CHALLENGES OF PERIOPERATIVE FELINE PAIN MANAGEMENT
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There are a number of factors that make cats different from dogs in terms of pain management, but there are more similarities than differences. The magnitude of pain experienced depends to a large extent on the type and degree of tissue injury and severity / extent of the inflammatory process. Experience has led to the generation of opinion-based tables ranking pain severity for animals, but observation of the individual patient’s response to analgesia is the only way to accurately gauge the painfulness of the condition. More severe pain means that analgesic needs will be greater, with need for stronger opioid type and higher doses, for multiple drugs classes (multimodal) therapy, and for potentially longer duration of treatment.

Premedication protocols that produce sedation are advantageous in healthy non cooperative cats to reduce the stress and pain involved with handling. It is essential to realize that when opioids, ketamine, or alpha 2 agonists are used prior to or during general anesthesia, the requirement for inhalant and injectable anesthetics can be significantly lessened. If this is not taken into account by reducing anesthetic doses, extreme anesthetic depth can lead to depression of respiration and cardiac output; risking morbidity or death. Decreased blood flow to the kidney, in combination with NSAID therapy risks nephrotoxicity.

For relatively minor pain, a single agent and even as few as one administered dose might be sufficient. Opioid-only, NSAID-only, or local anesthesia-only therapy may be used, depending on the situation. Many veterinary clinical pain studies have only evaluated single agent therapy and these may compare drugs of two different types (e.g. buprenorphine versus meloxicam). As the magnitude of pain increases, there is a necessity for adding a second type of analgesic. Multimodal analgesia is thus becoming widely appreciated in veterinary medicine. Some of the advantages are that drugs with longer actions (e.g. NSAIDS) may supplement during “troughs” in levels of another drug (opioid), or that if one drug is given at sub-therapeutic dose, the other may help to make up for this inefficacy.

Bandages, drains or splints, full bladder and stomach, gastric and esophageal ulceration may also contribute to acute pain; adjustments and supportive measures may result in relief and so it is important to realize that the injured body part may not be the only cause of pain. When pain is of a greater magnitude or duration than expected, despite attempts to treat it, one very important consideration is that healing is not progressing normally. In the author’s experience, in cats, this is a reason to suspect one of several complications; these include wound infection or dehiscence, nerve impingement by implants, sutures, fracture, ischemia, bandage or splint associated pain, neuroma formation, gastric or esophageal ulceration, bladder atony, cystitis, or urinary retention, delayed gastric emptying and pancreatitis. When pain is greater than expected, a thorough physical exam is mandatory and may require additional diagnostic testing.

Fear, anxiety and pain often make cats difficult to handle and to complicate the hospital experience. Thus pharmacologic and non-pharmacologic methods of reducing anxiety or fear may play a role in the overall amount of pain and stress. Anxiolytic medications, despite being considered devoid of analgesic properties, are arguably useful adjuncts in managing pain. Acepromazine may be given with the understanding that if significant untreated pain is present, the preferred option is to increase analgesia first. Alpha 2 agonists have both sedative and analgesic properties and are commonly used around the time of surgery or painful procedures. They can be given by infusion to those animals deemed to require both analgesia and sedation.
post surgically or after trauma, keeping in mind that some physical conditions might contraindicate the use of these drugs (i.e. cardiac insufficiency, shock).

A “fixed dose” opioid can be problematic, the dose may have to be increased to achieve the desired effect. So when an opioid is chosen from a dose table for a particular animal, it should be kept in mind that additional increments may be needed as one observes the analgesic effect and it is this “total” dose can be given going forward until pain levels decrease. Administration of an opioid at the time of surgery or after trauma is usually initiated by giving the drug intravenously or intramuscularly, however, oral-transmucosal delivery of buprenorphine in the cat results in rapid and thorough absorption and so this is a potential alternative route for this species. Subcutaneous injection of opioids is becoming recognized as suboptimal in terms of consistency of effect and duration. *Buprenorphine* is an opioid with a long expected duration – some reports indicate that doses may last for 8 – 12 hours, but this, too is often not the actual experience unless the dose is increased. The author commonly uses buprenorphine at 0.02 mg/kg in cats (and higher in some situations). Owners may be instructed to give oral transmucosal buprenorphine in the cat, when it is useful to continue opioid therapy treated at home. *Tramadol*, with its opioid-like effect has been prescribed for oral administration in cats. Some drawbacks to oral tramadol are that it is bitter tasting and many cats object strenuously after tasting it once, and also, we do not have good clinical efficacy data for oral use in cats for pain.

Clinical efficacy data are presently somewhat limited for *transdermal fentanyl* in cats. It is important to realize that the lag in onset after patch placement (of 6-12 hours), inconsistency of serum levels and thus presumably of effect means that some cats may not experience adequate pain relief. Use of this route must be preceded and/or supplemented by injection, or the patch must be in place prior to surgery. Skin temperature will affect the plasma level of fentanyl and thus contact with heating pads will elevate fentanyl levels.

Concern is often raised about the use of opioids in cats because of the incidence of undesirable effects such as dysphoria, hyperthermia, nausea, constipation and ileus, suppression of cough, respiratory depression and urinary retention. Careful monitoring, limitation of the course of therapy, reduction of the dose or switch to a “weaker” agonist-antagonist opioid usually resolves the problem. Decreased propulsive bowel motility leading to ileus can be caused by pain, handling of the bowel at surgery, inactivity, lack of oral intake and electrolyte imbalances as well as opioid use. Cough suppression and respiratory depression can be a concern when opioids are used in a patient with pneumonia or blood in the lung secondary to trauma. The reluctance to cough and breathe deeply are also impaired by chest wall or upper abdominal pain, thus there is a need to consider a balanced approach to relief of pain in such patients, using opioids and other analgesics. Animals may experience urinary retention when opioids acting at the mu receptor are used; this may be more profound after epidural morphine. Hyperthermia is a problem that can be seen after opioid use in some species, particularly after hydromorphone or oxymorphone administration in cats, and thus temperature monitoring is important. Behavioral changes, including euphoria and dysphoria, can also result. Many of the side effects of opioids can be reversed (including hyperthermia, dysphoria, ileus and urinary retention) by giving either a dose of butorphanol (0.1 mg/kg) or a small dose of naloxone (0.005 – 0.01 mg/kg) without increasing pain. Buprenorphine is not thought to be reversible unless very high doses of naloxone are given, but this is not usually a problem. Behavioral effects may also be controlled by switching to a “lesser” opioid or by use of sedation.
The relatively long apparent duration of action of NSAIDs, (12-24 hr) is particularly useful. NSAIDs are regarded as insufficient for moderate to severe pain, but they can be combined with other analgesic drugs. Practitioners should always consider a licensed drug unless no other options exist. COX 2 preferential NSAIDs are regarded as being less prone to causing gastrointestinal injury or platelet dysfunction. However, COX2 inhibition can retard tissue repair and COX 2 is required for preserving renal blood flow; COX 2 preferential NSAIDs are not without potential for harm. Use of any NSAID type is contraindicated with renal and hepatic dysfunction, dehydration or low cardiac output. Actual or potential compromise of the gastrointestinal mucosal barrier and concurrent use of corticosteroids are also contraindications to NSAID use. General anesthesia may reduce cardiac output and thus renal blood flow. When used prior to general anesthesia NSAID use risks further acute damage to the kidney. This is of special concern in elderly cats, in whom a degree of chronic renal dysfunction may exist without clinical or laboratory evidence. When blood pressure monitoring is not possible, then it is advisable to give NSAIDS to cats after anesthetic recovery, once a stable state is assured.

Local anesthetics can be very effective agents for control of acute pain, and are especially useful in combination with other analgesics. The author uses an injection of intratesticular lidocaine to reduce castration pain in cats, using 2 mg/kg divided between testicles and injected with a very small needle. Intravenous lidocaine is used in many veterinary species. However, several reports of concentrations and effects of IVL in cats indicate that it should not be used in this species, particularly intraoperatively, because of poor ability to metabolize the drug. Wound infusion catheters are an emerging new strategy to extend the duration of local anesthesia after surgery. The most studied surgical indication for wound infusion catheters in veterinary medicine is canine total canal ablation, but use for extensive soft tissue resection in cats (fibrosarcoma resection) is also reported. Currently, anecdotal reports are that practitioners are using such wound infusion catheters for limb amputation, intercostal and sternal thoracotomy, and major soft tissue tumor excision in cats. Intrawound (intermittent) infusion techniques with bupivacaine can be used in cats as long as the total dose of bupivacaine does not exceed 2 mg/kg/day. This often necessitates dilution of bupivacaine to ensure enough volume to be effective.

Ketamine is an extensively used component of anesthesia, but has some intriguing possibilities for an analgesic adjunct. Administration of even very low doses of ketamine reduces the required concentration of inhalant anesthetics required for surgery in dogs, horses and goats from approximately 20 – 50%, and this is likely to be the case in cats as well. Its anesthetic sparing action may be in part due to an analgesic effect that is present at low and sub-anesthetic dosages. In many species, subanesthetic or so called “low dose”, or “micro dose” ketamine is demonstrated to improve opioid sparing; prevent opioid tolerance; and reduce acute somatic and visceral pain. Because ketamine has a high therapeutic index and is relatively inexpensive, low dose ketamine infusions are now widely used as an analgesic adjunct in cats – both intraoperatively and postoperatively, for acute pain, even though clinical data to support its efficacy are still needed. Higher anesthetic doses of ketamine are thought to be relatively contraindicated in animals with high intraocular pressures, hypertrophic heart disease, tachyarrhythmias, and in central nervous system disorders, e.g. epilepsy and intracranial surgery. High dose ketamine is avoided in those patients because of its tendency to increase arterial blood pressure and heart rate, and to increase CNS excitation. Therefore, it may be prudent to avoid low dose ketamine in such patients until evidence of safety is demonstrated. When no contraindications exist, the routine incorporation of intraoperative low dose ketamine for
moderate to severe expected pain, or its addition to analgesic regimens represents a safe, inexpensive, and potentially effective technique when current therapy is not deemed sufficient.

The alpha2 adrenergic agonist drug class (*alpha-2 agonists*) produces analgesia which is accompanied by cardiovascular depression and sedation. Alpha 2 agonists have been studied for use in most animal species to produce sedation and anesthesia, generally in combination opioids or ketamine. The sedative plus analgesic actions of alpha 2 agonists are particularly useful to facilitate mildly painful procedures, and in hospitalized animals to calm anxious patients with acute pain. When used for sedation with an opioid pre- or postoperatively, doses significantly lower than the product label dose or even “microdose” administration of dexmedetomidine may be used in cats (0.001 – 0.005 mg/kg/hr). Significant concern exists about the cardiovascular depressant effects of alpha 2 agonists, and their use is recommended to be limited to animals with stable cardiovascular function.

The anticonvulsant drug *gabapentin* acts to reduce neuronal hyperexcitability, and has been used in humans for alleviation of neuropathic pain. There is currently significant interest in the use of gabapentin for a perioperative antihyperalgesic effect in humans. Although numerous reports support the efficacy of gabapentin in reducing post-operative pain in animal models, no clinical trials for its use at surgery have been reported in the clinical veterinary literature to date. Gabapentin in humans and animal models is synergistic with other analgesics and is currently used (empirically) for acute pain management in cats. Currently, gabapentin is only available in an oral formulation. It has sedative and anxiolytic properties, which may be additive with other analgesics and anesthetics. In the human and dog, gabapentin is relatively non toxic even at high doses, and has been used even in critically ill or systemically impaired animals. Dose reductions in situations of hepatic or renal insufficiency should be considered. The empirically advocated doses of gabapentin in the small animal patient with acute pain range from 2 – 5 mg/kg every 8 – 12 hours. Gabapentin, combined with opioids, tramadol, or NSAIDS may be a useful option for sustained analgesic therapy in cats with acute pain.
## Some feline premedication protocols

<table>
<thead>
<tr>
<th>Drugs</th>
<th>dose</th>
<th>comments</th>
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<tbody>
<tr>
<td>Butorphanol</td>
<td>0.3 mg/kg IM 0.2 mg/kg IV</td>
<td>For tractable cats when surgical pain is expected to be very minor, as butorphanol is not considered to be a strong or lasting opioid</td>
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<tr>
<td>Oxymorphone + acepromazine</td>
<td>0.1 mg/kg 0.02 – 0.05 mg/kg</td>
<td>Use higher dose of acepromazine in younger cats. Often results in a “euphoric” cat who tolerates catheter placement. Recoveries are usually good, but may see dysphoria (resolves after dose of 0.1 mg/kg butorphanol or 0.01 mg/kg buprenorphine IV). Add ketamine 5 mg/kg if cat is difficult (but see ketamine caution below).</td>
</tr>
<tr>
<td>Oxymorphone + acepromazine</td>
<td>0.1 mg/kg 0.02 – 0.05 mg/kg Use half of the IM dose if giving acepromazine IV.</td>
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<tr>
<td>Dexmedetomidine + Ketamine + Butorphanol or buprenorphine</td>
<td>0.01 - 0.02 mg/kg 2 – 8 mg/kg 0.2 mg/kg 0.01 mg/kg</td>
<td>IM cocktail useful for sedation for radiographs and exam of intractable cats – in this case use lower ketamine dose &amp; butorphanol. IM administration of higher ketamine dose &amp; buprenorphine will result in a state where minor surgery (castration) or pin removal/biopsy can be performed.</td>
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<tr>
<td>Glycopyrrolate</td>
<td>0.01 mg/kg</td>
<td>May be added to any protocol, especially if resting HR is &lt; 180. Under anesthesia, cats with HR &lt; 130 may have hypotension that is responsive to increasing the HR&gt;</td>
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<tr>
<td>ketamine</td>
<td>Generally avoided in cats w/ heart disease, because may increase left atrial pressures</td>
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