Analgesia has become an increasingly important aspect of veterinary patient care. Animals that have been injured or have undergone a surgical procedure are in obvious need of analgesia. Often, the most critically ill patients in an intensive care unit (ICU) do not get the benefit of analgesia; however, these patients require aggressive pain management. Numerous articles and textbooks have recently been published in response to increased interest in pain control. According to the recent veterinary literature, several pain-scoring systems have been developed using a total point system to help define the pain level and therefore the need for intervention. There is no universally accepted pain-scoring system for use in veterinary patients.

**ASSESSMENT AND PHYSIOLOGY OF PAIN**

Assessing the presence of pain in veterinary patients is often challenging because animals express pain clinically in a variety of ways. Signs that may be noted in painful animals include vocalization, trembling, splinting, reluctance to move, protection of a painful site, licking or mutilation of the affected area, or lameness. Other signs that may be referable to pain include atypical behavior, depression, anorexia, sleep deprivation, lack of grooming, aggressiveness, avoidance behavior, fear, anxiety, and apprehension. Physiologic signs that may be noted include salivation, mydriasis, tachypnea, tachycardia, hypertension, hyperglycemia, and elevated serum levels of corticotropin and cortisol (see box on page 434). Because of the detrimental physiologic effects of pain, it is imperative to recognize the presence of pain and initiate prompt, appropriate therapy in critically ill patients.

It has been argued that the presence of pain may be helpful in ill patients. For example, pain may prohibit an animal from using an injured leg or may help maintain blood pressure by inducing catecholamine release. However, it is known that pain induces many physiologic changes that may be detrimental to patients. Pain causes release of catecholamines, resulting in increased sympathetic tone and vasoconstriction. This may result in decreased gastrointestinal (GI) and urinary tone, decreased blood flow to the GI tract, GI ulcer formation, and increased skeletal muscle tone. Decreased regional blood flow to the pancreas may increase the incidence of pancreatitis.
Pain elicits the stress response, which can produce detrimental physiologic effects.

Increased sympathetic tone and vasoconstriction can lead to decreased oxygen delivery to tissue, increased systemic vascular resistance, and increased cardiac output from the compensatory increase in stroke volume and heart rate. Pain-induced tachycardia may increase the incidence of ventricular arrhythmias and increase myocardial work because of an elevation in metabolic rate and oxygen consumption.

Pain also induces increased secretion of corticotropin, cortisol, antidiuretic hormone, growth hormone, cAMP, renin, angiotensin II, aldosterone, glucagon, and interleukin-1. Pain can also decrease insulin and testosterone secretion. Excessive secretion of these hormones produces a catabolic state that is characterized by hyperglycemia, increased protein catabolism, lipolysis, renal retention of water and sodium, increased potassium excretion, and a decreased glomerular filtration rate. This catabolic response can lead to a negative energy balance and suppression of the immune status, potentially causing decreased wound healing and increased risk of postsurgical complications. An impaired immune system in critically ill patients contributes to increased risk of infection in wounds, catheter sites, and the pulmonary system.

Other effects of pain include self-mutilation, decreased appetite, decreased enteral activity (resulting in increased bacterial and enterotoxin translocation), and postoperative weight loss. The combination of these behavioral and physiologic effects results in longer hospitalization times, an increased requirement for interventional therapy such as enteral feeding tubes and antiemetics, and overall discomfort of ICU patients.

The changes that pain causes in the brain and spinal cord neurons result in heightened perception of pain (called central sensitization) after a period of stimulation. It is easier to prevent this sensitization via preemptive analgesia before pain starts than to treat subsequent hyperalgesia.

TREATMENT
Adequate pain relief promotes an animal’s overall well-being and has a positive effect on the speed and quality of recovery. Administering analgesics may not result in complete pain relief; however, the aim is to achieve a state in which the pain is bearable and some of the protective aspects of pain, such as inhibiting use of a fractured leg, still remain.

Once the presence of pain has been determined, there are several routes and techniques by which analgesia can be achieved. The type of treatment may depend on the severity of pain and the nature of the animal. It is vital that the underlying disease process be addressed while pain relief is provided.
Analgesia can be administered via the following routes: intravenous, subcutaneous, intramuscular, epidural, transmucosal, transdermal, local infiltration, oral, intraarticular, intrapleural, and intraperitoneal. Several classes of drugs can be used with these techniques. General drug classes that are commonly used include the following: opioids, α₂-adrenergic agonists, local anesthetics, NSAIDs, N-Methyl-D-aspartate (NMDA) antagonists, and adjuvant agents, including phenothiazines, benzodiazepines, and tricyclic antidepressants. Analgesics and their doses are listed in Table 1.

If analgesics can be administered before pain develops (i.e., preemptive analgesia), less drug therapy will be necessary to control pain.¹⁰¹¹ This is beneficial in patients undergoing scheduled surgery. However, preemptive analgesia may not always be possible, particularly in critically ill patients. To provide a significant benefit in ICU patients, analgesics should be administered as soon as possible following patient assessment.¹¹ In addition, it is important to develop an analgesic therapeutic plan that assesses the type and severity of the pain and the response to treatment. The assessment should include considerations for the expected duration of pain, routes and types of drugs that can be used according to an animal’s medical condition and disposition, and potential side effects of the analgesics. Patients should be reassessed frequently to ensure that the analgesic regimen is adequate and appropriate. Administering analgesics may be diagnostic when pain behavior is difficult to recognize.¹²

Established pain may be difficult to control with a single agent, necessitating combination therapy involving multiple classes of analgesics.¹¹ Because pain development and sensation may involve a multiplicity of pathways, one agent alone is often unlikely to completely alleviate pain, regardless of how high the dose is.¹² The combination of different drug classes may also overcome the problem of varying onset times and durations between drug classes. An example of combination analgesic therapy is administering opioids with NSAIDs.

**NSAIDs**

Because inflammation plays a significant role in the pain process, reducing or eliminating peripheral inflammation by administering NSAIDs should be considered. NSAIDs decrease the pain input to the central nervous system (CNS), which may aggravate central hypersensitivity.¹¹ Commercially available NSAIDs include carprofen, deracoxib, meloxicam, etodolac, and tepoxalin. The analgesic and antiinflammatory effects associated with NSAID administration are related to inhibition of cyclooxygenase (COX) enzyme isoforms.¹⁶ COX-1 is responsible for basal prostaglandin production for normal homeostatic processes within the body, including gastric mucous production, platelet function, and indirectly, hemostasis.¹⁶ COX-2 is found at sites of inflammation. It may be difficult to control with a single agent, necessitating combination therapy involving multiple classes of analgesics.¹¹ Because pain development and sensation may involve a multiplicity of pathways, one agent alone is often unlikely to completely alleviate pain, regardless of how high the dose is.¹² The combination of different drug classes may also overcome the problem of varying onset times and durations between drug classes. An example of combination analgesic therapy is administering opioids with NSAIDs.

Pain can lead to a catabolic state, causing a negative energy balance and suppressing the immune system.
<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand, Manufacturer</th>
<th>Dose and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylpromazine</td>
<td>Aceproject, Vetus Animal Health</td>
<td>0.01–0.05 mg/kg IM or IV q3–6h; do not exceed a total of 2 mg in large dogs</td>
</tr>
<tr>
<td></td>
<td>PromAce, Fort Dodge Animal Health</td>
<td></td>
</tr>
<tr>
<td>Atipamezole</td>
<td>Antisedan, Pfizer Animal Health</td>
<td>Reversing α₂-adrenergic agonists: 0.05–0.2 mg/kg IM, IV, or SC</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>Abbott Laboratories</td>
<td>Nerve block: 1–2 mg/kg SC q6h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dogs: 0.6–2 mg/kg epidurally</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cats: 0.5–1 mg/kg epidurally</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Buprenex, Reckitt &amp; Colman Pharmaceuticals, Inc</td>
<td>0.005–0.02 mg/kg IM or IV q6–8h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cats: 0.01–0.02 mg/kg q6–8h PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.003–0.006 mg/kg epidurally</td>
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<tr>
<td>Butorphanol</td>
<td>Torbutrol, Torbugesic-SA, Fort Dodge Animal Health</td>
<td>0.1–0.4 mg/kg IM or IV q1–4h</td>
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<tr>
<td></td>
<td></td>
<td>Partial reversal of μ-opioid agonists: 0.05–0.1 mg/kg IV</td>
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<tr>
<td></td>
<td></td>
<td>Loading dose: 0.1 mg/kg IV</td>
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<tr>
<td></td>
<td></td>
<td>Maintenance: 0.03–0.4 mg/kg/hr CRI</td>
</tr>
<tr>
<td>Carprofen</td>
<td>Rimadyl, Pfizer Animal Health</td>
<td>2–4 mg/kg SC (single dose)</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>Periactin, Merck</td>
<td>Dogs: 0.3–2 mg/kg PO bid</td>
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<tr>
<td></td>
<td></td>
<td>Cats: 2 mg/cat PO bid</td>
</tr>
<tr>
<td>Deracoxib</td>
<td>Deramaxx, Novartis Animal Health</td>
<td>Dogs: 1–2 mg/kg PO sid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative pain: 3–4 mg/kg PO sid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Should not be given for more than 7 days</td>
</tr>
<tr>
<td>Etorocolacin</td>
<td>EtoGesic, Fort Dodge Animal Health</td>
<td>Dogs: 5–15 mg/kg PO sid</td>
</tr>
<tr>
<td>Hydromorphone HCl</td>
<td>Baxter Healthcare Corp</td>
<td>Dogs: 0.05–0.2 mg/kg IM or SC; 0.05–0.1 mg/kg IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cats: 0.05–0.1 mg/kg IM or SC q3–4h; 0.03–0.05 mg/kg IV q3–4h</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Schein</td>
<td>No safe dose has been established; not recommended for use in small animals</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Ketaflo, Abbott Laboratories</td>
<td>Analgesia without sedation: 0.1–1 mg/kg IV</td>
</tr>
<tr>
<td></td>
<td>Ketaset, Fort Dodge Animal Health</td>
<td>Loading dose: 0.5 mg/kg IV</td>
</tr>
<tr>
<td></td>
<td>Vetalar, Bioniche Animal Health</td>
<td>Maintenance during surgery: 10 µg/kg/min CRI</td>
</tr>
<tr>
<td></td>
<td>Vetamine, Schering-Plough</td>
<td>Maintenance after surgery: 2 µg/kg/min CRI for 24 hr</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>1% preservative free, Abbott Laboratories</td>
<td>Nerve block: 1–2 mg/kg SC</td>
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<tr>
<td></td>
<td></td>
<td>Loading dose: 1–2 mg/kg IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintenance: 2–3 mg/kg/hr CRI</td>
</tr>
<tr>
<td></td>
<td>2% Lidocaine</td>
<td>Nerve block: 1–2 mg/kg SC</td>
</tr>
<tr>
<td></td>
<td>Phoenix Pharmaceuticals</td>
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istering corticosteroids and NSAIDs can potentiate the GI side effects of COX-1 inhibition; thus these two drugs are not recommended for use together.17

**NMDA ANTAGONISTS**

Ketamine has NMDA receptor antagonist activity.21 There are multiple binding sites at this receptor, with blockade resulting in the analgesic, amnestic, psychomimetic, and neuroprotective effects of ketamine.21 Ketamine can reverse central hypersensitivity due to prevention of the exaggerated response, wind-up activity, and central sensitization of wide dynamic-range neurons in the dorsal horn of the spinal cord.17 Ketamine, by acting as a noncompetitive NMDA receptor antagonist, prevents the response to nociceptive stimuli carried by afferent pain neurons called C fibers.22,21 Subanesthetic or low doses in dogs and cats (0.1 to 1 mg/kg IV) may have an analgesic effect without causing anesthesia or profound sedation. Ketamine may also be administered via constant-rate infusion (CRI) at a dose of 2 µg/kg/min.17,21 In addition, ketamine has been administered at a dose of 8 to 12 mg/kg PO q6h (in dogs) to provide pain relief following burn injuries.18

**OPIOIDS**

Opioids act centrally to limit the input of nociceptive information to the CNS, thereby reducing central hypersensitivity.17 Receptors in the brain and dorsal horn of the spinal cord receive impulses from peripheral nerves, which are modulated before being transmitted to higher centers.24 Opioids are most commonly used in critically ill patients because they have a rapid onset of action and are safe, reversible, and potent analgesics.18 Opioids should be intravenously titrated to effect slowly and carefully because critically ill patients may have altered drug pharmacokinetics.18 Opioid analgesics vary in effectiveness, depending

<table>
<thead>
<tr>
<th>Table 1. Analgesics and Their Doses (continued)</th>
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<tbody>
<tr>
<td><strong>Generic</strong></td>
</tr>
<tr>
<td>Lidocaine patch</td>
</tr>
<tr>
<td>Medetomidine</td>
</tr>
<tr>
<td>Meloxicam</td>
</tr>
<tr>
<td>Morphine (preservative free)</td>
</tr>
<tr>
<td>Morphine sulfate with preservative</td>
</tr>
<tr>
<td>Naloxone</td>
</tr>
<tr>
<td>Oxymorphone</td>
</tr>
<tr>
<td>Tepoxalin</td>
</tr>
<tr>
<td>Morphine–lidocaine–ketamine infusion</td>
</tr>
</tbody>
</table>
on which receptor is stimulated or which class of opioid is administered. There are four different classes of opioids: pure agonists, partial agonists, agonist–antagonists, and antagonists. Pure receptor agonist stimulation results in a pronounced analgesic effect. Partial agonists bind at the same receptor as the pure agonist but have a less pronounced effect. Agonist–antagonists have mixed effects, with an agonist effect at one type of receptor and an antagonist effect at a different type of receptor. This results in an analgesic effect at one receptor and no effect or a less pronounced effect at the other receptor. Opioid antagonists bind to the same receptor as agonists but cause no effect. They competitively displace the agonist from the receptor and therefore reverse the agonist effect. Partial agonists (e.g., buprenorphine [5 to 20 µg/kg IV, IM, or SC q6–8h]) and mixed agonist–antagonists (e.g., butorphanol [0.1 to 0.4 mg/kg IV q4h]) reach maximal effect at the upper end of the dose range. If the pain is severe or the analgesia is inadequate, additional doses of partial or mixed agonists–antagonists are unlikely to be effective. Using a combination of different classes of analgesics may be more effective than using a single agent in treating established pain.

In cats, all classes of opioids can be safely administered to provide analgesia. Morphine or oxymorphone (0.05 mg/kg titrated slowly IV) can be administered for analgesia; however, side effects such as hyperexcitability or agitation may occur. It has been shown that the onset of mydriasis following opioid administration correlates with adequate analgesia in cats; however, continual dosing after achieving mydriasis may result in adverse side effects such as dysphoria and agitation. It has recently been shown that buprenorphine (10 to 20 µg/kg PO q6–8h) is an effective analgesic in cats.

An advantage of opioids is that their effects can be reversed if necessary. Naloxone (0.02 to 0.1 mg/kg IV, IM, or SC) can be used to reverse the analgesic effect because it is a pure antagonist. Although naloxone can reverse CNS depression, respiratory depression, and bradycardia, the drug can also cause excitement, emergence delirium, aggression, and hyperalgesia. Low-dose naloxone (0.004 mg/kg titrated slowly IV) has been recommended to reverse CNS depression without affecting analgesia. In addition, the duration of effect for naloxone is relatively short (20 to 30 minutes) because of its rapid metabolism in dogs and cats, which may predispose patients to reanesthetization when the drug is used to reverse long-acting opioids. Agonist–antagonists such as butorphanol (0.05 to 0.1 mg/kg IV) may also be used to reverse sedation and respiratory depression from µ agonists. The benefit of using butorphanol as a reversal agent is that complete reversal of analgesia does not occur because of the κ agonist effects of butorphanol. In contrast, buprenorphine is more difficult to reverse than butorphanol because it is difficult to displace from the receptor.

**TRANSDERMAL ANALGESIA**

For analgesia with minimal systemic adverse reactions, administering topical analgesia in conjunction with existing analgesic treatments has been well-tolerated in patients. Fentanyl patches can be used to provide long-
term analgesia but may vary in effective time to onset and steady-state concentrations.18,20,29 Because of this variability, systemic analgesia must be provided until the patch becomes effective. Fentanyl uptake depends on dermal blood flow, hair, and obesity and may be greatly altered in hypovolemic or hypothermic patients. In dogs, it may take up to 24 hours to reach effectiveness.25 Cats may reach therapeutic levels in 6 to 12 hours and can maintain steady states for approximately 5 days.20,29 It should be noted that not all animals may reach therapeutic levels with the patch. If patients still appear to be painful 12 to 24 hours after patch placement, additional treatment with analgesics is necessary.25 Fentanyl patches are currently available in 25-, 75-, and 100-µg patches. If a lower dose is desired, part of the seal can be retained to prevent absorption.20 Fentanyl patches should not be cut or otherwise altered. Disposal of fentanyl patches should be specifically directed because there is potential for human abuse of fentanyl.

Lidoderm (Endo Pharmaceuticals), a 5% lidocaine patch, was recently introduced to the human and veterinary markets. Lidoderm was approved in 1999 by the FDA for treating postherpetic neuralgia in humans.28 Lidoderm is a nonwoven, polyester, felt-backed patch covered with a polyethylene terephthalate film release liner that should be removed before applying it to skin. Each adhesive patch, which is 10 × 14 cm, contains 700 mg of lidocaine and 50 mg/g adhesive in an aqueous base. Lidocaine penetration into intact skin is sufficient to produce an analgesic effect but does not result in complete sensory block. The Lidoderm patch can be safely worn for as long as 24 hours and provides analgesia without numbness or loss of sensitivity to touch or temperature.30 Therapeutic levels are achieved via absorption within 30 minutes, and toxic blood levels have not been documented.30 Unlike the fentanyl patch, the Lidoderm patch can be cut to fit patient size without affecting drug delivery.30 The most common adverse effect in humans was transient dermal reactions such as localized rash and pruritus.30 The lidocaine patch can be used in a back-to-back fashion because toxic blood levels do not develop, but the skin needs to be monitored for development of localized dermatitis.

Lidoderm patches provided adequate analgesia in horses with limb lameness for up to 11 hours with no detectable lidocaine blood levels.31 For placement of the patch on animals, the hair must be clipped and cleaned. The patch can be stapled in place with surgical staples to ensure appropriate contact with skin.31 Anecdotally, the Lidoderm patch has been used in dogs and cats to provide analgesia for severe skin abrasions and severe bruising as well as at the site of surgical incisions; no apparent toxic effects have been noted.

α₂-ADRENERGIC AGONISTS

α₂-Adrenergic agonists bind to receptors in the CNS, leading to sedation, peripheral vasoconstriction, bradycardia, respiratory depression, diuresis, muscle relaxation, and analgesia.25,32 Medetomidine is the most common α₂-adrenergic agonist administered in small animals. The sedative effects of medetomidine have a longer duration of action than do the analgesic effects, which last approximately 30 to 90 minutes.31 Low doses of medetomidine (1 to 10 µg/kg IV) are safe to use in stable patients and can be administered in conjunction with opioids to produce analgesic synergism and increase the analgesic duration to as long as 4 hours.25,33 In addition, medetomidine can be used to sedate distressed animals and for minor procedures (i.e., restraint and analgesia for radiographic positioning).25 As with opioids, the effects of α₂-adrenergic agonists can be reversed. Atipamezole (0.05 to 0.2 mg/kg IM, SC, or IV) is a specific α₂-adrenergic antagonist.26 Atipamezole reverses analgesia, sedation, and respiratory depression.26 Intramuscular or subcutaneous administration is preferred for reversal because intravenous administration leads to abrupt hypotension and/or reversal that may result in excitement.26

ACETYLPROMAZINE

Acetylpromazine (0.01 to 0.05 mg/kg IV, not to exceed a total of 2 mg) may be used in combination with opioids as an anxiolytic and sedative.25 Acetylpromazine should be used with caution because of risks of vasodilation and resultant profound hypotension and hypothermia.25 Acetylpromazine does not provide analgesia and should not be administered as a single agent if analgesia is desired.25 It may take up to 15 minutes before the sedative effect of an intravenous dose of acetylpromazine is clinically observed; therefore, repeated doses should be avoided until the full effect is evident.25 Acetylpromazine can be safely administered to ICU patients if given at low doses (0.005 to 0.01 mg/kg) in hemodynamically stable animals with adequate respiratory function.2

INFLTRATIVE AND LOCAL ANESTHETICS

Local anesthetics (e.g., lidocaine, bupivacaine) provide analgesia by blocking both specific nerve pathways and
action potential transmission in nerve fibers, including nociceptive fibers.\textsuperscript{17} Local anesthetics can be used for intercostal nerve blocks as well as intraperitoneal and intrathoracic administration. When using local anesthetics, the patient should be appropriately positioned so that the medication disperses over the desired site to enhance analgesia.\textsuperscript{17} Sodium bicarbonate (1 mEq/ml) may be added to lidocaine at a ratio of 1 to 2 parts bicarbonate to 8 to 9 parts lidocaine to decrease the burning sensation caused by administration of lidocaine alone.\textsuperscript{25} When using bupivacaine, a 1:30 ratio of sodium bicarbonate to bupivacaine is sufficient. Intrapleural or intraperitoneal 0.5\% bupivacaine (2 mg/kg q6h) can be administered for painful diseases and conditions (e.g., fractures, pancreatitis, septic peritonitis) or procedures (e.g., thoracotomy, placement of a thoracostomy tube).\textsuperscript{17,20} Intercostal nerve blocks can be performed to provide analgesia for rib fractures. Bupivacaine (1 to 1.5 mg/kg q6h; not to exceed 4 mg/kg on day 1) can be injected in the area of the intervertebral foramen on the caudal border of the rib to block the intercostal nerves.\textsuperscript{17} Bupivacaine can be administered intrapleurally via a thoracostomy tube to provide analgesia following thoracic surgery or tube placement because the presence of the tube itself may be painful. Bupivacaine can also be administered intraperitoneally (2 mg/kg q6h diluted in saline) and with a butterfly catheter to provide analgesia. Because bupivacaine is selectively cardiotoxic, only half the canine dose should be administered in cats.\textsuperscript{25} Potential side effects of bupivacaine include arrhythmias and reduced cardiac output; therefore, the drug should not be administered in animals with preexisting arrhythmias.\textsuperscript{25} In addition, because of the risk of cardiotoxicity, bupivacaine should not be administered if a pericardiectomy has been performed.\textsuperscript{17} Intrapleural bupivacaine may also interfere with ventilation by inducing diaphragmatic paralysis.\textsuperscript{25} Animals with good respiratory reserve capacity rarely develop clinically significant compromise, but administration of intrapleural anesthetics should be avoided in animals with marginal respiratory function.\textsuperscript{25} Toxicosis may occur with higher doses of lidocaine (>10 to 20 mg/kg) and bupivacaine (>4 mg/kg).\textsuperscript{17} Clinical signs of toxicosis may include seizures, cardiac arrhythmias, tachycardia, and cardiovascular collapse. The maximum safe dose for most species is 4 mg/kg of lidocaine and 1 to 2 mg/kg of bupivacaine.\textsuperscript{17} Administration of epinephrine, which normally enhances the duration of effect of local anesthetics, should be avoided in critically ill patients because it may lead to cardiac stimulation or ischemia from vasoconstriction.\textsuperscript{17}

**Epidural Analgesia**

Epidural analgesia can be administered to provide pain relief to the caudal half of the body or the forelimbs.\textsuperscript{17} Analgesia of the forelimbs can be achieved via use of an epidural catheter or large volumes of injectant (1 ml/5 kg blocks to the first lumbar vertebra; a larger volume results in a more cranial spread). Contraindications for use of epidural analgesia include trauma over the pelvic region (with loss of appropriate landmarks), septicemia, coagulopathy, CNS disease, skin infection over the site of injection, hypovolemic shock, and severe obesity.\textsuperscript{17,20,34,35} The technique for epidural analgesia has been described previously.\textsuperscript{17} Lower concentrations of local anesthetics can provide analgesia without secondary motor deficits.\textsuperscript{17} In addition, epidural opioids can provide analgesia without affecting motor function; nociceptive input is reduced but not completely abolished.\textsuperscript{17} Complete anesthesia can be achieved with higher doses of local anesthetics, resulting in motor paralysis of the rearlimbs.\textsuperscript{17} Higher doses may also lead to vasodilation and subsequent hypotension.\textsuperscript{17} In critically ill patients, lower doses of local anesthetics should be administered epidurally to avoid inducing hypotension. Morphine and bupivacaine are safe and effective epidural agents to administer in dogs and cats.\textsuperscript{14} Because of the lipid solubility and long duration of action of morphine, it is the opioid of choice for epidural administration.\textsuperscript{17} The dose of morphine in dogs ranges from

**New constant-rate infusions of analgesic combinations have shown promise and effectiveness in treating critically ill and traumatized patients.**
0.1 to 0.4 mg/kg, with a maximum volume of 6 ml. The onset of action of morphine delivered epidurally is 20 to 60 minutes, with a duration of 6 to 24 hours. Bupivacaine can be administered at a dose of 0.6 to 2 mg/kg (in dogs); however, the higher end of the dose may result in transient paralysis. The onset of action for bupivacaine can take up to 60 minutes, and the duration of action is similar to that for morphine. Administering buprenorphine may have some advantage because urinary retention is less likely. For cats, morphine can be administered at 0.16 mg/kg and bupivacaine at 1 mg/kg; these doses provide epidural analgesia for approximately 20 hours. This is a significantly longer duration than that of a single dose of systemically administered morphine. Preservative-free solution should be used in the epidural space to ensure that there is no chemical damage to the spinal cord; this is especially important for intrathecal or spinal administration. A one-time dose of preservative morphine in the epidural space is not considered dangerous.

An epidural catheter can be placed using the same landmarks as those for a single injection. The advantage of epidural catheterization is the ability to provide continuous analgesia without repeated epidural needle punctures. In addition, the catheter can be advanced cranially to improve analgesia to the front limbs or thoracic structures. Similar side effects of epidural catheterization occur with epidural injection. Catheters must be placed aseptically and maintained with sterility and care. Proper epidural catheter placement can be determined via a lateral radiograph after catheter placement. If the epidural catheter is not radiopaque, a low dose of myographic contrast agent can be used to view it. Catheters have been safely left in place for 1 to 332 hours. With epidural catheters, the total volume injected should be limited to 6 ml in a large dog. When using an epidural catheter, the following drugs and doses should be administered: morphine (0.1 mg/kg), bupivacaine (0.05 to 0.12 mg/kg), or buprenorphine (0.003 to 0.006 mg/kg).

Side effects of epidural anesthesia include vomiting, urinary retention, pruritus, and delayed hair growth at the clipped epidural site. Urinary retention can be treated or prevented by manually expressing the bladder or placing an indwelling urinary catheter. Another complication includes inadvertent subarachnoid space injection of drugs. In dogs, the dural sac ends before the lumbosacral space; therefore, care must be taken to avoid subarachnoid injection when injecting epidural drugs. If the subarachnoid space is penetrated, the nonpreservative drug may still be given; however, a significantly reduced dose (i.e., 50% to 75% of the original dose) should be administered. The lower dose is sufficient for an analgesic response because the roots of the spinal cord are more accessible within the subarachnoid space, where they are not protected by the dura.

Vomiting is a recognizable problem while administering a loading dose of analgesia in awake animals. This may be a function of the volume and speed of injection rather than the type of agent administered. Therefore, all drugs should be administered slowly into the epidural space. A CRI of morphine (0.3 mg/kg q24h) or bupivacaine (0.2 to 0.3 mg/kg q24h) can be given slowly into the epidural space using a syringe pump. Bupivacaine may be administered via CRI through an epidural catheter, but this may result in muscle weakness. If the weakness is excessive, the infusion should be promptly discontinued and the dose of bupivacaine reduced. Additional complications associated with epidural catheters include catheter dislodgement, discharge from the site, fecal contamination, line or filter breakage, and localized dermatitis. When complications occur, removal of the epidural catheter is recommended.

**CONSTANT-RATE INFUSION**

CRI of analgesics has the advantage of maintaining effective plasma concentrations for continued pain relief. All CRIs should be delivered by syringe pump for accurate dosing. To avoid histamine release that may occur with rapid intravenous morphine administration, a morphine CRI (0.1 to 1 mg/kg/hr) should be started after administering an initial loading dose (0.15 to 0.5 mg/kg IV, diluted) over 5 to 10 minutes. A CRI of morphine (0.12 mg/kg/hr) reportedly induces effects similar to intramuscular morphine (1 mg/kg q4h) in dogs undergoing laparotomy. Regardless of how morphine is administered, it results in bradycardia, hypothermia, and panting. Instead of morphine, other opioids can be administered if undesirable side effects occur. Butorphanol has been administered at a loading dose of 0.1 mg/kg, followed by an infusion of 0.03 to 0.4 mg/kg/hr. Lidocaine can also be administered for pain control via CRI at an initial loading dose of 1 to 2 mg/kg, followed by 0.025 mg/kg/min. Lidocaine doses as high as 2 to 3 mg/kg/hr IV have been reported.

COMPENDIUM  
June 2005
As previously discussed, ketamine given perioperatively may prevent “wind-up” pain from occurring and thereby reduce postoperative pain. Ketamine causes minimal cardiovascular depression, does not depress laryngeal protective reflexes, and produces less ventilatory depression compared with opioids. With low doses of ketamine, undesirable side effects such as dysphoria or hallucination do not seem to occur. Low-dose ketamine CRIs have been administered for intra- and postoperative analgesia in dogs. A loading dose of ketamine (0.5 mg/kg IV) can be followed by a CRI of 10 µg/kg/min. This should then be reduced to 2 µg/kg/min during the recovery phase. The CRI can be continued postoperatively as needed for analgesia.

Fentanyl can also be given to enhance analgesia, starting with a loading dose of 2 µg/kg IV immediately followed by 2 µg/kg/hr IV. This dose can be increased as needed up to 5 µg/kg/hr IV. Fentanyl is also a safe analgesic for cats when administered at a loading dose of 1 µg/kg IV followed by 0.1 µg/kg/min IV. In critically ill animals that are poor anesthetic candidates, fentanyl, in conjunction with propofol, can provide adequate, safe, cardiovascular-sparing anesthesia. Bradycardia may be an adverse effect.

**MORPHINE–LIDOCAINE–KETAMINE**

Morphine (3.3 µg/kg/min), lidocaine (50 µg/kg/min), and ketamine (10 µg/kg/min) can be administered as a CRI analgesic combination in dogs. These agents can be given separately or mixed together in a single bag. Using a combination of agents may result in enhanced analgesia through synergism and multiple receptor activation. Ketamine has been found to attenuate and reverse morphine tolerance in rodents and humans, thereby yielding an opioid-sparing effect and providing superior analgesia compared with either drug alone.

**CONCLUSION**

Administering analgesics in critically ill animals should be considered an integral part of a treatment regimen. Critically ill patients can present a challenge when clinicians assess the presence of pain and evaluate the response to analgesic therapy. Because of the physiologic effects of some analgesics, choosing the appropriate class of analgesic and route of administration may be challenging in ICU patients. Using multimodal therapy that emphasizes lower doses of different classes of drugs may be a safer and more effective way of achieving analgesia in critically ill patients.

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ARTICLE #3 CE TEST

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1. Which COX enzyme isoform is primarily involved with inflammation?
   a. COX-1  
   b. COX-2  
   c. COX-3  
   d. COX-4

2. An area of the CNS that is predominantly involved in nociception and where several analgesics exert their effects is the
   a. hypothalamus  
   b. lateral ventricles  
   c. limbic system  
   d. dorsal horn of the spinal cord

3. Which opioid when administered rapidly and intravenously may cause histamine release?
   a. buprenorphine  
   b. fentanyl  
   c. morphone  
   d. butorphanol

4. Histamine release can lead to
   a. vasodilation  
   b. vasoconstriction  
   c. bradycardia  
   d. hypertension

5. In dogs, fentanyl patches may require _____ hours of use to obtain therapeutic plasma levels.
   a. 1 to 2  
   b. 6  
   c. 72  
   d. 24

6. When giving an epidural injection, if the subarachnoid instead of epidural space is penetrated, the injection can still be given in the subarachnoid space. By how much should the dose be reduced when administering a drug into the subarachnoid space?
   a. no reduction; use the same dose  
   b. 10% to 25%  
   c. 20% to 25%  
   d. 60% to 70%
c. 30% to 40%
d. 50% to 75%

7. Which agent(s) is commonly used in CRIs?
   a. morphine
   b. lidocaine
   c. ketamine
   d. all of the above

8. Which systemically administered opioid reaches maximal effect at the upper limit of the dose range?
   a. morphine
   b. butorphanol
   c. fentanyl
   d. hydromorphone

9. Which agent could increase intracranial pressure by causing respiratory depression?
   a. morphine
   b. lidocaine
   c. carprofen
   d. meloxicam

10. Which agent has analgesic action via antagonism of the NMDA receptor?
    a. lidocaine
    b. fentanyl patches
    c. ketamine
    d. medetomidine

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In critically ill patients, adequate analgesia and sedation increase comfort, reduce stress response and facilitate diagnostic and therapeutic procedures. Analgesia and sedation may also have a beneficial impact on morbidity, particularly by reducing pulmonary complications such as atelectasis and pneumonia, and delirium or agitation with subsequent accidental extubation. The method and depth of analgesia and sedation should be adapted to the needs of the individual patient. While evaluation of analgesia and sedation is important, technical tools for assessment are generally unreliable. Accord In critically ill patients, adequate analgesia and sedation increase comfort, reduce stress response and facilitate diagnostic and therapeutic procedures. Analgesia and sedation may also have a beneficial impact on morbidity, particularly by reducing pulmonary complications such as atelectasis and pneumonia, and delirium or agitation with subsequent accidental extubation. The method and depth of analgesia and sedation should be adapted to the needs of the individual patient. While evaluation of analgesia and sedation is important, technical tools for assessment are generally unreliable.

Implementation of guidelines for rational analgesia and sedation would help to reduce patients' length of stay in the intensive care unit. Sedation and analgesia are an integral part of the management of critical patients in the Intensive Care Unit (ICU). The aim of sedoanalgesia is to offer patients maximum comfort with safety, reducing anxiety and disorientation, facilitating sleep, and ensuring adequate pain control. This likewise contributes to avoid interferences with the medical and nursing care received. Critically ill patients in the ICU are at risk of suffering anxiety, agitation, aggressivity, delirium and withdrawal syndrome (opioids, alcohol, nicotine, etc.). An accurate diagnosis of these clinical manifestations is