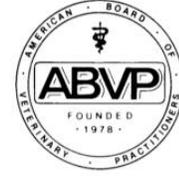




Recognition and Management of Pain in Cats

Susan Little, DVM, DABVP (Feline)
Bytown Cat Hospital, Ottawa, Canada
catvet@vin.com
@catvetsusan
<http://drsusanlittle.net>



Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (International Assoc. for the Study of Pain).

Pain is a component of many diseases and procedures in the cat and is an important welfare issue, but it has only been commonly discussed in recent years. Unfortunately, pain is still underappreciated and undertreated in cats. Studies in Canada and other countries show that cats receive analgesics less often than dogs and analgesia is often withheld for fear of adverse consequences. An important barrier is that recognizing the signs of pain and its impact on quality of life is challenging in cats. However, the effects of pain are detrimental to the animal's wellbeing in the short term, and pain interferes with healing and causes disease in the long term. Fortunately, therapeutic options have expanded as more pharmacological agents and adjunctive approaches are available.

Situations that require a pain management plan include:

- Peri-operative analgesia (before, during, and after surgery)
- Painful inflammatory or infectious conditions
- Non-surgical trauma
- Chronic painful conditions

Physiology of pain

Pain begins as a nociceptive stimulus (an event capable of damaging tissue, e.g., injury or surgical trauma) that is converted to an electrical signal (transduced) at the sensory receptor (nociceptor). The signal is then transmitted from the peripheral nerve via the spinal cord to the brain where pain perception occurs. The stimulus also produces an inflammatory response called peripheral sensitization where inflammatory mediators decrease the nociceptive threshold at the site of the injury. Understanding this 'pain pathway' allows clinicians to target multiple points with a combination of agents to produce effective analgesia.

If the nociceptive input persists so that the dorsal horn of the spinal cord receives repeated signals from the periphery, the spinal neurons become more excitable. This alteration in pain threshold over time is termed '**wind-up**'. Wind-up leads to central sensitization, so that the entire nervous system may become more sensitive. An increased sensitivity to noxious stimuli, either through a decrease in threshold or an increase in response, is called **hyperalgesia**. Hyperalgesia may be primary (at the original injury site) or secondary (distant from the original site). Hyperalgesia may be a useful mechanism to protect vulnerable tissues, but when it persists after the original cause of the pain has disappeared it becomes a disease in itself.

Sensitization of the central nervous system may contribute to **allodynia**, a painful response to a non-painful stimulus. It is caused by changes in the dorsal horn of the spinal cord so that non-noxious sensory information accesses the nociceptive system, causing the innocuous stimulus (e.g., a gentle touch or movement of air) to be perceived as pain. Both hyperalgesia and allodynia are notoriously difficult to treat, so that measures to prevent their establishment are important.

Adaptive pain is a normal consequence of injury and causes a protective response that results in withdrawal from or aversion to the pain-inducing event. Nociceptive pain and inflammatory pain (pain of healing) are types of adaptive pain. Adaptive pain contributes to survival by protecting the individual from further injury or promoting healing after injury by protecting the damaged tissues. If adaptive pain is not appropriately managed, neurophysiologic changes may occur that produce **maladaptive pain** – pain with no apparent cause or explanation that serves no purpose.

Neuropathic pain is an example of maladaptive pain. Neuropathic pain is initiated or caused by a lesion or dysfunction of the peripheral and/or central nervous system. Types of neuropathic pain in cats include diabetic neuropathy, spinal cord injury, orofacial pain syndrome, and cancer pain (e.g., compression of peripheral nerves by a tumor). Neuropathic pain is typically difficult to diagnose, chronic, severe, and difficult to treat.

Pain is a complicated multifactorial experience with sensory (how much the cat hurts), affective or emotional (how it makes the cat feel), and functional (impact on the cat's normal daily activities) components. Ideally, pain should be classified by the underlying causative mechanism (e.g., inflammatory or neuropathic). Identifying the underlying cause guides the choice of treatment; without this, treatment is empirical. The underlying cause may be simple or complex and some mechanisms of pain can co-exist, requiring several different treatment strategies. More information on this approach is found in the AAHA/AAFP pain management guidelines.

In addition to unnecessary suffering, inadequate pain management is associated with many detrimental effects in cats, including:

- Altered mentation (anxiety, lethargy, aggression)
- Inadequate nutritional intake leading to weight loss and a catabolic state
- Increase in stress hormones, leading to protein catabolism and delayed wound healing
- Impaired immune function, increased risk of infection
- Prolonged recoveries
- Impaired organ function, such as urine and fecal retention
- Self-mutilation of painful sites
- Altered physiological parameters that interfere with patient assessment

Signs of pain in cats

Signs of pain are more subtle in cats than in dogs and humans because cats may hide pain as a natural protective behavior. Cats should be considered similar to human infants, where pain evaluation is performed by assessing facial expression and body position. Physiologic parameters, such as heart rate, respiratory rate, blood pressure, and rectal temperature are poor indicators of pain in cats. The best way to assess pain in cats is to observe the patient before and during interaction and to evaluate body posture, facial expression, and response to handling, including palpation of surgical sites. Evaluations should be carried out repeatedly to monitor efficacy of analgesia and to determine if a change in the treatment plan is required. Ideally the same observer, which may be a trained veterinary technician, would score the patient during the entire hospitalization period.

Adult cats and seriously ill or obtunded patients are the most difficult to assess. Seriously ill cats may not be able to show behaviors associated with pain and yet may require management for severe pain. Adult cats are more stoic than kittens and their behavioral changes associated with pain may be subtle. As well, pain perception is an individual experience and behaviors vary among cats. Fear and stress may cause behaviors that are difficult to differentiate from pain. These factors make a standardized assessment of pain difficult in cats; there is currently no robustly tested or validated acute or chronic pain scale.

Visual analog or interactive visual analog scoring systems are available, and although not validated, they can be used by trained individuals. Return to normal behaviors is a sign of good pain control. Veterinary support staff can provide information on a patient's normal behavior before surgery and owners can provide valuable insight into what constitutes normal behavior for their cat at home.

Some indicators of pain in hospitalized cats include:

- Inability to sleep or rest
- Hiding in the back of the cage, reluctant to interact
- Change in attitude – anxious, irritable, aggressive or dull and quiet
- Reaction on palpation of a surgical site or affected organ (e.g., 'splinting', tensing, withdrawal, vocalizing)
- Change in facial expression – staring, dilated pupils, squinting
- Lack of food and water intake
- Lack of grooming
- Change in resting posture – hunched or lying flat out

Acute pain management

Peri-operative pain management is an important part of acute pain management in feline medicine. Other indications for acute pain management include cat bite wounds (cellulitis, abscess) as well as musculoskeletal injuries. Acceptance of the need for pain management is high among pet owners. Many minor and major surgical or diagnostic procedures in feline medicine will predictably cause some degree of pain. Unfortunately, some cats continue to be denied analgesia for procedures such as castration and many cats do not receive analgesia in the post-operative period even though pain can be expected to last for several days. Analgesia should never be an optional part of elective procedures where the owner is asked to accept or decline an extra cost. Whenever the clinician is unsure whether pain is present or may occur, it is humane to provide analgesia rather than withhold it until proof of pain is present. Whenever possible, validated pain assessment tools should be used. One such tool has been validated for assessment of postoperative pain in cats (UNESP-Botucatu multidimensional composite pain scale; see Resources).

Pain is easier to prevent than to treat. **Pre-emptive analgesia** is administration of analgesia before the painful stimulus occurs (e.g., before surgery and continuing into the peri- and post-operative periods), and is intended to prevent up-regulation of the CNS response to pain. A plan for analgesia is necessary because anesthetic agents are not analgesics – they simply prevent perception of pain while the animal is unconscious. **Multi-modal analgesia** is the use of more than one class of analgesic drug, thereby producing effects at multiple receptors to increase overall efficacy. Techniques such as local and regional nerve blocks or constant rate infusions (e.g., ketamine, morphine/lidocaine/ketamine, fentanyl, etc.) may be incorporated when appropriate. A multi-modal approach can be used for any type of pain (including chronic pain) and may allow for the use of lower doses of individual drugs. For example, an opioid (e.g., hydromorphone, buprenorphine) and a non-steroidal anti-inflammatory drug (e.g., meloxicam, robenacoxib) are often combined for feline elective procedures.

Several drugs (both licensed and off-label) are available for management of pain in cats (**Table 1**). Decisions about the most appropriate drug choices must take into account the status of the patient (e.g., renal, hepatic, intestinal function; hydration; concurrent diseases; severity of pain) and potential adverse effects of the drug. Each case should be assessed individually to determine the best analgesia plan. Patient and drug factors must be balanced against the danger of pain – uncontrolled pain sets in motion a cascade of detrimental effects that may increase morbidity and mortality.

Good nursing care is an important part of pain management for hospitalized cats. Patient comfort can be improved by providing soft bedding, warm water or warm air blankets to prevent hypothermia, a box or similar structure as a hiding place, quiet low stress environments, and respectful and gentle handling. Veterinary support staff, including veterinary technicians, plays an integral role in pain management through patient assessment and nursing care. More information is found in the AAFP/ISFM Feline-Friendly Nursing Care Guidelines.

Chronic pain management

Chronic pain (maldynia) serves no useful purpose and is considered a disorder in its own right. It has several definitions in human medicine: pain lasting longer than 1 month after healing of an injury, pain that recurs or persists over a period of 3 months or longer, or pain related to an injury that is expected to continue and/or get worse. It may be continuous or intermittent, and frequently leads to sleep disturbances, weight loss, and depression. Chronic pain accompanies many diseases in cats, including interstitial cystitis, neoplasia, dental and oral diseases, gastrointestinal disease, degenerative joint disease, and diabetic neuropathy. For some diseases, the treatment itself may cause pain (e.g., radiation damage or chemotherapy-induced neuropathy). Whenever possible, both the disease itself and the pain that is associated with it must be addressed. In some cases, such as arthritis, little can be done to slow or reverse the disease process, so the primary focus is to relieve pain.

Chronic pain is often slow and insidious in onset so that the accompanying behavioral changes can be subtle and easily missed. It can be difficult to be certain a cat is painful based on clinical assessment and owners may be convinced that some of the changes are just part of “getting old”. An analgesic trial can be helpful in these cases and should always be considered. A useful tool for the assessment of chronic pain (feline musculoskeletal pain index; see Resources) is in the process of being validated.

Periodically asking these questions and recording the answers is important for tracking response to therapy in chronic pain management. It can also be useful if the owner keeps a diary to note appetite, mobility, activity, grooming, and temperament and to compare entries over time. Having a written account can help monitor response to treatment. Needless to say, asking questions/reviewing the answers, performing a thorough physical examination, and reviewing the medical history will take time and appointments for cats with chronic diseases causing pain should be 20-30 min or more in length.

Treatment goals should be clear – in dealing with chronic pain, clinicians may be attempting to improve quality of life more than quantity of life. A goal should be restoring normal daily activities and normal behavior. Chronic diseases are not static, so that the treatment plan may need to be reviewed and adjusted periodically.

Environmental modification and enrichment may be an important component of treatment for cats with chronic disease. For example, cats with arthritis will benefit from gentle exercise, which can be increased by designing a complex environment (e.g., using cat towers, toys, hiding food to encourage foraging and hunting behavior). Ramps or steps may be useful to help the cat reach higher perches, such as window ledge. Litter boxes should be on the same level of the home where the cat spends most of its time, and should have low sides and be easy to get in and out of. It may help to elevate food and water bowls. Physical rehabilitation techniques including controlled exercise, passive range of motion exercises, and massage can be adapted from canine medicine. The benefits of these treatment strategies have not yet been evaluated in feline medicine. As well, studies evaluating the efficacy of acupuncture and laser therapy for pain management in cats are lacking.

Responsible use of NSAIDs in cats

NSAIDs reduce fever, pain, and inflammation by blocking COX enzymes. While NSAIDs vary in their selectivity for COX enzymes, the COX profile is not well understood for some products

used in feline medicine. Inhibition of COX-1 is reported to be the cause of most adverse effects such as gastric ulcers and blood dyscrasias. COX-2 preferential/selective drugs may be associated with fewer adverse effects, particularly on the gastrointestinal system. However, no NSAID is risk free. One problem in assessing risk of adverse effects is that species differences are recognized and very little feline-specific data are available. Another problem is that reported COX profiles vary with the type of assay used to measure activity. Patient selection, appropriate dosing, use of the lowest effective dose, and monitoring for early signs of toxicity are important in the use of all NSAIDs in cats.

Responsible use of NSAIDs includes administration of products licensed for use in cats and for the label indications whenever possible. However, licensing varies considerably from country to country. Pre-treatment laboratory evaluation is recommended to detect cats that are not suitable for NSAIDs. At a minimum, evaluation for healthy surgical patients should include BUN, creatinine, hematocrit, and total plasma protein. Evaluation of urine specific gravity is also helpful. For surgical patients, adequate anesthesia monitoring is a key component for safe use of any drug. Preventing hypoperfusion, hypovolemia, hypotension, and hypothermia improves outcomes. Post-operative treatment with NSAIDs should be with the same drug used initially as there are no data available on appropriate washout periods between different drugs in cats. Before long term therapy with an NSAID is started, patients should have a thorough physical examination, CBC, chemistry panel, and urinalysis. Risk of adverse effects is highest in older cats, cats receiving multiple drug therapies, and cats with renal, hepatic, cardiovascular, or gastrointestinal disease. In addition, NSAIDs should not be used concurrently with certain drugs, such as diuretics and corticosteroids. An initial re-assessment should be performed about 1 week after starting therapy and again about one month later. Thereafter, regular monitoring should occur during long term therapy (e.g., every 2-6 months), although the frequency will be dictated by factors such as the perceived risk for the individual patient, financial constraints of the owner, and owner compliance. The risk of adverse effects may be minimized by reducing the dose and frequency of administration to the lowest possible to control pain. Owners should always be informed of possible adverse effects and what signs to monitor for (e.g., vomiting, inappetence, lethargy) that warrant calling the veterinarian and stopping treatment. Information sheets for owners are available from drug manufacturers and in the ISFM/AAFP consensus guidelines on long-term use of NSAIDs in cats.

Table 1: Examples of drugs for treatment of acute and chronic pain in the cat

Drug and class	Dose (mg/kg)	Comments
Amantadine - NMDA antagonist	3-5 mg/kg, PO, q24 hrs	Has not been evaluated for toxicity in the cat. It may be a useful adjunct to NSAIDs in the treatment of cancer related pain and degenerative joint disease.
Amitriptyline - Tricyclic antidepressant	0.5-2.0 mg/kg, PO, q24 hrs	Well tolerated in cats. Somnolence (<10% of cats), weight gain, decreased grooming, and transient cystic calculi have been reported.
Buprenorphine - Opioid	Oral transmucosal, IV, IM, SC: 0.01-0.02 mg/kg, q8 hrs, or as needed Sustained release: 0.12-0.2 mg/kg SC q3 days	The oral transmucosal route is well tolerated by most cats, takes effect in 20-30 min. Vetergesic Multidose (10 mL) is reported to be more difficult to administer orally than single-use formulations without preservative.
Hydromorphone - Opioid	0.03-0.1 mg/kg, SC, IV, IM, q2-6 hrs	May cause hyperthermia and vomiting Opioid reversal (also reverses analgesia): naloxone 0.01 mg/kg, IM, SC IV buprenorphine may be used to counteract hyperthermia while maintaining analgesia
Transdermal fentanyl patch - Opioid	Average cat (3.5-5.0 kg): 25 µg/hour patch Smaller cats: 12.5 µg/hour patch	Uptake is highly variable. Time to onset of action is 6-12 hours. The patches may provide 3-5 days of analgesia in some cases. Following removal at 3 days, the decay in plasma levels following patch removal is slow. Liability issues should be considered when these are used in a home setting. Do not use in cats receiving psychoactive drugs. Do not use in combination with tramadol.
Gabapentin - Antiepileptic	3-10 mg/kg (or higher), PO, q12 hours	Effective adjunctive drug in cats where the underlying cause of pain is neuropathic.
Meloxicam (Metacam) - NSAID	Licensed in cats (Canada) <u>Injectable 5 mg/mL:</u> (peri-operative pain) 0.2 mg/kg SC or less before surgery, fluid therapy recommended <u>Oral suspension 0.5 mg/mL:</u> <i>Post-surgical pain:</i> 0.05 mg/kg, start 24 hrs after injectable dose, give q24 hrs for up to 2 more days <i>Acute, mild to moderate musculoskeletal disorders:</i> initial oral dose 0.1 mg/kg, followed 24 hrs later by 0.05 mg/kg q24 hrs for up to 4 more days.	COX-2 selective, preferential accumulation in inflamed sites, metabolized via oxidation, easy to titrate to lowest effective dose for chronic use. Owner education on risks and benefits of NSAID therapy is necessary. Chronic musculoskeletal pain label in other countries: <u>Oral suspension 0.5 mg/mL:</u> 0.1 mg/kg on day 1, followed 24 hrs later by 0.05 mg/kg q24 hrs; lower doses & every other day dosing can be effective
Robenacoxib	Licensed in cats (Canada)	First coxib licensed for cats (i.e., COX-2

<p>(Onsior) - NSAID</p>	<p>For acute pain & inflammation from cat bites/scratches, abscesses, musculoskeletal injuries; in cats over 2.5 kg and over 6 mths of age</p> <p><u>Tablet 6 mg</u>: 1 mg/kg (range 1-2.4 mg/kg), q24 hrs, up to 6 days</p>	<p>specific/COX-2 preferential/COX-1 sparing), preferential accumulation in inflamed sites. Palatable yeast-flavored tablet. Owner education on risks and benefits of NSAID therapy is necessary.</p> <p>Injectable 20 mg/mL licensed for dogs</p>
<p>Ketoprofen (Anafen) - NSAID</p>	<p>Licensed in cats (Canada) For musculoskeletal pain, trauma, post-surgical pain, fever <u>Injectable 10 mg/mL, tablet 5 mg</u>: 2 mg/kg SC once, followed 24 hrs later by oral 1 mg/kg q24 hrs for 4 more days</p>	<p>No published data on COX profile in cats, best reserved for post-operative use as it affects platelet function. Owner education on risks and benefits of NSAID therapy is necessary.</p>
<p>Tolfenamic acid (Tolfedine) - NSAID</p>	<p>Licensed in cats (Canada) For fever and upper respiratory diseases <u>Tablets 6, 20, 60 mg</u>: 4 mg/kg q24 hrs for 3-5 days</p>	<p>COX profile & pharmacokinetics poorly described in cats, concentrated in many organs including kidneys, caution with pre-surgical use due to significant anti-platelet activity. Owner education on risks and benefits of NSAID therapy is necessary.</p> <p>Manufacturer issued warning in October 2011 about adverse effects when used in kittens.</p> <p>Injectable 40 mg/mL not licensed in cats</p>
<p>Tramadol - Mixed analgesic</p>	<p>1-2 mg/kg, PO, q12-24 hrs</p>	<p>Metabolism is slower in the cat than the dog, and the production of the M1 metabolite is very much greater, leading to a greater tendency to see 'opioid' like side effects (pupil dilation, euphoria). Very unpalatable even when compounded. Do not use in cats receiving psychoactive drugs.</p>
<p>Maropitant (Cerenia) - NK-1 antagonist</p>	<p>Injectable 10 mg/mL Tablet 16 mg 0.5-1 mg/kg SC, PO q24 hrs</p>	<p>Blocks the action of substance P (neurokinin 1), may provide analgesia for nociceptive (somatic and visceral) pain, marked variation in individual responses.</p>

Recommended reading

- Bortolami E, Love EJ. Practical use of opioids in cats: a state-of-the-art, evidence-based review. *J Feline Med Surg* 2015, 17(4):283–311. <http://www.catvets.com/guidelines/practice-guidelines/pain-management-guidelines>
- Carney HC, Little S, Brownlee-Tomasso D, et al. AAFP and ISFM Feline-Friendly Nursing Care Guidelines. *J Feline Med Surg*. 2012; 14: 337-49. <http://www.catvets.com/professionals/guidelines/publications/>
- Epstein ME, Rodan I, Griffenhagen G, Kadrlík J, Petty MC, Robertson SA, et al. 2015 AAHA/AAFP Pain Management Guidelines for Dogs and Cats. *J Feline Med Surg* 2015;17(3):251–72. https://www.aaha.org/professional/resources/guidelines_and_implementation_toolkits.aspx
- Gurney MA. Pharmacological options for intra-operative and early postoperative analgesia: an update. *J Small Anim Pract*. 2012; 53: 377-86.
- McKune C and Robertson S: Analgesia. In Little S (editor): *The Cat: Clinical Medicine and Management*, St. Louis, 2012, Saunders Elsevier.
- Meintjes RA. An overview of the physiology of pain for the veterinarian. *Vet J*. 2012; 193: 344-8.
- Robertson S: Palliative medicine: pain assessment and management. In Little S (editor): *The Cat: Clinical Medicine and Management*, St. Louis, 2012, Saunders Elsevier.
- Sparkes AH, Heiene R, Lascelles BDX et al: ISFM and AAFP consensus guidelines: Long-term use of NSAIDs in cats, *J Feline Med Surg* 12: 521, 2010. <http://www.catvets.com/professionals/guidelines/publications/>
- WSAVA Global Pain Council Guidelines for Recognition, Assessment, and Treatment of Pain (2014): <http://www.wsava.org/guidelines/global-pain-council-guidelines>

Resources

- UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats: <http://www.animalpain.com.br>
- Feline musculoskeletal pain index, North Carolina State University: <http://www.cvm.ncsu.edu/docs/cprl/fmpi.html>
- Cat Healthy: Pain assessment and management: <http://www.cathealthy.ca>
- International Veterinary Academy of Pain Management: <http://ivapm.evetsites.net/>
- Veterinary Anesthesia & Analgesia Support Group: <http://www.vasg.org/>
- American Animal Hospital Assoc. client handout – **How to Tell if Your Cat is in Pain**: https://www.aahanet.org/graphics/CustomContent/Cats_in_Pain_Client_Handout.pdf
- Novartis Animal Health – **Identifying Pain in Your Cat**: <http://www.onsior.com/cat/identifying/>
- **Boehringer Ingelheim – Arthritis and Your Cat**: <http://www.metacam.co.uk/cats/cats.html>