

Peer Reviewed

Pain Management in Cats

PROFILE

Definitions

- Pain is an aversive sensory experience that causes response with protective motor actions, resulting in learned avoidance of the experience.¹ In addition to the sensory experience, there is an affective/emotional component.²

- *Adaptive pain*, which is defined as an appropriate hypersensitive response to a potentially damaging stimulus, is responsive to medication.³

- *Maladaptive pain* (commonly referred to as wind-up pain), defined as spontaneous hypersensitivity resulting from abnormal processing of a stimulus by the central nervous system (CNS), does not respond to treatment.³

- *Allodynia* is pain caused by a stimulus that

does not normally provoke pain, according to the International Association for the Study of Pain.⁴ Allodynia can be a component of maladaptive pain.²

- In cats, assessment of pain sensation cannot

be determined by measuring plasma cortisol or beta-endorphin concentrations.⁵

- Heart rate, respiratory rate, body temperature, and response to approaching humans or to stroking cannot be used reliably to determine amount of pain being experienced.⁵

- Postoperative pain can be assessed by response to palpation, or by a visual or interactive analog scale.⁵

- Incidence of clinical signs of degenerative joint disease or osteoarthritis in younger cats is estimated to be 34%; incidence in geriatric cats (15 years and older) increases up to 90%. Pain associated with interstitial cystitis may be more prevalent than previously thought because outward signs (eg, urinating outside the litter box) may not always be present.^{6,7}

Causes & Risk Factors

- Acute pain in cats is most commonly associated with trauma or postoperative pain. Other causes (eg, lower urinary tract disease, pancreatitis, inflammatory bowel disease, cholangiohepatitis, pleuritis, upper respiratory tract infections, and obstruction) should be investigated if the cause is not readily apparent.

CONTINUES

FIND MORE

Go to page 24 to see **Determining Pain Scores in Cats** or download it at cliniciansbrief.com.

CNS = central nervous system

- Causes of chronic pain are varied but may include degenerative joint disease, dental and gum disease, neoplasia, interstitial cystitis, dermatitis, and chronic wounds.⁸
- Risks for acute or chronic pain vary according to cause of the pain stimulus, but the risk for chronic pain increases with age.
- Risk for maladaptive pain increases when adaptive pain is not appropriately managed.

Pathophysiology

- Maladaptive pain develops when adaptive pain is untreated for a prolonged period, resulting in sensitization of dorsal horn neurons. Maladaptive pain may be present with or following resolution of adaptive pain.
- As the threshold for pain sensation is lowered, wind-up pain develops in both the peripheral and central nervous systems. Pain wind-up can worsen acute pain and cause chronic maladaptive pain.
- Nociceptors throughout the body can convert a chemical, thermal, or mechanical stimulus into an electrical impulse through a process termed *transduction*. This impulse is transmitted from the periphery to the dorsal horn of the spinal cord, then the brain and thalamus, and finally the cerebral cortex.⁹

Signs

Acute Pain

- Hiding or holding head down, squinting the eyes (**Figure 1**)
- Licking or biting the surgical site
- Hunched back, resisting movement
- Ignoring attempts by humans to interact
- Not urinating (even with a full bladder), eating, or drinking^{8,10}

Cats in acute pain hold their heads down and squint their eyes, or they may hide their heads. When in a crate or cage, they often have hunched backs and do not move around or respond to humans.



Chronic Pain

Signs of chronic pain in cats may be markedly different from those seen in dogs. Cats that demonstrate aggression or have pain that does not respond to opioids or NSAIDs may have maladaptive pain.

- Changes in behavior—less social with owners, aggression toward members of the household, urinating outside litter box
- Decreased appetite, weight loss, and disinterest in normal activities; however, these signs have many causes¹¹
- Signs of chronic pain attributed to “normal aging” include increased sleeping; decreased jumping, climbing, or overall activity; and reluctance to be petted¹⁰

DIAGNOSIS

- Diagnosing the cause of pain is important to its elimination or, at least, to its control. Repeated examinations are vital to anticipate changes needed in pain management (**Figures 2 and 3**).
- Pain management may need to change with progressive diseases (eg, osteoarthritis, cancer, intervertebral disk disease) or in hospice patients.²
- Owners should learn the signs of pain in cats and how these differ from signs in dogs. In some cases, clinic visits for repeat examinations to assess effectiveness of pain management stress the cat extensively; the owner’s assessment of the cat’s comfort level may be employed in those cases.

TREATMENT

Precautions

Compared with other species, cats have fewer hepatic phase II enzymes (such as uridine 5-diphosphate-glucuronosyltransferase); therefore, they cannot metabolize drugs that are excreted as glucuronide conjugates.⁸ Consequently, some dosages and dosing intervals may be very differ-

ent in cats compared to dogs. For example, drugs such as acetaminophen (paracetamol) are toxic to cats. Several NSAIDs are also very slowly metabolized and should be avoided.

Analgesia Strategies

Perioperative Analgesia

Opioids may reduce anesthetic requirements in patients undergoing elective surgery. Local anesthetics and perioperative NSAIDs not only prevent acute pain but also decrease the risk for maladaptive pain.² However, clinicians must account for risks associated with preexisting conditions, such as liver disease, renal disease, gastrointestinal disorders, blood clotting abnormalities, and drug hypersensitivities.

Postoperative Analgesia

For many procedures, pain continues beyond the first 12 to 24 hours. Abrupt cessation of analgesia can result in maladaptive pain and delayed healing and recovery from surgery. After the patient is stable and can eat/drink following surgery, pain management should be modified to a regimen that can be continued by the owner. This allows the practitioner to assess the efficacy of the analgesic protocol and make adjustments as necessary before sending the patient home.

Chronic Pain Analgesia

- **NSAIDs**, such as meloxicam, can control chronic pain and improve quality of life for many cats.
- Anecdotal reports suggest that the NMDA antagonist **amantadine** may also be useful for treating chronic and maladaptive pain.
- **Gabapentin**, which inhibits not only neuropathic pain but also pain associated with inflammation,¹² has been used with some success in cats with lumbar nerve root entrapment due to fractures or degenerative disk changes. I have also had success using it (3 mg/kg PO Q12 H) to relieve pain associated with feline osteoarthritis.
- **Amitriptyline**, a tricyclic antidepressant, may



Cats with well-managed postoperative pain will look at an observer but not move away as the person approaches or touches the operative site. Mydriasis can occur secondary to opioid administration.



This cat has a chronic condition that is well managed as seen here by its ability to rest comfortably, face outward in the cage, and not move away as an observer approaches.

offer another mode of treatment for chronic pain associated with osteoarthritis and inflammatory bowel disease.

MEDICATIONS

Opioids

Due to genetic variability of opioid receptors, one opioid may work well as an analgesic in one cat but not in another.^{8,13,14} Following declaw surgery, an opioid (such as buprenorphine) may be more effective than an NSAID.

- **Hydromorphone**: Shown to cause nausea and vomiting in cats, especially when administered subcutaneously.¹⁵ Has been associated with elevated body temperature up to 108.5° F at doses of 0.1 mg/kg; lower intravenous doses (0.025–0.05 mg/kg) do not produce such increases but may not provide sufficient pain relief.⁸ Morphine is not frequently used in cats because it also causes vomiting and has a slow onset of action.^{8,16}
- **Oxymorphone**: Provides excellent analgesic effects that may be enhanced by addition of acepromazine.¹⁷ Hyperthermia is not commonly encountered at low doses.

CONTINUES

NMDA = N-methyl-d-aspartic acid; NSAID = nonsteroidal antiinflammatory drug

FIND MORE

See Aids & Resources, back page, for references & suggested reading.

Oxymorphone may be used with intravenous medetomidine, an alpha-2 adrenoceptor antagonist, for sedation.

- **Butorphanol:** Effective for visceral but not somatic analgesia. Reported to be effective for pain related to interstitial cystitis; however, its ceiling effect prevents dose increases from producing greater analgesia.¹⁴ Butorphanol's duration of action is less than 90 minutes when given intravenously. Oral administration is possible, but the tablet may be difficult to administer; there are also no published data on the bioavailability of butorphanol following oral administration in cats.⁸
- **Buprenorphine:** Available as a liquid that is absorbed by transmucosal uptake; has excellent bioavailability. Analgesia can last 6 hours regardless of the route of administration.
- **Fentanyl transdermal patches:** Used in cats; however, the plasma concentrations achieved are variable; some may never achieve an analgesic concentration.¹⁸ Cats must be monitored closely for signs that pain is adequately controlled.
- **Tramadol:** Oral tramadol (10 mg/kg) was shown to lower minimum alveolar concentration (MAC) of sevoflurane in cats if given 5 minutes before induction; however, some cats vomited or hypersalivated following administration of this high dose.¹⁹ Further investigation is needed before it can be recommended. Oral tramadol is bitter and can be difficult to administer.

NSAIDs

For soft-tissue surgery (eg, ovariohysterectomy), an NSAID, such as meloxicam or ketoprofen, may provide adequate analgesia.^{8,20}

NSAIDs inhibit cyclooxygenase (COX) enzymes 1 and 2 with variable effects on gastric mucosal integrity, platelet function, and renal autoregulation. Because many are metabolized by glucuronidation in the liver (except for meloxicam, which undergoes oxidation), frequent dosing may cause drug accumulation and toxicity.⁸

Long-term meloxicam use for chronic pain in cats is not approved by the FDA (only a single dose is approved); however, long-term use at the lowest possible dose can provide improved com-

fort in cats. I monitor renal function, hepatic enzyme levels, and packed cell volume monthly to detect early signs of toxicity. If gastrointestinal erosions are suspected (due to decreases in packed cell volume and diminished liver or renal function), discontinuation of therapy is recommended.

- **Carprofen:** Has a highly variable half-life of anywhere from 9 to 49 hours depending on the individual cat; it is not recommended.^{21,22} However, it has been approved for use in other countries and may be effective when administered as a single dose.
- **Meloxicam:** A COX-2 selective NSAID that may be used for postoperative pain or chronic pain. In my experience, meloxicam combined with buprenorphine can provide adequate postoperative analgesia, and most owners are able to administer these medications at home. Studies have shown that as many as 18% of cats can develop gastrointestinal upset while receiving meloxicam, but generally these effects are not sufficiently severe to require withdrawal of the medication.^{23,24} Low-dose oral meloxicam has been shown to be effective for osteoarthritis pain in 85% of cases.^{8,25} Cats had no signs of renal side effects after 5 months of continuous use, although 4% did develop gastrointestinal upset.²⁵ In cats with normal serum biochemical profiles, I use an induction dose of 0.1 mg/kg, then 0.1 mg per cat Q 24 H thereafter while monitoring blood analysis monthly.

NMDA Antagonists

- **Ketamine:** Most widely recognized NMDA antagonist. Has analgesic properties that specifically inhibit central sensitization, or wind-up pain, and maladaptive pain. Low-dose infusions of ketamine produce analgesia; however, it can cause significant hyperalgesia in cats that are not experiencing painful stimuli.²⁶ Since effects of ketamine in cats have not been clearly defined, its use in clinical settings may not be warranted postoperatively, but it may be used as a component of anesthesia induction protocol.
- **Amantadine:** Has been reported to successfully control chronic pain in cats and may be better suited for maladaptive chronic pain than other

COX = cyclooxygenase;
CRI = constant rate infusion;
FDA = Food & Drug Administration; MAC = minimum alveolar concentration; NMDA = N-methyl-D-aspartic acid; NSAID = nonsteroidal antiinflammatory drug

analgesics.^{8,11,27} Amantadine is excreted unchanged in the urine, so the duration of action is prolonged in cats with renal insufficiency; the toxic dose in cats is 30 mg/kg. Side effects that can occur with lower doses include anxiety, restlessness, and dry mouth. Amantadine has been used with NSAIDs in dogs to treat pain associated with osteoarthritis and osteosarcoma; there are anecdotal reports of its successful use in cats with similar conditions.^{8,12}

Gabapentin

Gabapentin's mechanism of action is unknown, but it has been used adjunctively to treat neuropathic and inflammation-associated pain in humans. It has also been used in combination with an NSAID to manage osteoarthritis in dogs¹² and has been successfully used alone in cats for pain associated with lumbar nerve root entrapment from fractures or degenerative disk disease.²⁸ Because gabapentin is excreted in the urine, dosage and frequency must be adjusted for patients with renal insufficiency.²⁸ I successfully treated a cat that had osteoarthritis-related pain and chronic liver disease with a combination of gabapentin (3 mg/kg PO Q 12 H) and meloxicam (0.1 mg PO Q 4 days).

Tricyclic Antidepressants

Pain associated with interstitial cystitis has been successfully treated with amitriptyline, but some cats may have subsidence of clinical signs within several days even when no treatment is administered. Amitriptyline may have some benefit in the treatment of chronic pain from osteoarthritis or inflammatory bowel disease, but more research is needed to assess its efficacy for these conditions.⁸

FOLLOW-UP

Patient Monitoring

Cats receiving chronic analgesic therapy should have physical examinations, complete blood counts, urinalyses, and serum biochemical profiles performed once monthly or more frequently if they have concurrent chronic illnesses, such as renal or liver disease. Treatment of the underlying condition is always the foremost concern, and response to that treatment ultimately determines the prognosis.

TX AT A GLANCE

<i>Drug</i>	<i>Dose</i>
Amantadine	3–5 mg/kg PO Q 24 H
Amitriptyline	2.5–12.5 mg per cat PO Q 24 H
Buprenorphine	0.005–0.02 buccally, IM, IV, SC Q 6–12 H
Butorphanol	0.2–0.4 mg/kg IM, IV, SC Q 1–4 H or 0.5–1.0 mg/kg PO Q 6–8 H
Fentanyl	2–4 mcg/kg IV (CRI) Q H or 12.5–25 mcg (transdermal patch) Q H
Gabapentin	2.5–5 mg/kg PO Q 12 H
Hydromorphone	0.025–0.05 mg/kg IV, IM Q 2–4 H (poor analgesic effect at this dose)
Ketamine	0.1–0.3 mg/kg IV (CRI) Q H or 0.1–1 mg/kg IM, SC Q 4–6 H
Meloxicam	0.1 mg/kg PO single dose, then 0.01–0.03 mg/kg PO Q 24–96 H
Oxymorphone	0.01–0.03 mg/kg IM, IV, SC Q 2–6 H Given with medetomidine (0.01 mg/kg IV) for sedation

COMPLICATIONS

Long-term use of any analgesic requires careful monitoring because agents used may not remain effective as the disease being treated progresses. Gastrointestinal upset, renal disease, liver disease, and other complications may develop over time and require drug doses or dosing intervals to be adjusted accordingly. Occasionally, drugs may have to be discontinued.

FUTURE CONSIDERATIONS

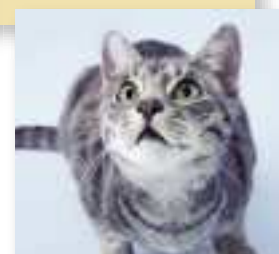
In the future, more options will become available to veterinarians for the treatment of pain in cats; however, these drugs must be adequately investigated for safety and efficacy before they can be recommended for widespread use. Until then, recognizing pain in cats is the first challenge to overcome, followed by adequately treating that pain.

IN GENERAL

Relative Cost

Management of acute pain (perioperatively or postoperatively): \$–\$\$\$ (depending on treatment plan used, cause of the pain, and duration of treatment)

Management of chronic pain: \$–\$\$\$ monthly (depending on medications)



Cost Key

\$ = < \$100
 \$\$ = \$100–\$250
 \$\$\$ = \$250–\$500
 \$\$\$\$ = \$500–\$1000
 \$\$\$\$\$ = > \$1000