

# Analgesia for the Critically Ill Dog or Cat: An Update

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## KEYWORDS

- Acute pain • Local anesthesia • Wound infusion
- Intravenous analgesia

Significant pain frequently accompanies acute illness<sup>1</sup> and is almost always present following surgery or trauma. This pain is considered acute in character and, as such, is intimately tied to the neurologic process of nociception. This feature is important for several clinically relevant reasons. First, acute pain contributes to the intensity of the postinjury stress response and, if poorly managed, may increase the risk of complications.<sup>2–4</sup> Nociception and the stress response to pain modify the immune response in complex ways that can produce immunosuppression. There is clinical evidence, at least in humans, that this sequela becomes most problematic in critical illness when the stress response is excessive and contributes to morbidity and mortality. Second, sustained nociception triggers the adaptive response of central sensitization. The subsequent development of hyperalgesia and allodynia intensifies pain and creates more challenges for the patient and the caregiver. Finally, acute pain usually responds, at least to some extent, to straightforward pharmacologic approaches, and drug therapy is an essential component of management of most patients that have significant acute pain. Anyone who has experience knows, however, that there is tremendous variation in patient response; some animals appear completely comfortable with modest drug therapy, whereas others that have similar conditions have distressing pain that is comparatively refractory to multiple drugs and all efforts at nonpharmacologic intervention.

Assessment of acute pain is beyond the scope of this review but serves as the basis for recognition of pain and evaluating patient response to therapy. Because injury and inflammation reliably produce nociception, pain is assumed to be present in animals that have these conditions, and at least some form of treatment should be considered regardless of clinical signs. Significant advancement toward the goals of including pain assessment in every physical examination (as in the Pain as a Vital Sign concept adopted by the International Veterinary Academy of Pain Management) and adoption of standardized assessment methods (as required by the American Animal Hospital Association for member hospitals) have occurred in the last 5 years.

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Nonpharmacologic approaches to pain management remain the basis for all other therapy. Meticulous surgical technique limits tissue injury and postoperative nociception. Careful and compassionate nursing care must maintain hygiene, prevent thirst and hunger, properly position and cushion immobile patients, and support the metabolic processes of healing. Protecting naturally timid animals from excessive exposure to the clinic environment reduces the stress of the hospital experience, whereas engaging more energetic, gregarious animals serves to distract them from their pain. Family visits in the hospital keep the animal rooted in the knowledge that they have not lost their home. Physical therapy to prevent edema, thrombosis, and stiffening of joints and muscles is beneficial to many, particularly those that have chronic pain from osteoarthritis. We are only beginning to appreciate the value of physical rehabilitation therapy in animals following significant illness or injury, particularly in those that have major musculoskeletal injury and repair.

Opioids and nonsteroidal anti-inflammatory drugs are the two most important drug classes for acute pain management. For a more in-depth review of the use of these drugs in hospitalized patients, the reader is referred to the earlier version of this review (see the *Veterinary Clinics of North America* 2000) and the companion chapters in this issue. Two approaches that have seen increasing use in the companion animal ICU at North Carolina State University are presented in this review: the use of local anesthetics and the continuous-rate infusion of multiple agents.

## LOCAL ANESTHETICS

Local anesthetics remain the only class of drug capable of completely blocking nociception from injury or surgery. Because of the efficacy of local anesthesia for intraoperative analgesia,<sup>5-8</sup> there has been considerable interest in expanding the role of these drugs for postoperative analgesia. Areas of interest include continuous intravenous (IV) infusions of lidocaine; continuous or intermittent infusion of local anesthetics into wounds, body cavities, and near nerves; regional analgesia with repeated epidural administration; and topical application of lidocaine.

Continuous nerve block with an infusion of drug remains the only available method to continuously block nociception. In theory, local anesthesia can provide complete analgesia of wounds. In practice, reaching this goal can be challenging. Many traumatic injuries produce damage that is too diffuse to allow a complete response to local anesthesia; however, the nature of many elective surgical procedures allows for the effective control of pain with local anesthetics applied before, during, or after the procedure.

Whereas splash blocks,<sup>9,10</sup> superficial infusion,<sup>11</sup> or single injections<sup>5</sup> of local anesthetics into wounds often fail to provide improved analgesia or provide only modest benefit, regional anesthesia (see the article by Lemke and Valverde found elsewhere in this issue) appears to provide substantial benefit.

In the author's experience, excellent postoperative anesthesia can often be obtained by performing a continuous nerve block or local wound infiltration by placing a fenestrated anesthetic delivery catheter into the surgical site before wound closure or near a nerve or nerve group that innervates the affected tissue. Although considerable clinical evaluation of continuous nerve blocks has been conducted in humans, comparatively little has been published regarding the technique in animals.

Precisely manufactured wound infusion catheters are available commercially (eg, veterinary perineural catheters, ReCathCo, Allison Park, Pennsylvania, [www.recathco.com](http://www.recathco.com)) or may be fashioned by hand using tubing such as 0.05-inch (outside diameter) polyethylene tubing. This sterile product may be purchased in individual 12-inch or 36-inch lengths (eg, Intramedic PE 90 polyethylene tubing, Becton-Dickenson, Franklin Lakes,

New Jersey, [www.bd.com](http://www.bd.com)) or in bulk packages (100 feet) of nonsterile tubing (eg, Intramedic PE 90 Polyethylene Tubing [Non-Sterile], Becton-Dickenson). To fashion local anesthetic delivery catheters out of polyethylene tubing, the following materials are needed:

- 1 Intramedic PE 90 polyethylene tubing (Becton-Dickenson)
- 1 insulin syringe with a 27- to 28-gauge needle
- 1 Luer adapter (Intramedic 20-gauge tubing adapter, Becton-Dickenson)
- 1 empty sterile 3-mL syringe
- 1 cigarette lighter
- 1 scissors
- 1 injection cap
- 64" × 4" gauze sponges or any other soft padded material
- 1 pair of examination gloves
- 1 syringe loaded with the agent of choice

If prepared in advance, the catheters can be made under clean conditions and then gas sterilized. If prepared at the time of surgery, all materials except the cigarette lighter (which is held by an assistant) must be sterile.

The catheter tubing may be cut into appropriate lengths (usually 12–36 inches). The cigarette lighter is used to flame the end of the catheter sufficiently to melt the plastic. When the catheter begins to melt, the operator pinches off the melted tip and draws it to a point, protecting fingers with the examination gloves, a gauze sponge, or both. A Luer adapter is firmly seated into the open end of the catheter, and a test injection of air is used to confirm that the seal at the tip is complete. If any air escapes the test injection, the tip is reheated and another attempt to seal it is made.

When sealed, the end of the catheter is rested on the sponge padding and the operator uses the insulin needle to perforate the tubing completely through both sides, beginning 5 mm proximal to the sealed tip and continuing every 5 to 10 mm up the desired length of tube. The purpose of the sponge padding is to prevent the needle tip from butting against the table work surface underneath and becoming dull. When the working length (or infusion surface—the total length of the portion of tube with perforations) exceeds 10 cm, the holes should be spaced approximately 10 mm apart to limit their total number. As each hole is placed, the catheter should be rotated 90° to prevent the holes from opening in the same plane. The length of the infusion surface of the catheter is determined by its desired use and location. If the goal is nerve block, and the catheter is to be implanted adjacent to (1) the brachial plexus, (2) a peripheral nerve (eg, a radial nerve block), or (3) the transected stump of a large nerve (eg, the sciatic and femoral nerves in a rear limb amputation), then the working surface need not be much longer than 5 cm. If the catheter is to be implanted into the long axis of a surgical wound, then it should be long enough to extend the length of the entire wound. At the time of packaging, the Luer adapter may be left on the catheter or may be removed and placed alongside the catheter in its package to facilitate catheter placement during surgery. A variety of lengths can be prepared and gas sterilized so that they are available for immediate use (**Table 1**).

Just before positioning the catheter in a patient, the device is primed with the anesthetic agent to be used. An injection cap with a Luer-Loc fitting may be connected to the catheter adapter. A common practice in the author's hospital is to connect the Luer adapter to a length of extension tubing that is, in turn, connected to a bacterial filter fitted with an injection cap. Regardless of the materials used, the entire system is purged with the local anesthetic agent of choice before placement into the patient. The most common agent used in the author's hospital is bupivacaine 0.25%. Using

**Table 1**  
**Wound infusion catheter lengths used frequently at the North Carolina State University veterinary teaching hospital**

Catheter Tubing Length (cm)	Length of Infusion Surface (cm)
25	5
30	10
45	15
45	20
60	25
60	30
60	35
75	40

a sterile syringe, the drug is injected into the catheter with some force, and the operator observes the infusion surface to verify that droplets of the solution are present at every hole.

When the catheter is to be used as a perineural infusion device, it may be (1) placed by direct visualization of the nerve (eg, during limb amputation), (2) passed through a long needle that is advanced to the desired location by recognition of anatomic landmarks, or (3) advanced to the desired location through an IV catheter that was guided to the proper location by use of an electrical nerve stimulator. The use of electrical nerve stimulators was previously described by Mahler and Reece.<sup>12</sup> When the catheter is passed to the nerve through an IV catheter or needle, the Luer adapter, if attached, is temporarily removed from the proximal end of the tubing to allow the catheter or needle to be removed.

When using the catheter to infuse local anesthetic directly into the surgical wound, some principles regarding placement should be followed to optimize efficacy of the device. The author's clinical experience and practice on cadavers suggest that effective anesthesia is most likely to occur for tissues that lie within 2 cm of the catheter after the wound has been closed. Therefore, whenever possible, the catheter should be positioned into the deepest layer of the wound and include the most dorsal margin that contains proximal portions of the nerve axons that serve the wound area. The shape of the path that the catheter takes should bring the infusion surface into contact with as much tissue as possible. For irregular wounds, for example, the surgeon must lay the catheter in a serpentine path and loosely anchor the catheter at strategic points with a loop of absorbable suture. Any anchoring sutures must be loose enough to allow eventual withdrawal of the catheter. When a nerve is within the wound, a portion of the working surface of the catheter must be in close approximation to that tissue. When multiple tissue planes are present (eg, in a deep muscle incision in the pelvic limb), the catheter may need to wind its way across several tissue plane boundaries. More than one catheter may be needed to bring enough tissue into contact with local anesthetic. When exiting the catheter, the proximal end is tunneled subcutaneously and exits the skin through a separate stab incision that is created at least 3 cm from the surgical wound margin. Increasing the length of the subcutaneous tunnel increases the barrier to bacterial migration along the surface of the catheter. Following wound closure, the catheter at the exit site is anchored to the skin with 00 monofilament nylon suture or by enclosing it in a bilayer of 1-inch (2.54-cm) waterproof white tape and suturing the tape to the skin. If tape is not used, then the suture is passed

through the skin under the catheter, and a square knot is placed to complete a loop that does not incorporate the catheter; two long ends are left to tie around the catheter in a series of knots that are snug but not so tight as to collapse it.

The first injection of local anesthetic should be administered before recovery from general anesthesia. Estimating the optimal volume of drug to be administered is often an educated guess based on the clinician's impression of the size, depth, and complexity of the wound. In some patients (eg, a large dog that has a total ear canal ablation), the ratio of volume needed to body size is relatively small, and a concentrated- form of anesthetic may be used. When the volume of infusate needed is judged to be large, however, 0.25% bupivacaine is often preferred over the 0.5% concentration because it provides nearly as intense anesthesia but with twice the volume to spread through the area. Either concentration needs to be administered at 4- to 6-hour intervals to maintain adequate anesthesia, so the clinician must calculate a volume that does not produce local anesthetic toxicity. In the case of bupivacaine, the total daily dose should probably not exceed 4 mg/kg in dogs<sup>13,14</sup> and 2 mg/kg in cats. The injection should be made with some force (5–20 psi) because slow injections under low pressure often yield erratic distribution of drug from the catheter. It is because of this erratic distribution that the author does not administer local anesthetics through these catheters as a slow continuous infusion despite the fact that continuous infusion with portable pumps accounts for a large proportion of the use of this technique in humans. The reasons for the erratic drug distribution are complex and currently under investigation by the North Carolina State University Comparative Pain Research Laboratory.

The second dose of bupivacaine should be administered at 4 hours. If the patient objects to the injection, then it should be immediately halted and the operator should wait 10 minutes for the injected proportion to numb the tissue in the immediate vicinity of the catheter. Discomfort is due to the "sting" (low pH) of the solution and the pressure entering the tissue. In many patients, the injection can be finished after this waiting period, with much less reaction.

Subsequent doses of drug are administered at 4- to 6-hour intervals and are modified according to the patient's clinical signs. In most of the author's patients, the catheter is used for 1 to 3 days and then removed. Prior to removal of the device, the clinician allows at least 6 hours to pass from the time of the last injection to confirm that the patient is comfortable without the local anesthetic.

## **ANALGESIC DRUGS ADMINISTERED INTRAVENOUSLY BY CONTINUOUS-RATE INFUSION**

For animals being treated with IV fluids that also require analgesic therapy, continuous infusion of analgesic drugs is convenient and often more effective than intermittent administration in response to patient signs. "Cookbook" formulations can be used for intraoperative fluid therapy and have the advantage of being made the same way and given at the same rate for every patient. Drug therapy can also be tailored to meet individual needs for postoperative or postinjury patients or animals that have other painful conditions such as pancreatitis, burns, severe dermatitis, and so forth. Drugs used most frequently in the North Carolina State University ICU are listed in **Table 2**.

All of these agents appear stable for several days in combination, and in any commonly used IV fluid.<sup>15</sup> When used within a few days, there is no need to protect the solution from light. When used in combination, the dosages for each of these drugs can be at the low end of the suggested range.

Drug	Species	Infusion Rate
Morphine	Canine	0.05–0.2 mg/kg/h
Hydromorphone	Canine	0.0125–0.05 mg/kg/h
Buprenorphine	Canine	2–4 $\mu$ g/kg/h
	Feline	1–3 $\mu$ g/kg/h
Fentanyl	Canine	2–6 $\mu$ g/kg/h
	Feline	2–4 $\mu$ g/kg/h
Lidocaine	Canine	2–4 mg/kg/h
Ketamine	Both	0.2–0.6 mg/kg/h
Medetomidine	Canine	1–3 $\mu$ g/kg/h
	Feline	0.5–2 $\mu$ g/kg/h

### Opioids

Useful agents include hydromorphone and morphine in dogs, and fentanyl and buprenorphine in cats and small dogs. Hydromorphone should be avoided in cats due to the high incidence of drug-induced hyperthermia.<sup>16,17</sup> Morphine is an inexpensive choice for large dogs. Fentanyl is particularly useful when the clinician plans to transition the patient to a fentanyl patch. In that case, the infusion rate of fentanyl is adjusted to reach optimal effect before a patch is applied; the infusion is then tapered and discontinued over the next 8 to 24 hours while observing patient response. If the patient does well on the infusion but poorly when transitioned to the patch, failure of the patch should be suspected. A 25- $\mu$ g patch provides approximately 10  $\mu$ g/h of fentanyl to healthy cats, but delivery is highly variable.<sup>18–20</sup> For small cats, a 12.5- $\mu$ g patch is available.

### $\alpha_2$ -Adrenergic Agonists

The  $\alpha_2$ -adrenergic agonists have marked sedative and analgesic properties that make them useful as preanesthetics and as analgesic adjuncts following surgery or injury. Commercially available drugs in this class include xylazine, medetomidine, and dexmedetomidine. Although xylazine is inexpensive and commonly used as part of preanesthetic protocols for relatively healthy animals, at the author's hospital, it is less effective as a sedative at low doses than the newer agents. Medetomidine consists of a racemic mixture of the *d*- and *l*- optical isomers; the inactive *l*- form is absent from dexmedetomidine, and this drug is twice as potent (not twice as efficacious) as the racemate.<sup>21–23</sup> All of these drugs have clear and profound cardiovascular effects. When administered to healthy dogs, medetomidine increases systemic vascular resistance and produces substantial reductions in heart rate and cardiac output. These effects are fully realized within seconds after IV bolus administration, and a dose of as little as 5  $\mu$ g/kg IV has the full cardiovascular effect seen with higher dosages.<sup>24</sup> Nevertheless, the author has used continuous-rate infusions of medetomidine in dogs (and occasionally in cats) in an ICU environment for many years. The drug is particularly useful to assist sedation in vigorous, young animals following major elective surgical procedures. The patient must be hemodynamically stable and free of significant cardiac disease. In practice, the drug is administered IV as a continuous-rate infusion with no loading dose at an infusion rate of 1 to 3  $\mu$ g/kg/h. Sedation ensues within an hour and generally peaks within 2 hours. The  $\alpha_2$ -adrenergic agonists rarely

suffice as sole analgesic therapy but appear to intensify the analgesia and sedation obtained from other drug classes.<sup>25,26</sup>

### **Lidocaine**

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Intravenous infusion of lidocaine provides some measure of analgesia, likely by a combination of mechanisms that includes reduction of ectopic activity by damaged primary afferent neurons.<sup>27</sup> The drug should not be administered to sick cats or cats under anesthesia because it causes significant cardiovascular depression in that species.<sup>28</sup> When local infusion of local anesthetics is being used, systemic administration should not be used, or the total dose must be calculated from both routes and the daily dosage not exceeded. Lidocaine 5% dermal patches are available in the United States (eg, Lidoderm, Endo Pharmaceuticals, Chadds Ford, Pennsylvania, [www.lidoderm.com](http://www.lidoderm.com)) and may be effective for painful superficial dermatologic conditions in dogs. Although some systemic absorption of lidocaine occurs in dogs following placement of the 700-mg 5% lidocaine patch, the concentration achieved is much lower than what is obtained by IV infusion and may be too low to provide meaningful systemic analgesia for acute pain.<sup>29</sup>

### **Ketamine**

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The role of ketamine in postinjury analgesia is presently unclear. Although the drug is a competitive *N*-methyl-*D*-aspartate receptor antagonist that has modest efficacy to inhibit central sensitization following injury, the results of clinical trials in human patients have been ambiguous.<sup>30</sup> Small studies addressing its use in veterinary patients suggest that there is some efficacy for analgesia and recovery of normal behaviors postoperatively.<sup>31–33</sup>

## **APPROACH**

The use of standardized “recipes” for adding constant amounts of these drugs to IV fluids (eg, “morphine-lidocaine-ketamine”) is an excellent method to provide a background of analgesia to patients during surgery and in the immediate perioperative period. In this system, everyone involved—doctors and staff—know they have to make the analgesic-fluid mix the same way, and hospital staff learn over time how animals respond to a particular approach. An advantage of this approach is that it becomes an easy way to incorporate analgesia therapy into a busy surgical practice with a low chance of making mistakes in preparation. Because of the wide variation in patient needs for analgesia, however, the author prefers to tailor drug infusion to meet individual patient needs during the first 1 to 3 days postoperatively in animals that require support with intravenous fluids.

A commonly employed treatment for patients in pain in the author’s ICU that need sleep is to combine an opioid with lidocaine, ketamine, and medetomidine (for dogs) or with ketamine and medetomidine (for cats) (**Box 1**). This approach is particularly useful for vigorous postoperative patients that require sedation to sleep the night after surgery.

The most convenient method is to add any analgesic medications to fluids that are formulated to provide the maintenance needs for the patient. These are typically low-sodium fluids (eg, one-half or one-fourth strength saline, or commercial maintenance solutions with 40 mEq/L sodium) administered to maintain fluid homeostasis and at infusion rates that never change. Any additional fluid needs (eg, to make up for losses due to drainage, vomiting, diarrhea, polyuria, or excess evaporation) are met with a second fluid set run through the same IV catheter.

**Box 1****Example of a tailored drug infusion plan**

For this technique, plan on adding the drugs to a bag of fluids for which the administration rate will not change, which usually means picking a fluid and administration rate calculated to provide maintenance needs for water. For example, to calculate a drug plan for a 20-kg dog that is to receive morphine, lidocaine, ketamine, and medetomidine for the first 8 to 24 hours postoperatively, drug doses to consider might include

Morphine:  $0.1 \text{ mg/kg/h} \times 20 \text{ kg} = 2 \text{ mg/h}$

Lidocaine:  $2.5 \text{ mg/kg/h} \times 20 \text{ kg} = 50 \text{ mg/h}$

Ketamine:  $0.1 \text{ mg/kg/h} \times 20 \text{ kg} = 2 \text{ mg/h}$

Medetomidine:  $2.0 \text{ } \mu\text{g/kg/h} \times 20 \text{ kg} = 40 \text{ } \mu\text{g/h}$

The maintenance fluid administration rate for a dog this size lying quietly in a cage is roughly 800 mL/d or 33 mL/h. Therefore, a 1-L bag contains 1000/33 or 30 hour's worth of treatment, and to a 1-L bag one must add

Morphine:  $2 \text{ mg/h} \times 30 \text{ hours} = 60 \text{ mg} = 4 \text{ mL}$

Lidocaine:  $50 \text{ mg/h} \times 30 \text{ hours} = 1500 \text{ mg} = 75 \text{ mL}$

Ketamine:  $2 \text{ mg/h} \times 30 \text{ hours} = 60 \text{ mg} = 0.6 \text{ mL}$

Medetomidine:  $40 \text{ } \mu\text{g/h} \times 30 \text{ hours} = 1200 \text{ } \mu\text{g} = 1.2 \text{ mL}$

If the drugs are added to a 1-L bag of fluid, the final volume is greater than a liter—in this case 1081 mL. Therefore, 81 mL should be removed from the bag before addition of the medications.

Considerations regarding the use of continuous infusions include the following:

- Morphine (and to a lesser extent hydromorphone) tends to produce increased sedation and side effects when used at a dosage of  $>0.1 \text{ mg/kg/h}$  ( $>0.05 \text{ mg/kg/h}$  for hydromorphone) for more than 12 hours; therefore, the infusion rate must often be reduced by that time.
- Ketamine may provide some protection against central hypersensitivity at dosages too low to produce obvious clinical signs of ketamine treatment. In the author's experience, infusion rates of  $\leq 0.2 \text{ mg/kg/h}$  are less likely to produce the characteristic behavioral side effects of the drug.
- A reliable sign in cats of significant central effects of opioids is mydriasis. When pupils are dilated and are accompanied by signs of dysphoria, the infusion should be interrupted for 1 to 6 hours and restarted at a lower rate. Cats with dilated pupils should be kept in quiet, darkened cages whenever possible.
- The delay to peak sedation seen with a constant-rate infusion of  $\alpha_2$ -adrenergic agonists is problematic if rapid sedation is required to address emergence delirium. In this case, a dose of  $1 \text{ } \mu\text{g/mL}$  may be diluted into 10 mL of saline and administered to the patient 1 mL ( $0.1 \text{ } \mu\text{g/kg}$ ) at a time, titrated to effect.
- Sedation and respiratory depression from opioids and medetomidine are much more likely when the animal is hypothermic. Caregivers should verify satisfactory recovery of consciousness and body temperature after surgery before sedation with these agents and provide heat support as needed.
- If sedation with any agent is excessive, the clinician should interrupt the infusion for up to a few hours and restart it at a lower rate or lower drug concentration.
- For cats and small dogs, 250-mL bags should be used or an in-line burette should be installed to meter the fluid. Putting all additives into such a container instead of a large bag limits waste and makes it easier to change the infusion mix.

- If additional fluids are needed, one should piggyback a separate bag and administration set onto the primary IV set at an injection port and administer as needed; the rate of the medicated fluid should not be changed.
- When first learning how to use drug infusions, one should start with lower dosages and gradually use higher infusion rates as the care team gains confidence and experience. The first few applications of the technique should be on patients whose infusion can begin before noon. Generally, by the time 4 to 6 hours have passed, drug effects and clinical signs will reach a plateau. After gaining confidence with this technique, some patients that receive fluids unattended overnight can be treated in this manner, assuming an electronic fluid pump is used and the drug effects reach a plateau by the end of the work day.
- Most postinjury and postoperative patients benefit from the addition of oral non-steroidal anti-inflammatory drug therapy in addition to the infusion, providing there are no contraindications.
- As the patient recovers the ability to drink and as less drug is needed, the IV fluid rate can be slowed proportionately.

### GABAPENTIN

Gabapentin is a structural analog of  $\gamma$ -aminobutyric acid introduced in 1993 as an anticonvulsant and later approved for treatment of the human chronic pain syndrome of postherpetic neuralgia. Its antinociceptive mechanism may be multifactorial but appears to include inhibition of neuronal voltage-dependent calcium channels, a process that reduces the release of excitatory neurotransmitters in nociceptive substrate of the spinal cord.<sup>34</sup> Although it is commonly used as an adjunct therapy for chronic pain in dogs and cats, there is growing interest in its use as an adjunct analgesic for the treatment of acute pain in veterinary patients because of recent trends in human medicine.<sup>35</sup> A common starting dose is 2 to 5 mg/kg twice a day, adjusted upward if needed or downward if sedation or ataxia develop. Gabapentin is started as soon as the animal tolerates oral medications while being treated concurrently with established drugs.

### SUMMARY

Acute pain is a physiologically appropriate consequence of injury and inflammation but, in hospitalized patients, may increase complications from an exaggerated stress response. Because it is usually caused by nociception, drug therapy is often an effective component of patient management. Although the drugs used for analgesia have many potential side effects, when used properly and in combination, it is almost always possible to provide meaningful and safe analgesia to even critically ill patients.

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