosally to cats.
Nalbuphine	0·3–0·5 q 2–4h	0·2–0·4 q 2–4h	IM, IV	
Buprenorphine	0·01–0·02 q 4–8h	0·02–0·04 q 4–8h	IM, IV, OTM [cats]	
Naloxone (antagonist)	0·04 q 0·5–1h*	0·04 q 0·5–1h*	IM, IV†	Dilute and titrate IV dose to effect when reversing opioid side effects in painful patients. Mix 0.1 mL (cats, small dogs) or 0.25 mL of naloxone (0.4 mg/mL) with 5–10 mL saline. To avoid adverse effects, titrate this at 1mL/min until the side effects have subsided; using this technique analgesic effects will be maintained. Repeat as required after ~ 20–30 min. If administering IM, give an initial dose of 0.01mg/kg and repeat at 10 min intervals until opioid side effects have been antagonized. Analgesia cannot be guaranteed using the IM route.
Nalmefene (antagonist)	0·25–0·30 μg/kg q 1–2h	0·25–0·30 μg/kg q 1–2h	IM, IV	

*Lower dosages are recommended to start for patients with health problems. †Titration of dose is recommended to avoid adverse effects. ‡Bolus or loading doses should be given slowly or to effect to avoid sudden bradycardia and hypotension.

part of multimodal analgesia. Mixing of different groups of opioids (i.e. buprenorphine and butorphanol) can result in unpredictable effects and it may not offer any advantages.

Special considerations

Opioid tolerance is widely reported in humans but is rarely a problem with short-term use in veterinary medicine. There are reports of opioids causing hyperalgesia in humans and rats; however, this has not been documented yet in small animal practice.

13. NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

What they are

NSAIDs are drugs that exert antipyretic, anti-inflammatory and analgesic effects. NSAIDs are the mainstays of relief from mild-to-moderate pain. Chemically they can be divided into salicylates (ASA) and carboxylic acid derivatives. The latter comprise most drugs: indoles (indomethacin), proprionic acids (carprofen), enolic acids (phenylbutazone), oxicams (meloxicam), fenamates (mefenamic acid) and coxibs (deracoxib, firocoxib, robenacoxib). Availability of veterinary licensed products with a COX-1 sparing and COX-2 preferential profile has improved the safety profile of this class of drugs.[75] Most drugs are commonly administered per os but some drugs exist in injectable form. NSAIDs are generally metabolized in the liver and may have active metabolites.[76]

How they work

NSAIDs influence the expression of arachidonic acid derivatives in the body. This relates largely to the production of prostaglandins catalyzed by the enzyme cyclooxygenase (COX); however, for salicylates inhibition of nuclear factor kappa-B (NF-κB) may have an important role, and dual inhibitors (tepoxalin), inhibit lipoxygenase (LOX), reducing leukotriene production.

COX exists in two forms: COX-1 and COX-2. COX-1 produces a range of prostaglandins (PGs) and thromboxanes involved in many physiological processes including vascular homeostasis, gastroprotection, renal blood flow, blood clotting, reproduction, wound healing, bone metabolism, nerve development and growth, and immune responses while COX-2 products are mainly PGE_2 and prostacyclin – both important mediators of inflammation, although having hemostatic, gastrointestinal and important renal constitutive functions as well.

Both COX-1 and COX-2 are expressed constitutively, but are also induced in higher concentrations at times of inflammation and in certain cancer types. COX-1 and COX-2 are present within the spinal cord where the PGs produced function as nociceptive neurotransmitters independent of an inflammatory response. At the brain stem, NSAIDs induce antinociception by activating the descending inhibitory pathway inhibiting transmission of pain signals at the dorsal horn.[77] While COX selectivity may be beneficial to reduce side effects and inflammation (the main indication of these drugs), it is important to note that both enzyme forms are required at certain concentrations for normal body functions. The specificity of NSAIDs for COX-1 vs. COX-2 form is species-specific. The 50%-inhibitory concentration ratio ($IC50_{COX\text{-}1}$: $IC50_{COX\text{-}2}$) is a measure of how much drug is needed to inhibit each isoenzyme by 50%. The actual value to the ratio, however, depends on the method, the test situation and assay used, and no clinically relevant gold standard for comparing NSAID inhibiton of each isoenzyme has been established. The comparison of selectivity between single drugs on the basis of this ratio remains difficult.

Paracetamol (acetaminophen) is a non-acidic NSAID that likely acts on a splice variant of COX-1 present in the central nervous system, and it may influence the opioidenergic, serotonergic and cannabinoid systems. Paracetamol has analgesic and antipyretic effects but little if any anti-inflammatory activity. It has been used for chronic pain in dogs as part of a multimodal approach with minimal gastrointestinal effects. While it seems a promising treatment option due to good central analgesic and antipyretic effects in dogs, it should not be given to cats.[78] Paracetamol readily induces methaemoglobinemia in cats. Dipyrone (metamizole) is a weak NSAID with analgesic, antipyretic and spasmolytic properties. Its mechanism of action appears to be related to the inhibition of both peripheral and central COX enzymes. The administration of metamizol (25–35 mg/kg TID IV) has been shown to provide adequate postoperative analgesia after ovariohysterectomy in dogs.[77] Since this is a phenolic compound, it should be used with caution in cats.

Indications

NSAIDs are effective analgesics and of significant benefit across the spectrum of pain intensities. NSAIDs are administered in the perioperative period, as well as in other acute and chronic pain states such as OA, cancer and other inflammatory conditions.[79] In moderate-to-severe pain they should be used as part of a multi-modal protocol. When used for chronic pain conditions (e.g. OA pain), they are often titrated to the lowest effective dose although there is no evidence that downward dose titration results in greater safety.

There are individual differences, however, in their clinical effectiveness and in case of an unsatisfactory response, switching NSAID may be warranted, and should follow a washout period of several days (this has not been scientifically supported). Particular caution is advised when switching from a non-selective, or COX-1 selective to a COX-2 selective drug.[80] Should mucosal erosions be present, or suspected, caution should be exercised if using COX-2 selective drugs, as these may retard mucosal healing.[81]

Table 2 provides dosing recommendations for NSAIDs.

Table 2. Non-steroidal anti-inflammatory drugs (NSAIDs): canine and feline dosing recommendations[a]

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	Once Once per day
		Cats: 0·3 mg/kg SC _____ Or, Up to 0·2 mg/kg SC 0·05 mg/kg PO	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	Once on Day 1 Once per day to follow; use the lowest effective dose
		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
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/acute musculoskeletal	Dogs: 2 mg/kg SC 1 mg/kg PO	Once followed by oral Once daily
		Cats: 2 mg/kg SC 1 mg/kg PO	Once followed by oral Once daily for total of 6 days or as licensed Once daily; use lowest effective dose
	Chronic pain	Dogs: 1 mg/kg PO	
Carprofen[d]	Surgical pain	Dogs: 4 or 4·4 mg/kg SC, IV, PO 2 or 2·2 mg/kg SC, IV, PO	Once per day for up to 4 days Every 12h for up to 4 days
		Cats: 2 to 4 mg/kg SC, IV	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
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
Tepoxalin[d]	Chronic pain	Dogs: 10 mg/kg PO	Once daily; use lowest effective dose

Table 2. (Continued)

DRUG	INDICATION	SPECIES, DOSEb, ROUTEc	FREQUENCY
Tolfenamic acid	Acute and chronic pain	Dogs: 4 mg/kg SC, IM, PO Cats: as for dogs	Once daily for 3 to 5 days. Repeat once per week.
Flunixin meglumine	Pyrexia	Dogs and Cats: 0·25 mg/kg SC	Once
	Surgical and ophthalmological procedures	Dogs and Cats: 0·25–1·0 mg/kg SC	Every 12 to 24h for 1 or 2 treatments
Ketorolac	Surgical pain	Dogs: 0·3 mg/kg IV, IM, SC	Every 12h for 1 to 2 treatments
		Cats: 0·2 mg/kg IM	Every 12h for 1 to 2 treatments
	Panosteitis	Dogs: 10 mg/dog > 30 kg, PO 5 mg/dog >20 kg<30 kg, PO	Once daily for 2–3 days
Piroxicam	Inflammation of the lower urinary tract	Dogs: 0·3 mg/kg, PO	Once daily for 2 treatments, then every 2 days
Paracetamol (acetaminophen)	Surgical/acute or chronic pain	Dogs ONLY: DO NOT USE IN CATS 10–15 mg/kg PO 10 mg/kg IV over 15 mins	Every 8–12h
Aspirin	Surgical/acute or chronic pain	Dogs: 10 mg/kg PO	Every 12h

[a] See text for details on the contraindications for use
[b] Dose based on lean body weight
[c] IV, intravenously; SC, subcutaneously; IM, intramuscularly; PO, per os
[d] Indicates a veterinary licensed version of this pharmaceutical exists in some countries. The label will provide the best information as to product use relevant to the country licensed in.

Contraindications

In a few patients NSAIDs may cause adverse effects: these are most commonly 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. Similarly, NSAIDs should be used cautiously in animals with pre-existing renal disease and, if contemplated, should follow a risk-benefit assessment and close monitoring regimen appropriate for the patient's condition. Periodic monitoring is recommended with long-term use. NSAIDs with selective COX-1 antagonism (e.g., ketoprofen, aspirin, ketorolac) have been reported to cause inhibition of coagulation via anti-thromboxane activity. This class of NSAIDs should be avoided preoperatively, and only administered postoperatively when adequate clot formation has occurred (usually upon completion of surgery), this is especially important for non-compressible surgical procedures and dental extractions.[82,83] While there is no clear evidence stating that the use of NSAIDs in patients with hepatic disease is an absolute contraindication, gastrointestinal ulceration is known to be more frequent in animals with hepatic disease. Paracetamol should not be used in cats.

Drug interactions

NSAIDs should not be given together with other drugs that affect arachidonic acid derivatives and leukotrienes. A higher incidence of severe side effects is described when co-administered with corticosteroids. COX-2 inhibitors should not be co-administered with aspirin, since this may enhance the risk of gastrointestinal mucosal injury. NSAIDs should be given very cautiously when ACE-inhibitors, diuretics, warfarin, phenobarbitone or chemotherapeutics are administered, if at all.[82]

14. ALPHA$_2$ ADRENOCEPTOR AGONISTS

What they are

Alpha$_2$ adrenoceptor agonists are non-controlled drugs (xylazine, romifidine and [dex] medetomidine) that produce sedation and hypnosis, analgesia and muscle relaxation. The analgesic effects are normally short-lived in comparison with the sedative effects of these drugs. They vary in their receptor specificity and potency (xylazine < romifidine < [dex] medetomidine). Alpha$_2$ adrenoceptor agonists have the benefit of sedative reversibility when an antagonist (atipamezole or yohimbine) is given; however, analgesia is also reversed. Dexmedetomidine is the pharmacologically active enantiomer found in the racemic preparation of medetomidine, and is approximately (with specific differences) twice as potent as the latter. Sedative effects vary from 30 min to 90 min depending on the drug, route of administration and dose used. These drugs are metabolized by the liver and excreted by the kidneys.[84]

How they work

These drugs bind to different alpha$_2$ adrenoceptor subtype receptors in the dorsal horn of the spinal cord (spinal analgesia), cerebral cortex and locus ceruleus (sedation and supraspinal analgesia) which are present on noradrenergic and non-noradrenergic neurons. Noradrenaline (norepinephrine) is the endogenous ligand for these receptors. These drugs inhibit the release of excitatory neurotransmitters through complex signal transduction and intracellular mechanisms causing membrane hyperpolarization in a similar way to opioid analgesic drugs. Alpha$_2$ agonists also bind to their receptors in the vascular endothelium causing peripheral vasoconstriction with increases in systemic and pulmonary vascular resistance while decreasing cardiac output in a dose-dependent manner. Consequently, a reflex or centrally-mediated bradycardia and bradyarrhythmias (first and second degree atrioventricular block) may be observed.[85]

Indications

Alpha$_2$ adrenoceptor agonists are widely used for sedation for non-invasive procedures (radiographs, ultrasound examinations, minor laceration repair, wound debridement, bandage placement, biopsies, etc) and as part of neuroleptanalgesia and balanced anaesthesia protocols. They are considered analgesic adjuvants in a variety of clinical settings as they can supplement analgesia while reducing stress response. Small doses may be administered during recovery from anaesthesia, particularly in cases of emergence delirium and dysphoria. Their use is generally reserved to healthy animals that can tolerate significant haemodynamic changesand/or with feral and/or aggressive animals.[86] Further studies may elucidate the advantages and disadvantages of these drugs when administered by other routes of administration (continuous rate infusion, oral transmucosal, epidural, intra-articular and/or part of local anaesthetic blocks).[87]

Side effects

Most common side effects include hyper and/or hypotension, bradycardia, hypothermia, decreases in sympathetic tone and gastrointestinal motility, increases in urinary output, transient hypoinsulinaemia and hyperglycaemia. Other less common side effects such as emesis, salivation, bradyarrhythmias may be observed.[88,89]

Contraindications

These include animals with cardiopulmonary disease with or without arrhythmias or conduction disturbances, significant systemic disease, preexisting hypo/hypertension, diabetes mellitus and liver/renal failure. Caution should be exercised when using in patients with trauma. The use of anticholinergics in combination with alpha$_2$ agonists may be contraindicated if peripheral vasoconstriction and possible hypertension are present.

Drug interactions

Concurrent use of alpha$_2$ adrenoceptor agonists and opioids may improve analgesia due to a synergistic effect. These drugs have significant injectable and inhalant anaesthetic-sparing effects. Opioid requirements are usually reduced when alpha$_2$ adrenoceptor drugs are used.[87]

Special considerations

Some animals appear unaffected by the administration of alpha2 adrenoceptor agonist drugs.

15. LOCAL ANAESTHETICS

What they are

Local anaesthetics (LAs) are drugs that reversibly bind to Na_+ channels and block impulse conduction in nerve impulses. LAs contain an aromatic ring (lipophilic) at one end and an ionizable group at the other and an intermediate chain in between, which can be either an ester (tetracaine, procaine, benzocaine) or an amide (lidocaine, bupivacaine, ropivacaine, mepivacaine, prilocaine and their respective mono-isomers). Potency is directly related to lipid solubility while onset is inversely associated with pKa and lipophilicity; increased protein binding and potency, and the vasoactivity of the LAs correlate with increased duration of action. The intermediate chain determines their metabolism (amides, liver; esters, liver and pseudocholinesterases in plasma). LAs are the main drugs used for loco-regional anaesthesia and analgesia.[90]

How they work

LAs stabilize the cell membrane, rendering it non-susceptible to electrical stimuli by altering Na_+-channel conformation. LAs block small unmyelinated C-fibres and myelinated Aδ fibres before other sensory and motor fibres (unmyelinated A_γ, Aβ and Aα). In a neuraxial blockade (epidural, intrathecal) from least to most sensitive to LAs are: autonomic, pain, proprioception, and motor fibers. Recovery of sensation is expected to be in the reverse order. In a peripheral nerve block (brachial plexus), in contrast, fibre sensitivity

from least to most is: motor, proximal sensitive, distal sensitive.[91] When administered systemically, lidocaine blocks the ectopic afferent neural activity at the NMDA receptor within the dorsal horn.

Indications

Topical anaesthesia. To aid intubation, lidocaine spray. To desensitize only the skin and upper subcutaneous layers, eutectic mixture of LAs
(EMLA) cream (lidocaine and prilocaine) (generally used to aid vascular catheterization). To desensitize mucous membranes, lidocaine gel. Studies in humans and animal models have indicated that lidocaine patches provide analgesia of the skin and underlying tissues and can reach deep tissues to provide perioperative analgesia, for example for joint surgery and large surgical wounds.[92,93]

Infiltration anaesthesia: consists of injection of LAs into tissues that surround the area of interest or into joints. Blocking transmission of stimuli in defined, specific, peripheral nerves represents the larger part of loco-regional applications. These techniques can be accomplished by using anatomical knowledge or, in case of some distal limb blocks, even by palpation of the nerve itself. LAs can also be delivered through diffusion (wound soaker) catheters placed within large wounds, especially amputation sites. This technique is best applied as part of a multimodal analgesic protocol.

Neuraxial blockade can be achieved by either epidural or intrathecal application of LAs. Other drugs (opioids, alpha$_2$ agonists, and others) can also be applied via these routes either alone or together with LAs provided they are sterile and preservative free. It should be noted that single use of morphine with preservative has been used epidurally without problems – repeat dosing should be avoided.

Systemic: lidocaine can be administered intravenously either as a bolus or as a constant rate infusion in dogs to provide pro-kinetic, anti-arrhythmic, inhalant-anaesthetic sparing and anti-inflammatory effects.

Contraindications

Ester (prilocaine, benzocaine) LAs may cause allergic reactions in some animals and methaemoglobinaemia in cats. Loco-regional, particularly neuraxial techniques, should not be performed if there is skin infection at the puncture site. Other contraindications for neuraxial blockade include coagulation disorders, spinal cord trauma, hypovolaemia and septicaemia. Toxicities usually result from high plasma concentrations affecting the central nervous system first (except bupivacaine) before cardiovascular depression and death.[94] Central nervous toxicity may manifest as head pressing, star gazing and with increasing doses as stupor and coma. Due to its cardiotoxicity, bupivacaine should not be used intravenously. Other signs of toxicity may include allergic reactions and range from urticaria to anaphylaxis. If clinical signs of toxicity occur, the administration/infusion should be stopped immediately and in severe cases of cardiac signs, an intravenous lipid emulsion (4 mL/kg bolus, followed by 10 min of 0·5 mL/kg/min of Intralipid®) can be administered to augment chances of survival in cardiac arrest after bupivacaine overdose.[95]

Caution

When combining different local anaesthetics, do not exceed the maximum dose of either drug.

Drug interactions

Adrenaline (epinephrine) may be added as a local vasoconstrictor to decrease tissue absorption (1:200,000 = 5 μg/mL; 1:400,000 = 2·5 μg/mL) and increase duration of effect; with erroneous intravascular injection this may cause short-lived tachycardia. This formulation must not be injected into the extremities due to the risk of tissue necrosis.

The maximum recommended doses are based on clinical experience, and designated, species-specific studies are needed to confirm these in dogs and cats. If using lidocaine spray for intubation, the amount of lidocaine used needs to be taken into consideration in total lidocaine dosing. (The dose per spray for xylocaine is 10 mg per spray action and for 'Intubeaze' it is 2-4 mg).

Table 3. Local anaesthetics

Agent	Relative lipid solubility	Relative potency	pKa	Onset (min)	Plasma protein binding (%)	Duration (min)	Maximum recommended dose (mg/kg) Dogs/Cats
Low potency, short duration							
Procaine 0.5–1%*1		1	8.9	Slow	6	60–90	12/6
Chloroprocaine 2*–3 %1		1	9.1	Fast	7	30–60	12/6
Intermediate potency and duration							
Mepivacaine 1.5%2		2	7.6	Fast (3–10)	75	120–240	4.5/3
Prilocaine1		2	7.7	Fast (1–4)	55	120–240	8/4
Lidocaine 1–2%3.6		2	7.7	Fast (5–10)	65	90–200	8/6
Articaine52		4	7.8	Fast (2–5)	65	30–45	7/3
High potency, long duration							
Tetracaine *0.1–0.5%80		8	8.6	Slow (20–60)	80	180–600	3/1
Bupivacaine 0.25–0.75%30	30	8	8.1	Intermediate (10–20)	95	180–600	2/1.5
Levobupivacaine 0.125-0.75%		8	8.1	Intermediate (10-15)	96	180-600	2/unknown
Etidocaine 0.5–1.5%140		6	7.7	Fast	95	180–600	8/4
Ropivacaine 0.75%14		4	8.1	Intermediate (15–20)	94	90–360	3/1.5

*Ester local anaesthetics

There is no convincing scientific evidence for the beneficial effect of mixing two local anethestic drugs and there may even be a decrease in duration of effect or a prolongation of onset of one local anaesthetics when adding another one.

Repeat dosing of local anaesthetics is usually based on the duration of action (e.g. bupivacaine, every 6 hours), but the optimal doses to use for repeat dosing have not been determined, nor have the pharmacokinetics of repeat dosing in clinical patients been fully elucidated.

There may be differences between a calculated maximum dose of the local anaesthetic and the volume required. These volume deficits can be augmented with NaCl 0·9% solution; however, this dilutes the local anaesthetic and reduces effectiveness. For lidocaine and bupivacaine, concentrations of <0·125% and <0·25%, respectively, are not recommended.

16. ANALGESIC DELIVERY TECHNIQUES AND TOOLS

The method by which a drug is delivered can have a significant effect on its efficacy. Drug delivery systems (DDS) are important to minimize toxicity and improve efficacy.

Techniques

Sustained release systems include any DDS that achieves slow release of a drug over an extended period of time (days). Such systems provide 'hands-off ' analgesia, minimize systemic side effects and drug accumulation, reduce fluctuations in drug plasma concentrations and may not require infusion devices.[96]

A new long-acting transdermal fentanyl solution has been shown to produce similar postoperative analgesia to buprenorphine in dogs undergoing surgery. Population pharmacokinetics and safety of this compound have been reported in this species.[97,98] Transdermal patches (fentanyl, lidocaine and buprenorphine) are adhesive patches that are placed on the skin to deliver a specific dose of drug through the skin and into the plasma. The patch provides a controlled release of the drug through a porous membrane with a drug reservoir.[73,93,99] In cats, the analgesic effects of fentanyl patches can be highly variable due to the individual variability in its pharmacokinetics. In dogs undergoing orthopaedic surgery, this compound appears to provide adequate postoperative analgesia when administered with a NSAID.[73] Fentanyl patches have a long onset period and must be in place at least 12h (cats) to 24 hours (dogs) before analgesia is required. Therefore, other analgesic drugs should be available in the meantime.

Constant rate infusion: continuous administration of a set dose regimen through an electronic delivery device in order to maintain constant plasma levels.

Target-controlled infusion: based on complex algorithms, infusion rates are administered by a delivery device to obtain a specific plasma (effect site) concentration in order to produce a desired effect.

Tools

Infusion devices: Volumetric infusion pumps work with different delivery systems (peristaltic, piston, shuttle). They can deliver high volumes with low accuracy (±10%). Syringe pumps use a stepper motor with a drive screw and are suitable for administering potent and more concentrated analgesics with high accuracy (±5%). A calculator feature allows the user to enter body weight, drug concentration and the infusion rate.[100]

Wound infusion catheters: These are flexible indwelling catheters that are embedded near, or in, surgical sites that are used to deliver intermittent infusions of local anaesthetics[101] (continuous infusions have been show to lead to unequal distribution).[102]

Electrical nerve locators (ENLs): These devices can be used to facilitate neural blockade of brachial plexus, tibial and femoral nerves, epidurals, among other local blocks. Clinical use of ENLs helps with needle placement and may shorten onset time, prolong duration of action, and reduce risk for nerve injury. They consist of a constant-current generator (low frequency and duration) that is connected to an insulated needle and a remote electrode that is attached to the skin. The needle is advanced toward the nerve until the desired motor response is obtained. The volume of local anaesthetic to be injected varies from 0·05–0·3 mL/kg. As the solution is injected, the nerve is mechanically displaced and motor response is lost.[103]

Epidural catheters: Catheterization is usually accomplished by using commercial kits (19-, 20- and 24-gauge sizes) that include the catheter and a Tuohy needle, which has a curved bevel that facilitates direction of the threaded catheter through the epidural space. These catheters are usually inserted through the lumbo-sacral intervertebral space and allow intermittent or continuous administration of analgesic drugs for prolonged postoperative periods or animals in severe pain. Dislodgement or coiling, and contamination of the catheter are the most common complications with this technique.[104]

17. ADJUNCTIVE DRUGS

There are several drugs that can be incorporated into a pain management protocol that do not fall into the major traditional classes of analgesic. These include ketamine (at sub-anaesthetic doses), amantadine, gabapentin, imipramine and amitriptyline. These drugs

are not considered 'standalone' analgesic agents and are most often used in conjunction with opioids, NSAIDs, local anaesthetics and alpha$_2$ adrenoceptor agonists. Ketamine is used intravenously on a short-term basis – amantadine, gabapentin, imipramine and amitriptyline are given orally and are used long-term. These drugs may play a more prominent role in the treatment of chronic (maladaptive) pain as we gather more scientific and clinical trial based information on their use in dogs and cats.

Ketamine

Mode of action: By binding to NMDA receptors, ketamine can modulate central sensitization and exert an anti-hyperalgesic effect. Ketamine may also act at opioid, monoaminergic and muscarinic receptors and at voltage sensitive Ca_{++} channels.

Indications: As part of a multimodal perioperative pain management plan for major surgery, in trauma patients or as part of a desensitization treatment for chronic pain patients. For surgery, treatment should be started prior to surgery and continued for up to 24 hours afterwards. Ketamine is administered in addition to other analgesic agents such as opioids and NSAIDs. Beneficial effects including improved appetite and lower pain scores have been shown after soft tissue and major orthopaedic surgery. In trauma patients treatment should begin as soon as possible after initial triage.

Recommended dose: Dogs, bolus (loading dose); 0·5–1·0 mg/kg IV followed by constant rate infusion (CRI) at 0·12–0·6 mg/kg/h; the higher infusion rates are used during surgery and then tapered following surgery, and in severe pain states where dosages >2mg/kg may be required. Cats, bolus (loading dose); 0·5 mg/kg IV followed by constant rate infusion at 0·3–1·2 mg/kg/h; some cats will be sedated at these doses.

Amantadine

Mode of action: Inhibition of NMDA responses; may cause NMDA receptors to remain closed.

Indications: Dogs with osteoarthritic pain that is refractory to NSAID treatment alone. Amantadine may be beneficial in patients with other long-standing pain syndromes with a neuropathic component.

Recommended dose: Dogs: 3–5 mg/kg per os, once daily.[105] Pharmacokinetic data are available in cats but there are no published clinical data on its use as an adjunctive analgesic agent; however, doses similar to those used in dogs are recommended. Amantadine is excreted renally and this should be taken into consideration when it is used in animals with decreased renal function. High doses (40 mg/kg and above) are known to cause seizures.

Gabapentin

Mode of action: Not yet fully elucidated; gabapentin may modulate pain by altering trafficking of the alpha$_2(\delta)$ calcium channel subunits, by suppressing glutamate and substance P and modulating GABA receptors located in the dorsal horn of the spinal cord.[106] Gabapentin activates the descending inhibitory pathway by inducing norepinephrine release which subsequently induces analgesia due to spinal alpha$_2$ adrenoceptor stimulation.

Indications: Developed as an anti-seizure medication, gabapentin has been used perioperatively in laboratory animals with induced nerve damage, and as part of a multimodal treatment regimen in humans with long-standing pain with a neuropathic component. There are very few published studies assessing its analgesic action in dogs for the treatment of acute surgical pain,[107,108] and its use in cats with pain related to major trauma unresponsive to traditional analgesic therapy.[109] Human and laboratory animal studies, and anecdotal veterinary evidence, supports further studies for prophylaxis against, and for, long-standing pain with a known or potential neuropathic component (e.g., diabetic neuropathy, pelvic trauma, amputation, IVDD) in both cats and dogs.[110,111]

Recommended dose: Start treatment at 10mg/kg per os for dogs q8-12h, 5mg/kg per os for cats q12h and increase or decrease depending on therapeutic response. Treatment is frequently required for several weeks and gradual withdrawal is recommended. Side effects may include sedation and ataxia.

Imipramine and amitriptyline

Mode of action: Tricyclic antidepressants (TCAs) block reuptake of catecholamines, thereby enhancing adrenergic transmission. Amitriptyline also has NMDA receptor antagonist properties and less potential for serotonin toxicity when compared to imipramine.

Indications: TCAs may be effective adjunctive analgesics for a range of neuropathic conditions and can be used in combination with environmental modifiers for treatment of cats with inflammatory bowel disease and feline lower urinary tract disease (FLUTD).[112,113] The addition of imipramine or amitriptyline may prove successful in managing refractory chronic pain.

Recommended doses: Amitriptyline, dogs: 1–2 mg/kg orally q12–24h; cats: 2·5–12·5 mg/cat orally q24h. Imipramine, dogs: 0·5–1 mg/kg orally q8h; cats 2·5–5 mg/cat orally q12h. Many of these products are unpalatable and may require creative methods of administration. Clinical improvement can be seen within 48 hours of initiating amitriptyline treatment when combined with other analgesics, or when used in combination with corticosteroids for feline inflammatory bowel disease, and continued improvement may be seen over time. It has been reported that it can take up to 2–4 weeks for these drugs to achieve maximal effectiveness.[113] However, environmental modification is an essential component of treatment.

Duloxetine

Mode of action: Serotonin re-uptake inhibitor (SRI) and noradrenaline (norepinephrine) re-uptake inhibitor (NRI) mixed compounds.

Indications: Duloxetine, a mixed SRI and NRI, is approved in humans for the treatment of diabetic neuropathy,[114] and in both neuropathic and inflammatory pain models analgesic activity has been demonstrated.[115] Some reports suggest that mixed compounds may be beneficial for the treatment of neuropathic pain, whereas compounds with greater affinity for noradrenaline (norepinephrine) re-uptake inhibition may be more beneficial for the treatment of visceral pain.[115] As these agents gain more popularity in human medicine for treating neuropathic pain they are likely to be used more widely in animals; however, caution should be used extrapolating from humans to animals and species-specific studies should be undertaken.

Some analgesic (some pure mu agonists) or adjunctive analgesic agents with SRI capability (e.g. tramadol, imipramine, duloxetin) may, when combined, induce serotonin toxicity. This may be more of a concern when the patient is also receiving selective SRIs (e.g. fluoexitine [Reconcile, Prozac]), TCAs, monoamine oxidase inhibitors (e.g. selegiline [L-Deprenyl, Anipryl]) prescribed for anxiety in dogs.[113] The serotonin syndrome is characterized by neuromuscular hyperactivity, fever, tachycardia, tachypnea and agitation.[114]

PLT (Prednoleucotropin)

PLT is a mixture of two drugs; cinchophen, a NSAID, and prednisolone, a corticosteroid. It is licensed in the UK for the treatment of osteoarthritis in dogs.

18. NON-ANALGESIC DRUGS IN THE MANAGEMENT OF THE PAINFUL PATIENT

Glucocorticosteroid (GCs)

GCs are among the most misused class of drugs in veterinary medicine. There is little evidence-based medicine that supports the administration of these drugs in the clinical setting for analgesia. These drugs are useful in the management of hypoadrenocorticism, allergic and autoimmune disorders, and specific inflammatory conditions. It is the resolution of these illnesses that confers the analgesia. The combination of GCs with NSAIDs is contraindicated due to the increased incidence of side effects.[116]

Inhalant anaesthetics

These are used for general anaesthesia in animals. They have favourable pharmacokinetic characteristics with predictable and rapid adjustment of anaesthetic depth. Most common agents are halothane, isoflurane and sevofurane but none have analgesic properties.

Maropitant

Maropitant is a neurokinin-1 receptor (NK-1) antagonist used to treat and prevent emesis in dogs by blocking NK-1 receptors in the chemoreceptor trigger zone in the CNS. The NK-1 receptor and its ligand, substance P, are present in spinal cord sensory afferents involved in nociception and substance P vesicles are present in spinal cord ascending projections to brain areas used for nociceptive processing. Studies in mice and rabbits have demonstrated that NK-1 receptor antagonists consistently induce analgesia to visceral noxious stimulation. Maropitant may decrease inhalant anaesthetic requirements after IV administration in dogs. At this point, there is no clear evidence that maropitant should be used as an analgesic in the clinical setting.[117]

Acepromazine (ACP)

ACP is one the most widely used tranquillisers in veterinary medicine; it has no analgesic properties. The administration of ACP decreases injectable and inhalant anaesthetic requirements while decreasing blood pressure, cardiac output and stroke volume.[118] ACP is widely used in the perioperative period (neuroleptanalgesia) and may cause hypothermia.

19. PHYSICAL REHABILITATION

Physical rehabilitation is the objective assessment, diagnosis and treatment of musculoskeletal and neurological impairments including but not limited to acute, subacute and chronic pain in tissues including intra-articular, capsular, ligamentous, muscular, central and peripheral neural tissues. The physical rehabilitation assessment utilizes careful evaluation of posture, gait, function, strength, muscle extensibility, passive range of motion and joint play to create a problem list and develop an assessment from which targeted treatment interventions are developed.[119]

Treatments for pain may include physical modalities, manual therapy and therapeutic exercise. Choice of treatment intervention should be based on the target tissue healing response and the chronicity of the injury which determines treatment frequency, intensity and duration. Reassessment of response to treatment should occur at each treatment. Overall, the greatest efficacy is seen with exercise
and cooling modalities.

Therapeutic exercise

Exercises improve blood and lymph flow, increase soft tissue support to skeletal and spinal structures, increase tendon and ligament pliability. Simple exercise such as static weight-bearing can generally be utilized in the acute phase of injury, with gradual amplification

of difficulty as healing progresses and strength improves. In humans, exercise is has been shown to provide very significant levels of pain relief, with analgesic effects as large or larger than those seen with NSAIDs associated with strengthening and aerobic exercise.[120]

Physical modalities

Physical modalities can be used to diminish pain, promote soft tissue healing, improve muscle extensibility and facilitate muscle strengthening. Physical modalities that have been studied in human and animal models include but are not limited to the following.

Thermotherapy (heat): Application of heat to tissues increases distensibility and increases blood flow to facilitate healing. Heat activates heat-sensitive nociceptors and may be pro-nociceptive early in disease states, but can have analgesic effects after the inflammatory state has subsided, when muscle and fascia restrictions predominate.[121]

Cryotherapy: Cooling techniques are inexpensive, readily available, are associated with robust evidence of analgesia and can substantially reduce the degree of damage in acute injury. Mechanisms for these effects include decreased bleeding and swelling due to local vasoconstriction, reduced pain via local effects as well as facilitation of descending inhibitory mechanisms.[122]

Laser: Application of low level laser therapy (660 nm, 9 J/cm_2) has been shown to decrease indicators of neuropathic pain and increase function in a rodent model of peripheral nerve entrapment neuropathy.[123]

Electrical stimulation: Transcutaneus electrical nerve stimulation (TENS) provides analgesia for about half of human patients with moderate pain.[124]

Phonophoresis: Application of pulsed therapeutic ultrasound for percutaneous lidocaine absorption increases the analgesic effect when compared to continuous ultrasound.[125]

Pulsed electromagnetic therapy: Application of non-thermal, non-invasive electromagnetic therapy can result in pain reduction in humans with knee OA.[126]

Shock wave therapy: Deformation of tissues using high-intensity sound waves leads to a cascade of beneficial effects such as neovascularisation ingrowth, reversal of chronic inflammation, stimulation of collagen and analgesia,[127] and in humans with lower back pain.

Manual techniques

The application of hands-on treatments can effect tissues mechanically and physiologically to decrease pain, increase circulation, reduce swelling, increase soft tissue extensibility and normalize joint mobility:

Joint mobilization: In human and rat models manual application of forces through inflamed and non-inflamed joints increases mechanical nociceptive thresholds.[128]

Trigger point pressure: Manual treatment of trigger points can have beneficial effects, however in healthy human subjects, mechanical stimulation of trigger points induces central sensitization[129] and antagonist muscle activity.[130] Manual treatment of trigger points should be complimentary to other pain treatments.[131]

Massage: See Section 23.

20. DIET AND SUPPLEMENTS

Based in Part on WSAVA Nutrition Assessment Guidelines Committee Dietary factors and dietary supplements with beneficial effects on pain (see references and further reading).[36,132-152] It should be noted that dietary supplements do not require proof of safety, efficacy, or quality control to be marketed. Therefore careful selection of type, dose, and brand is important to avoid toxicities or lack of efficacy.

Optimal body condition (4-5/9)

Weight loss in dogs and cats that are even mildly overweight can significantly reduce pain from OA and other orthopaedic conditions. This is one of the reasons that nutrition screening evaluation is a critical component of the examination of every pet, but particularly those in which pain is identified. When pain is identified, a more thorough nutritional evaluation is warranted to determine the cause of overweight body condition. Based on this information, a specific plan can be developed for the animal to achieve optimal body condition.

Optimal nutrition (especially in young growing animals)

Fast growth rate can increase the risk of developmental orthopaedic diseases, especially in large and giant breed dogs. These diseases not only affect the young animal but also can contribute to OA and pain in later life. Nutritionally unbalanced diets are especially detrimental during growth so careful attention should be paid to all animals' diet histories during this critical phase. Dogs and cats should be fed a diet that meets growth requirements until at least 1 year of age (up to 18 months in giant-breed dogs).

Dietary supplements with potential benefits for pain management

Omega-3 polyunsaturated fatty acids:

- The omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have anti-inflammatory effects which may reduce inflammation and pain from OA

- Indications – adjunctive treatment for chronic pain. Studies conducted in dogs and cats suggest modest benefits of EPA and DHA on pain from OA. High doses of omega-3 fatty acids may alter platelet function and may cause gastrointestinal side effects in some animals
- The optimal dose has not been determined but studies of dietary omega-3 fatty acids at a dose of 0·41 g/100 kcal EPA and 0·34 g/100 kcal DHA (approximately 170 mg/kg EPA and 140 mg/kg DHA from the canine studies) have shown benefit. Veterinary diets marketed for dogs with OA are all enriched in omega-3 fatty acids but the amounts vary. Omega-3 fatty acids (i.e., EPA+DHA) also can be provided as supplements
- The total EPA+DHA dose is the primary factor to consider; the ratio of omega-3 to omega-6 fatty acids appears to be of much lower importance
- Note that there are other omega-3 fatty acids (e.g. the plant-based omega-3 fatty acid, alpha-linolenic acid) which do not have similar effects to EPA and DHA. Therefore, it is important to assess the total dose of EPA and DHA, rather than just the dose of total omega-3 fatty acids.

Glucosamine and chondroitin

- Glucosamine and chondroitin may have benefits in OA through their anti-inflammatory effects. There is no evidence for 'chondroprotective effects'
- Indications – adjunctive treatment for chronic pain. Studies of glucosamine and chondroitin have been contradictory in terms of beneficial effects on pain; effects appear to be low to modest, at best. Glucosamine is an amino sugar, and although no adverse effects on glucose regulation have been seen in studies of healthy dogs or cats, studies of glucosamine supplementation in diabetic animals has not been reported
- The optimal dose has not been determined.

Green-lipped mussels (Perna canaliculus)

- Components of green-lipped mussels include omega-3 fatty acids (EPA, DHA, and eicosatetraenoic acid [ETA]), chondroitin, glutamine, zinc, copper, manganese, and vitamins C and E. Although the exact mechanism of action is unknown, green-lipped mussels appear to have anti-inflammatory effects
- Indications – adjunctive treatment for chronic pain. Both supplemental and dietary green-lipped mussels have been studied in dogs. Not all studies showed positive results but this may be related to study design issues
- Adverse effects are unlikely
- The optimal dose is unknown. One study which provided 11 mg/kg body weight/day showed no significant effects, while studies providing approximately 17–75 mg/kg body weight/day had positive results. Some veterinary diets and certain over-the-counter diets contain supplemental green-lipped mussels.

The strength of evidence for benefits on pain and locomotion is low for other supplements (hydroxycitric acid, turmeric extract (P54FP), beta-1,3/1,6 glucans, gelatin hydrosylate, undenatured type II collagen, special milk protein concentrate). Avocado and Soy unsaponifiables are oily compounds that have been evaluated as disease-sparing agents in dogs, humans and horses. These supplements are standardized at 1/3 avocado and 2/3 soy. In preclinical studies inhibition of IL-1β and stimulation of collagen synthesis by chondrocytes have been identified. In the very limited clinical data in dogs and horses, there appears to be a disease modifying effect, but an analgesic augmentation is less evident.[153-155]

21. NURSING AND SUPPORTIVE CARE

Quality nursing care (tender loving care) should be applied to small animals as an adjunct to other therapies for managing pain and stress. It is important to create an environment where the animal is emotionally and physically comfortable.[156-159]

Assess the entire animal – not just the painful part. Other areas of pain will often be found. Stress and anxiety can intensify pain. The following actions can all reduce stress and anxiety: sitting with the animal, turning down the lights, decreasing noise, keeping cats and dogs separate. The environment may affect pain.

Nursing care techniques

Massage: Gentle pressure, compression and rocking can soothe patients both physically and psychologically if they are accustomed to close human contact.

Application of warmth or cold: Cold compress during acute injury can reduce swelling and provide analgesia. Cold compress generally needs to be in place for 15–20 minutes to be effective. Warm compress is generally more comfortable after the acute phase has

passed, but can aid tissue relaxation and as a precursor to massage or stretching. Warm compress generally needs to be in place for 10–15 minutes.

Patient handling: When handling and moving an animal avoid painful areas (surgical/trauma site, osteoarthritic joints, etc.), even when the animal is anaesthetized or sedated to avoid inflicting a painful stimulus which can begin a new pain cascade. Long bone injuries should always be immobilized with a cast or splint before moving the patient.

Bedding and positioning: The creation of a soft, cushioned surface for the animal to rest on will help prevent additional pain. Laying for long periods on a hard or cold surface is very uncomfortable and predisposes to anxiety, heightening the sensation of pain and the potential for decubital ulcers. Rolled blankets or pillows can facilitate the patient being able to choose the most comfortable body posture. Furthermore, the patient can be assisted with positioning that encourages elevation of injured limbs to reduce oedema, or facilitates ventilation.

Changing positions: Turning, a patient (down side up) every 4 hours prevents muscle stiffness, decubital ulcers, pulmonary atelectasis, and gives an opportunity for pain assessment and analgesic adjustment if required.

22. ACUPUNCTURE

What it is

Acupuncture is the placement of fine needles at defined locations in the body that are rich in neurovascular or muscular structures in order to stimulate an endogenous response directed at analgesia, healing and immune modulation. Acupressure is the application of pressure to the same specific point locations for similar indications.[160]

Mode of action

Neuroanatomical approach: Due to the complexity of constructing and interpreting placebo controlled trials in acupuncture, the practice of acupuncture rests heavily on physiological data showing measurable changes in endogenous analgesic mechanisms. There is considerable evidence of measurable physiological effects, for example: enkephalins, endorphins, serotonin, norepinepherine, purines, glutamate, neurokinin, cannabinoid, ion channel modifiers, modification of transcription, and through additional modification of associated cell types such as interneurons, microglia and astrocytes. A body of work has developed showing the effects of acupuncture as neuro-modulation. From this evidence a logical and rational approach to treatment can be made, utilizing point locations that are based upon known neuro-anatomy and effects measured through fMRI, chemical changes, and microscopic deformation of soft tissue structures.[161] While these points often occur in the same locations as the meridian points, the rationale for their use is often different when approaching acupuncture from an evidence-based perspective, and has been shown to be more effective and repeatable between practitioners.[162]

Metaphysical approach: Acupuncture can be based on a metaphysical framework that involves moving invisible energy, called chi or xi. This approach has added to the clinical expertise of acupuncture treatment for pain, but cannot be corroborated by research, as chi is, by definition, immeasurable.

Indications

Somatic pain including: Spinal conditions, post-surgical conditions, trauma, wounds, chronic pain such as osteo-arthritis.[163]

Visceral pain: May be targeted with superficial treatments such as acupuncture due to the overlap of neural innervation along myotomes, dermatomes and shared locations of spinal processing.

Myofascial trigger point pain: Often described as 'dry needling' by physical therapists.

Side effects

Risks of acupuncture are very low and include unintentional puncture of vital structures (especially lungs), infection (especially without the use of sterile, single-use needles), and introduction of foreign material. Intentional implantation of foreign material (such as gold beads or pieces of metal) cannot be recommended, and has been shown to cause long-term harm to patients.

Special considerations

Acupuncture is a complex intervention, and requires additional training. However, the supplies are accessible, and acupuncture is seldom regulated in the same fashion as pain-controlling pharmaceuticals.

Sterile, single use needles are essential. Advanced training in acupuncture is available in many regions throughout the world. Acupuncture can be integrated into veterinary pain treatments with an understanding of muscle function and anatomy and nerve function and anatomy.

Several human studies have shown efficacy of acupressure, a modality that is not limited to individuals trained in the placement of needles.

Acupuncture is a valuable adjunct, when used properly, to pharmaceutical approaches, and is meant to be used in a multi-modal regimen rather than a stand-alone therapy in most instances.

23. MEDICAL MASSAGE

What it is

The manipulation of soft tissues in order to generate a change in texture, mobility, blood flow and lymphatic drainage; and to provide relief from stress, anxiety and pain.

Mode of action

The pressure generated by massage strokes generates changes in various measurable physiological phenomena on tissue and cellular levels, within the chain of electrochemical reactions in the local area of massage, as well as in the organism as a whole.[164,165]

Tissue effects: Collagen deformation releases fascia restrictions and improves regional blood flow. Direct pressure releases myofascial trigger points in affected and compensatory muscle groups. Soft, stroking massage techniques mobilize oedema and lymphatic fluid.

Cellular effects: When direct mechanical pressure is applied, the signal is rapidly transferred from the cell surface receptors to distinct structures in the cell and nucleus, including ion channels, nuclear pores, nucleoli, chromosomes, and perhaps even individual genes, independent of ongoing chemical signaling mechanisms.[166] Furthermore, mechanical stimuli (massage or soft tissue mobilization) have been shown to stimulate healing through fibroblast function and recruitment.[166]

Homeostatic effects: A reduction in stress hormones and an increase in endorphins, serotonin, norepinepherine results from massage and tissue mobilization.[167]

Indications

After a thorough myofascial and pain evaluation have been performed, and appropriate treatment has been initiated, the practitioner and/or nursing staff can apply medical massage to the following cases:[166–171]

- Stress and anxiety: Touch, gentle stroking, gentle compression and rocking
- Allodynia: Gentle compression, laying on of hands
- Postoperative: Focus on compensatory muscles
- Gastrointestinal disease/discomfort: Work on back muscles
- Amputation: Focus on compensatory muscles, massage opposite limb
- Geriatric: Gentle massage for tight muscles can help alleviate pain associated with age-related diseases, even if the tension is not directly related to the reason for hospitalization
- Vestibular: Focus on cervical muscles, assess and massage scapular muscles as needed
- Respiratory (therapy depends on level of patient stress). Can perform calming massage (laying on hands, gentle compression, rocking) or work specifically on compensatory muscles
- Pneumonia: Gentle tapotements (cup hands and alternately tap) cranial and caudal over rib cage, massage latissimus.

Contraindications[172]

- Elevated body temperature (> 104° F [39·5° C])
- Massaging a swollen postoperative limb that could release clots into the systemic circulation
- Shock, open or bleeding wound, acute sprain or trauma – torn muscle, internal bleeding, diseases of the nervous system, acute nerve irritation, pregnancy, neoplasia, inflammatory conditions, fungal skin issues, acute stages of viral diseases, patient unable to provide feedback (heavy sedation, anaesthesia, mentally inappropriate, loss of sensation from neurologic injury, etc.)
- Massage must be carefully titrated to the individual needs and requirements. Massage that is too firm can lead to more muscle and fascial tension, and increase the stress response.

24. SALVAGE SURGICAL PROCEDURES

In some cases a surgical approach to the alleviation of pain is a good option. This may be chosen because pharmacological and adjunctive therapies such as acupuncture, rehabilitation and dietary intervention have failed, for example severe and incapacitating DJD. Examples of these techniques are listed below. Many of the patients undergoing these procedures will have been in pain for a considerable period of time, and comprehensive analgesic techniques should be employed to prevent acute pain on top of a sensitized state resulting in upregulation of chronic postoperative pain that will compromise outcome as has clearly been shown in humans.

Limb amputation

Indications: Irreparable limb fracture, appendicular osteosarcoma, otherwise inoperable neoplasia, as an alternative to complex internal or external fixation of a limb fracture, to prevent damage to the distal limb following brachial plexus avulsion, salvage procedure following failed fracture repair.

In most cases recovery time is rapid and animals adapt well to having three limbs. Amputation is best reserved for animals that have no musculoskeletal disease in their other limbs and are not overweight or obese.

Total joint replacement

Indications: To relieve pain in a diseased joint.

These procedures (total hip replacement, total elbow replacement, total knee replacement, custom joint replacement) are technically advanced and demanding procedures requiring specialized equipment. If performed correctly, they can eliminate all joint pain.

Excision arthroplasty

Indications: To relieve pain in a diseased joint.

Conditions that cause pain in the joint include DJD, subluxation, luxation, and intra-articular fracture. Most often performed in the hip joint (femoral head and neck excision) this procedure is less technically demanding than total joint replacement and can be performed to relieve pain in the hip joint of dogs (especially small and medium sized dogs) and cats with good success. However, effective perioperative analgesic techniques and aggressive physical rehabilitation are required to optimize outcome.

Arthrodesis

Indications: To relieve pain in a diseased joint

Arthrodesis techniques aim to permanently eliminate movement of a joint and the pain associated with this; however, the procedure usually results in mechanical (functional) lameness.

Denervation

Indications: To relieve pain when medical therapies have failed, as an alternative to arthrodesis.

Sensory denervation techniques have been described for the canine hip (coxofemoral joint) and elbow. In most cases this technique is performed to alleviate the pain related to DJD in these joints when other treatments such as medical, surgical and adjunctive therapies have failed. Motor function can usually be well maintained when these procedures are correctly performed.

The procedures outlined above constitute major surgery with the potential to cause severe pain (acute and persistent) if adequate perioperative analgesia is not provided for a sufficient duration of time. A multimodal approach is recommended with an emphasis on local analgesia.

SECTION 3: PAIN MANAGEMENT PROTOCOLS

25. CASTRATION AND OVARIOHYSTERECTOMY/OVARIECTOMY: CATS

Castration and ovariohysterectomy/ovariectomy performed in cats are associated with pain of varying severity which is influenced by the degree of surgical trauma. For this reason surgery should be performed with careful tissue handling and adherence to good surgical principles. General anaesthesia and preventive/multimodal analgesia techniques are strongly recommended. There are many options available for perioperative management. The protocol below is one example. Postoperative treatment with analgesics may be required for up to 3 days after surgery.

Castration

Preoperative:

- Neuroleptanalgesia to include opioid + acepromazine (0·01–0·05 mg/kg) OR alpha$_2$ +/- ketamine (5–10 mg/kg IM: the higher doses are selected for cats that are more difficult to handle)
- Induction of anaesthesia: In some cats an opioid, an alpha$_2$ adrenoceptor agonist and ketamine will provide sufficient analgesia and anaesthesia for a castration
  - Intravenous: Propofol to effect (3–10 mg/kg), ketamine (3–5 mg/kg) + diazepam or midazolam (0·25 mg/kg), or alfaxalone (3–5 mg/kg). Note: if an alpha$_2$ adrenoceptor agonist has been used preoperatively these doses may be lower
  - Intramuscular: An alpha$_2$ adrenoceptor agonist + ketamine (5–10 mg/kg) or tiletamine/zolazepam (3–4 mg/kg).

Maintenance of anaesthesia: Inhalation anaesthesia or ketamine or propofol or alfaxalone IV to effect. Note: in many cases a castration can be completed without the need for maintenance anaesthesia drugs; however, there should be a plan for extending the anaesthesia time in the event the cat becomes responsive or complications arise. Equipment should also be available for endotracheal intubation.

Local anaesthetic techniques: Intra-testicular block and pre- and/or post-surgery skin infiltration with lidocaine.

Postoperative analgesia: NSAID.

Protocol without controlled drugs
Preoperative: combination of a NSAID and an alpha$_2$ adrenoceptor agonist.
Otherwise as above.

Protocol with limited availability of analgesic drugs
Preoperative: Alpha$_2$ adrenoceptor agonist ± NSAID.
Induction and maintenance of anaesthesia: Any available induction agents; injectable or inhalant.
Local anaesthetic techniques: Intra-testicular block and pre- and / or post-surgery skin infiltration with lidocaine.
Postoperative analgesia: NSAID.

Ovariohysterectomy/ovariectomy

Preoperative:
- Analgesia: Opioid ± ketamine (5–10 mg/kg IM: the higher doses are selected for cats that are more difficult to handle)
- Sedation: Acepromazine (0·01–0·05 mg/kg IM) or alpha$_2$adrenoceptor agonist
- Induction of anaesthesia:
  - Intravenous: Propofol to effect (3–10 mg/kg), ketamine (3–5 mg/kg) + diazepam or midazolam (0·25 mg/kg), or alfaxalone (3–5 mg/kg). Note: if an alpha$_2$adrenoceptor agonist has been used preoperatively these doses may be lower
  - Intramuscular: An alpha$_2$ adrenoceptor agonist + ketamine (5–10 mg/kg) or tiletamine/zolazepam (3–4 mg/kg).

Maintenance of anaesthesia: Inhalation anaesthesia or ketamine or propofol or alfaxalone IV to effect (1/3 or 1/2 of initial dose).
Note: in many cases an ovariohysterectomy or ovariectomy can be completed without the need for maintenance anaesthesia drugs; however, there should be a plan for extending the anaesthesia time in the event the cat becomes responsive or complications arise; venous access is recommended.
Local anaesthetic techniques: Incisional and intraperitoneal/ovarium ligament block with lidocaine.
Postoperative analgesia: NSAID.

Protocol without controlled drugs:
Preoperative: Combination of a NSAID and an alpha$_2$ adrenoceptor agonist.
Otherwise as above.

Protocol with limited availability of analgesic drugs:
Preoperative: Alpha$_2$ adrenoceptor agonist ± NSAID.
Induction and maintenance of anaesthesia: Any available induction agents; injectable or inhalant.
Local anaesthetic techniques: Epidural or incisional and intraperitoneal/ovarium ligament block with lidocaine.
Postoperative analgesia: NSAID.
Analgesia may be supplemented after most surgical techniques by application of non-drug modalities such as cold therapy, laser therapy, acupuncture, nursing care, mild exercise and massage.

26. CASTRATION AND OVARIOHYSTERECTOMY/OVARIECTOMY: DOGS

Castration and ovariohysterectomy/ovariectomy performed in dogs is associated with pain of varying severity and is influenced by the degree of surgical trauma. General anaesthesia and preemptive/multimodal analgesia techniques are strongly recommended. There are many options available for perioperative management; below are examples of some. Postoperative treatment with analgesics may be required for up to 5 days after surgery. The same NSAID should be used pre- and postoperatively.

Protocol for castration

Preoperative:
- Analgesia: Opioid
- Sedation: Acepromazine and/or benzodiazepines (midazolam or diazepam 0·25–0·4 mg/kg IM; diazepam is best given IV - painful IM); alpha$_2$ adrenoceptor agonist
- Induction of anaesthesia:
  - Intravenous: Propofol to effect (3–5 mg/kg), ketamine (3–5 mg/kg) + diazepam or midazolam (0·25 mg/kg), or alfaxalone (1–2 mg/kg)
  - Intramuscular: Alpha$_2$adrenoceptoragonist + ketamine (3–5 mg/kg) or tiletamine/zolazepam (3–4 mg/kg).

Maintenance of anaesthesia: Inhalation anaesthesia or propofol, alfaxalone or ketamine ($_1/_3$ or ½ of initial dose) to effect; venous access is recommended. Equipment should also be available for endotracheal intubation.

Local anaesthetic techniques: Intra-testicular block, incisional block.
Postoperative analgesia: NSAID.

Protocol without controlled drugs:
Preoperative: Combination of a NSAID and an alpha$_2$ adrenoceptor agonist ± tramadol (2–5 mg/kg IM)
Otherwise as above.

Protocol with limited availability of analgesic drugs:
Preoperative: Alpha$_2$ adrenoceptor agonist ± NSAID.
Induction and maintenance of anaesthesia: Any available injectable or inhalant agent; venous access is recommended.
Local anaesthetic techniques: Intra-testicular block, incisional block.
Postoperative analgesia: NSAID.

Protocol for ovariohysterectomy/ovariectomy

Preoperative:
- Analgesia: Opioid
- Sedation: Acepromazine and/or benzodiazepines or alpha$_2$ adrenoceptor agonist
- Induction of anaesthesia:
  - Intravenous: Propofol to effect (3–5 mg/kg), ketamine (3–5 mg/kg) + diazepam/midazolam (0·25 mg/kg) or alfaxalone (1–2 mg/kg).
  - Intramuscular: Alpha$_2$ adrenoceptor agonist + ketamine (5·0–7·5 mg/kg) or tiletamine/zolazepam (3–4 mg/kg).

Maintenance of anaesthesia: Inhalation anaesthesia, or propofol, alfaxolone, ketamine ($_1/_3$ or ½ of initial dose) to effect; venous access is recommended.
Local anaesthetic techniques: Incisional and intraperitoneal/ovarium ligament block.
Postoperative analgesia: NSAID.

Protocol without controlled drugs:
Preoperative: Combination of a NSAID and an alpha$_2$ adrenoceptor agonist ± tramadol (2–5 mg/kg IM).
Otherwise as above.

Protocol with limited availability of analgesic drugs:
Preoperative: Alpha$_2$ adrenoceptor agonist ± NSAID.
Induction and maintenance of anaesthesia: Any available induction agent; venous access is recommended.
Local anaesthetic techniques: epidural or incisional and intraperitoneal/ovarium ligament block.
Postoperative analgesia: NSAID.

Analgesia may be supplemented after most surgical techniques by application of non-drug modalities such as cold therapy, laser therapy, acupuncture, mild exercise, nursing care and massage.

27. ORTHOPAEDIC SURGERY

Orthopaedic surgery can result in moderate-to-severe postoperative pain. Surgery should be performed under general anaesthesia combined with aggressive perioperative analgesia. Preventive and multimodal analgesic techniques should be employed for all procedures. The balance between pre-, intra- and postoperative analgesia will depend on the severity of the preoperative condition and the location and magnitude of surgical trauma. Frequent pain assessment should be performed and when pain is not successfully controlled, alternative or additional analgesics or analgesic techniques should be employed to improve patient comfort. NSAIDs provide excellent perioperative analgesia, and should be used unless contraindicated. The administration of an approved NSAID is recommended. The same NSAID should be used postoperatively as is used preoperatively – that is, switching between drugs should be avoided. Nerve transection (e.g. during limb amputation) or manipulation, may lead to severe chronic pain (neuropathic pain). In such cases, anecdotal evidence suggests gabapentin, included in a multimodal regimen, may have a role in prevention of chronic neuropathic pain in veterinary patients; however, no suitably designed clinical studies have investigated this. (refer to Section 17 Adjunctive Analgesia & Section 36 Neuropathic Pain).

Note: The choice of opioid, alpha$_2$ adrenoceptor agonist or NSAID used will vary based on availability, personal preferences and contraindications. Loco-regional anaesthetic techniques such as intra-articular, incisional and specific nerve blocks, wound infusion catheters or combinations thereof before and/or after surgery are highly recommended in all cases. Such techniques become mandatory when opioids and other controlled analgesic drugs are not available. Longer acting local anaesthetic agents such as bupivacaine or ropivacaine are recommended due to their prolonged duration of action. The systemic administration of lidocaine is contraindicated in cats due to its cardiovascular depressant effects.

Protocol for orthopaedic surgery

Preoperative: Combination of an opioid and a NSAID, ± alpha$_2$ adrenoceptor agonist, ± ketamine (cats).
Intraoperative: Boluses and/or infusions of opioids, alpha$_2$ adrenoceptor agonists, ketamine and/or lidocaine. These drugs may not be required if an effective local anaesthetic block has been performed.
Immediate postoperative (24 hours): Combination of a NSAID (if not administered preoperatively) and continue intraoperative infusions or boluses with gradual reduction in doses. Adjunctive analgesics, non-drug therapies (especially cold therapy), careful padding and positioning, and gentle massage of compensatory regions (back, and non-operated limbs)
Later postoperative days: Opioid administration (injectable, transdermal, oral, transmucosal) with titration to effect and gradual discontinuation and/or NSAIDs. Icing of the affected regions should be continued for a minimum of 3 days, at which point it can be alternated with heat therapy prior to stretching and gentle weight-bearing (with icing following these therapies). Adjunctive analgesics including lidocaine patches (evidence supports their use in human studies) and non-drug therapies, local anaesthetic administration via a diffusion catheter may be employed until discharge from hospital if needed.

Example of a protocol for dogs undergoing femoral fracture repair

Preoperative: NSAID (24 h dose; ideally one approved for dogs), morphine 0·5 mg/kg IM, acepromazine 0·05 mg/kg IM.
Induction of anaesthesia: propofol to effect IV.
Maintenance of anaesthesia: Inhalation anaesthesia with lumbosacral epidural administration of bupivacaine 0·5% (1 mL/5 kg before surgery.
Immediate postoperative (for 24 h): Morphine 0·3–0·5 mg/kg IM (every 4–6 h depending on evaluation or as needed), icing, range of motion, and other non-drug techniques.
Later postoperative days: Buprenorphine 0·01 mg/kg IM, q6–8h for up to 3 days and NSAID (same drug as preoperative, starting 24h after preoperative dose), q24h for up to 7 days after surgery and continue with non-drug techniques.

Example of a protocol for cats undergoing femoral fracture repair

Preoperative: NSAID (24h dose; ideally one approved for cats), morphine 0·3 mg/kg IM, medetomidine 0·01 mg/kg IM.
Induction of anaesthesia: Propofol to effect IV.
Maintenance of anaesthesia: Inhalation anaesthesia with lumbosacral epidural administration of 0·5% bupivacaine (1 mL/5kg before surgery).
Immediate postoperative (for 24h): Morphine 0·2–0·3 mg/kg IM (every 4–6h depending on evaluation or as needed), icing, range of motion, and other non-drug therapies.
Later postoperative days: Buprenorphine 0·02 mg/kg IM or OTM, q6–8h for up to 3 days after surgery and NSAID (same drug as preoperative, starting 24h after preoperative dose), q24h for up to 7 days after surgery. Please see label for approved NSAIDs for use in cats. Continue with non-drug techniques.

Protocol without controlled drugs:
See above, without the opioid. Injectable tramadol may be administered in the perioperative period. The use of local anaesthetic techniques, particularly regional blocks, intravenous lidocaine infusion intra- and postoperative, non-drug therapies combined with NSAIDs becomes critical when opioids are not available.

Protocol with limited availability of analgesic drugs:
See above without the opioid. Non-drug therapies, ketamine, and lidocaine infusions, and acupuncture may be used in the intraoperative period. A combination of low dose alpha$_2$ adrenoceptor agonist, tramadol, NSAID (not if administered preoperatively), non-drug therapies, further regional blocks or continuous wound block (wound catheters) are employed in the immediate postoperative period. Continuous intra-articular infusions of local anaesthetic are contraindicated as this can result in significant cartilage damage, and the risk of ascending contamination leading to infectionis high. For later postoperative days, NSAIDs are administered as required-paracetamol (acetaminophen) (not in cats) or dypirone, amantadine and/or gabapentin, non-drug therapies are employed.

If pain is severe, cannot be controlled with the available resources and is likely to be prolonged, euthanasia should be considered.

28. SOFT TISSUE SURGERY

Soft tissue surgery may cause mild, moderate or severe postoperative pain. Preventive and multimodal analgesic techniques should be employed and local anaesthetic techniques included whenever possible. The balance between pre-, intra- and postoperative analgesia will
depend on the severity of the preoperative condition and the location and magnitude of surgical trauma. Where postoperative pain is not
successfully controlled with NSAIDs, alternative or additional analgesics or analgesic techniques should be employed. Major soft tissue

surgery may lead to chronic pain which may have a neuropathic component. To date no veterinary studies have been performed assessing
the benefit of adding gabapentin to the perioperative anaesthetic and analgesic protocol in surgical situations where there is significant nerve damage. However, based on its use in human medicine there may be potential value for use in the prevention of neuropathic pain.

Note: The choice of opioid, alpha$_2$ adrenoceptor agonist or NSAID used will vary based on availability and contraindications. Loco-regional anaesthetic techniques such as intra-articular, incisional and specific nerve blocks, wound infusion catheters or combinations thereof before and/or after surgery are highly recommended in all cases. Such techniques become mandatory when opioids and other controlled analgesic drugs are not available.

Minor soft tissue surgery

Pre-and intraoperative: Combination of an opioid, NSAID ± alpha$_2$ adrenoceptor agonist ± ketamine (cats). Local anaesthetic techniques.
Postoperative analgesia: NSAIDs (unless administered preoperatively) ± opioid and/or non-drug therapies.

Protocol without controlled drugs:
Same as above but without the opioid.

Protocol with limited availability of analgesic drugs:
Pre- and intraoperative: Combination of alpha$_2$ adrenoceptor agonists, tramadol, a NSAID and local anaesthetic technique.

Immediate and later postoperative (24h): NSAID (unless administered preoperatively), paracetamol (acetaminophen) (not in cats) or dypirone, and non-drug therapies.

Major soft tissue surgery

Preoperative: Same as for minor soft tissue surgery.
Intraoperative: Boluses or infusions of opioids ± alpha$_2$ adrenoceptor agonists ± ketamine ± lidocaine. These drugs may not be required if an effective local anaesthetic block has been performed.
Immediate and later postoperative (24 hours): NSAID (unless administered preoperatively), continuous infusions or boluses of drugs used intraoperatively as needed ± other adjunctive drugs and non-drug therapies such as cold therapy and acupuncture.

Example of a protocol for a dog undergoing a perineal hernia repair

Preoperative: NSAID (24h dose; ideally one approved in dogs), morphine 0.5 mg/kg IM, and acepromazine 0.02 mg/kg IM.
Induction of anaesthesia: ketamine 5 mg/kg and diazepam 0.25 mg/kg IV, or to effect.
Maintenance of anaesthesia: Inhalation anaesthesia with lumbosacral epidural administration of 0.5% bupivacaine (1 mL/5kg before surgery).
Immediate postoperative (24h): Morphine 0.3 mg/kg IM (every 4–6h depending on evaluation, or as needed), non-drug techniques such as cold therapy.
Later postoperative days: NSAID (same drug as preoperative, starting 24h after preoperative dose), q24h and buprenorphine 0.01 mg/kg IM, q8h up to 3 days postoperatively.

Example of a protocol for a cat undergoing a surgical removal of injection site sarcoma

Preoperative: NSAID (24h dose; ideally one approved in cats), morphine 0.2 mg/kg IM, ketamine 5 mg/kg and midazolam 0.25 mg/kg IM.
Induction of anaesthesia: Propofol to effect IV.
Maintenance of anaesthesia: Inhalation anaesthesia with constant rate infusions of fentanyl 10 μg/kg/h following a loading dose of 2 μg/kg IV and ketamine 0.6 mg/kg/h. Infiltration anaesthesia with local anaesthetics.
Immediate postoperative (24h): Constant rate infusions of fentanyl 1–3 μg/kg/h and ketamine 0.12 mg/kg/h. Cold therapy ± acupuncture. Wound therapy catheter with administration of bupivacaine 0.5% (up to 2 mg/kg).
Later postoperative days: NSAID (same drug as preoperative, starting 24h after preoperative dose) and buprenorphine 0.02 mg/kg IM, q6–8h up to 3 days postoperatively.

Protocol without controlled drugs:
See above, without the opioid. Injectable tramadol may be administered in the perioperative period. The use of local anaesthetic techniques, particularly regional blocks, lidocaine infusion intra- and postoperative, non-drug therapies combined with NSAIDs becomes critical when opioids are not available.

Protocol with limited availability of analgesic drugs:
See above without opioids. A combination of low dose alpha$_2$ adrenoreceptor agonist, NSAID (unless administered preoperatively), gabapentin, paracetamol (acetaminophen) (not in cats) or dipyrone, amantadine, non-drug therapies, further regional blocks or continuous wound block (wound catheters).

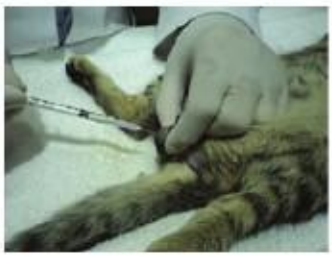
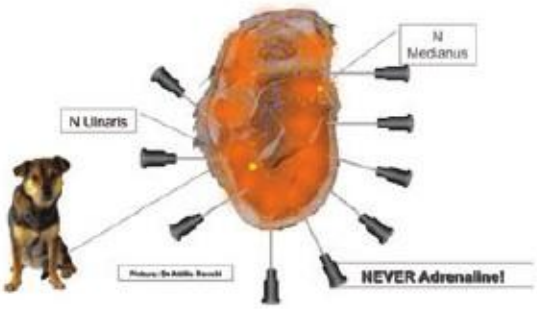
Later postoperative days: NSAID as required non-drug therapies, further regional blocks or continuous wound block (wound catheters).

If pain cannot be controlled or ameliorated with available techniques and the prognosis is poor, consider euthanasia.

29. LOCO-REGIONAL TECHNIQUES

For all loco-regional anaesthetic techniques described herewithin, it is imperative to maintain sterile injection techniques (clipping and sterile preparation of the injection site). The techniques are described to be performed on the anaesthetized or deeply sedated (with analgesia as these are painul to perform) animal. After needle placement and before injection of local anaesthetic, an attempt to draw blood has to be made. If blood can be withdrawn, injections are not made, but the needle is repositioned. While many landmarks and nerves themselves can be palpated transcutaneously, use of neurostimulator or ultrasound localization techniques can reduce the risk of incomplete blocks and damage to the nervous, vascular and other structures. Where available, the use of a nerve stimulator may result in muscle contraction and limb extension/flexion and aid in correct needle placement. The volumes recommended in this text reflect the collective experience of the authors based on published data and the correct needle placement. The desensitized area of the limbs is indicated by the coloured area in the limb pictogram.

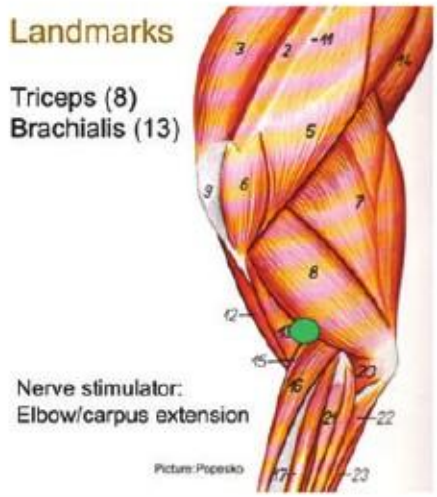
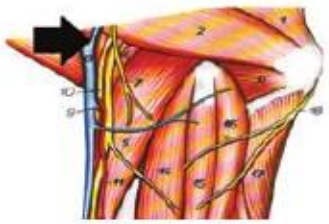
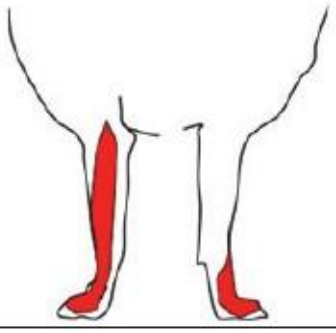
Infiltration anaesthesia

Intratesticular block Where: Could be anywhere on the body, where there is enough superficial or organ soft tissue available to infiltrate: A surgical site, for example incisional line block, extirpation of a small tumour, particularly useful for ovariectomies with intraoperative injection into the cranial edge of the ovarian ligament (0·2–0·3 mL/side in cats; 0·5–2 mL/side in dogs) and in orchiectomies (0·2–0·3 mL/side in cats; 0·5–1 mL/side in dogs). What: Lidocaine with or without adrenaline (epinephrine), bupivacaine, mepivacaine, ropivacaine, sterile NaCl or water for injections may be added to increase volume. Technique: By injecting in an inverse pyramide or V-shape around/along the incision site. Usually performed 'blindly'. Desensitizes: Pyramidal or V-shaped tissue area of injection site or testicles or ovaries.	Picture courtesy of Dr Paulo VM Steagall 
Ring block Where: Distal limb or tail. What: Lidocaine, bupivacaine, mepivacaine, ropivacaine, , sterile NaCl or water for injections may be added to increase volume. Never adrenaline (epinephrine). Technique: By injecting at 0·3–0·6 mm depth around the limb to infiltrate around sensitive nerves and branches withouth individually localizing them. Desensitizes: Frontlimb: N. ulnaris, N. medianus, N. radialis.	
Intraperitoneal anaesthesia Intraperitoneal blocks are a useful adjunct to other analgesics following abdominal surgery and for pain associated with intra-abdominal conditions, particularly when opioids may not be available for use due to regulatory restrictions. Recommended to be given under general anaesthesia to avoid laceration or puncture of abdominal organs and peritonitis. Where: Intraperitoneal space during or after abdominal exploratory including ovariohysterectomy, or for painful intra-abdominal conditions (e.g. pancreatitis).	

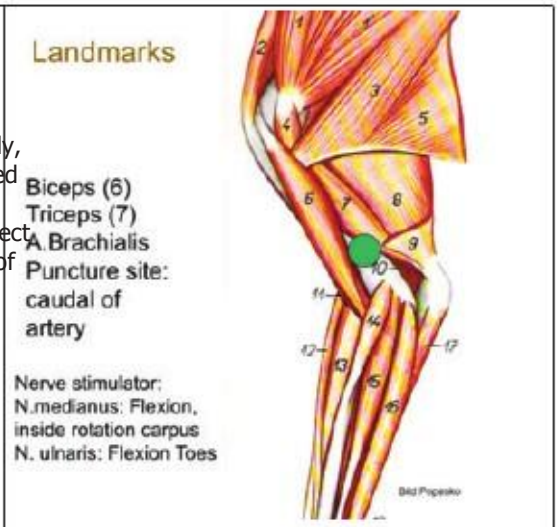
What: Bupivacaine 0·5% (2 mg/kg in the dog; 1 mg/kg in the cat). How: Bupivacaine is diluted in 2 mL/kg and can be instilled directly into the intraperitoneal space before abdominal closure in dogs or cats undergoing abdominal exploratory surgery. Aseptic technique is required. Caution: For cases without an open abdomen, it is essential to follow instructions given at www.wsava.org prior to performing this technique as patient and local anaesthetic solution preparation, landmarks, catheter type, and an immobile patient is required to avoid inadvertent laceration of abdominal organs. Desensitizes: Peritoneum, abdominal viscera.	

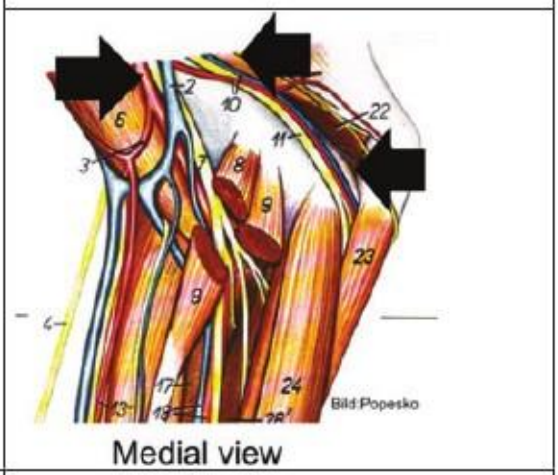
Limb nerve blocks

For peripheral nerve blocks, lidocaine, bupivacaine, mepivacaine, ropivacaine can be used according to the doses suggested in Table 3; sterile NaCl or water for injections may be added to increase volume. Lidocaine may be used with or without adrenaline (epinephrine) (1:200,000), unless otherwise indicated.

N. Radialis Where: Thoracic limb, lateral side of elbow. Volume: Approximately 0·1 mL/kg. Technique: Injection control under palpation of nerve (top figure, 10) and landmarks (centre figure: triceps muscle caudo-dorsally [8], radial carpal extensor muscle craniodistally [16], biceps muscle [12] and brachial muscle [13], at green dot), care has to be taken to avoid the cephalic vein in close proximity to the injection site (bottom figure, black arrow); correct placement of a nerve stimulator tip results in elbow/carpus extension.	  Lateral view
Desensitizes – Red areas of figure.	Picture courtesy of Dr Isabelle Iff, www.vas-int.com 

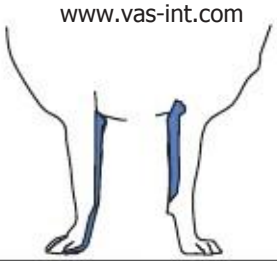
Nn. Medianus, ulnaris
Where: Thoracic limb, medial side of elbow.
Volume: Approximately 0·1 mL/kg.
Technique: Injection control under palpation of nerves (top figure [7 and 11], lower picture) and landmarks (top picture: triceps muscle [7,8] dorsally, biceps muscle [6] cranioventrally, at green dot). Injection sites are indicated by the black arrows in the lower picture. Care has to be taken to avoid the arterial and venous structures in close proximity to the injection sites. Correct placement of the nerve stimulator tip results in flexion and inside rotation of the carpus (n. medianus) and flexion of the toes (n.ulnaris).



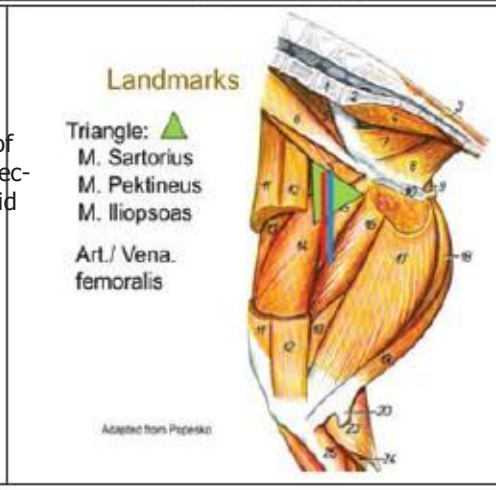


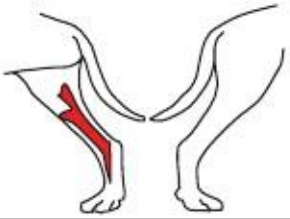
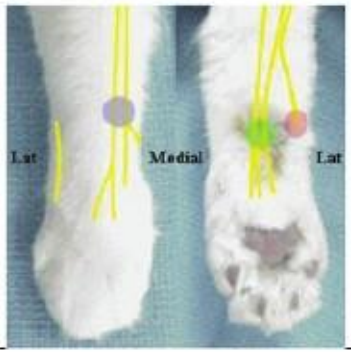
Desensitizes: Blue areas of figure.

Picture courtesy of Dr Isabelle Iff, www.vas-int.com

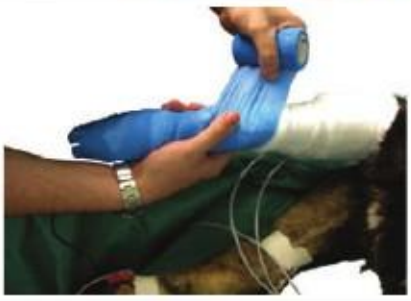


Nn. Femoralis, saphenous
Where: Pelvic limb, medial side of thigh, proximal.
Volume: Approximately 0·1 mL/kg.
Technique: animal in lateral recumbency with one hindlimb on a table and the other abducted and stretched away. Injection control under palpation of the triangled area of injection through landmarks (Sartorius muscle (12), pectineous muscle (15) and iliopsoas muscle (5)). Care has to be taken to avoid the femoral artery and vein in close proximity to the injection site. Correct placement of the nerve stimulator tip results in extension of the knee joint.

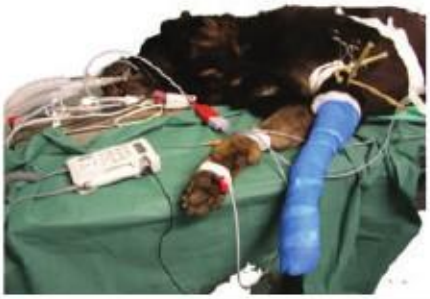


Desensitizes: Red area of figure.	Picture courtesy of Dr Isabelle Iff, www.vas-int.com 
Digital nerve blocks (RUMM) Where: At the distal thoracic limb: the superficial branches of the radial, the dorsal and palmar branches of the ulnar, musculocutaneous and median nerve, particularly useful for toe amputations. Volume: 0.1–0.2 mL at each of the injection sites. Technique: Injection control under palpation of the nerves (yellow lines) or ultrasound is possible. Injection sites (red, green and violet dots) are lateral and proximal to the accessory carpal pad, and the dorso-medial aspect of the proximal carpus. Desensitizes: Foot pad, toes and claws.	Picture courtesy of Dr Bob Stein, www.vasg.org 

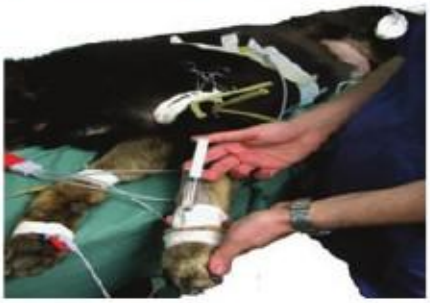
Intravenous regional anaesthesia (IVRA/Bier-block)

Where: In the limbs, distal to the elbows or the knee joints.	
Technique: The limb to be blocked is shaved and the catheter puncture site aseptically prepared (picture 1).	Pictures courtesy of Dr Attilio Rocchi 
An intravenous catheter is placed into the distal limb (picture 2).	
The distal limb is rendered low (empty) in circulating blood by applying a pressure bandage to it from distal towards proximal (picture 3) and a tourniquet to prevent new influx of blood into the limb.	

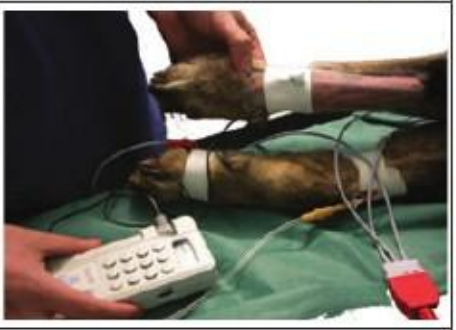
The tourniquet is placed just proximal to the elbow or the knee joint (picture 4) and the bandage subsequently removed.



The circulating blood of this part of the limb is replaced by lidocaine (picture 5).



Stimulation of the distal nerves of the limb using a nerve stimulator for percutaneous stimulation should not result in any muscle twitches (picture 6).

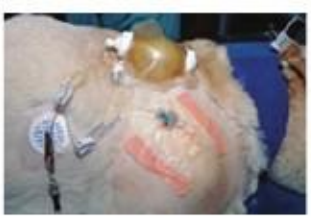


What: 5–15 mL in dogs with or without NaCl to augment the volume are injected into the previously placed catheter. Observe maximum doses. The lidocaine will retrogradely perfuse the tissues and produce a block in the whole distal limb up to the tourniquet. The limb is devoid of circulating blood, making surgical visualization easier, particularly during surgery of the food pad.
Desensitizes: Limb distal to tourniquet.
Caution: Never leave the tourniquet on for longer than 90 or less than 30 minutes. Open the tourniquet slowly, as outrush of lidocaine into the systemic circulation may cause side effects.
Side effects: Are rare. Most side effects are due to improper placement of the block, or use of incorrect or faulty equipment. Hyper- and hypotension may result from tourniquet placement/loosening. Systemic (CNS) toxicity after tourniquet loosening may, however, occur.

Wound soaker catheters

Where: Anywhere, where a wound soaker catheter can be implanted into or alongside a surgical site. This technique is particularly helpful for limb amputations, total ear canal ablations, serial mammary gland or larger tumour excisions. Local anaesthetic with or without adjuncts can be administered over time. Wound soaker catheters are specifically designed to distribute injectate evenly over the tissues that surround the length of the catheter.
How: During a surgery or under surgically sterile conditions a wound soaker catheter can be implanted into the wound or alongside incision lines or around the affected nerves and tissues.
What: Local anaesthetics as a bolus injection. Lidocaine or mepivacaine at 1–2 mg/kg bolus injection. Ropivacaine and bupivacaine can be administered intermittently at 1–2 mg/kg. The catheter can be left in place for 1–3 days, occasionally and with very strict aseptic precautions longer. Side effects are rare.
Desensitizes: The wound specific to placement.

Picture courtesy of Dr Christine Egger



Intra-articular blocks

Where: Application into the capsule of all limb joints. This is particularly useful for perioperative analgesia in patients undergoing joint surgery or arthroscopy. However, application can also be very helpful in chronic pain patients and, as in horses, for lameness diagnostics. Perioperative analgesia may last as long as 24 hours.
Technique: Meticulous care has to be applied to an aseptic technique (clipping, surgically preparing, draping and sterile gloves are to be used). Careful injection into the joint cavity is then performed, without injuring the articular surface. The details of the technique depend largely on the joint.
What: Lidocaine 1 mg/kg, bupivacaine 0·5 mg/kg, morphine 0·1 mg/kg. Other drugs are under investigation. When multiple joints have to be injected, total doses must not exceed maximum doses for the specific drug and species.
Desensitizes: Single joints, and, maybe due to leakage or diffusion, peri-articular tissues.

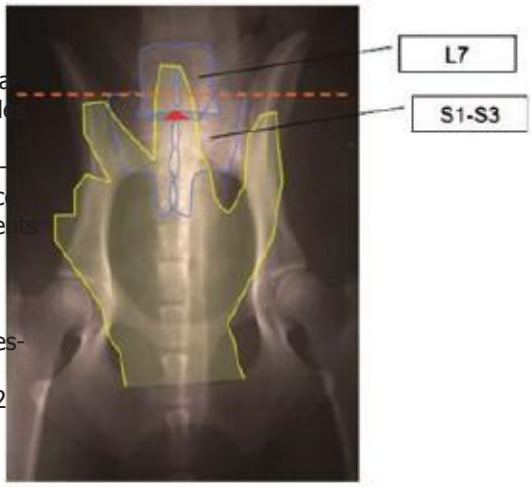
Neuraxial blocks

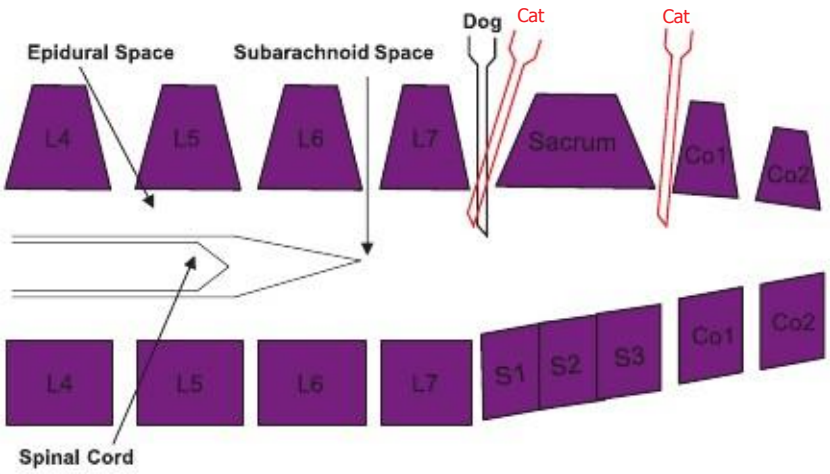
Cautions: Absolute contraindications to neuraxial anaesthetic techniques are infections (including skin) at the puncture site, sepsis, coagulation impairments, particularly thrombocytopenia, and change of anatomical landmarks (such as in multiple pelvic fractures) in absence of imaging techniques employable (radiography, ultrasound). Meticulous care has to be applied to sterile preparation of the puncture site and to all material used. Relative contraindications: In obese and pregnant animals, the size of the epidural and spinal compartments may be varied and puncture more difficult.

Neuraxial blocks should be performed only by appropriately trained individuals and drugs used should be sterile and preservative free. Single epidural injections of morphine with preservative have been used with few complications but preservative-free is essential for repeated injections.

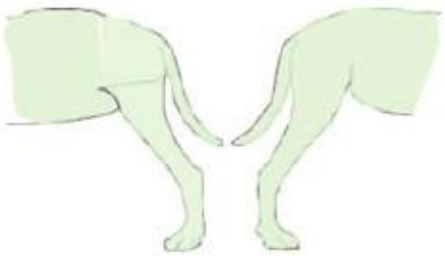
Epidural
Where: At the lumbosacral junction, between the ligamentum flavum and the dura mater, or in cats also at the sacro-coccigeal junction. The lumbosacral junction can be palpated with the two tuberositas ischiaticae to the side and the dorsal processes on the midline as shown in the radiograph.

What: 0·2 mL/kg up to a total of 6 mL using a spinal needle of appropriate size and length. The volume of the injectate is of paramount importance to the cranial spread of the injected drugs and thereby to the spinal segments reached by the drug. The volume indicated here will produce a spread up to L1-L2. Slow injection is also very important to achieve a homogenous distribution of the drug within the epidural space and not produce 'patchy' analgesia leaving some spinal nerves uncovered by drug action. Local anaesthetics; morphine may be added at 0·1 mg/kg or buprenorphine at 0·012 mg/kg, or medetomidine may be added at 0·001 mg/kg,or ketamine (0·4–2 mg/kg), sterile NaCl or water for injections may be added to increase volume, with or without adrenalin (1:200,000).





How: Difficulty of identification of the epidural space remains a factor for block failure. Several techniques may be used to identify correct needle placement in to epidural space:

The 'hanging-drop' technique is a positive control mechanism, by which a drop of NaCl placed in the needle hub is "sucked" into the needle and epidural space by the vacuum prevailing this virtual space. The 'loss-of-resistance' technique uses the different resistances (using NaCl or air) that the single tissue layers pose against needle advancement as indicators for the type of tissue the needle tip is advancing through. This test can be made 'manually', it is even more effective, if the pressure is measured and displayed. A first peak is encountered as the needle passes through the skin, the underlying subcutaneous tissues causes a decline in pressure, followed by a steady plateau as the needle is advanced through the muscle layers to be followed by a second, high peak in pressure, as the ligamentum flavum is encountered. Thereafter, a loss of resistance indicates needle tip placement in the epidural space. If the needle is advanced further, pressure increases again passing through the dura mater into the subdural/intrathecal/spinal space. For the experienced user, ultrasound guidance may provide a useful help to increase block security.	Picture courtesy of Dr Isabelle Iff, www.vas-int.com  Picture courtesy of Dr Isabelle Iff, www.vas-int.com 
Desensitizes:	Picture courtesy of Dr Isabelle Iff, www.vas-int.com 
Side effects: Hypotension, hypothermia, urinary retention (especially in males), infections, slowed hair regrowth.	

30. OPHTHALMIC PROCEDURES

Procedures of the eye, eyelid and surrounding tissues are usually associated with mild to severe pain. Regional anaesthesia techniques in ophthalmology are important to achieve excellent analgesia in the intra- and early postoperative period, and to produce akinesia. Where an immobile eye is required, neuromuscular blockade is preferred, provided appropriate facilities to ventilate are available.[173] The latter can be accomplished by anaesthetizing the zygomatic, lacrimal and ophthalmic nerves as shown in Figure 6. Insert the needle ventral to the zygomatic process, rostral to the cranial border of the vertical mandibular ramus and advance the needle in a caudo-medio-dorsal direction until the tip reaches the orbital fissure. Inject lidocaine 2% alone (0·25–0·5 mL) with or without 1:200,000 adrenaline (epinephrine). This should produce desensitization and immobility of the eye. This procedure should only be performed by trained personnel.

The conjunctiva and the cornea can also be desensitized by topical application of local anaesthetic drops (proxymetacaine, tetracaine, proparacaine). The number of applications should be limited since repetitive application particularly with tetracaine may cause epithelial or stromal keratitis.[174] Topical application of local anaesthetic usually lasts about 15 minutes. While additional applications will deepen the degree of analgesia this also increases the risk for keratitis. Application of artifical tears is essential.

Where enucleation is performed a bupivacaine splash block can be applied once the globe is removed and haemorrhage is controlled, to provide up to 6 hours of partial analgesia. An NSAID and/or opioid is also required for optimal analgesia. Retrobulbar anaesthesia can be performed to produce local anaesthesia of the eye (Nn. Opticus, oculomotorius, trochlear, ophthalmicus and

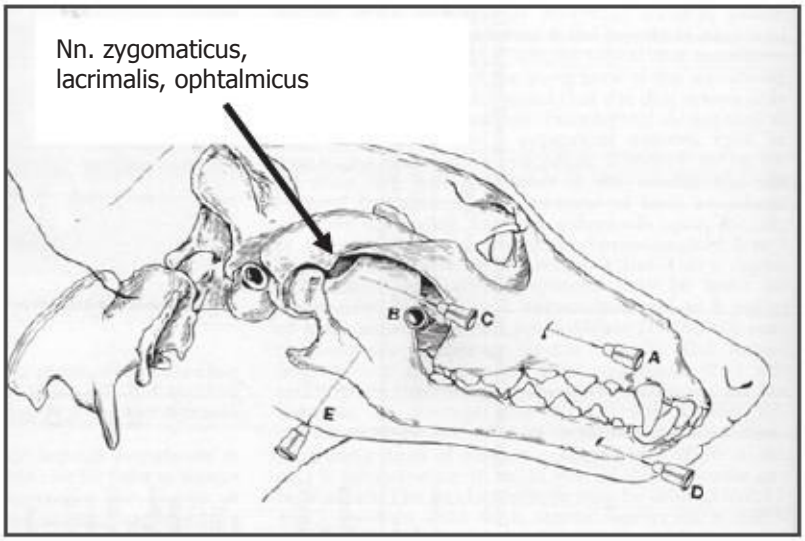


FIG 6. Motor blockade by anaesthetizing the zygomatic, lacrimal and ophthalmic nerve. Picture reprinted with permission by Isabelle Iff. www.vas-int.com

maxillaris and N. abducens). The injection technique is not associated with high complication rates, as puncture of the globe, ciliary or scleral vessels or the optic nerve are rarely observed. High resistance to injection, however, may be indicative for intraneural injection into the optic nerve, and the injection must be stopped immediatedly and the needle repositioned: the curved needle should be inserted at the lateral third of the eye and directed medially and 1–3 mL of lidocaine alone or lidocaine with 1:200,000 adrenaline (epinephrine) are injected slowly after having assured (through aspiration) that no blood vessel is punctured.[175]

Lidocaine (1 mg/kg IV bolus followed by CRI at 0·025 mg/kg/min) may provide intraoperative analgesia similar to that provided by morphine in dogs undergoing ocular surgery.[176] However, caution should be used when combining CRI lidocaine with local administration of local anaesthetics to avoid toxicity. Lidocaine CRI is not recommended in cats.

The use of systemic NSAIDs (starting 24h before surgery) in ophthalmologic procedures is indicated, as they produce analgesia and decrease the risk of uveitis and acqueous humour-PGE production which leads to posterior chamber flare. As always care must be taken to avoid NSAID-induced side effects.[177]

Intra- and postoperative administration of opioids and/or alpha$_2$ adrenoceptor agonists may improve the analgesic effects of local anaesthetics and NSAIDs. Morphine produces miosis in dogs and mydriasis in cats. Opioids (e.g. methadone and buprenorphine), that do not cause vomiting and associated increases in intraocular pressure (IOP), are usually preferred.

The use of ketamine (0·5–1 mg/kg) has been associated with increased intraocular pressure due to increases in extraocular muscle tone. While there are clear species differences, and some conflicting results, it should be used with caution in patients where increased IOP may result in expulsion of ocular contents (e.g. corneal trauma) or any other manoeuvre that could potentially increase IOP (e.g. neck leashes). If ketamine is used, other drugs (such as benzodiazepines or alpha$_2$ agonists) may be administered concomittantly to mitigate potential ketamine-induced increases in IOP.

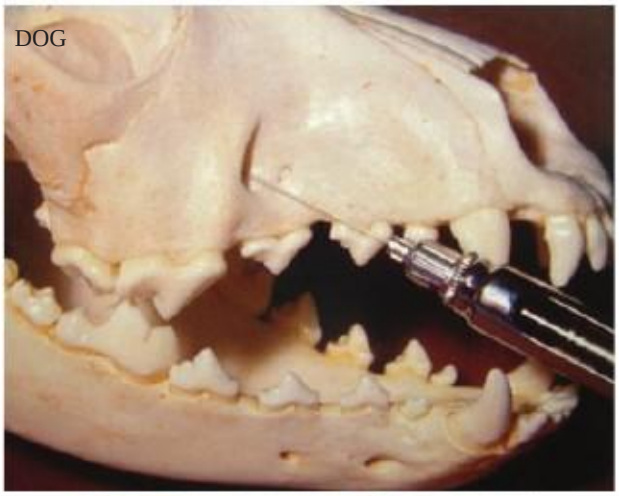
Cool packs can be used to reduce swelling. For postoperative analgesia, NSAIDs can be given (systemic and/or topical) or, if pain is considered to be more severe or persistent, the addition of tramadol (4 mg/kg PO q8h) may be considered where available. Patients should receive artificial tears for 1–3 days postoperatively as general anaesthesia and opioids decrease tear production.[178]

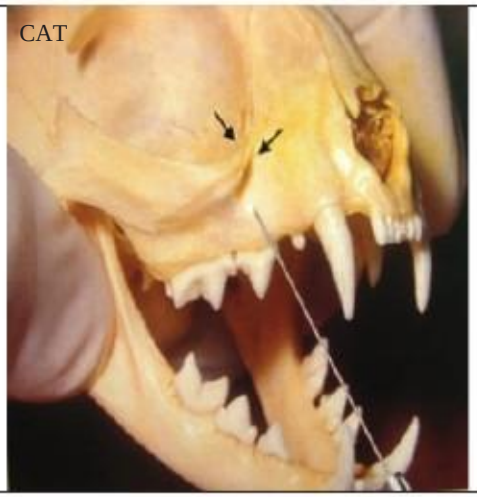
31. DENTAL PROCEDURES

Procedures in the oral cavity – including teeth cleaning should be performed under general anaesthesia with a secured airway (endotracheal intubation). All precautions, safety measurements, monitoring rules and standards apply.[179] While simple teeth cleaning may be associated with only a minor degree of pain, gingivectomy, tooth extractions, root canal therapy and interventions of soft tissue and bony structures of the oral cavity are associated with moderate-to-severe pain. Refer to Table 3 for dosing instructions.

For painful procedures in the oral cavity, inclusion of loco-regional anaesthetic techniques is of paramount importance[180] and the most common dental blocks are therefore herein described. The landmarks for needle insertion can be palpated either transmucosally or transcutaneously. If the latter is done, an aseptic injection technique is mandatory. After needle placement aspiration, with the syringe attached, is performed to confirm that the needle has not been inserted into a blood vessel. If blood is drawn into the syringe, do not inject, remove the needle slightly and re-test. If resistance to injection is experienced, do not continue as this may be associated with perineural injection with the potential of nerve damage.

Infraorbital block
Blocks: Nn. Infraorbitalis and alveolaris superior.
Desensitizes: Upper lip and skin of the upper lip from rostral end to the infraorbital foramen, dorsal part of the nasal cavity, ipsilateral superior incisors. With application of digital pressure over the foramen for one minute the local anaesthetic agent will diffuse caudally to the ptyergopalatine fossa and block the entire quadrant.
Technique: The needle is inserted transmucosally (intraorally), just apical to the third maxillary premolar through the mucosal vestibule for only a few mm into the entrance of the palpable infraorbital foramen in dorso-caudo and slightly medial direction. Care has to be taken to not advance the needle too far, as damage to ocular, vascular or neural structures may occur.
Volume: 0·2–1·5 mL per side.

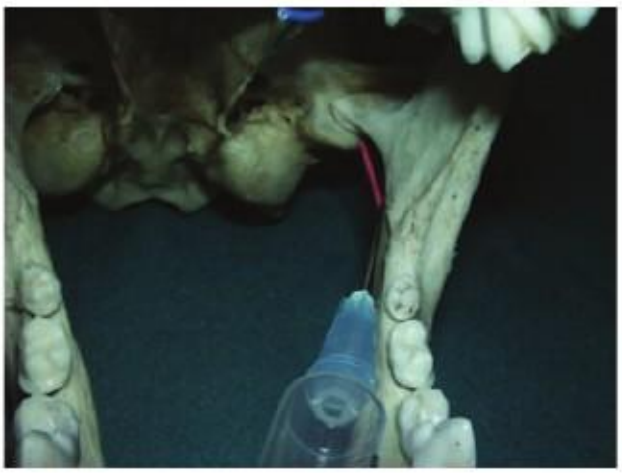


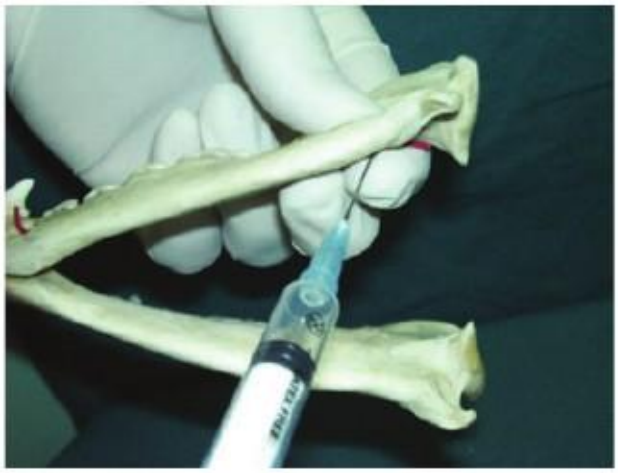


Inferior alveolar block:
Blocks: N. Inferior alveolar.
Desensitizes: Ipsilateral lower jaw and teeth with buccal and labial mucosa, skin of lower lip.
Technique - transmucosal, intraoral approach: With the animal in sternal recumbency and the mouth wide open, in larger dogs, the mandibular foramen may be palpated in the ventral fourth of the vertical part of the mandible, caudally to the last mandibular tooth and an intramucosal deposit of local anaesthetics be made.
Technique - transcutaneous, extraoral approach: On the medial side of the vertical part of the mandible, the angular process can be palpated and the needle is inserted just cranial to that and parallel to the mandible advanced for 0·5–2 cm.

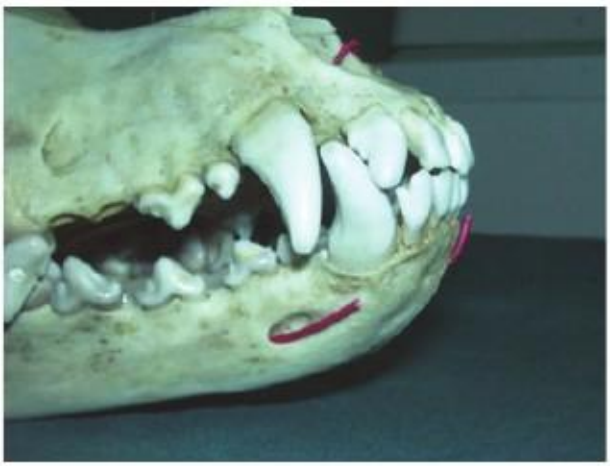
The needle should be centred over the notch on the ventral aspect of the ramus in dogs and directed to the midpoint of the zygomatic arch in both dogs and cats.

Care has to be taken not to harm the lingual or hypoglosseal nerves which may result in loss of motor function of the tongue and subsequent self-mutilation.
Volume: Intraoral technique: 0·2–1·5 mL per side; extraoral technique: 0·2–1·5 mL.

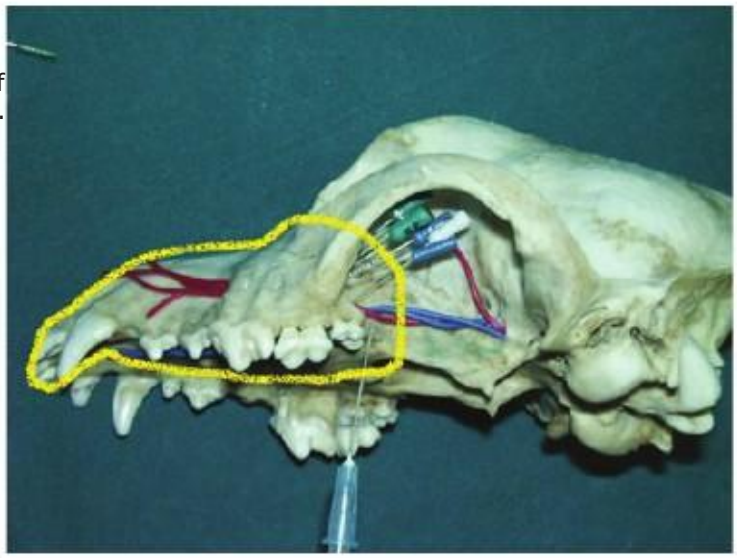




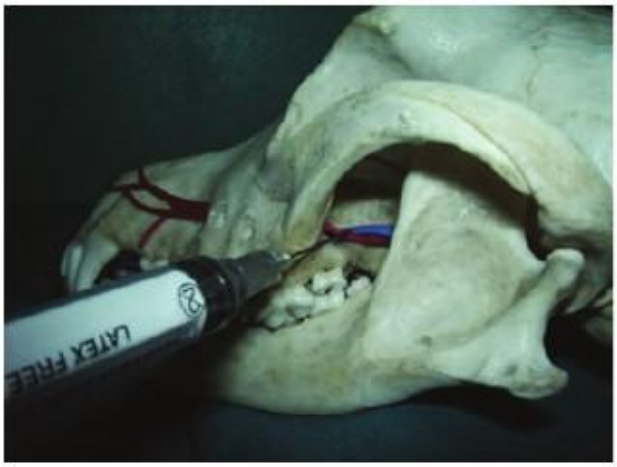
Mental block:
Blocks: N. alveolaris mandibularis.
Desensitizes: Ipsilateral inferior incisors.
Technique: The needle is inserted transmucosally (intraorally) perpendicular to the direction of the canal and nerve; in cats and smaller dogs even the larger mental foramen is usually not palpable and the landmarks can be the frenulum labiale and the first and second mandibular premolar teeth between which the needle is inserted to a depth of 2/3 of the height of the mandible. In larger dogs, the foramen may be palpated. In small animals the needle is not inserted into the foramen to avoid neural damage.
Volume: 0·2–1 mL per side.



Maxillary block:
Blocks: N. maxillaries.
Desensitizes: Ipsilateral maxilla and maxillary teeth, roof of nasal cavity, skin of lateral part of nose and upper lip.



Technique – intraoral behind the last molar tooth: This transmucosal, intraoral technique is easiest performed with the animal in dorsal recumbency, when with a wide opening of the mouth a soft deflection in the mucosa can be palpated just behind the last molar tooth.

The needle is inserted into the mucosa at the palpated deflection in a dorsal direction. This technique is safe, but may not desensitize the last maxillary teeth. Technique – extraoral, at the fossa pterygopalatina: This transcutaneous, extraoral technique requires some expertise in order to avoid ocular, neural or vascular damage and is best performed with the animal in lateral recumbency. The needle is inserted perpendicularly to the skin along the ventral border of the zygomatic process and advanced in medio-rostral direction to the fossa. This can accomplished with less risk with an infraorbital block. Volume: Intraoral technique: 0·2–0·5 mL per side; extraoral technique: 0·2–2 mL per side.	

Furthermore, using very fine needles (26G and higher) local anaesthetics can be injected into the lateral peridontal ligament to desensitize single dental pockets, but feasibility is somewhat lower in dogs and cats than in humans. The use of cool packs to reduce the amount of swelling particularly due to intraoperative trauma and while the patient is anaesthetized should be taken into consideration.[181]

32. EMERGENCY AND CRITICAL CARE

In addition to analgesia for pain control, many injured or ill animals will require analgesia to facilitate restraint, diagnostic and emergency procedures.[171, 182-186] As each animal will present with varying levels of injury or illness and be experiencing different degrees of pain, individual drug selection, and dosing to effect is essential, rather than considering a standard regimen for all patients. Painful animals may also be aggressive and chemical restraint is required to protect staff, and the patient from further (self-inflicted or iatrogenic) injury, and to facilitate a physical examination. These animals may appear stable even with severe injury or illness (especially cats) due to the 'fight or flight' response. Where blood or fluid loss may be present or suspected, fluid therapy is commenced prior to careful titration of the opioid to avoid potential adverse effects with standard dosing.

The use of NSAIDs in the emergency patient should be withheld until the volume, cardiovascular and renal status of patients is determined to be within normal limits and with no potential for deterioration. NSAIDs should never be administered to patients with evidence of/potential hemorrhage.

Due to the variability of diagnoses, animals admitted for ongoing critical care experience a variable degree of pain, which contributes to a catabolic state in these patients. In addition to the primary problem, there are the additive effects of pain due to placement/presence of IV, urinary, thoracic and abdominal catheters and drains. Many patients undergo frequent manipulations and procedures also contributing to the overall pain experienced. When considering analgesic selection, potential adverse effects should be minimized due to the often compromised organ function of these patients. Opioid analgesics and ketamine can still be used in patients with renal and hepatic insufficiency. Initial low dosing of the analgesic titrated to effect is required to reach therapeutic levels and avoid adverse effects; however, ongoing dosing with adjustments will be dependent on the individual patient as metabolism and excretion will be reduced (see below). Analgesia must be withdrawn slowly to avoid an abrupt return to a hyperalgesic state should pain still be present. Where the re-appearance of pain is identified, return to the previous dose for several more hours followed again by slow withdrawal. Analgesia and the induction of restful sleep is the goal. Continuous rate infusions are useful to achieve this. The following drugs, approximate dosages and combinations, are suggested for moderate to severe pain. Initially, start with a lower dose of an opioid. Should further analgesia be required, add lidocaine (not cats), or ketamine if needed. Where drug availability is limited, select a regimen from the following based on availability:

For severe pain opioids alone will not be sufficient and higher dosages than those in Table 4 may be required. Should adverse effects begin but pain is still not controlled, introduce ketamine. Add lidocaine if ketamine cannot control the pain.

•Loading dosages: Titrate the opioid slowly to effect first, if needed add ketamine, if needed add lidocaine 2 mg/kg
•CRI: The continuous dosing regimen is based on the loading dose and expected duration of action. Clinical experience indicates that the fentanyl and ketamine loading dose can be used as the hourly infusion even though the expected duration of a single dose is ~30 mins. For hydromorphone, methadone and morphine, the effective loading dose can then be used as the CRI dose over a 4-hour period (divide by 4 for the hourly dose) with frequent assessment and modification as duration of action may be prolonged, especially

Table 4

Drug	Approx Loading Dose: titrate to effect	Approx CRI/time period based on loading dose
Fentanyl	2-5+ μg/kg	3-5+ μg/kg/h
Hydromorphone	0·04-0·05+mg/kg	0·01-0·015+ mg/kg/h
Methadone	0·2-1·0mg/kg	0·05-0·2mg/kg/h
Morphine	0·3mg/kg	0·1mg/kg/h
Ketamine	0·2-2+mg/kg	0·2-2+mg/kg
Lidocaine	Dogs only 2mg/kg	1-2mg/kg/h

where renal or hepatic dysfunction is present. Should the patient appear overdosed at any period of time, the CRI can be stopped for 30 minutes, or less if signs subside, and reinstituted at one-half the previous dose rate. Or, careful titration of naloxone to reverse side effects (unless an emergency< 0.002mg/kg may suffice; higher doses may result in hyperalgesia, hyperexcitability, cardiac arrhythmias and aggression. Refer to Table 1 for instructions). Where there are no contraindications/compromised organ function for NSAID use, addition is recommended where pain cannot be managed.

Where opioids are not available, lidocaine and ketamine as above, epidural anaesthesia, intrapleural or intra-abdominal local anaesthesia where indicated, diffusion catheters and various local blocks for post-surgical analgesia can be administered.

Anecdotally acupuncture has been used as an appropriate adjunct for the critically ill patient. There are minimal risks or side effects of acupuncture, although very debilitated patients may require fewer needles.

Other modalities to include in the critically ill patient are proper use of warmth for muscle spasm or pain, cold for regions of acute injury or inflammation, gentle pressure support for appendicular regions that are painful (or sometimes for abdominal pain). Furthermore, proper padding and positioning, patient mobilization and nursing care are critical for comfort in these patients.

33. MEDICAL PAIN

Medical pain discussed here is a 'catch-all' for conditions not primarily associated with surgery or trauma (examples below); however, they
may occur secondarily. Treating the underlying problem alleviates discomfort; however, analgesics are required during the healing process.

Abdominal, pelvic and thoracic visceral pain[187,188] occurs in conditions associated with distension and/or inflammation of hollow organs, ischaemia, pulmonary thrombosis, acute enlargement of solid organs resulting in stretching of the capsule and inflammation of any organ (e.g. pancreatitis, acute kidney injury, pneumonia/pleuritis). Visceral pain tends to be diffuse in nature; however, pain can be localized to an area within the cavity when pressure is applied externally. Thoracic visceral pain may be elicited on abdominal palpation; visceral pain may also be exhibited as referred pain at a distant cutaneous site.

Dermatologic diseases cause inflammation resulting in mild to excruciating pain (e.g. necrotizing fasciitis). Specific therapy to treat the underlying problem should alleviate the discomfort but analgesics may be required to manage pain effectively.

Further examples of medical pain and their severity can be found in Section 9.

Suggested analgesic regimens

Opioids are the first choice drugs in many emergency and critically ill patients.

Severe pain refer to critically ill above

1. mu agonist opioid (Table 4) commencing at the mid- higher dosage and titrate to effect.
2. NSAIDs, when haemodynamically stable and no contraindications, in combination with any of the opioids above
3. Locoregional anaesthetic techniques
4. Ketamine and/or lidocaine (dogs only) CRI
5. Intrapleural and intraperitoneal blocks for visceral pain (www.wsava.org)

Moderate pain

1. Low-medium dose mu agonist opioid, IV followed by CRI: fentanyl, hydromorphone , methadone or morphine. (Refer to Table 4 for dosing). If only pethidine (meperidine) opioid available: 5–10 mg/kg IM or SC; Frequent IM or SC injections are painful and stressful and should be avoided where possible. OR
2. NSAID when haemodynamically stable and no contraindications, either alone or in combination with an opioid OR
3. Buprenorphine 0·02–0·04 mg/kg IV or OTM q4-8h for 3–5 days cats, 0·01–0·02 mg/kg IV q4-8h dogs, 0·02–0·04 mg/kg OTM small dogs (<10kg) for 3–5 days OR

4. Butorphanol 0·2–0·4 mg/kg IV q1–2h cats and dogs or CRI at 0·2 mg/kg/h after the loading dose

Mild to moderate pain (non-hospitalized or hospitalized patients)
1. NSAID of choice where not contraindicated AND/OR 2. Buprenorphine 0·02-0·04 mg/kg OTM q6-8h for 3–5 days cats, 0·02-0·04 mg/kg OTM q6–8h small dogs (<10kg) for 3–5 days OR
3. Tramadol 5mg/kg PO q8-12h for dogs, 2 mg/kg PO cats q12h may be of benefit, although there is little published evidence to support this
4. Lidocaine 2% viscous[a] 1:1 to aluminium hydroxide 64 mg/mL, (max dose 0·4mL/kg q8h) is effective in treating oral & esophageal lesions [b] (personal communication, KM)
[a]Lidodan 2%, Montreal, Canada (or similar product based on individual country). [b]Abrams-Ogg A. Oncologic emergencies. In: Mathews KA, ed. Emergency & Critical Care Manual 2nd ed. Lifelearn, Guelph,Canada: 2006: 448.

Adjunctive therapies (to be used with all levels of pain where indicated)

- Anti-emetics are indicated where nausea and vomiting are present
- Acupuncture may be very useful for gastrointestinal and urinary cases in particular. Acupuncture may also be of benefit as an anti-emetic technique
- Medical massage and warm compress are recommended where indicated
- Environmental enhancement to reduce stress and anxiety. Pheromonatherapy may be helpful in cats[189] and dogs.

34. PREGNANT OR LACTATING PATIENTS

Very little information is available about the pharmacology of analgesic drugs in dogs and cats during pregnancy and lactation; some information is presented from studies in humans and laboratory species.[190]

Pregnancy

Physiological changes associated with the maternal-placental-foetal unit alter drug pharmacodynamics, pharmacokinetics and distribution to the foetus.[191] The maternal factors that may alter drug absorption are decreased gastrointestinal motility, oesophageal reflux and vomiting; and an increased cutaneous blood flow, which may enhance absorption of transdermally administered drugs.[191] Increased total body water, increased total body fat, reduced serum albumin, altered hepatic enzymatic activity and increased renal function are all factors that may alter the response of pregnant animals to analgesic drugs.[191]

The placental barrier is considered to be a lipoprotein, therefore drugs with high lipid solubility are permeable.[192] Drugs that are polar, ionized, protein-bound or water soluble are less likely to cross the placenta into the foetus.

Opioids: Currently, opioids are commonly used for analgesia in pregnant dogs and cats. Methadone, morphine and hydromorphone are used during pregnancy in humans.[192] Fentanyl, pethidine (meperidine), butorphanol and nalbuphine are more lipid soluble, and therefore may reach higher concentrations in the foeti.[192] Opioids are frequently used preoperatively for caesarian section, and most puppies and kittens are successfully delivered and are vigorous.[193] If the puppies or kittens are depressed after delivery, alongside provision of warmth, stimulation, and oxygen and application of suction as required, a drop of naloxone placed sublingually should reverse these effects; however repeat dosing may be required.[194,195] Buprenorphine resulted in lack of milk production in animal studies, which may be a problem following casesarian.[196,197]

NSAIDs: Due to possible teratogenicity and development-interfering effects, it is advised that NSAIDs are not administered to pregnant animals.[198]

Ketamine: Ketamine rapidly crosses the placenta; however, no foetal effects have been observed during organogenesis and near delivery in rats, mice, rabbits and dogs.[199] Ketamine increases uterine tone and should be avoided during pregnancy.[199] An in-depth review of caesarean section in dogs is available.[200]

Alpha$_2$ adrenoceptor agonists: Reduce uterine blood flow. Xylazine should not be used during pregnancy. Evidence regarding the use of medetomidine and dexmedetomidine in dogs and cats during pregnancy is not available.

Local anaesthetics: Generally considered to be safe and non-teratogenic[201] – they are highly recommended.

Herbal analgesic medications: Due to a lack of information, these should be avoided

Caesarean Section

The physiologic changes associated with pregnancy outlined above influence the choice of anaesthetic and analgesic drugs for caesarean section in queens and bitches. All anaesthetic and analgesic agents cross the placental barrier.

There is more evidence-based information on caesarean section and neonatal vitality and survival for dogs than cats. Premedication is normally recommended to decrease maternal stress and anxiety and to reduce the doses of induction and maintenance agents; in addition the use of opioids provides pre-emptive analgesia. Decreased gastrointestinal motility and the enlarged uterus increase the risk of vomiting and aspiration. Aspiration of gastric contents is thought to contribute to maternal mortality.[195] For this reason if opioids are given preoperatively choose those that are less likely to cause emesis (e.g. buprenorphine, butorphanol, methadone and pethidine); intubation is always warranted to protect the airway and also for delivery of oxygen. Rapid control of the airway is essential therefore mask induction with an inhalant agent is not recommended. The administration of opioids prior to delivery has not been shown to adversely affect the outcome for the offspring.[202] If opioids have been administered to the dam and the offspring are bradycardic, naloxone can be administered via the umbilical vein or sublingually.

Due to their high oxygen requirements and reduced functional residual capacity of the lungs, pregnant animals are at risk for hypoxaemia and oxygen desaturation can occur rapidly at induction of anaesthesia. Pre-oxygenation (3–5 minutes) using a face mask is recommended.[203] Many animals undergoing caesarean section are dehydrated and even in elective situations, fluid losses can be large therefore intravenous fluids are recommended and should be started prior to induction of anaesthesia.

Drugs that are known to increase maternal and/or neonatal mortality include the alpha$_2$- adrenergic agonist xylazine and the inhalant agent methoxyflurane.[195,202] There are no data on the effect of the newer alpha$_2$-adrenoceptor agonists, medetomidine and dexmedetomidine, on anaesthetic risk associated with caesarean section. However due to the potential for emesis and cardiovascular depression, these drugs as a class are best avoided.

There is some controversy regarding the use of NSAIDs in this setting due to potential uptake and negative effects in the suckling offspring. However, only a small percentage of the dam's dose of NSAID is secreted in milk and a single post-operative dose is regarded as a suitable compromise. NSAIDS should only be given if hypovolaemia and hypotension have been corrected (see Section 13 for details).

Neonatal vitality: In one study[204] respiratory rate (RR) and neurologic reflexes of puppies were compared after dams received ketamine/midazolam, thiopentone, propofol or an epidural local anaesthetic. The RR was higher after epidural anaesthesia and neurologic reflexes were best after epidural, followed by propofol, thiopentone and ketamine/midazolam. See below for precautions on using epidural analgesia as a sole technique. Moon[202] also reported that although ketamine did not increase puppy mortality it decreased the vigour of new-born puppies, therefore resuscitation efforts should be aggressive if ketamine is used. There was no difference in survival between puppies whose dams received propofol or alfaxalone.[205] However, using a modified Apgar score puppy vitality was found to be superior when alfaxalone was used. There is a lack of published information on kitten vitality after caesarean delivery.

Elective situation
Preoperative: IM or IV opioid ± acepromazine (lower doses [0·01-0·03 mg/kg IM or IV] are usually sufficient). An opioid normally provides adequate sedation for venous access however acepromazine can be used if the dam is difficult to manage and requires more sedation than an opioid alone can provide.
Induction and maintenance of anaesthesia: IV alfaxalone to effect (3-5 mg/kg) or IV propofol to effect (3-10 mg/kg). Where propofol or alfaxalone are not available, ketamine or thiopentone could potentially be used with the understanding that they may decrease vigour of the offspring and resuscitation efforts should be aggressive. Following intubation, anaesthesia can be maintained with isoflurane. NOTE: The dam's requirements for inhalant agents may be reduced by 25-40% at term. Anaesthesia can be maintained with repeated boluses or a continuous rate infusion of propofol, but intubation and administration of oxygen is still required.
Local anaesthetic techniques: Pre-incisional and / or post incisional line block (lidocaine or bupivacaine).
Epidural/ Spinal analgesic techniques: Morphine can be administered pre- or post-operatively to provide up to 18-20 hours of analgesia. See Section 29 for details.
Postoperative analgesia: NSAIDs, one dose; see Section for details. Opioids can be continued.

Emergency situation with compromised dam
Preoperative: Fentanyl IV (3-5 μg/kg).
Induction and maintenance of anaesthesia: IV etomidate (1-2 mg/kg) ± diazepam or midazolam (0·25 mg/kg), IV ketamine (3-5 mg/kg) plus diazepam or midazolam (0·25 mg/kg); midazolam is shorter acting in both dam and offspring so is preferred when available. Following intubation anaesthesia can be maintained with isoflurane and fentanyl can be repeated.
Local anaesthetic techniques: See above
Epidural/ Spinal analgesic techniques: See above
Postoperative analgesia: NSAIDs should only be considered if the bitch or queen is normovolaemic and normotensive. For choice of drugs see Section 13 for details. Opioids can be continued.

Protocol without controlled drugs
Preoperative: Acepromazine unless the bitch or queen is volume depleted. If the dam is compromised do not administer premedication drugs.

Induction and maintenance of anaesthesia: IV alfaxalone to effect (3-5 mg/kg), propofol to effect (3-10 mg/kg) or etomidate (1-2 mg/kg). Following intubation anaesthesia can be maintained with isoflurane. Anaesthesia can be maintained with repeated boluses or a continuous rate infusion of propofol, but intubation and administration of oxygen is still required.
Local anaesthetic techniques: See above
Epidural/ Spinal analgesic techniques: See above
Postoperative analgesia: NSAIDs, one dose; see Section 13 for details.

Protocol with limited availability of anaesthetic and analgesic drugs
Preoperative: Acepromazine (see indication for use above).
Induction and maintenance of anaesthesia: Depending on availability of drugs, choose from the protocols above.
Local anaesthetic techniques: Epidural local anaesthetic (lidocaine) can be used as a sole technique but with caution. NOTE: due to the decreased size of the epidural space in pregnant animals smaller volumes (25-30% reduction) of epidural local anaesthetic drugs are used. Epidural local anaesthetics cause sympathetic blockade with resultant vasodilation and hypotension which can be prevented or treated with intravenous fluids, but could be especially detrimental in compromised dams. With this technique the dam is conscious and therefore not intubated so there is an increased risk of aspiration; oxygen should be administered by face mask. The dam will also require to be manually restrained for surgery. See Section 29 for details on technique.
Postoperative analgesia: NSAIDs one dose; for choice of drugs see Section 13 for details.

Lactation

Characteristics of a drug which would facilitate secretion into milk are high lipid solubility, low molecular weight and the non-ionized (charged) state. It is estimated that the neonate receives approximately 1% to 2% of the maternal dose of a drug.[206] Where analgesia is essential and there are concerns for potential toxicity in the offspring, the milk should be pumped and discarded for 12h before resuming suckling, and puppies and kittens should be bottle fed.
Opioids: The lipid solubility of the opioid influences its appearance in the milk; pethidine (meperidine)>sufentanil>fentanyl>morphine>hydromorphone, therefore a more hydrophilic opioid, such as morphine, may appear in smaller amounts than a more lipid-soluble opioid such as pethidine. It is recommended that suckling occurs after peak levels of the opioid have waned. Pethidine (meperidine), butorphanol, nalbuphine are not recommended.[207,208] Where opioids are selected for analgesia, mothers and offspring should be carefully observed and monitored for signs of opioid adverse effects.
NSAIDs: Most NSAIDs are not lipid soluble, are highly protein bound to plasma proteins and may be present to a great degree in an ionised form in the plasma. It has been suggested that a single use of an NSAID is safe in nursing human mothers. Until studies are performed in lactating cats and dogs, NSAIDs should be administered with caution and as single doses only. Hemorrhage is a potential concern following the administration of non-COX selective, or COX-1 selective NSAIDs immediately after caesarian section, or even natural birth.[190,207] In general, paracetamol is safe for use in dogs, but cannot be administered to cats.
Local anaesthetics: Lidocaine and its metabolites have low lipid solubility; at therapeutic doses the concentrations in milk are small and unlikely to be a risk. Incision line infiltration is highly recommended.
Ketamine: No reports on passage into breast milk were found, but it is expected to pass into breast milk.[208]
Herbal analgesic medications: Due to a a lack of information, these should be avoided.

35. NEONATAL AND PAEDIATRIC PATIENTS

Studies in neonates and infants show that when anaesthesia or analgesia was withheld, altered pain sensitivity and increased anxiety occurred with subsequent painful experiences, when compared to children receiving analgesia.[209] This suggests that infants retain a 'memory' of a painful experience with subsequent altered response to a painful stimulus. This has also been shown in laboratory animals.[210]

The term paediatric generally refers to the first six months of life. Due to important physiological changes which occur during this time frame, a further demarcation is defined as: neonatal (0–2 weeks), infant (2–6 weeks) weanling, (6–12 weeks) and juvenile (3–6 months). This distinction is made to highlight the metabolic changes that occur during these periods of maturation.[211]

There tends to be apprehension in administering analgesic drugs, especially opioids, to young animals due to the often cited 'decreased ability for drug metabolism and high risk of overdose'. While this may be a potential concern in the neonate, it is not necessarily so through all stages of maturation. While there are no reports in the veterinary literature suggesting increased dosing should be considered in the young cat or dog, personal experience with intensive monitoring of the young (3–6 month old) animal has shown opioid doses for analgesia may be equal to, and can be higher than, a mature adult emphasizing that administering the analgesic to effect, rather than a pre-determined dose, is the most important method of clinical dosing.[190] However, young animals can be susceptible to the sedative effects of opioids. Opioids can be reversed with careful titration of naloxone should there be clinical evidence of CNS depression and respiratory depression, hypotension and bradycardia (unless an emergency,

<0·002mg/kg may suffice; higher doses may result in hyperalgesia, hyperexcitability, cardiac arrhythmias and aggression. Refer to Table 1 for instructions). For all these reasons, frequent pain assessment and treatment should be evaluated on a case-by-case basis and tailored to patient needs.

The neonate has reduced clearance of many drugs as compared with older individuals largely because of:

- The greater body water content leading to a higher volume of distribution
- A larger fraction of body mass that consists of highly perfused tissues
- A lower plasma concentration of proteins that bind drugs
- Incomplete maturation of their hepatic-enzymes systems.[212]

The hepatorenal system continues to develop until 3–6 weeks of age; this may result in reduced metabolism and excretion, which may require alterations in dosing and dosing intervals.[210] For all young animals, the presence of milk in the stomach may inhibit the absorption of some orally administered drugs, potentially resulting in lower blood concentrations.

Opioids

Lower doses of fentanyl or morphine are required for analgesia in the neonate (0–2 weeks) when compared to the 5-week-old puppy[213] or kitten. Puppies and kittens are also more sensitive to the sedative and respiratory depressant effects of morphine than adults. Fentanyl may be a more suitable opioid in the young paediatric and neonatal puppy or kitten; however, as it is short-acting continuous IV access and titration are required.[213,214] Buprenorphine may be an alternative, and associated with minimal respiratory depression. Hydromorphone, oxymorphone and methadone may also be used; however, as with all opioids, starting at or below the lowest dose of the range and increasing to effect is recommended. Opioids can be reversed with titration of naloxone should there be clinical evidence of overdosing.

Non-steroidal anti-inflammatory drugs

NSAIDs are not recommended for animals less than 6 weeks of age; however, for some NSAIDs the age is older. It is essential to consult the package insert of all NSAIDs prior to using in young animals.

Local anaesthetics

Local anaesthetics are recommended, but careful dosing according to accurate body weight is imperative. Lidocaine is painful when infiltrated even with 27–30 gauge needles.[214] To reduce pain, buffering (a 20:1 mixture of local anaesthetic with 1 mEq/mL sodium bicarbonate; e.g. lidocaine 2% = 2mL:0·1mL), warming (36–37°) and slow administration is recommended. Mepivacaine does not induce pain on injection. A maximum dose of local anaesthetic is half the adult dose[215] for both kittens and puppies up to 10 days of age.

Topical LA creams (EMLA® Cream; AstraZeneca LP, Wilmington, DE, USA [prescription only mixture of lidocaine 2·5% and prilocaine 2·5%]; MAXILINE®4, Ferndale Laboratories, Ferndale, MI, USA [over-the-counter. Onset time faster than EMLA cream]; ELA-Max® or L.M.X™; Ferndale Laboratories, Ferndale, MI, USA [liposome-encapsulated formulation of 4% lidocaine (OTC)]) are effective when used on intact skin to provide anaesthesia for IV catheter placement, blood collection, lumbar puncture and other minor superficial procedures.[216,217] The creams should be covered with an occlusive dressing for at least 30 minutes prior to the procedure. Products containing adrenaline (epinephrine) should be avoided. Lidocaine 2% is also available as a sterile gel, and is used for local desensitization of the vaginal vault or penis prior to urinary catheter placement.

Alpha$_2$ adrenoceptor agonists

Alpha$_2$ agents are sedative analgesics and are not recommended due to the cardiovascular effects.

Sedatives

These should not be used in young animals, especially when less than 12 weeks of age.[218] Most sedatives have no analgesic properties and if used may mask pain behaviours.

Nursing

Suckling is analgesic in rat and human infants. Where any painful procedure is required in young animals, contact with the mother as soon as possible is recommended.[219] Other feeding procedures can provide distraction-related analgesia and comfort.

36. NEUROPATHIC PAIN

Neuropathic pain[55] requires several classes of medications and procedures as it cannot be adequately managed with a single pharmacological or non-pharmacological therapy.[57,58,91,104,220,221] Prior to, and during any surgical procedure, various different analgesic drugs

and modalities can be used to reduce the inciting nociceptive afferent impulse. Many of these are continued postoperatively to reduce both peripheral (PNS) and central (CNS) sensitization.

NSAIDs

There is evidence to support an inflammatory response driving the pathophysiological changes of the peripheral and central nervous systems resulting in neuropathic pain and augmentation of pain processing by spinal prostanoids.[222,223] While no studies are reported at this time, human clinical trials are currently underway investigating various modalities to target specific components of the neuro-inflammatory process. It is advised that NSAIDs be used in the treatment of neuropathic pain.

Opioids

Opioids may be included in a multimodal regimen to manage neuropathic pain, but not as a stand alone analgesic. Opioids may have reduced effectiveness, where tactile allodynia (Abeta stimulus) is a component of neuropathic pain and where opioid receptors in the descending inhibitory pathway are reduced or inactivated, which may occur in neuropathic pain. Also, the closer the nervous system lesion is to the CNS, the less effective opioids may be; peripheral nerve injuries tend to respond better to opioid therapy than nerve root injuries, which respond better than spinal cord injuries.[220] The shorter half-life of fentanyl is an advantage in patients with acute CNS or PNS pain/injury as withdrawal for assessment is more easily planned. Opioids with less propensity to cause emesis (e.g., fentanyl, methadone, butorphanol) should be titrated cautiously in any trauma patient to avoid potential vomiting and wretching, which will cause a marked and sudden increase in intracranial pressure in patients with known, suspected or occult brain injury. The naloxone titration technique to reverse side effects of opioids is recommended (see Table 1). Buprenorphine OTM may be suitable for continuing home management for cats and small dogs.

NMDA antagonists

Low-dose ketamine is frequently used pre-, intra, and postoperatively to prevent[224] and treat neuropathic pain.[225,226] Following the administration of an opioid and an NSAID (when not contraindicated), an IV loading dose >0·5–4 mg/kg (to effect) of ketamine is administered, followed by a CRI 0·2–2+mg/kg/h. Amantadine (3–5 mg/kg once daily orally) may be continued after ketamine is discontinued for longer-term therapy at home.[227,]

Local anaesthetics

Lidocaine systemically administered has been shown to be effective in the treatment of several neuropathic pain disorders.[228,229] Lidocaine infusions should not be used in cats. Lidocaine 5% dermal patches may be of benefit where pain originates. Pharmacokinetic studies of the lidocaine patch in dogs are reported;[92] however, no analgesic efficacy studies have been reported in dogs or cats for IV infusions or transdermal patches for neuropathic or chronic pain.

Anti-epileptics

Studies in humans and laboratory animals indicate that perioperative administration of gabapentin to animals with nerve injury may reduce the potential establishment of, or ongoing, neuropathic pain.[230,231] Based on blood concentrations in dogs, dose at 10 mg/kg PO q8h (5 mg/kg PO q12h in cats), increasing as needed to effect (dose range 10–15 mg/kg in dogs). The dose limiting side effect is sedation. Some animals need several weeks to months for resolution of pain, or longer. A benefit of long term administration of gabapentin following trauma was reported in three cats;[109] however, to date there are no prospective veterinary studies investigating the long-term effects of multimodal analgesia including gabapentin.

Alpha$_2$ adrenoceptor agonists

Medetomidine and dexmedetomidine may be added to a multimodal regimen.[232,233] As an example, dexmedetomidine (1–2 μg/kg/h), in addition to low-dose fentanyl (3–4 μg/kg/h) and corticosteroids, can be effective for management of the severe pain associated with meningitis in the dog. Intra- and postoperative pain management for intervertebral disc herniation is another example. No observed adverse effects are noted at this low dose other than potential for increased urinary output.

Acupuncture and medical massage

These should be included in the analgesic regimen as soon as possible. Neuropathic pain is difficult to manage with pharmaceutical agents alone, therefore the use of acupuncture and other integrative techniques should be included as adjuncts to a multimodal pharmaceutical regimen.

Serotonin and norephinephrine re-uptake inhibitors

These (e.g., amitriptyline, dogs: 1–2 mg/kg orally q12–24h; cats: 2·5–12·5 mg/cat orally q24h, gabapentin [see above]) may be beneficial as a home medication in combination with those listed above, as the descending inhibitory system appears to be dysfunctional in neuropathic states.[234]

37. DEGENERATIVE JOINT DISEASE

The management of DJD has grown in complexity in the past decade, and there are many recommendations for treatment of the pain and dysfunction associated with this disease. These include, but are not limited to, surgical intervention, systemic analgesic therapy (NSAIDs, paracetamol [acetaminophen] [not in cats], corticosteroids), local pharmacologic therapy (transcutaneous; intra-articular), home-based exercises, clinic-based therapeutic exercises, weight optimization, nutritional supplementation, massage, acupuncture, laser therapy, heat/cold therapy, neuromuscular electrical stimulation, transcutaneous electrical stimulation and joint mobilization. However, it should be remembered that DJD in any patient is not a single 'type' of problem – indeed, it is now becoming recognized that DJD presents differently in the growing, versus middle-aged, versus older cat or dog. DJD presenting at different 'life-stages' requires different approaches to optimize care. For example, in the growing dog surgical intervention may be a first line treatment in an attempt to limit the disease progression and the likelihood of pain in the future.

Regardless of the stage of disease or the treatments selected, the veterinarian should aim to maximize the benefit and minimize the risks associated with managing this disease. The mainstays of treatment involve methods to alleviate pain, and at all stages NSAIDs are the most predictable analgesics.

In cats and dogs, the broad categories of treatments for OA pain can be summarized as:

Non-surgery, non-drug treatment

- Weight management
- Diet modulation (type; amount)
- Exercise
- Physical rehabilitation and physical modalities
- Environmental modification
- Nutritional supplements
- Acupuncture.

Drugs

- 'Base' analgesics
  - NSAIDs
  - Paracetamol (acetaminophen) (not in cats)
  - Corticosteroids (treating the underlying immune-mediated disease resulting in polyarthritis)
- Adjunctive analgesics (e.g. tramadol, amantadine, gabapentin, tricyclic antidepressants)
- Postulated disease modifying drugs (e.g. polysulfated glycosaminoglycan)
- Neuroablative procedures.

Surgery

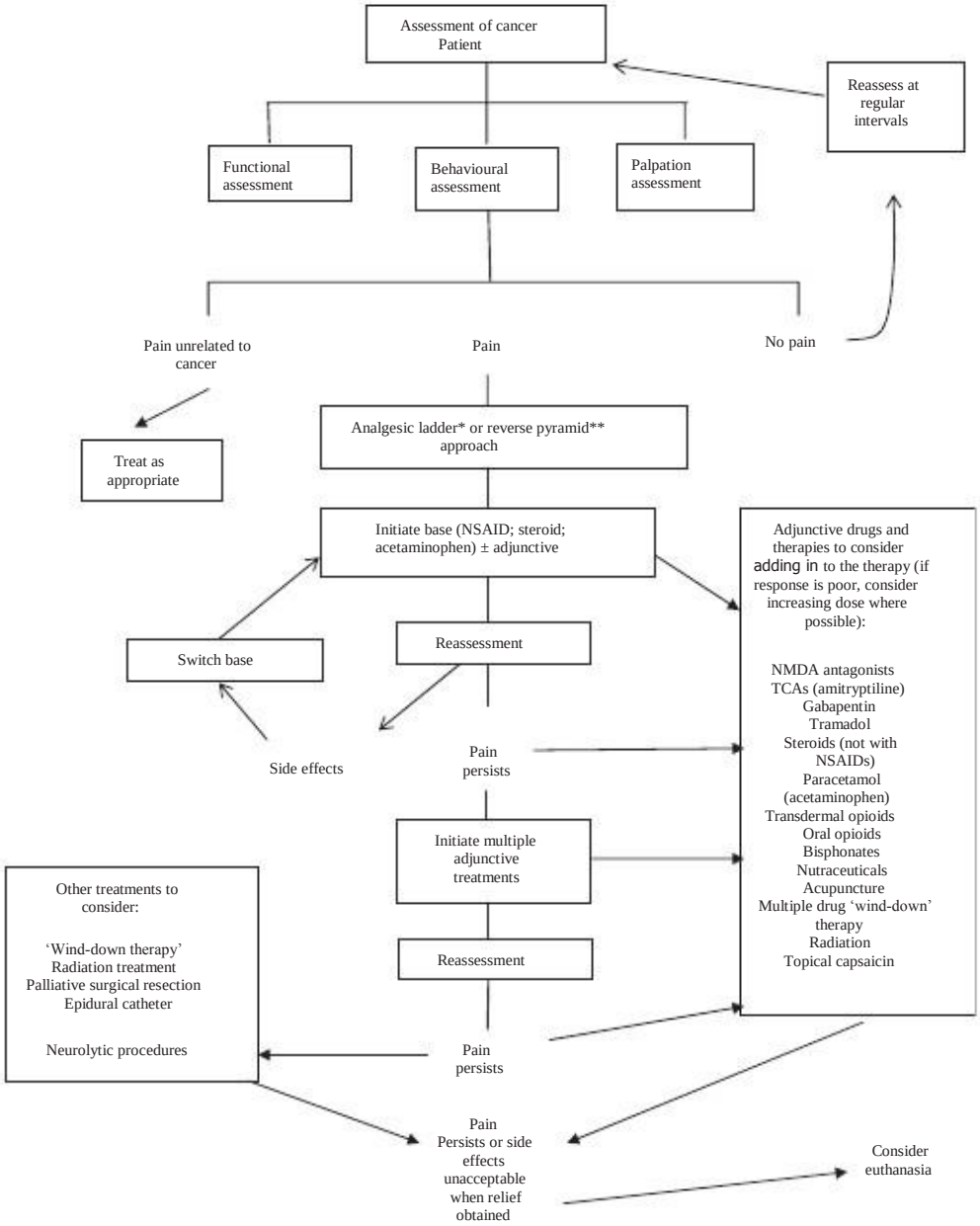
- Joint replacement (hip, elbow, knee)
- Excision arthroplasty
- Arthrodesis
- Joint dennervation
- Stem cell therapies.

Currently, the greatest weight of evidence for efficacy is for weight management, NSAIDs, dietary optimization (amount and content), and exercise.[134,235]

38. CANCER-RELATED PAIN

Cancer pain has varying degrees of severity that is dependent on duration, location and type of cancer. Inflammation due to tumour necrosis or direct pressure causes pain. Pain may originate from nerve root compression, from muscle spasms in the area of the lesions or directly from lesions, or from tissue that has been infiltrated. Most patients with cancer suffer pain to some degree. Some cancers such as lymphomas and leukaemia have a lower incidence of pain suffering in humans. However, even in these, the pain can be excruciating. The incidence and severity of pain associated with various cancer types in animals is not well documented.

One of the best documented is bone pain. Metastatic involvement of bone is a frequent cause of pain results from direct invasion of the bone, microfractures, increased pressure of endosteum, distortion of the periosteum or perilesional inflammation. Another important mechanism in the genesis of bone pain is the release of chemical mediators such as amines, peptides, fatty acids, potassium



* analgesic ladder, gradual addition of analgesic medications until adequate comfort is achieved
** reverse pyramid, initial aggressive multimodal approach, removing analgesic medications providing comfort maintained

Figure 7.

and prostaglandins. Cancer pain, and bone pain in particular, is often associated with neuropathic like clinical signs. Therapies that decrease tumour activity, are anti-inflammatory, or are targeted against the changes in neuropathic pain can all have efficacy in cancer pain.

A particular type of bone pain is called 'incident' or 'movement-related pain'. In humans, the pain is described as dull, constant and gradually increasing in intensity; movement and pressure worsen it. Incident pain usually has a sudden onset, reaching peak pain intensity within a few minutes and is a cause of breakthrough pain in a large number of human patients.

A multimodal drug approach to the control of cancer pain is recommended.[236-238] NSAIDs are recommended with the addition of opioids and adjunctive drugs (such as gabapentin) as needed. Other modalities that can prove beneficial are bisphosphonates (clodronate, disodium pamidronate, ibandronate), chemotherapy and radiotherapy. Non-drug therapies should be used concurrently. The combination of acupuncture with drug therapy appears to be superior to either alone.[239] Other forms of adjunctive therapy tend to improve quality of life in cancer patients, although it is not known if they directly induce analgesia.

The following algorithm is suggested (Figure 7). Dosages for analgesics selected can be found in the respective Sections.

39. WSAVA HUMANE EUTHANASIA OVERVIEW

The termination of companion animal life through euthanasia may be required for a variety of medical, behavioural, and animal population
control reasons. Key animal welfare concerns and issues relative to selection of the method for humane euthanasia are outlined as follows:

- Stress avoidance (where possible)
- Stress mitigation (where likely or inevitable):
  - Animals being euthanized are not viewed by other animals
  - Bodies of euthanized animals are not viewed by other animals
- Humane method (will vary based upon local availability of restraint/drugs):
  - Performed by competent, trained personnel
  - Giving due consideration to the safety of those performing euthanasia
  - Minimally painful/stressful for the animal being euthanized
  - Rapid
  - Reliable
  - Death confirmed before animal remains are disposed of
  - Minimizes distress to public
- Protocol without drug restrictions:
  - Pre-euthanasia sedation/tranquilization followed by IV lethal drug or mixture of drugs (e.g. acepromazine/alpha$_2$ may be administered via SQ/IM routes followed by IV pentobarbital overdose). IV bolus must be administered via IV catheter or after confirming venous access
  - In cases where pets are fractious/anxious, profound sedation may be followed by intraperitoneal injection of pentobarbital. Sedation must be adequate to abolish any reaction to needle puncture of the abdomen
  - Use of CO, CO_2 chambers, anoxia, foaming agents and cyanide are unacceptable when alternative methods of euthanasia are available
- Protocols where legal availability of drugs is restricted:
  - Profound sedation or anaesthesia followed by IV potassium chloride or magnesium sulfate, or gunshot
  - Gunshot (where sedation is not available this procedure must be performed by trained personnel)
- Remains removal management in large-scale euthanasia events ought to consider environmental/wildlife impacts:
  - Relative to tissue residues of injectable drugs
  - Relative to contamination of soil/groundwater with animal decomposition/waste
  - Relative to environmental impacts of cremation/open air cremation
  - Relative to public sentiment regarding animal disposition
  - Relative to possibility of other animals seeing, smelling or finding and eating the carcasses.

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Dietary supplements with potential benefits in pain management

Prepared by: Narda G. Robinson, DO, DVM, MS, DABMA, FAAMA
Director, CSU Center for Comparative and Integrative Pain Medicine, Assistant Professor, Department of Clinical Sciences, Founder and Director, Medical Acupuncture for Veterinarians Program

Nursing care as an adjunctive non-pharmacologic treatment for pain

Prepared by: Nicole DiPierre BA, RVT, CCRP, CCMT

Medical massage as an adjunctive non-pharmacologic treatment for pain

Prepared by: Nicole DiPierre BA, RVT, CCRP, CCMT

Physical rehabilitation for pain management

Prepared by: Sasha Foster, MSPT, CCRT

Perioperative analgesia for dental procedures

Reviewed by: Ian J. Haws, DVM, FAVD, DACVD
Animal Dental Care, Guelph, Ontario, Canada (animaldentalcare.com)

Perioperative analgesia for ophthalmic procedures

Reviewed by: Chantale Pinard DVM, MSc, DACVO
Assistant Professor – Ophthalmology, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada

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