Chapter 20

Local and Regional Anesthetic and Analgesic Techniques: Dogs

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Introduction

The popularity of local anesthetic-induced neural blockade in dogs has increased over the past several years. A major driving force behind this increased usage is acceptance of the concept of blocking multimodal pathways to control animals' pain and suffering. Unlike most general anesthetics, which block the perception of pain by inducing anesthesia in an unconscious patient, local anesthesia and regional anesthesia completely block transmission of noxious impulses in a region of the body of a conscious patient. General anesthesia may be advantageous in dogs that are considered difficult to sedate and restrain for surgery and where complete immobilization and relaxation of the patient are required. Local and regional anesthesia also decreases the quantity of opioid and inhalation anesthetic required to obtain the desired plane of anesthesia intraoperatively.[1] Topical anesthesia, infiltration anesthesia, field blocks, selected nerve blocks of the head (anesthesia of the maxilla, upper teeth, eye and orbit, mandible, and lower teeth), anesthesia of the foot and leg (ring block, brachial plexus block, and intravenous regional anesthesia), multiple intercostal nerve blocks, lumbosacral epidural anesthesia, and continuous epidural anesthesia are all logical techniques for providing surgical analgesia and anesthesia in dogs that are considered at risk for inhalant or intravenous anesthesia (Table 20.1). Continuous interpleural analgesia and epidural opioid analgesia can be used to relieve postoperative pain following general anesthesia.

This chapter provides a general overview of the most commonly used local and regional anesthetic techniques for surgical and postoperative pain relief in dogs, emphasizing methodology, advantages, and disadvantages. The pharmacology of local anesthetic drugs, highlighting the mechanisms of action, relevant pharmacology and pharmacokinetics, toxicity, and potential drug interactions, are discussed in Chapter 14.

Topical Anesthesia

Many local anesthetics are effective when placed topically on mucous membranes and may be used in the mouth, tracheobronchial tree, esophagus, and genitourinary tract. Local anesthetics used topically include lidocaine (2% to 5%), proparacaine (0.5%), tetracaine (0.5% to 2.0%), butacaine (2%), and cocaine (4% to 10%). Preparations include injectables that are applied topically, cream, ointment, jelly, powder, and aerosol. Injectable preparations of lidocaine (0.5% to 5.0%), available in ampules and vials, with and without epinephrine (1:50,000 to 1:200,000), can be used for infiltration (0.5% to 1.0%) and nerve block (1% to 2%), and applied topically to mucous membranes (1% to 5%). Topical local anesthetic agents can relieve pain during cleaning or dressing of wounds, although their effect is highly variable.

Table 20.1. Classification and degree of required dexterity for producing local and regional anesthetic techniques in dogs.

Classification	Techniques	Required Manual Dexterity and Experience
Terminal anesthesia	Topical	+
	Intravenous regional anesthesia	++
Infiltration anesthesia	Subcutaneous, intramuscular injection	+
	Subpleural injection	++
	Ring block	+
Perineural anesthesia	Nerve blocks on the head	++
	Nerve blocks on the legs	+++
	Brachial plexus block	++
	Intercostal nerve block	+
Spinal anesthesia	Lumbosacral epidural anesthesia	++
	Continuous epidural anesthesia (catheter technique)	+++
	Lumbar subarachnoid anesthesia	+++
Postoperative analgesia	Epidural opioid analgesia	++
	Continuous epidural opioid analgesia (catheter technique)	+++
	Interpleural regional analgesia (catheter technique)	+++
Therapeutic analgesia	Anesthesia of the cervicothoracic ganglion	+++
	Anesthesia of the lumbar sympathetic ganglia	+++

+, little; ++, some; +++, considerable.

The lowest effective dose of topical anesthetic should always be used in order to prevent toxicity from excessive drug plasma concentrations.[2] Time between application of topical anesthetics and onset of anesthesia is generally longer, and pain relief less, than that achieved with infiltration anesthesia. A 2% to 4% solution of lidocaine used for topical anesthesia on mucous membranes produces effects in approximately 5 min and lasts for 30 min.

Local instillation of proparacaine (0.5%), tetracaine (0.5% to 1.0%), butacaine (2%), piperocaine (2%), oxybuprocaine (0.4%), or cocaine (1% to 4%) into the conjunctival sac anesthetizes the cornea and conjunctiva for short procedures (e.g., removal of hypertrophied gland of the third eyelid). Proparacaine (0.5%) has been advocated as an excellent topical anesthetic for examination of a painful eye, removal of foreign bodies, sutures, obtaining conjunctival scrapings, and subconjunctival injections.[3] Anesthesia occurs rapidly (1 to 6 min), lasts for 10 to 15 min after single instillation, and may last for up to 2 h after repeated instillation without untoward effects (e.g., irritation or epithelial damage).[4] A series of three to five instillations of 1 or 2 drops of proparacaine at approximately 1-min intervals may be necessary to produce satisfactory anesthesia of the cornea and conjunctiva. Topical anesthesia is very safe, is simple to apply, and can be repeated, although dogs may resent the application of cold solutions. Data on vascular uptake and maximum blood concentration are not available, large interpatient variability should be expected, and potential for bacterial contamination exists.[5]

Local anesthetic sprays (10% lidocaine or 14% to 20% benzocaine) anesthetize the mucosa up to a depth of 2 mm within 1 to 2 min after application. Anesthesia lasts for approximately 15 to 20 min. The movable nozzle (Jetco nozzle) of the spray can enable easy access to the site of application. Pressure on the nozzle with the forefinger delivers a specific quantity of the anesthetic each second (10 mg of lidocaine from a 10% lidocaine spray can). The average expulsion rate from a benzocaine (Cetacaine) spray can is 200 mg/s.

Endotracheal tubes are frequently coated with local anesthetic jells but should not be lubricated with jelly containing 20% benzocaine hydrochloride. Topical sprays and ointments containing 14% to 20% benzocaine reproducibly cause dose-dependent methemoglobinemia. Preparations with over 8% benzocaine include Hurricane Spray (20%), Hurricane Topical Anesthetic Gel (20%) and Liquid (20%), Camphophenique Sting Relief Formula (20%), Dermoplast Anesthetic Pain Relief (20%), and Cetacaine Spray (14%).[6] Exposure of the tracheal mucosa to topical benzocaine oxidizes blood hemoglobin in dogs in proportion to the absorbed dose within 10 min. Methemoglobin cannot bind oxygen or carbon dioxide.[7] Dogs are usually asymptomatic when concentrations of methemoglobin are less than 20%, but show fatigue, weakness, dyspnea, and tachycardia at concentrations between 20% and 50%.[8] Laryngeal sprays containing benzocaine should be used with caution, and if signs of cyanosis and respiratory distress develop, methemoglobinemia should be considered. In general, benzocaine should be used sparingly and cautiously while continuously monitoring for cyanosis. Patients at risk of hypoxia after using benzocaine topical anesthesia should receive oxygen[6] and intravenous methylene blue (1.5 mg/kg) therapy.[8]

One of the oldest forms of topical anesthesia is superficial cooling. Ethyl chloride can be used to freeze a small local area of skin for punctures, skin biopsy, or incision of small abscesses. Ethyl chloride is sprayed on the skin for 3 to 7 s from an inverted bottle and a distance of 10 to 20 cm, with the jet stream aimed so that it meets the skin at an acute angle to lessen the shock of impact (Fig. 20.1). Surface anesthesia results from cooling (<4°C), which occurs during the evaporation process. Attempts to freeze large skin areas by using ethyl chloride are contraindicated be-

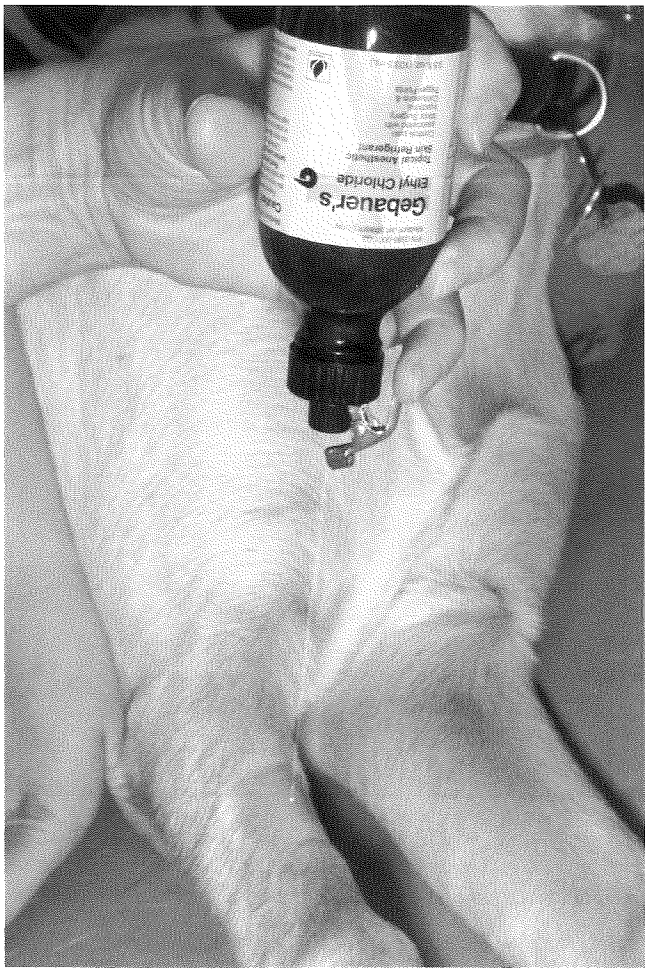

Fig. 20.1. Ethyl chloride is sprayed on the skin to produce surface anesthesia.

cause of the potential for frostbite. Ethyl chloride's brief action (<2 min), ability to produce a freezing sensation, and flammability when exposed to open flames and electric sparks (electrocauterization) limit its use. Inhalation of ethyl chloride should be avoided because it may produce narcotic and general anesthetic effects, or fatal coma with respiratory and cardiac arrest.

Pontocaine cream and a liposomal tetracaine preparation (0.5% tetracaine encapsulated into phospholipid vehicles) effectively penetrate human skin within 30 to 60 min of application, producing long-lasting (>4 h) analgesia.[9] The most clinically usable cream contains a 5% eutectic mixture of 2.5% lidocaine and 2.5% prilocaine (EMLA cream), which overcomes the human stratum corneum barrier within 1 h of topical application without adverse effects.[10] The usefulness of EMLA cream in dogs has been reported.[11]

Infiltration Anesthesia

Local infiltration of local anesthetics requires their extravascular placement by direct injection and may be the most reliable and safest of all the local anesthetic techniques (Table 20.1). Lidocaine (0.5% to 2.0%) is the local anesthetic most often used for infiltration. Only sharp and sterile needles should be used. Local anesthesia can be produced by multiple intradermal or subcutaneous injections of 0.3 to 0.5 mL of local anesthetic solution by using a 2.5-cm, 22- to 25-gauge needle or by using a longer needle (3.75 to 5.0 cm) and slowly injecting local anesthetic while advancing the needle along the line of proposed incision (linear infiltration). Pain is minimal if the needle is advanced slowly into the first desensitized wheal and successive injections are made at the periphery of the advancing wheal. This technique assures that the dog senses only the initial needle insertion. Intradermal deposition of local anesthetic over a superficial abscess, cyst, or hematoma is a routine procedure. Infection along the filtration site will not occur if the needle has not entered the abscess. The amount of local anesthetic used for infiltration anesthesia depends on the size of the area to be anesthetized. Approximately 2 to 5 mg/kg of lidocaine or mepivacaine and 4 to 6 mg/kg of procaine without epinephrine may be used to diffuse into surrounding tissue from the site of injection and anesthetize the nerve fibers and endings. Large amounts of relatively dilute solutions are often infiltrated into operative sites. The lowest possible concentration of local anesthetic that will produce the desired effect should be administered. For example, an average dog (20 kg) will tolerate approximately 50 mL of 0.5% lidocaine without demonstrating signs of toxicity, whereas only 20 to 30 mL of 1% lidocaine or 10 to 15 mL of 2% lidocaine can be injected. The local anesthetic may be diluted in 0.9% sodium chloride solution (not with sterile water) to a 0.25% solution if a large volume of local anesthetic is needed for infiltration of a large operative area. The total dose of drug administered should be reduced by 30% to 40% in old dogs (>8 years) and sick or cachectic dogs in poor condition.[12]

Alternatively, approximately 5 to 8 mg/kg of local anesthetic with epinephrine (1:200,000) may be used for infiltration to produce local vasoconstriction, which reduces absorption rates (30%) and helps to maintain a high drug concentration at the nerve fiber, thus increasing the local anesthetic effect and duration (50%). Local anesthetics containing epinephrine should not be injected into tissues supplied by end arteries (e.g., ears and tail) or in thin and dark-skinned dogs (e.g., poodles) because of the risk of severe vasoconstriction, local ischemia, and necrosis. Epinephrine increases the potential risk of cardiac arrhythmias (e.g., sinus tachycardia, ventricular tachycardia, and ventricular fibrillation in a halothane-sensitized heart), although this has not been a problem when administered in conjunction with lidocaine in dogs. Hearts sensitized to ventricular arrhythmias with halothane do not develop serious ventricular arrhythmias when given lidocaine (1.3 to 7.9 mg/kg) containing epinephrine (0.3 to 1.9 mg/kg) in doses found in lidocaine-epinephrine mixtures used commonly for local anesthesia.[13] Subfascial and intra-arterial injections must be avoided.

Continuous-Infiltration Anesthesia

This can be accomplished by the use of a continuous catheter-insertion system and a disposable infusion pump (Fig. 20.2).[14] A sterile multipore catheter is placed within the surgical incision

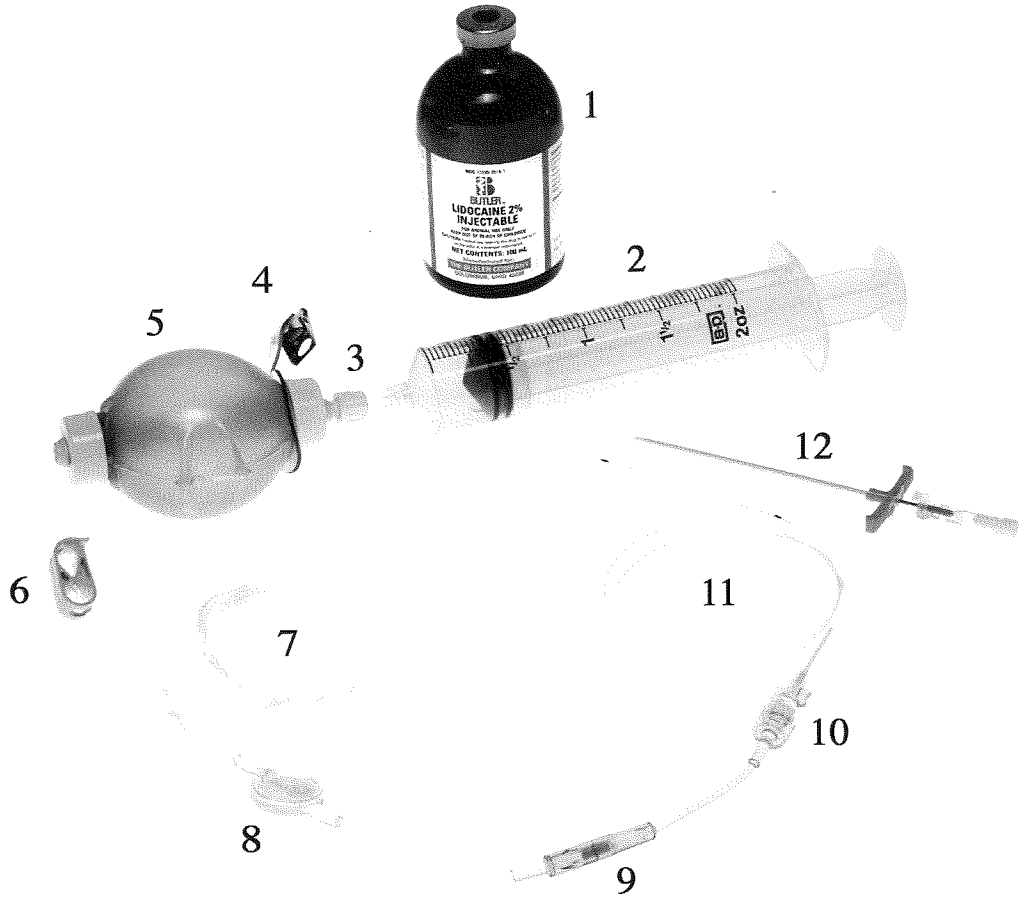

Fig. 20.2. Pain management system for continuous local anesthetic infiltration. The Pain Buster Soaker/ON-Q (I-Flow, Lake Forest, CA) provides continuous administration of local anesthetic into the surgery site for 1 to 5 days: (1) 100 mL of 2% lidocaine hydrochloride solution; (2) 60-mL syringe; (3) fill port with protection cap; (4) E-clip to secure the pump; (5) Pain Buster pump; (6) clamp; (7) pump tubing; (8) filter; (9) flow restrictor, 2-mL/h flow rate if placed in direct contact with the skin (31°C); (10) luer lock on the catheter connector; (11) radiopaque, fenestrated soaker catheter, with a 20-gauge, 59-cm long, 6.5–cm infusion segment; and (12) split-introducer sheath with the needle partially withdrawn from the needle guard.

(e.g., total ear-canal ablation with lateral bulla osteotomy [Fig. 20.3A], forelimb amputation [Fig. 20.3B], or median and lateral thoracotomies) at the end of the surgical procedure. The catheter is connected to an elastomeric reservoir infusion pump (Pain Buster Soaker system; Orthopedics, Vista, CA), which is filled with local anesthetic (i.e., lidocaine, mepivacaine, or ropivacaine) to its full capacity (65, 100, 270, or 335 mL) to deliver the local anesthetic at a constant rate (0.5, 2.0, 4.0, or 5.0 mL/h) for several days. The Pain Buster Soaker technique is generally well tolerated, producing good postoperative analgesia for up to 50 h, with no acute local anesthetic toxicity, hemodynamic instability, or breakthrough pain.[15] Side effects, such as nystagmus, restlessness, apprehension, and vomiting, are readily treated by removing the pump.

Field Block

This technique can be used for anesthetizing large areas. First, intradermal or subcutaneous linear infiltration is produced around the lesion as previously described. Local anesthetic is then deposited in the deeper tissues by passing the needle through the desensitized skin far enough to infiltrate the deep nerves supplying the area (Fig. 20.4).[16]

Intraperitoneal Infusion

The efficacy of intraperitoneal administration of either lidocaine (2%, 8.8 mg/kg with epinephrine 5 µg/mL), bupivacaine (0.75%, 2.2 mg/kg), or 0.9% sodium chloride solution, and additional subcutaneous injection of 2 mL of the assigned solution prior to incisional closure, has been evaluated for analgesia in 10 dogs upon completion of ovariohysterectomy.[17] Surgery was performed with the patient under general anesthesia (acepromazine-butorphanol-thiopental-isoflurane). No adverse side effects were observed. Pain scores, using the visual analogue scale (VAS), peaked for all groups at 0.5 h and returned to baseline by 18 h. Dogs in the bupivacaine group had significantly lower pain scores at 0.5 h than did the dogs in the 0.9% saline group. Butorphanol and/or acepromazine (0.22 mg/kg intramuscularly [IM] or intravenously [IV]) was given to provide supplemental analgesia to 7 of 10 dogs in the saline group, 4 of 10 dogs in the

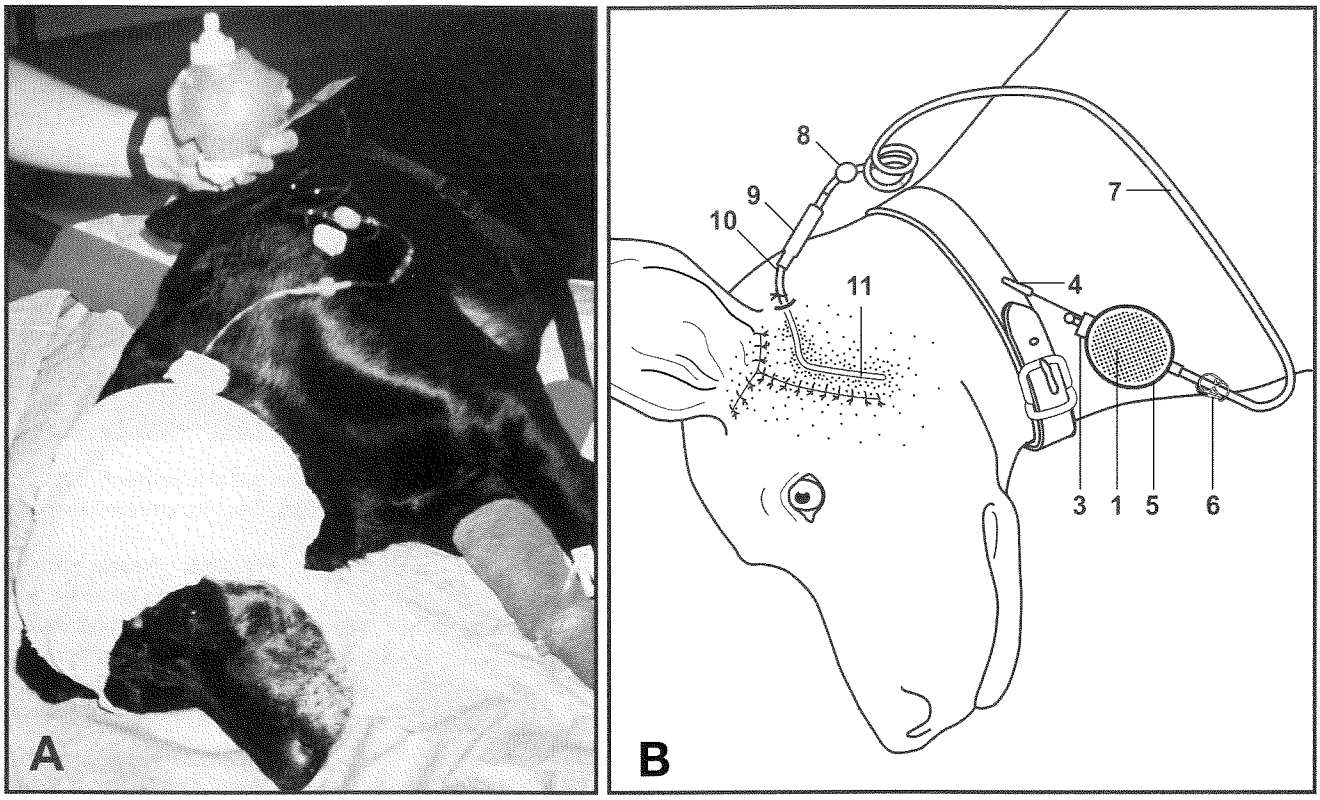

Fig. 20.3. Pain therapy by using the Pain Buster Soaker: black Labrador (39 kg) after total ear-canal ablation **(A)**. The Pain Buster pump is placed into a protective bag hanging beneath the neck. Lidocaine (2%) continuously infiltrates the wounds at a constant rate (2 mL/h) for several days. The numbers refer to the same system components as described in Fig. 20.2 **(B)**.

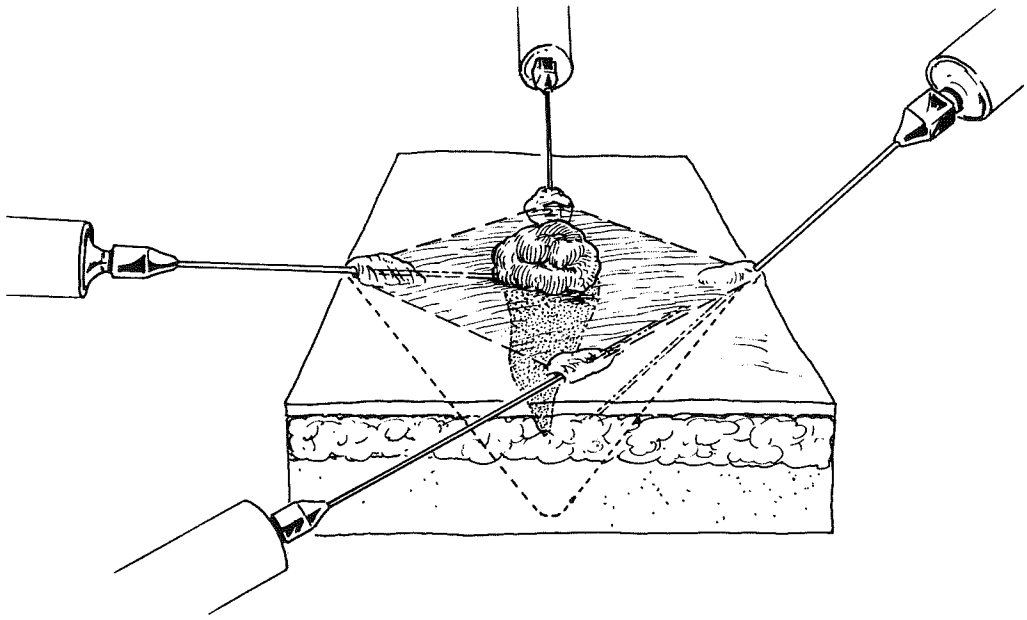

Fig. 20.4. Field block producing walls of anesthesia enclosing the surgical field.

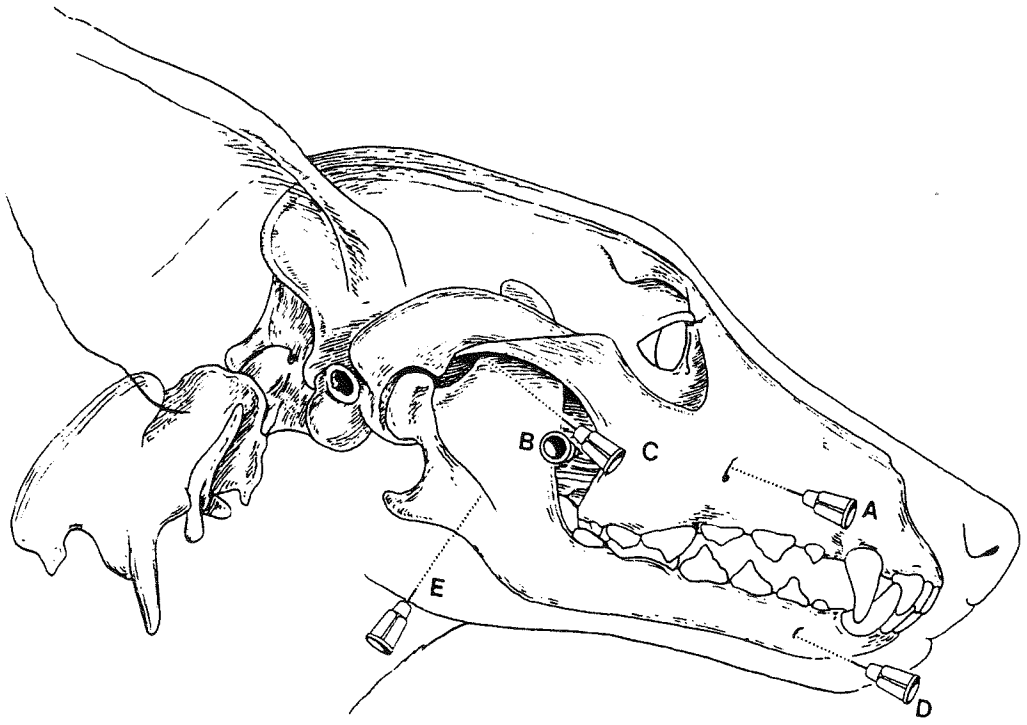

Fig. 20.5. Needle placement for producing nerve blocks on the head: infraorbital (A), maxillary (B), zygomatic, lacrimal, and ophthalmic (C), mandibular (E), and mental (D) nerves.

lidocaine group, and 2 of 10 dogs in the bupivacaine group. These findings can be interpreted as support for the use of intraperitoneal and subcutaneous bupivacaine for postoperative analgesia following ovariohysterectomy in dogs.[17,18]

Nerve Blocks

Injection of local anesthetic solution into the connective tissue surrounding a particular nerve produces loss of sensation (sensory nerve block) and/or paralysis (motor nerve block) in the region supplied by the nerves (regional anesthesia). Smaller volumes (1 to 2 mL) of local anesthetic are needed to produce nerve blocks when compared with a field block, thereby reducing the danger of toxicity.

Three supplemental methods of pain relief in 31 anesthetized dogs undergoing total ear-canal ablation with lateral bulla osteotomy have been compared.[19] The use of systemic opioids alone (e.g., oxymorphone, 0.05 mg/kg IV), intraoperative splash block, using bupivacaine (0.5% solution, 1.0 mg/kg per ear), and preoperative nerve block of the great auricular nerve (cervical nerve II) and the auriculotemporal nerve (cranial nerve V), using bupivacaine (0.5% solution, 0.5 mL per site), provided similar pain relief, although 33% of the dogs required additional analgesia or tranquilization after surgery. Rectal temperature, pulse rate, respiratory rate, and postoperative serum cortisol concentrations in dogs were not significantly different among groups ($P < 0.05$).

Regional Anesthesia of the Head

The administration of local anesthetic around the infraorbital, maxillary, ophthalmic, mental, and alveolar mandibular nerves provides valuable and practical advantages over general anesthesia when combined with effective sedation (Fig. 20.5). Each nerve may be desensitized by injecting 1 to 2 mL of a 2% lidocaine hydrochloride solution by using a 2.5- to 5-cm, 20- to 25-gauge needle.

The infraorbital nerve is desensitized at its point of emergence from the infraorbital canal. The needle is inserted either intraorally[20] or extraorally approximately 1 cm cranial to the bony lip of the infraorbital foramen.[21,22] The needle is advanced to the infraorbital foramen, which can be found between the dorsal border of the zygomatic process and the gum of the upper canine tooth (Fig. 20.5A). Successful injections desensitize the upper lip and nose, the roof of nasal cavity, and the surrounding skin up to the infraorbital foramen.

The maxillary nerve must be desensitized to completely desensitize the maxilla, upper teeth, nose, and upper lip. The needle is placed percutaneously along the ventral border of the zygomatic process approximately 0.5 cm caudal to the lateral canthus of the eye and is advanced into close proximity of the pterygopalatine fossa (Figs. 20.5B and 20.6). Local anesthetic is administered at the point where the maxillary nerve courses perpendicular to the palatine bone between the maxillary foramen and foramen rotundum.[20,21]

Eye and Orbit

Anesthesia of the eye and orbit is produced by desensitizing the ophthalmic division of the trigeminal nerve. General anesthesia for ophthalmic procedures has increased in popularity; however, retention of ocular reflexes during light and medium planes of general anesthesia in dogs can disturb the surgical field. Regional anesthesia, by anesthesia of ophthalmic nerves, produces immo-

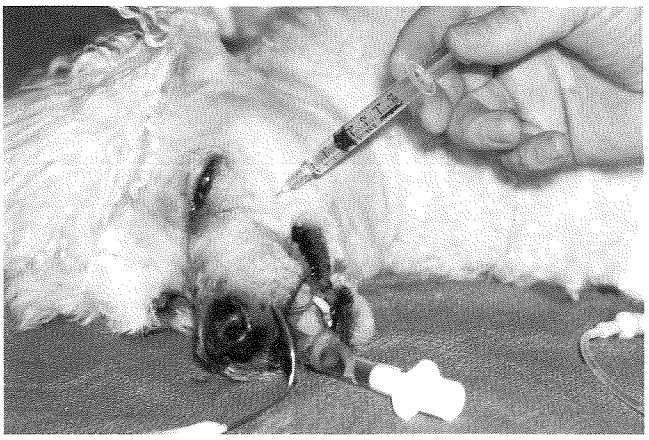

Fig. 20.6. Anesthesia of the maxillary nerve in a poodle (32 kg) after partial maxillectomy: site and direction of the inserted needle.

bility of the eye in addition to sensory anesthesia, and prevents the oculocardiac reflex, which can cause bradycardia, arrhythmias, and cardiac arrest as result of traction on the extrinsic muscles of the eye. A 2.5-cm, 22-gauge needle is inserted ventral to the zygomatic process at the level of the lateral canthus. The point of the needle should be approximately 0.5 cm cranial to the anterior border of the vertical portion of the ramus of the mandible. The needle is advanced medial to the ramus of the mandible in a mediodorsal and somewhat caudal direction until it reaches the lacrimal, zygomatic, and ophthalmic nerves at the orbital fissure (Fig. 20.5C). Deposition of 2 mL of local anesthetic at this site produces akinesia of the globe because of the proximity of the abducens, oculomotor, and trochlear nerves to the ophthalmic nerve. Motor block is assessed by cessation of the following eye movements: laterally, caused by the lateral rectus muscle (abducens nerve); and upward, downward, medially, and laterally, caused by the superior, inferior, medial, and lateral rectus muscles, respectively (oculomotor nerve). The superior oblique muscle rotates the eye downward and laterally (oculomotor nerve), whereas the inferior oblique muscle rotates the globe upward and laterally (trochlear nerve).[23]

Retrobulbar or peribulbar anesthesia for local anesthesia of the eye runs the risk of direct subarachnoid injection, peribulbar hemorrhage, globe perforation, and intravascular injection.[5,23,24] When performing retrobulbar anesthesia, the risk of puncturing the globe is minimal if a 7.5-cm, 20-gauge needle is inserted at the lateral canthus through the anesthetized conjunctiva and is advanced past the globe toward the opposite mandibular joint until the base of the orbit is encountered.[20] When performing peribulbar anesthesia, the potential for puncturing ciliary and scleral blood vessels is minimal if a 5-cm curved needle (0.5-mm internal diameter) conformed to the roof of the orbit is inserted through the anesthetized conjunctival sac at the vertical meridian (Fig. 20.7).[25] Directing the needle away from the globe and toward the orbit also minimizes the risk of perforating the globe.

Injection of local anesthetic into the optic sheath can cause respiratory arrest attributable to the infiltration of local anesthetic into the subarachnoid space of the central nervous system (CNS).[24] The pressure generated by injection into the optic nerve sheath or intrascleral injection is three or four times that produced by injection into the retrobulbar adipose tissue (135 vs. 35 mm Hg).[24] Increased resistance encountered during retrobulbar block should serve as a warning, mandating redirection of the needle in order to prevent subarachnoid injection.

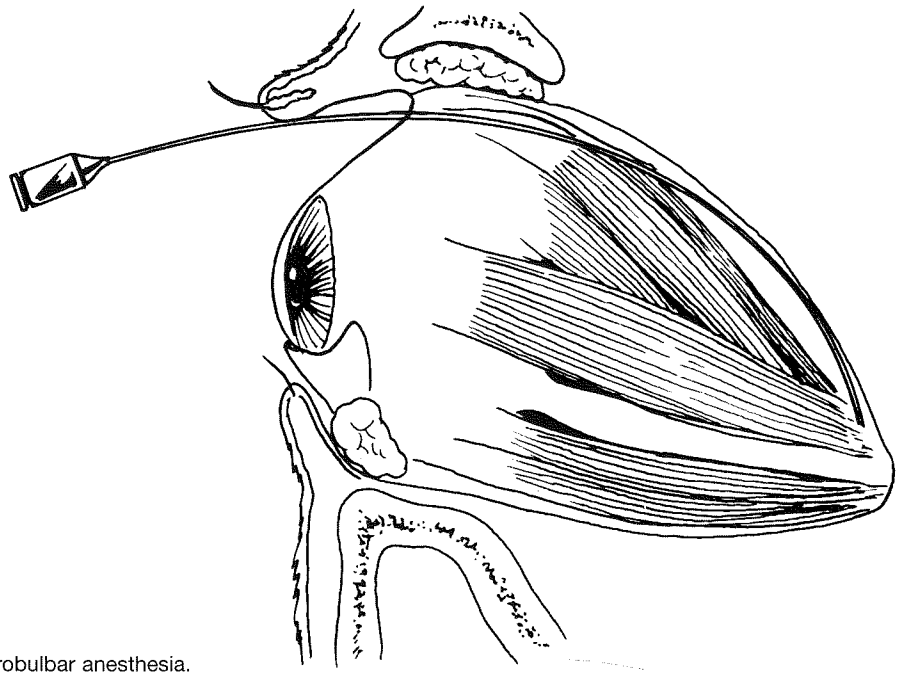

Fig. 20.7. Needle placement for producing retrobulbar anesthesia.

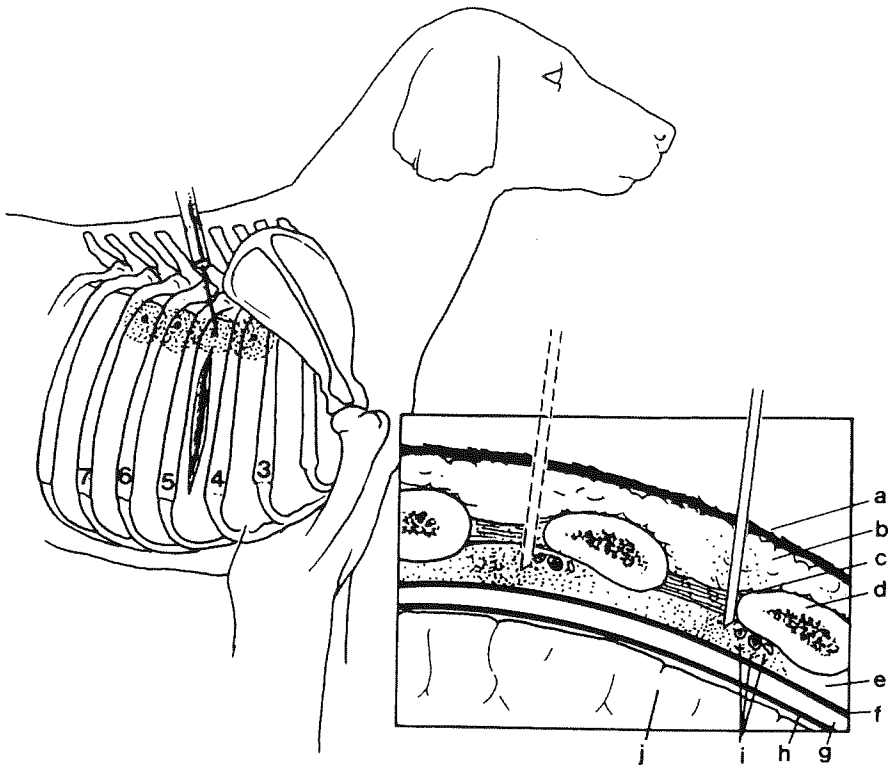

Fig. 20.8. Needle placement for inducing intercostal nerve blocks. **Inset:** (a) skin, (b) subcutaneous tissue, (c) intercostal muscles, (d) rib, (e) subcostal space, (f) pleura costalis and fascia, (g) interpleural space, (h) pleura pulmonalis, (i) intercostal artery, vein, and nerve, and (j) lung.

Lower Lip

This can be desensitized by percutaneously inserting a 2.5-cm, 22- to 25-gauge needle rostral to the mental foramen at the level of the second premolar tooth. Approximately 1 to 2 mL of local anesthetic is deposited in close proximity to the mental nerve (Fig. 20.5D).

Mandible and Lower Teeth

The mandible (including molars, premolars, canine, incisors, skin) and the mucosa of the chin and lower lip can be desensitized by injecting 1 to 2 mL of the local anesthetic in close proximity to the inferior alveolar branch of the mandibular nerve as it enters the mandibular canal at the mandibular foramen (Fig. 20.5E). A 2.5-cm, 22-gauge needle is inserted at the lower angle of the jaw approximately 0.5 cm rostral to the angular process and is advanced 1 to 2 cm dorsally along the medial surface of the ramus of the mandible to the palpable lip of the mandibular foramen.[20,22]

Intercostal Nerve Block

Intercostal nerve blocks may be used for relieving pain during and after thoracotomy, pleural drainage, and rib fractures, thereby minimizing the need for systemic analgesics that may depress respiration. They are not recommended for dogs with pulmonary diseases, which impair blood-gas exchange, or for dogs that cannot be observed for several hours after injection because of the potential for clinically delayed pneumothorax.

A minimum of two adjacent intercostal spaces both cranial and caudal to the incision or injury site are selectively blocked because of overlap of nerve supply.[26] The site for needle placement is the caudal border of the rib (R3-6) near the intervertebral foramen (Fig. 20.8). Approximately 0.25 to 1.0 mL of 0.25% or 0.5% bupivacaine hydrochloride per site, with or without epinephrine 1:200,000, is deposited. Small volumes and/or diluted local anesthetic solutions should be used as initial pain therapy so that the total dose does not exceed 3 mg/kg. Small dogs receive 0.25 mL/site, medium dogs 0.5 mL/site, and large dogs 1.0 mL/site. Postthoracotomy pain is generally controlled for 3 to 6 h after successful block.[26] Heart rate, respiratory rate, hematocrit, plasma protein, blood pH, arterial oxygen partial pressure (PaO_2), and arterial carbon dioxide partial pressure ($PaCO_2$) do not change significantly in halothane-anesthetized dogs after intercostal nerve block.[26,27] Prolonged analgesia may be achieved by repeated administrations of local anesthetics, although a patient may not tolerate multiple percutaneous injections. Intercostal nerve block produces relatively high blood concentrations of local anesthetic for a given dose;[28,29] therefore, the risk of toxic blood concentrations is greater.

Selective intercostal nerve block is easily performed because of the proximity of each nerve to its adjacent rib.[30] The intercostal nerves can be visualized beneath the parietal pleura during thoracotomy. This technique provides consistent analgesia and does not produce respiratory depression, with subsequent hypercarbia and hypoxemia, which is a more frequent problem in dogs administered intramuscular or intravenous opioids.[26,31] Because intercostal bupivacaine (0.5%, 0.5 to 1.0 mL) abolishes nociceptive input only from tissues supplied by the intercostal nerves,

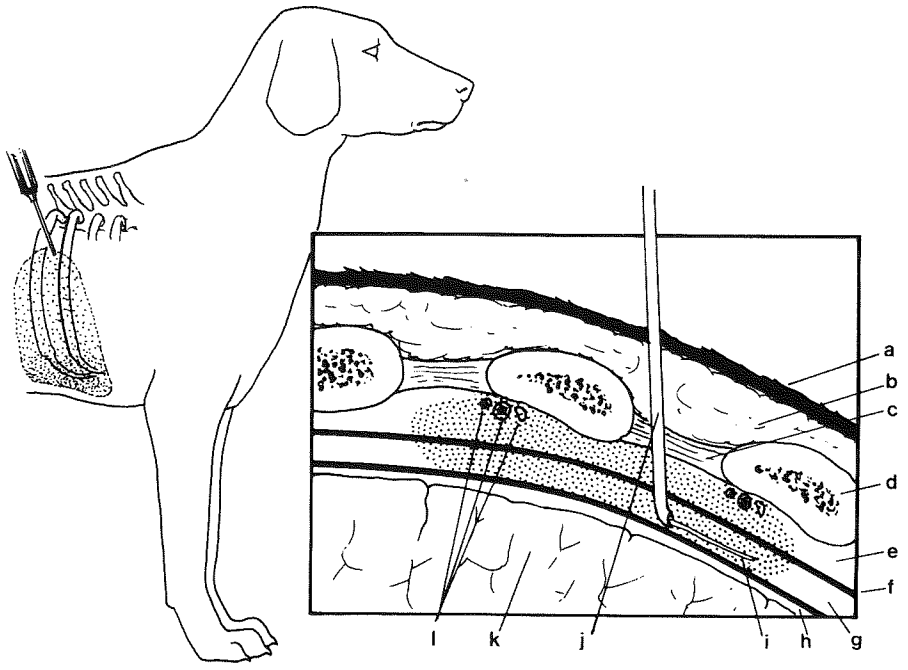

Fig. 20.9. Interpleural catheter placement. **Inset:** (a) skin, (b) subcutaneous tissue, (c) intercostal muscles, (d) rib, (e) subcostal space, (f) pleura costalis and fascia, (g) interpleural space, (h) pleura pulmonalis, (i) catheter, (j) Tuohy needle, (k) lung, and (l) intercostal artery, vein and nerve.

but not from the whole surgical site, additional analgesia with preoperatively administered epidural morphine (0.1 mg/kg) has been suggested to improve both intraoperative and immediate postoperative analgesia in dogs after thoracotomy.[32]

Interpleural Regional Analgesia

Interpleural injection of local anesthetics is a relatively new option for managing certain types of acute and chronic pain originating from thoracic and upper abdominal structures in humans.[33] Pain from rib fractures, metastasis to the chest wall, pleura, and mediastinum, mastectomy, chronic pancreatitis, cholecystectomy, renal surgery, abdominal cancer, and posthepatic neuralgesia can be relieved by intermittent or continuous administration of local anesthetic into the pleural space through a catheter, without the systemic effects commonly observed after the use of parenterally administered (IM or IV) opioids.[34] Most clinical studies have been performed in patients recovering from gallbladder surgery. Less frequently, this technique has been used for pain relief in patients with multiple fractured ribs; other indications are uncommon.[35] Reports in the current literature provide evidence both supporting[36,37] and opposing[38–40] the effectiveness of postoperative pain management via interpleural analgesia after thoracotomy for pulmonary surgery in humans. The mechanisms of pain relief produced by interpleural analgesia are not fully understood, but at least three different sites of actions have been hypothesized: (a) retrograde diffusion of local anesthetic through the parietal pleura, causing intercostal nerve block;[41,42] (b) unilateral block of the thoracic sympathetic chain and splanchnic nerves;[43] and (c) diffusion of the anesthetic into the ipsilateral brachial plexus, resulting in a parietal block.[33]

The technique requires the insertion of a catheter into the pleural space of sedated or anesthetized dogs.[26,44–51] The catheter is placed into the pleural space either percutaneously or prior to closure of a thoracotomy (Fig. 20.9). Percutaneous placement of a catheter into the pleural space is difficult to perform on dogs with pleural fibrosis, because thickening of the pleura makes identification of the pleural space guesswork. The dog should be sedated, and the skin, subcutaneous tissues, periosteum, and parietal pleura over the caudal border of the rib should first be desensitized with 1 to 2 mL of 2% lidocaine solution, using a 2.5- to 5-cm, 20- to 22-gauge needle. A 5.0-cm × 1.4-mm outer diameter, 17-gauge Huber point (Tuohy) needle is then used for catheter placement. The stylet is removed and the needle filled with sterile saline until a meniscus is seen at the needle's hub. The needle is then advanced until a clicking sensation is perceived as the needle tip perforates the parietal pleura or until the meniscus disappears when the needle tip enters the pleural space (hanging-drop technique).

The hanging-drop technique for the identification of the subatmospheric pleural pressure is not always reliable because the meniscus may also disappear when the needle passes through the intercostal muscles. Alternatively, a freely moving 10-mL glass syringe is attached to the needle. The syringe and needle are then advanced as a unit. On entering the pleural space, the plunger of the syringe is drawn inward by the negative pressure of the interpleural space.[34] Some veterinarians place the catheter in the tissue plane superficial to the parietal pleura, close to or in the subcostal space (e in Fig. 20.9), in order to produce a more effective block attributable to a decreased loss of local anesthetic through thoracic drainage tubes.[35] A catheter (6- to 10-cm length of fenestrated medical grade silastic tubing, 2-mm inside diameter) can

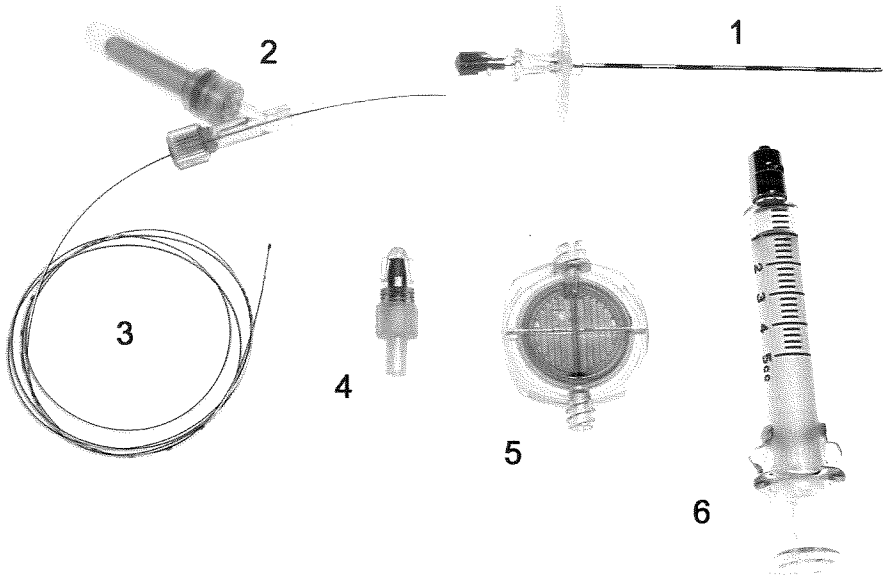

Fig. 20.10. Interpleural tray for continuous interpleural analgesia. The basic Pleurocert procedure set contains (1) Tuohy needle (1.7 × 80 mm, 16 gauge × 31/4 inches), (2) Y piece with control balloon, (3) radiopaque polyamide catheter (0.65 × 1.05 × 1000 mm), (4) screw connector, (5) luer lock antibacteria injection filter (0.2 μm), and (6) 5-mL glass syringe.

be introduced and advanced 3 to 5 cm beyond the needle tip with minimal resistance after the needle tip is placed subpleurally.

A technique has been developed to insert the catheter without disconnection to minimize the risk of pneumothorax.[52] The technique involves the use of a Tuohy needle to which a Y piece with a latex balloon and catheter is attached (Fig. 20.10). The needle is inserted until the balloon collapses under the negative pressure of the pleural cavity; the catheter is then advanced as required. The needle is then carefully withdrawn over the catheter, and the catheter is left in place.

Approximately 1 to 2 mg of bupivacaine/kg (0.5%, with or without 5 μg of epinephrine/mL) is injected over 1 to 2 min following negative aspiration of air or blood through the catheter. The catheter is then cleared with 2 mL of physiological saline solution. Bolus interpleural bupivacaine is effective in relieving postthoracotomy pain for 3 to 12 h.[26] The addition of epinephrine (5 μg/mL) to the local anesthetic solution may or may not increase the duration of analgesia and decrease the plasma concentration of the local anesthetic.

Complications, such as lung trauma, bleeding, and pneumothorax, are occasionally reported with the blind percutaneous insertion technique in humans.[53] The balloon technique is superior to other methods (i.e., loss-of-resistance technique, low-friction syringe-piston movement, and infusion technique). Sterile sets for single continuous interpleural analgesia are available that contain a Tuohy needle, catheter, control balloon, flat antibacterial injection filter, screw connector, screwdriver, and drape (Fig. 20.10).

A catheter can be placed in the open chest by inserting the Tuohy needle through the skin over the rib at a site that is at least two intercostal spaces caudal to the incision while care is taken to retract the lung. The catheter is then passed through the needle and placed 3 to 5 cm subpleurally under direct vision. Local anesthetic is injected in the usual manner. The ventral tip of the catheter is best anchored by using one encircling suture of surgical gut (3.0) in the intercostal space at the site of puncture.

Positioning of the catheter will affect the site of intercostal nerve blockade and is attributable to gravity-induced pooling of the local anesthetic within the interpleural space.[44,45,54] Dogs that recover from lateral thoracotomy should be placed with the incision side down. Dogs that have had a sternotomy should be placed in sternal recumbency for approximately 10 min to allow the local anesthetic to pool near the incision and adjacent intercostal nerves. The external portion of the catheter should be anchored with tape, sutured to the skin, and covered with a no-occlusive-type dressing that allows air circulation. Reportedly, analgesia produced by interpleural infusion in dogs is similar to analgesia produced by morphine (0.5 mg/kg subcutaneously) or selective intercostal nerve block with bupivacaine (0.5 mL of 0.5% bupivacaine per site), but lasts longer (3 to 12 h).[26] Dogs treated with 1.5 mg of interpleural bupivacaine/kg through an interpleural catheter do not demonstrate significant changes in heart rate, respiratory rate, hematocrit, plasma protein, blood pH, or $PaCO_2$.[26,49,50,51]

Studies have been performed to evaluate cardiovascular effects of low-dose interpleural bupivacaine (0.5%, 1.5 mg/kg), high-dose interpleural bupivacaine (0.5%, 3 mg/kg), and high-dose interpleural bupivacaine (0.5%, 3 mg/kg) with epinephrine 1:200,000 (5 μg/mL) in four dogs recovering from diazepam-ketamine-1.2% halothane and oxygen anesthesia.[47,49] The local anesthetic drugs were administered via an interpleural catheter (25 cm long) that was advanced through a 17-gauge needle at the left or right eighth intercostal space. Pneumothorax or any other pulmonary complication was not observed in any of the dogs evaluated radiographically. The low dosage rate (1.5 mg/kg) of 0.5% bupivacaine produced no significant ($P < 0.05$) alterations in heart rate, systolic, diastolic, and mean arterial blood pressure, cardiac output, and pulmonary arterial blood pressure, respiratory rate, and end-tidal carbon dioxide. Cardiac output, expressed as a percentage of change from baseline, was significantly higher in dogs receiving the low dosage (1.5 mg/kg) than dogs receiving

the high dosage (3 mg/kg) of interpleural bupivacaine (126% ± 6% vs. 94% ± 6% change). Mean plasma concentrations of bupivacaine peaked 5 to 15 min after interpleural injection. Mean plasma concentrations of bupivacaine in individual dogs were variable and did not significantly ($P < 0.05$) differ among dogs treated with the low dose (1.5 mg/kg), high dose (3 mg/kg), and high dose (3 mg/kg) with epinephrine (1:200,000) of interpleural bupivacaine (0.5%).[49] Mean arterial blood pressure was decreased to 28 mm Hg in one dog 15 min after interpleural administration of 3 mg of bupivacaine/kg and was decreased to 37 mm Hg in one dog receiving 3 mg of bupivacaine/kg with epinephrine. This dog also demonstrated apnea for approximately 6 min and required positive-pressure ventilation. The maximum plasma concentration of bupivacaine in these hypotensive dogs was 3.4 and 3.6 μg/mL, respectively.[49] The high dosage rate (3 mg/kg) for interpleural administration is not recommended because it may cause hypotension in some individual animals. Careful patient monitoring is advised if dosages approach 3 mg/kg. The addition of epinephrine 5 μg/mL may not be of any advantage because it does not attenuate peak plasma concentrations.[49]

The effects of interpleural bupivacaine (0.5%, 1.5 mg/kg), intramuscular morphine (1.0 mg/kg), or interpleural morphine (0.1 mg/kg) have also been compared. Interpleural bupivacaine produced longer analgesia, less work of breathing, fewer blood-gas alterations, and earlier return to normal pulmonary function in the first 5 to 8 h after thoracotomy.[50] Interpleural administration of morphine (0.1 mg/kg) did not appear to provide any advantages in terms of analgesia or pulmonary function when compared with the intramuscular administration of morphine (1.0 mg/kg). These results differ from other experimental trials in dogs receiving either 0.5% bupivacaine (1.5 mg/kg) interpleurally, morphine (1.0 mg/kg) IM, or morphine (1.0 mg/kg) interpleurally.[51] Medium sternotomy significantly decreased pH, PaO_2, mean oxygen saturation of hemoglobin, and dynamic compliance; and significantly increased $PaCO_2$, alveolar-arterial difference in the partial pressure of oxygen, pulmonary resistance, and work of breathing. The effects of interpleural administration of bupivacaine and morphine were similar to effects of intramuscular administration of morphine and provided little or no additional benefit. It is not known what the effects of dilution by pleural fluid, such as blood and serum, and loss of local anesthetic through the thoracotomy tube are on overall efficacy. The dose of interpleural bupivacaine may have been inadequate in this study, considering that sternotomy may be more painful than intercostal thoracotomy.

The optimum total dose, concentration, or volume of interpleural bupivacaine in sick dogs have not been reported. Theoretically, one or two of the three branches of the phrenic nerve can be blocked, leaving the remaining branch(es) intact. Isolated contraction of the costal portion of the diaphragm without contraction of the crural portion may result in paradoxical respiration with negative intra-abdominal pressure.[46] The catheter is usually removed 24 h after thoracotomy when postoperative pain has normally decreased. Long-term use (over several weeks) of an interpleural catheter is possible if the catheter is subcutaneously tunneled.[55]

The administration of interpleural bupivacaine is greatly facilitated in dogs in which a chest tube has been placed for evacuation of air (Fig. 20.11). Interpleural regional analgesia has limitations but also several distinct advantages over the more traditional intercostal nerve block or the administration of parenteral opioids. The procedure is technically simple to perform. Only one needle stick is needed, in contrast to multiple sites of injection when performing an intercostal nerve block. Pain relief lasts longer and is less likely to produce CNS and respiratory depression than after the use of parenteral opioids. Interpleural administration of the local anesthetic (lidocaine or bupivacaine) approximately 30 min prior to removal of the chest tube helps to prevent pain associated with the tube removal.

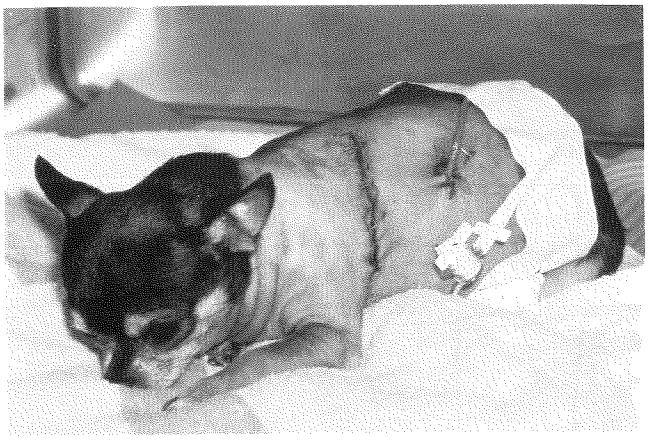

Fig. 20.11. Pain therapy in a Chihuahua (2 kg) recovering from left lateral thoracotomy and correction of a patent ductus arteriosus Botalli: 0.5% bupivacaine (1.5 mg/kg) was administered into a chest tube, which was placed interpleurally (total dose = 3 mg = 0.6 mL), and then the chest tube was cleared from the anesthetic with 0.6 mL of 0.9% sterile sodium chloride.

Infection, tachyphylaxis to local anesthetic, high anesthetic blood concentration, systemic toxicity from local anesthesia, unilateral sympathetic block (evidenced as a Horner's syndrome) and increased subcutaneous skin temperature of the affected side, pleural effusion, phrenic nerve paralysis or paresis, and catheter-related complications (e.g., intrapulmonary placement of catheter) do not occur if the procedure is performed properly. Pain relief is minimal in people and dogs with a misplaced catheter, loss of local anesthetic in the chest tube, excessive bleeding into the pleural space, or altered diffusion within the parietal pleura after mechanical irritation by the surgical procedure.[56] A dilution of local anesthetic by pleural exudation appears to play a subordinate role in humans because a relationship between a loss of chest tube fluid and interpleural analgesic requirement or pain scores could not be demonstrated.[40] Care must be taken to avoid the serious potential complication of pneumothorax, particularly when this method is used bilaterally.[57]

Anesthesia of the Foot and Leg

Several techniques may be used to induce anesthesia of the foot and leg successfully: (a) infiltration of tissues around the limb by

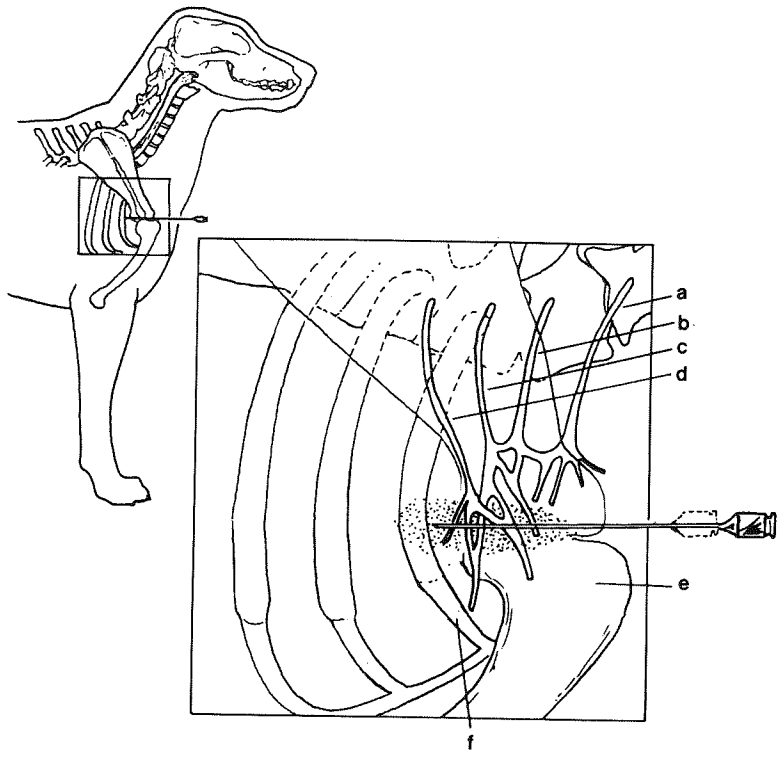

Fig. 20.12. Needle placement for brachial plexus block. **Inset:** ventral branches of (a) sixth, (b) seventh, (c) eighth cervical, and (d) first thoracic spinal nerves; (e) tuberosity of humerus; and (f) first rib.

using local anesthetic solution (ring block), (b) intra-articular injection of local anesthetic, (c) infiltration of the brachial plexus with local anesthetic solution (brachial plexus block), (d) injection of local anesthetic into an accessible superficial vein in an extremity that is isolated from the general circulation by placing a tourniquet proximal to the injection site (intravenous regional anesthesia), (e) perineural infiltration of sensory nerves in the limbs (nerve block), and (f) injection of local anesthetic solution into the lumbosacral epidural space to induce anesthesia of the hind legs,

Ring Block

Local infiltration and field block around the distal extremity may be performed with a 2- to 5-cm, 22- to 23-gauge standard needle. Intradermal wheals around a superficial lesion and subcutaneous infiltration around the limb are performed by using a short (<3 cm) and fine (23- to 25-gauge) needle.

Intra-articular Analgesia

A prospective study has compared the analgesic effect of the intra-articular administration of bupivacaine (0.5%, 0.5 mL/kg), preservative-free morphine (morphine sulfate [Duramorph] injection, USP; Elkins-Sinn, Cherry Hill, NJ) at a dose of 0.1 mg/kg diluted with 0.9% sodium chloride to a volume of 0.5 mL/kg or with 0.9% sodium chloride (0.5 mL/kg).[58] Dogs in the bupivacaine and morphine groups required less supplemental analgesia when morphine (0.5 mg/kg IM) at 6 and 24 h was used after cranial cruciate ligament repair than did the dogs in the 0.9% sodium chloride group. Intra-articular morphine provided some analgesia, as indicated by cumulative pain scores and measurement of pain threshold in both stifles by using a spring-action load–measuring device (Pain Diagnostics and Thermography, Great Neck, NY), but not to the same level as intra-articular bupivacaine. Intra-articular morphine (0.1 mg/kg) did not produce the bradycardia, respiratory depression, or hypotension that might be observed after systemic administration of morphine. Ongoing inflammation is apparently needed for intra-articular opioids to produce noticeable antinociceptive effects.[59]

Brachial Plexus Block

Brachial plexus block is suitable for operations on the front limb within or distal to the elbow.[60–62] The technique should be done in well-sedated standing or laterally recumbent dogs. A 7.5-cm, 20- to 22-gauge needle is inserted medial to the shoulder joint and directed parallel to the vertebral column toward the costochondral junction (Fig. 20.12). In larger dogs, approximately 10 to 15 mL of 2% lidocaine hydrochloride solution with 1:200,000 epinephrine is injected slowly as the needle is withdrawn, if no blood is aspirated into the syringe, thereby placing local anesthetic in close proximity to the radial, median, ulnar, musculocutaneous, and axillary nerves. Gradual loss of sensation and motor function occurs within 10 to 15 min. Anesthesia lasts for approximately 2 h, and total recovery requires approximately 6 h.

A peripheral nerve stimulator can be used to accurately locate the radial, median, ulnar, musculocutaneous, and axillary nerves, thereby reducing the dose of local anesthetic for successful brachial plexus blockade in dogs.[62] One electrode (the alligator clip on the positively charged lead wire [red plug]) from the nerve locator is attached to the skin, while the other electrode (the alligator clip on the negatively charged lead wire [black plug]) is attached to the proximal portion of the insulated needle (0.72 × 10.8 mm, 22 gauge × 4.25 inches). A 20-mL syringe

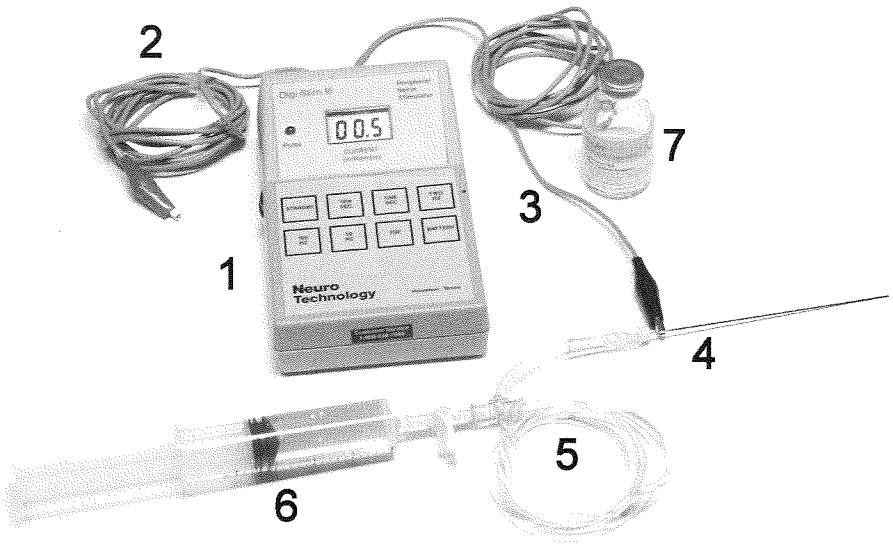

Fig. 20.13. (1) Peripheral nerve-stimulator used as an aid in accurately locating nerves when performing nerve-block procedures: The nerve locator is set at 2 Hz and low output (0.5 mA); the 0.5-mA current delivered to the patient is displayed; (2) the lead wire with red plug (+) and alligator clip for the patient's electrode; (3) the lead wire with black plug (−) and alligator clip for the needle; (4) Stimex insulated needle (22 gauge, 4.25 inches, 0.72 × 10.79 mm); (5) extension set; (6) 20-mL syringe with three-way stopcock, filled with (7) 0.2% ropivacaine hydrochloride.

containing the local anesthetic agent (2% lidocaine, 0.5% ropivacaine, or 0.5% bupivacaine, diluted with 0.9% sodium chloride solution to make a 0.375% concentration) is attached to a three-way stopcock, a fluid extension set, and the needle (Fig. 20.13). As the needle is inserted medial to the scapulohumeral joint toward the costochondral junction of the first rib, medial to the scapula but outside the thorax, the nerve stimulator is turned on to 2 Hz and 1.0 mA. As the paw begins to twitch, the needle is precisely placed to obtain maximal twitch with as little current (<0.5 mA) as possible. At this point, the syringe is aspirated to ensure that it is not in a blood vessel, and 0.1 to 0.2 mL of the anesthetic is injected until the twitch disappears. The technique is repeated three or more times, by fanning the needle dorsal and ventral from the initial placement. Direct deposition of the local anesthetic on the nerves at a maximum dose of 1.5 mg/kg of lidocaine, ropivacaine, or bupivacaine will produce good brachial plexus blockade. By using a nerve stimulator, a total dose of 4 mg of bupivacaine with 5 μg/mL of epinephrine was effective in providing anesthesia for middiaphyseal osteotomies of the humerus followed by intramedullary pin fixation in 11 of 12 dogs sedated with acepromazine and anesthetized with propofol.[62] Analgesia lasted for 11.1 ± 0.5 h.[62]

Brachial plexus block is relatively simple and safe to perform and produces selective anesthesia and relaxation of the limb distal to the elbow joint (Fig. 20.14). The relatively long waiting period (15 to 30 min) required to attain maximal anesthesia and some occasional failures to obtain complete anesthesia, particularly in fat dogs, are disadvantages of the technique.

Fig. 20.14. Anesthesia of the brachial plexus of the left thoracic limb in a conscious dog.

Intravenous Regional Anesthesia

Intravenous regional anesthesia (IVRA) is a rapid and reliable method for producing short-term (<2 h) anesthesia of the extremities. The clinical value of IVRA in humans is well established. The IVRA technique is also known as *Bier block*.[63] Little information on clinical experiences with IVRA in dogs exists, even

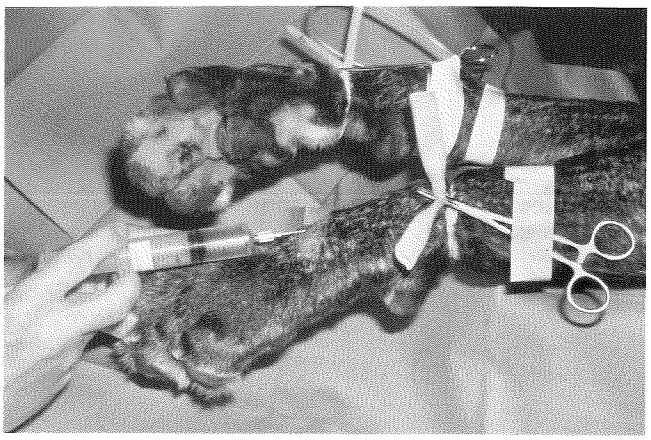

Fig. 20.15. Intravenous regional anesthesia in a sedated bullmastiff (80 kg) in right lateral recumbency for skin biopsies at the palmar paws of both front legs. A rubber tourniquet is placed distal to the carpus (right foot) and proximal to the carpus (left foot). The tourniquets are secured with hemostatic forceps, which are taped to the skin. Injection of 12 mL of 1% lidocaine hydrochloride solution (1.5 mg/kg per leg) into the cephalic vein is shown.

though it appears to be a simple, safe, and practical method for providing 60 to 90 min of regional anesthesia in an extremity distal to a tourniquet (Fig. 20.15).[64,65] The technique is best accomplished in dogs by placing an intravenous catheter in an appropriate and accessible vein (e.g., the cephalic or lateral saphenous vein) distal to the tourniquet. The limb is first desanguinated by wrapping it with an Esmarch bandage. A rubber tourniquet is placed around the limb proximal to the Esmarch bandage. The tourniquet must be tight enough to overcome arterial blood pressure.[66] Once the tourniquet is secured, the Esmarch bandage is unwrapped, and 2.5 to 5 mg/kg lidocaine is injected IV with light pressure. A period of 5 to 10 min is required to achieve maximum anesthesia before beginning the surgical procedure. Diluted concentrations (0.25% and 0.5%) of lidocaine produce adequate sensory blockade as long as the tourniquet is applied. By avoiding leakage and keeping the local anesthetic isolated in the limb, the incidence and severity of toxic symptoms are decreased and the percentage of successful blocks increased.[66] Complications resulting from blood-flow deprivation to the limb or from the dose of anesthetic used do not occur if the procedure is limited to 90 min.

Once the tourniquet is removed, sensation returns within 5 to 15 min and residual analgesia remains for up to 30 min. Minimal effects on heart rate, respiratory rate, or the electrocardiogram have been noted in dogs after removal of the tourniquet.[64] The site and mechanism of local anesthetic action in IVRA are unclear but may involve desensitization of major nerve trunks and/or sensory nerve endings.[67] Unlike the desensitization described in other nerve blocks, the onset of anesthesia and muscle paralysis begins distally and progresses proximally; thus, the local anesthetic should be injected as distally as possible in the limb to be anesthetized (Fig. 20.16). The blood-free surgery site

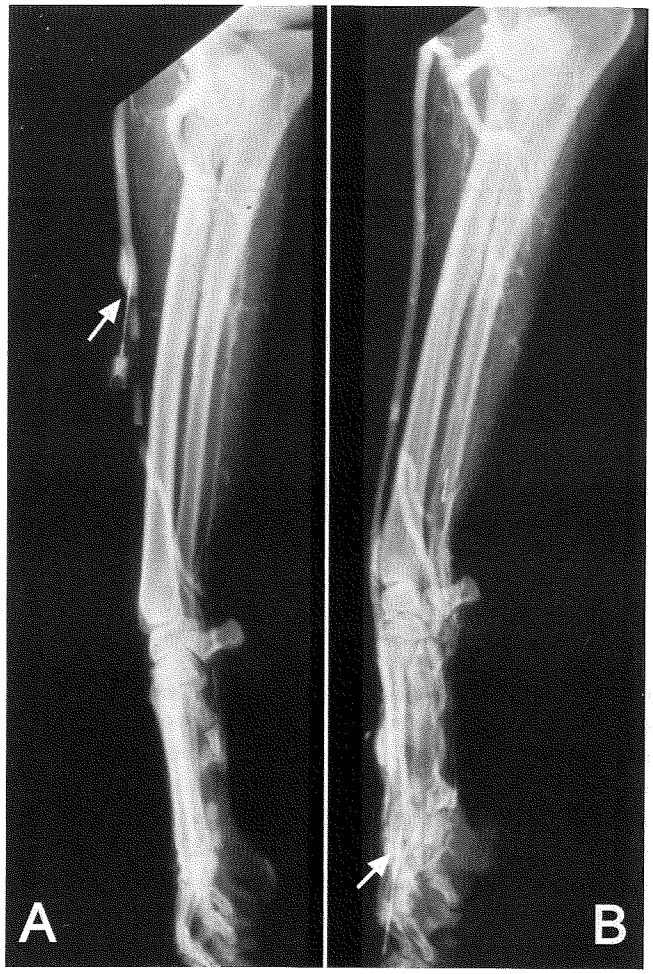

Fig. 20.16. Radiographs of the left forelimb of a German shepherd (35 kg). **A:** A mixture of 3 mL of 2% lidocaine hydrochloride solution and 3 mL of Omnipaque 300 was injected into the cephalic vein at a proximal site. Retrograde dissipation of the anesthetic was prohibited by venous valves; thus, anesthesia of the limb did not develop. **B:** The injection was repeated at a distal site 1 week later, thereby inducing anesthesia of the limb distal to the tourniquet. The *arrow* indicates the injection site.

is ideal for taking biopsy samples and removing a foreign body from the paws. Prolonged procedures (>90 min) may produce tourniquet-induced ischemia, which is associated with pain and increased blood pressure. If pain occurs, it is often difficult to control and requires induction of general anesthesia.[68] Reversible shock occurs if the tourniquet is removed after 4 h; and sepsis, endotoxemia, and death occur if the tourniquet is removed after 8 to 10 h. Bupivacaine should not be used for this technique because of the increased potential for cardiovascular collapse and death associated with its use IV.[69–72]

Nerve Blocks of the Limbs

Specific nerve blocks in the front limbs (radial, ulnar, median, and musculocutaneous nerves) and hind limbs (tibial, peroneal, and saphenous nerves) of dogs have been described.[73] These

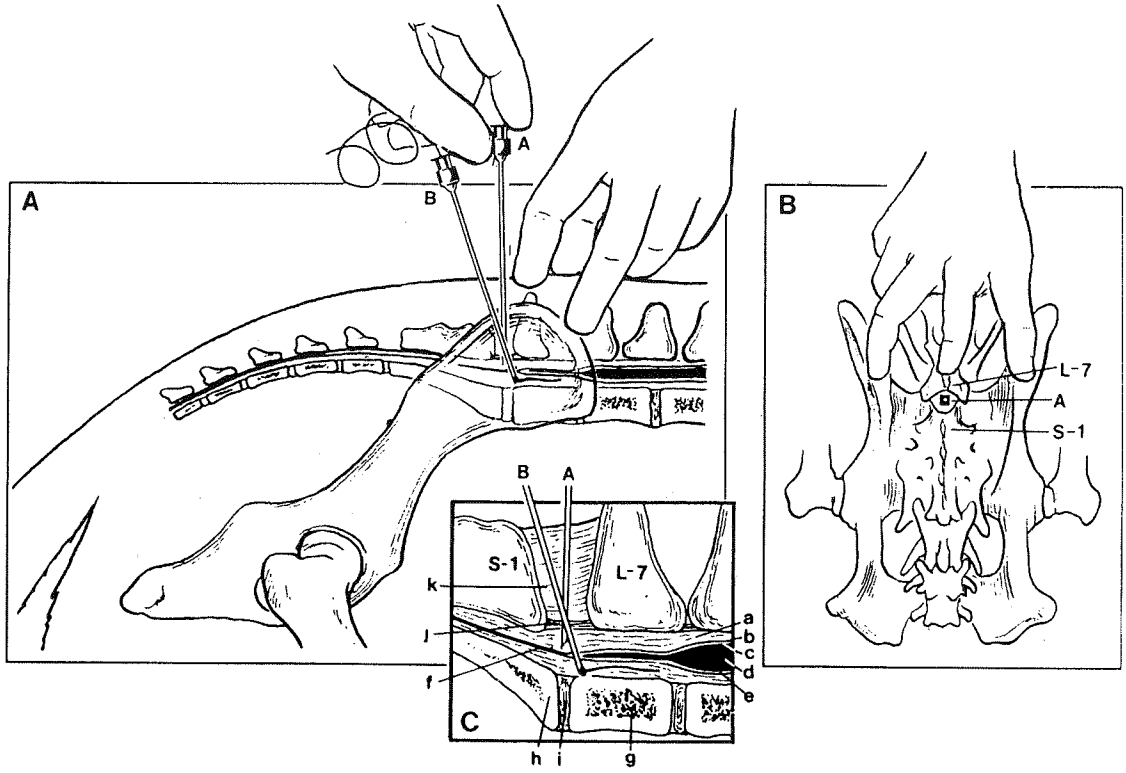

Fig. 20.17. **A:** Aseptic needle placement, using sterile surgical gloves, into the lumbosacral epidural space of a dog (A) and catheter placement for continuous epidural anesthesia using a local anesthetic and/or analgesia using an opioid (B). **B:** Dorsal view. Palpation of the dorsal spinous process of the L7 vertebra and dorsoiliac wings. **C:** Inset: (a) epidural space with fat and connective tissue, (b) dura mater, (c) arachnoid membrane, (d) spinal cord, (e) cerebrospinal fluid, (f) cauda equina, (g) seventh lumbar (L7) vertebra, (h) first sacral (S1) vertebra, (i) intervertebral disc, (j) interarcuate ligament (ligamentum flavum), and (k) interspinous ligament.

techniques are rarely used in clinical small animal practice because of difficulty in locating the proper site for injection of local anesthetic and the substitution of simpler methods (e.g., IVRA and epidural anesthesia).

Lumbosacral Epidural Anesthesia

This technique is noted for its simplicity, safety, and effectiveness, and is one of the most frequently used regional anesthetic techniques described for surgical procedures caudal to the umbilicus in dogs.[74–98] Epidural anesthesia is frequently recommended for cesarean section because, unlike other anesthetic techniques, it does not depress the puppies. The bitch remains awake and able to take care of her puppies immediately after surgery.

Dogs are generally sedated, tranquilized, or anesthetized to reduce fear and apprehension and then are placed either in sternal recumbency (for bilateral anesthesia) or in lateral recumbency (for ipsilateral anesthesia). The hind limbs can be extended cranially to maximally separate the lumbar vertebrae, making identification of the lumbosacral space easier.

The anesthetic procedure is not technically difficult when performed by an experienced clinician. The epidural space is located between the inner and outer layers of the dura mater (Fig. 20.17). It contains nerves (cauda equina), fat, blood vessels, lymphatics, and occasionally the end of the spinal cord with its surrounding meninges (arachnoid and dura mater). The subarachnoid space contains cerebrospinal fluid (CSF). After a thorough surgical preparation, the local anesthetic solution is injected through a disposable 2.5- to 7.5-cm, 20- to 22-gauge spinal needle as a single dose or is injected through a catheter that is inserted at least 1.5 to 2.0 cm beyond the end of an 18- or 17-gauge Huber-point (Tuohy) or 18-gauge Crawford needle (continuous technique [Figs. 20.17 and 20.20]). A 2.5-cm, 22-gauge spinal needle is used for small dogs, a 3.8-cm, 20-gauge needle for medium-sized dogs, and a 7.5-cm 18-gauge needle for large dogs. Important landmarks for needle placement are easily identified in most dogs. The iliac prominences on either side of the spine are palpated by using the thumb and middle finger of one hand (Fig. 20.17). The spinous process of the seventh lumbar (L7) vertebra is located with the index finger. The lumbosacral (L7-S1) interspace should be palpated from both the cranial and caudal directions by moving the finger on the dorsal spinous processes of L6 to L7 and S2 to S1. This will help to avoid inadvertent placement of the needle into the L6 to L7 interspace. The needle must be placed correctly on the midline and caudal to the L7 spinous process, and is inserted until a distinct popping sensation is felt as the needle point penetrates the interarcuate ligament. Tail

movement may indicate that the needle has engaged nerve tissue. The epidural space is best identified by the *loss-of-resistance test*, using either an air-filled or a saline-filled syringe. Deliberate injection of 3 to 4 mL of air into the epidural space of dogs weighing 20 to 27 kg results in bubble formation that can persist for 24 h. The bubbles, however, are not large or numerous enough to impede transfer of local anesthetic across the meninges and into the CSF, spinal roots, and cord, nor do they localize in any particular region (e.g., nerve roots); thus, subsequent injection of local anesthetic does not result in patchy anesthesia or inadequacies attributable to bubbles.[99] Subcutaneous crepitation may be felt at the site of skin penetration if air has been injected outside the epidural space.

After the needle has been placed, the stylet is removed from the needle hub and the stylet is carefully examined for CSF or blood smears. Also, the needle (or catheter) should be carefully inspected for flow of CSF or blood before the local anesthetic is administered. If inadvertent subarachnoid puncture occurs, as indicated by the presence of CSF, the procedure may either be abandoned or the intended epidural dose reduced by at least 50%. The presence of blood indicates penetration of the ventral venous plexus, after which the needle should be repositioned epidurally. Obtaining CSF at the L7 to S1 site is not uncommon, even though the subarachnoid space of dogs usually ends cranial to the lumbosacral interspace. The spinal cord and meninges in younger and smaller dogs may occasionally extend into the lumbosacral vertebral junction.[100] A subarachnoid injection may be made if CSF is encountered, with the precaution that 1 mL of local anesthetic per 10 kg of body weight is then injected over a 1-min period.[90,93] The reduced dose should avoid *total spinal anesthesia* with cardiovascular and respiratory depression or collapse. If blood is encountered, the needle is withdrawn and cleansed, and another attempt is made to place it into the epidural space. Intravascular injection of local anesthetic can cause systemic toxicity, which is characterized by convulsions, cardiopulmonary depression, and the absence of regional anesthesia[70,71,101] Inadvertent subarachnoid administration of small amounts (2 mL) of fresh autologous blood aspirated from the venous plexus during attempted lumbar epidural puncture in dogs may cause pelvic limb spasm. If this occurs, most dogs recover rapidly and demonstrate no signs of meningeal irritation, long-term neurological sequelae, or neuropathological changes.[102] To avoid excessive cranial advancement of neural blockade, it is also good practice to elevate the dog's head for approximately 5 min immediately after completion of the epidural administration of the anesthetic.

The shape and bevel orientation of the spinal needle affect the size of the dural defect. Large dural defects in humans may result in post–lumbar puncture headache attributable to a postulated increased CSF leak. The dural defect produced by a 22-gauge needle is smaller than that produced by a 22-gauge Quincke needle (27,400 vs. 39,400 μm^2). Likewise, a bevel orientation parallel rather perpendicular to the dural fibers causes smaller dural defects (39,400 vs. 73,300 μm^2), because the needle splits rather than cuts the longitudinal dural fibers.[103] It is also important to administer the calculated dose of local anesthetic at the body temperature of the dog and slow enough (over 45 to 60 s) to avoid causing pain.

Local Anesthetic Drugs

A variety of local anesthetics of different concentrations and doses, and combinations of different local anesthetic drugs, have been used to produce epidural anesthesia in dogs and have induced a wide spectrum of sensory and motor blockades.[81,89,93,96,97,104–109] The selected local anesthetic and dosage (concentration and volume) depends on a dog's size, the desired extent of anesthesia, and the desired onset and duration of anesthetic effect. A test dose of 0.5 to 1.0 mL of 2% lidocaine hydrochloride solution produces almost immediate dilation of the external anal sphincter, followed by relaxation of the tail and ataxia of pelvic limbs, within 3 to 5 min. Approximately 1 mL of 2% lidocaine per 4.5 kg of body weight will completely anesthetize the pelvic limbs and posterior abdomen caudal to the first lumbar (L1) vertebra within 10 to 15 min after administration.[81] The flexor-pinch reflex of pelvic limbs will be absent in 5 to 10 min after injection.[77] Clinical experience indicates that the disappearance of the toe reflexes is associated with surgical anesthesia from midthorax to coccyx sufficient for abdominal surgery.[78] The latent period is prolonged to 20 to 30 min if 0.75% bupivacaine hydrochloride is administered and is attributable to the drug's low solubility and slow uptake by nervous tissue.[93] Good anesthesia for abdominal and orthopedic surgeries caudal to the diaphragm is generally achieved by administering 1 mL/5 kg (maximum, 20 mL) of 2% lidocaine or 0.5% bupivacaine, both with freshly added 1:200,000 epinephrine.

A reduced volume of 2% lidocaine (1 mL/6 kg) is generally satisfactory for epidural anesthesia in dogs for cesarean section. The reason for the (approximately 25%) decrease in dose requirement during pregnancy is unclear.[110] Several theories have been proposed: (a) distension of epidural veins, which decreases the size of the epidural space, and/or increase in the spread of local anesthetic;[111] (b) hormonal changes, which influence proteins that affect membrane sensitivity;[112] and (c) chronic exposure to progesterone, which alters the permeability of intercellular connective-tissue matrix, thereby facilitating diffusion of local anesthetics across the nerve sheath.[113] It is rarely necessary to inject more than 3 mg of lidocaine/kg of body weight for epidural anesthesia during cesarean section in dogs.

The anesthesia duration obtained from the deposition of epidural local anesthetic drugs primarily depends on the drug selected, the dermatomal level of anesthesia, and the presence or absence of epinephrine (Table 20.2). Postoperative analgesia (after general anesthesia) lasts longer when epidural anesthesia is performed at the end of surgery, and is attributable to a diminished intensity of the painful stimulus. Two percent solutions of procaine, lidocaine, and carbocaine have provided satisfactory anesthesia and muscle relaxation for 60 to 120 min. Epidural bupivacaine (0.75%) and etidocaine (1%) have induced surgical anesthesia for periods lasting from 4 to 6 h. Surgical anesthesia caudal to the last rib is produced and gradually converted into a phase of postoperative analgesia lasting for 24 h without affecting motor activity or cardiopulmonary function, if a combination of 0.7 to 1.0 mL/10-cm vertex-coccyx distance of 0.5% bupiva-

Table 20.2. Commonly used local anesthetic drugs and doses for peripheral and epidural block procedures in conscious dogs.

Local Anesthetic			Usual Doses (mg/kg)		Toxic Doses, IV (mg/kg)				
Generic Name	Trade Name (Manufacturer)	Conc. (%)	With Epinephrine	Without Epinephrine	Convulsive	Lethal	Approximate Onset of Motor and Sensory Block (min)	Approximate Duration of Motor and Sensory Block (h)	Motor Block
Ester linked									
Procaine	Novocaine (Withrop Laboratories)	1–2	8	6	36	100	10–15	0.5	±
Chloroprocaine	Nesacaine (Pennwalt)	1.0–1.5	8	6	—	—	7–15	0.5–1.0	±
Amide linked									
Lidocaine	Xylocaine (Astra Pharmaceutical Products)	0.5–2.0	7	5	11–20	16–28	10–15	1–2	+
Mepivacaine	Carbocaine (Breon Laboratories)	1–2	7	5	29	—	5–10	2.0–2.5	+
Bupivacaine	Marcaine (Breon Laboratories)	0.25–0.5	3	2	3.5–4.5	5–11	20–30	2.5–6.0	±
Ropivacaine	LEA 103 (Breon Laboratories)	0.5	5	3	4.9	—	5–15	2.5–4.0	+
Etidocaine	Duranest (Astra Pharmaceutical Products)	0.5–0.75	5	3	4.5	20	5–10	2–5	+++

Conc., concentration; IV, intravenous; ±, inconsistent motor nerve block; +, weak motor nerve block; +++, strong motor nerve block.

caine hydrochloride solution and 0.1 mg/kg of morphine hydrochloride is injected epidurally.[114]

The efficacy of bupivacaine and ropivacaine for producing lumbar epidural and subarachnoid anesthesia in dogs has been compared.[104] Various concentrations of ropivacaine (0.25%, 0.5%, 0.75%, and 1.0%) and bupivacaine (0.25%, 0.5%, and 0.75%) with a constant 3-mL epidural volume and 1-mL subarachnoid volume of ropivacaine and bupivacaine were assessed. Epidural blockade was also performed using solutions of ropivacaine and bupivacaine that contained epinephrine (1:200,000). There were no signs of adverse reactions, irreversible block, or other sequelae in any of the dogs studied. Onset of motor blockade (time from the completion of the injection until a dog's pelvic limbs cannot support weight) ranged from 1.7 to 4.1 min following subarachnoid injection. There were no differences in the onset of motor blockade between various anesthetic solutions. Duration of motor blockade (time from onset of motor blockade until the dog could support its own weight) ranged from 103 min (0.75% ropivacaine) to 163 min (0.75% bupivacaine). Solutions of 0.25% ropivacaine and 0.25% bupivacaine failed to induce complete loss of weight support following epidural injection. Onset of motor blockade varied between 5 and 9 min with the use of higher concentrations (>0.25%) and was inversely related to dose. Duration of motor blockade ranged from 141 min (0.5% ropivacaine) to 258 min (0.75% bupivacaine). The similar onset times for both drugs were related to their similar p*Ka* (ropivacaine, 8.0; and bupivacaine, 8.1). The decreased motor-blocking potency of ropivacaine is consistent with its low lipid solubility. Epinephrine failed to prolong the duration of motor blockade for either drug. Little difference in vascular activity may exist between ropivacaine and bupivacaine when injected into the epidural space of dogs.[104]

A direct comparison between the effect of epidural bupivacaine and ropivacaine, using 0.5% and 0.75% solutions and 0.14- and 0.22-mL/kg volumes, on analgesia at the perineum (S3 dermatome), right and left hind-toe web (L5 to L7 dermatomes), flank (L2 to L5 dermatomes), and caudodorsal rib areas (T12 to L1 dermatomes), and associated cardiopulmonary effects (heart rate, systemic arterial blood pressure, pH, $PaCO_2$, PaO_2 bicarbonate, and base excess) in six dogs sedated with acepromazine (0.075 mg/kg IM) has been reported.[109] Sterile local anesthetic drugs were slowly administered (rate, 3 mL/min) into the epidural space at the lumbosacral junction via implantable vascular access ports.[115] The results of this study indicate that 0.22 mL/kg of 0.5% bupivacaine and ropivacaine produce greater anesthesia success at dermatomes L5 to L7 than does 0.5% at 0.14 mL/kg (>80% vs. <70% success), a similar extent of anesthesia, and mild cardiopulmonary changes. Varying the bupivacaine concentration did not affect the duration of perineal analgesia. Perineal analgesia with 0.5% and 0.75% ropivacaine has been reported to be slightly shorter than that achieved with 0.5% and 0.75% bupivacaine (115 to 140 vs. 137 to 145 min).[109]

Lidocaine and Bupivacaine Combination

The effects of epidural administration of lidocaine (2%, 5 mg/kg with epinephrine 1:200,000), bupivacaine (0.5%, 1.25 mg/kg with epinephrine 1:200,000), and lidocaine (2%, 2.5 mg/kg with epinephrine 1:200,0000) combined with bupivacaine (0.5%, 0.61 mg/kg with epinephrine 1:200,000) on the time of interdigital reflex loss, duration of analgesia and muscle relaxation, and cardiorespiratory effects in six dogs, weighing 5 to 10 kg, have been compared.[97] The combination of epidural bupivacaine with lidocaine achieves a shorter time to sphincter relaxation than does bupivacaine alone (23 ± 2 vs. 84 ± 23 s), longer analgesia than lidocaine alone (94 ± 8 vs. 54 ± 5 min), and longer muscle relaxation than either lidocaine (102 ± 8 vs. 59 ± 6 min) or bupivacaine (102 ± 8 vs. 57 ± 20 min). The combination of epidural lidocaine and bupivacaine produces minimal changes in arterial oxygen saturation, end-tidal carbon dioxide, respiratory and heart rates, and mean arterial blood pressure, and appears to be the best choice for maintaining anesthesia when surgical time is prolonged.[97]

Pharmacokinetics and Pharmacodynamic Properties

Local anesthetics injected epidurally may enter the CSF,[74,116] epidural venous blood, or lymph[80] and become partitioned in epidural fat. Epidurally administered drugs are dispersed by entering the lymphatic system by diffusion into the dural lymphatic vessels located at the level of the nerve roots, by leakage of local anesthetic drug out of the vertebral canal through the intervertebral foramina, and by vascular absorption and systemic redistribution.[117]

The pharmacokinetics of bupivacaine and ropivacaine after lumbar epidural administrations of either drug (0.75% solution, 3-mL volume with or without 1:200,000 epinephrine) in dogs have been determined.[70] Both drugs have a similar pharmacokinetic profile. Peak arterial concentrations of bupivacaine and ropivacaine occur within 5 to 10 min after injection and were less than 1 μg/mL. The addition of epinephrine did not consistently decrease the clearance (C_{max}) of either agent.

The disposition and pharmacological effects of bupivacaine[118] and, most recently, those of the S(−) isomer of bupivacaine[119] after intravenous and epidural administration in dogs have been reported. Bupivacaine (1.0 mg/kg IV) resulted in a mean ± standard deviation half-life of 34.5 ± 7.8 min, a mean plasma clearance of 20.2 ± 7.4 mL/kg/min, and a mean volume of distribution at a steady state of 0.7 ± 0.2 L/kg. After epidural administration of 0.5% bupivacaine (1.8 mg/kg), the peak plasma concentration was 1.4 ± 0.4 μg/mL approximately 5 min after administration. Onset and duration of anesthesia were 2.3 ± 2.2 min and 158 ± 49 min, respectively. The mean bupivacaine plasma concentration ranged between 0.2 and 1.4 μg/mL, and the half-life was 179 ± 34 min.[118] After intravenous administration of a 1-mg/kg dose of the S(−) isomer of bupivacaine (0.5%), the mean ± standard deviation half-life was 33.5 ± 17 min, the mean plasma clearance was 21 ± 11 mL/kg/min, and the mean volume of distribution at steady state was 0.8 ± 0.2 L/kg. Mean peak plasma concentration was 2.6 ± 0.7 μg/mL. Following epidural administration of the same dose peak plasma concentration decreased to 0.9 ± 0.5 μg/mL. Motor block began immediately after completion of epidural injection and lasted for 3 to 4 h.[119]

It has been shown that epidural anesthesia that extends as far

cranially as the anterior thoracic dermatomes (T3 to T5) does not adversely change cardiovascular function, respiratory rate, arterial blood pH, and gas tensions (PaO_2 and $PaCO_2$) in conscious dogs or those sedated with methadone (0.8 mg/kg), acepromazine (0.3 mg/kg), or atropine (0.6 to 1.2 mg).[89] In awake healthy dogs, it is thought that compensation for markedly attenuated spinal sympathetic outflow during thoracic epidural anesthesia is accomplished by increasing endogenous vasopressin concentrations to support arterial blood pressure.[120,121] Severe hypotension (with mean arterial blood pressure < 60 mm Hg) can occur in aged and sick dogs with suppressed neurally mediated renin release or when endogenous vasopressin is prevented from acting on its vasopressin receptors.[79,121] Hypotension should be treated with intravenous crystalloid solutions (20 to 30 mL/kg) and/or a vasopressor (e.g., phenylephrine or ephedrine).[122] Hepatic and renal blood flow generally remains stable in dogs undergoing epidural anesthesia until the T1 to L3 spinal cord segments begin to be blocked. Arterial blood pressure can decrease to less than 30% to 40% of the preepidural anesthesia value with a high epidural block. Ephedrine (2.5 μg/kg/min) has been used successfully to rescue hypotensive dogs and return blood-flow values during high epidural anesthesia.[123]

High epidural anesthesia to the T1 myotomal level has been associated with increased intrathoracic volume at end expiration via an increase in intrathoracic tissue volume and the amount of gas in the lungs at end expiration (functional residual capacity).[124] It has been postulated that the increases in thoracic tissue volume are attributable to increases in intrathoracic blood volume. Thoracic epidural block before the production of experimental hemorrhagic shock has been advocated as potentially therapeutic.[95] Endocardial blood flow improves, and determinants of myocardial oxygen consumption decrease.[125]

Rectal temperature usually remains unchanged during epidural anesthesia in dogs. If hypothermia occurs after epidural injections, the cause might be redistribution of heat within the body.[126] In humans, fluctuation in skin temperature of the limbs (but not the trunk) and an absence of sweating (dogs have no sweat glands except in the paws)[127] may reflect changes in sympathetic activity after epidural nerve blockade.[94,128] Increased skin temperature in the pelvic limbs (1.2°C) and paws (2.0°C), coupled with decreased skin temperature in the thoracic limbs and thorax (−0.6°C), after bupivacaine lumbar epidural administration has been observed in conscious dogs.

Epidural anesthesia likely suppresses the markers of stress as represented by serum levels of andrenocorticotropic hormone, beta-endorphin, epinephrine, and norepinephrine.[120,129] In addition, epidural anesthesia may inhibit host-defense mechanisms against various microorganisms less than does general anesthesia.[130]

Adverse Effects

Adverse effects associated with epidural and subarachnoid anesthesia in dogs include (a) hypoventilation secondary to respiratory muscle paralysis, which is attributable to the spread of local anesthetic to the cervical spinal segments; (b) hypotension, Horner's syndrome (Fig. 20.18), and hypoglycemia caused by sympathetic blockade; (c) Shiff-Sherrington–like reflexes; and (d) muscular twitches, coma, convulsion, and circulatory depression caused by toxic plasma concentrations of local anesthetic. Improper injection technique can cause delay in onset of anesthesia, unilateral hind-limb paresis, partial anesthesia of the tail or the perineal region, and sepsis.[131,132]

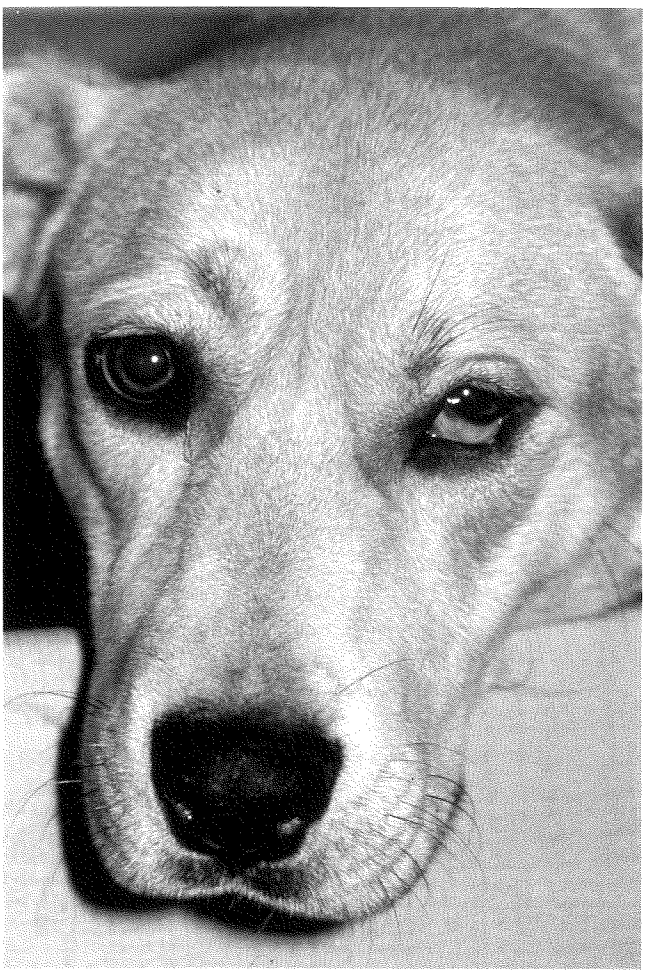

Fig. 20.18. Unilateral Horner's syndrome (i.e., ptosis, miosis, and enophthalmus) in a golden retriever (35 kg) with ipsilateral paresis of the left thoracic limb, after overdose (12 mL of 2% lidocaine) via lumbosacral epidural anesthesia.

Although epidural anesthesia has been referred to as the ideal anesthetic procedure for bitches in dystocia,[77,133,134] respiratory depression can be a serious complication. Changes from a thoracic to a diaphragmatic (abdominal) pattern of breathing indicate at least partial motor block of the intercostal musculature, which may not be reflected by changes in arterial pH, PaO_2, or $PaCO_2$. The use of preblock oxygenation, proper doses of local anesthetic, and slight elevation of the head, neck, and thorax minimize this problem. The presence of paresis of the nictitating membrane of the eye (Fig. 20.18), which derives its sympathetic nerve supply from the first three thoracic spinal segments, is evidence that most, if not all, of the sympathetic outflow has been blocked by extensive epidural spread.

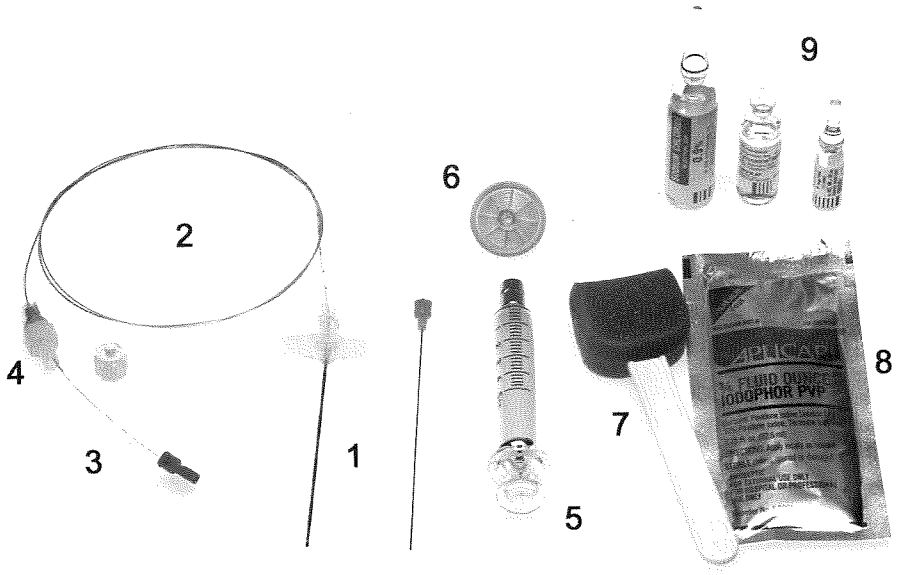

Fig. 20.19. Epidural trays for continuous epidural anesthesia. The basic sterile and single-use regional anesthesia delivery system contains (1) Tuohy needle (1.3 × 87 mm, 18 gauge × 31/2 inches), plastic hub, and detachable wing; (2) radiopaque (polytetrafluoroethylene) catheter with open end and stylet (0.9 × 1000 mm, 20 gauge × 36 inches); (3) catheter stylet; (4) catheter connector with luer plug; (5) 5-mL glass syringe; (6) epidural filter; (7) swabs; (8) iodine packet; and (9) 5 mL of lidocaine hydrochloride 1%, 1-mL epinephrine injection 1:200,000, and 10-mL sodium chloride injection 0.9%.

Anecdotal reports about delayed hair regrowth after epidural analgesia in dogs, though controversial, have been difficult to confirm. In one study, hair regrowth was complete after 4 months, and there was no difference in hair length among groups, indicating that neither epidural analgesia nor scrubbing or clipping seemed to affect hair regrowth in at least the limited number of dogs in this study.[135] In a more recent retrospective study, 8 of 72 dogs were reported to have delayed hair growth after epidural administration of morphine with or without bupivacaine.[136]

Complications with epidural anesthetic techniques can be prevented in most instances by following several basic rules, which include careful selection of drugs and dosage, aspiration before injection (to assure that the tip of the needle is not in a blood vessel or subarachnoid space), and injection of test doses.[96]

Absolute contraindications for epidural anesthetic techniques include infection at the lumbosacral puncture site, uncorrected hypovolemia, bleeding disorders, therapeutic or physiological anticoagulation, degenerative central or peripheral axonal diseases, and anatomical abnormalities that would make epidural anesthesia difficult. Bacteremia, neurological disorders, and minidose heparin therapy are relative contraindications. The benefits of epidural anesthesia often outweigh the risks.[137]

Continuous Epidural Anesthesia

The indications, advantages, contraindications, and complications associated with continuous epidural anesthesia in dogs are similar to those of the single-injection method. Additional advantages of continuous epidural anesthesia are the ability to tailor the anesthesia duration to the length of operation and to maintain a route for injecting epidural opioids during surgery and postoperatively.[86,114,138]

Despite numerous reports describing continuous epidural anesthesia in dogs, epidural catheters are not used routinely because of technical difficulties; the potential to damage the spinal cord, meninges, and nerves; the risk of infection; and catheter-related problems. Nevertheless, insertion of plastic catheters into the epidural space of dogs is relatively simple and safe, once practiced. Local anesthetics and/or opioids may be administered to produce continuous epidural anesthesia by placing a commercially available epidural catheter through an 18- or 17-gauge Huber-point (Tuohy) needle or 18-gauge Crawford needle into the epidural space (Fig. 20.19). Self-prepared sterile 20-gauge catheters (e.g., polyethylene tubing PE 160) may also be used.

A comprehensive selection of epidural products and accessories exists for use in people and can be adapted for dogs, thus making the technique in dogs easier and safer. Epidural trays contain an 8.7-cm, 18-gauge Tuohy needle and a 20-gauge catheter set with a radiopaque Teflon (polytetrafluoroethylene) catheter that resists kinking, with either an open rounded-tip or a closed-tip atraumatic catheter with lateral flow side ports, a thread-assist guidewire that eliminates the need for a stylet, a catheter connector that attaches quickly and securely without possibility of crushing the catheter, a luer-slip glass syringe, and a variety of syringes, needles, sterile preparation solutions, and sponges (Fig. 20.19). The theoretical advantages of the multiple side-port epidural catheter include even distribution of local anesthetic, less chance of clotting (because fibrin is less likely to collect on the side), and the ability to have a completely rounded and therefore atraumatic tip. Catheters should be placed, following strict aseptic technique, by using mask, gown, drapes, and prophylactic antibiotics. A skin preparation, using dry gauze dressings with or without antibiotic ointment (povidone iodine, Neosporin ointment [bacitracin, neomycin, and polymyxin B], or Bactroban ointment [mupirocin]), is very effective in preventing infection. A sterile 4 × 4-inch gauze or OpSite IV 3000 brand of dressing, which collects only minimal fluid underneath it, is tightly adhered to the skin and should be replaced daily or more often as needed to keep the wound dry. Plastic occlusive dressings are not ideal because they collect bacteria of normal skin

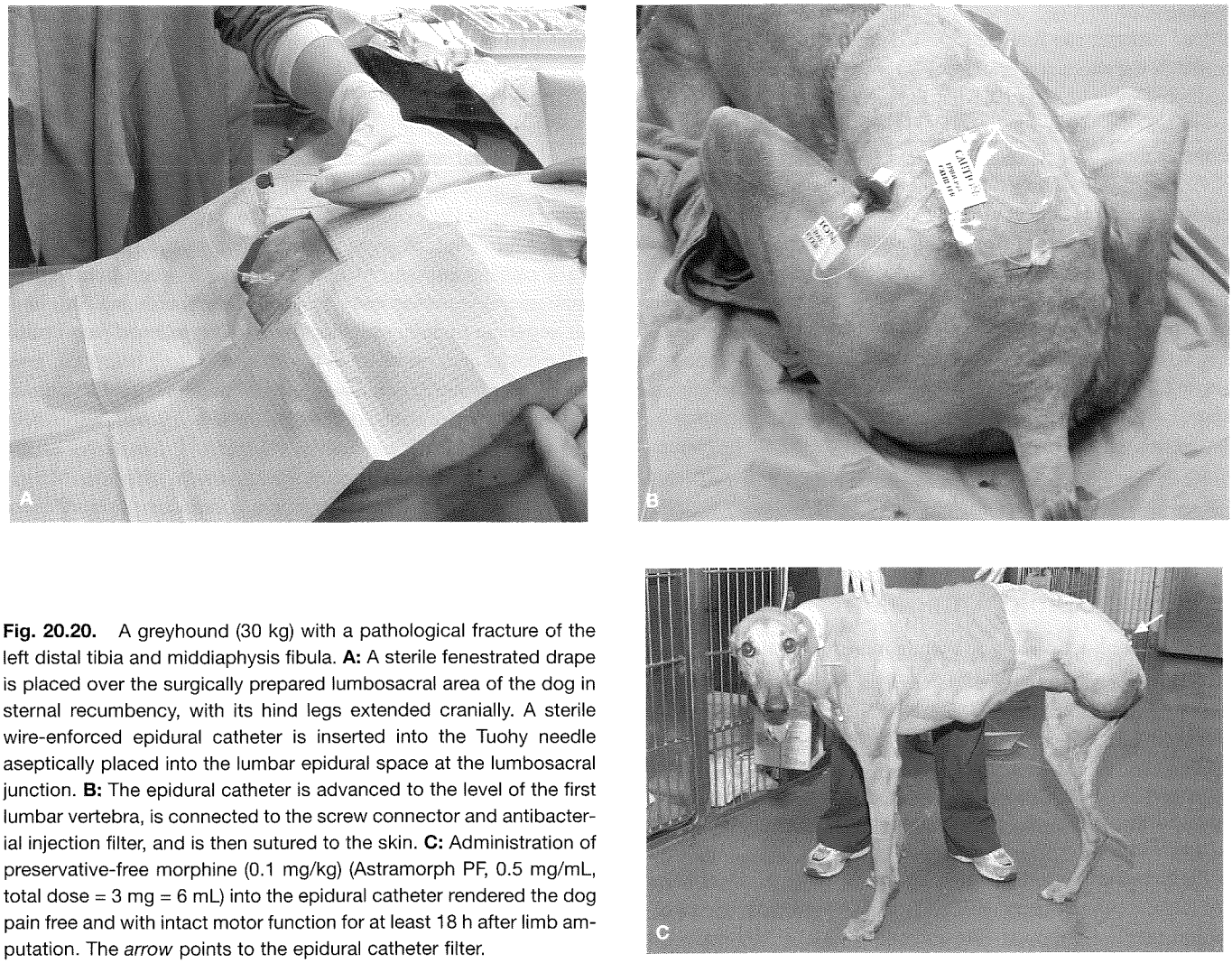

Fig. 20.20. A greyhound (30 kg) with a pathological fracture of the left distal tibia and middiaphysis fibula. **A:** A sterile fenestrated drape is placed over the surgically prepared lumbosacral area of the dog in sternal recumbency, with its hind legs extended cranially. A sterile wire-enforced epidural catheter is inserted into the Tuohy needle aseptically placed into the lumbar epidural space at the lumbosacral junction. **B:** The epidural catheter is advanced to the level of the first lumbar vertebra, is connected to the screw connector and antibacterial injection filter, and is then sutured to the skin. **C:** Administration of preservative-free morphine (0.1 mg/kg) (Astramorph PF, 0.5 mg/mL, total dose = 3 mg = 6 mL) into the epidural catheter rendered the dog pain free and with intact motor function for at least 18 h after limb amputation. The *arrow* points to the epidural catheter filter.

and wound secretions in constant exposure to the catheter site. The use of postoperatively administered systemic antibiotics is debated and is usually reserved for patients with a compromised immune system (e.g., diabetics). A thorough surgical preparation, using soap, antiseptic, or Hibiclens scrub (chlorhexidine cleanser), dramatically reduces the concentration of bacteria on the skin.

The Tuohy needle is placed into the epidural space between the L7 and S1 intervertebral space, similar to the single-injection epidural block technique. Catheterization is facilitated by first desensitizing the lumbosacral space with a small amount (2 mL) of 2% lidocaine. The Tuohy needle is inserted at a 15° to 45° angle from the vertical position with the bevel directed cranially (Figs. 20.17 and 20.20) and is advanced until the epidural space has been entered. The three techniques previously discussed—hanging drop, loss of resistance to air, and loss of resistance to saline—may be more readily performed in dogs that are positioned in sternal rather than lateral recumbency. Because the techniques may not always be ultimate proof that the needle has been placed epidurally, aspiration of the plunger before injection should verify whether a vein has been entered. At this point, catheters with a stylet are preferred. A slight resistance is usually encountered when the catheter passes through the tip of the Tuohy needle. Special markings on the catheter denote the distance the catheter has been advanced. The catheter is advanced at least two to three markings beyond the hub of the needle, which ensures that at least 2 to 3 cm of catheter has entered the epidural space. Flushing the needle with saline, rotating the needle, and advancing the catheter while slowly withdrawing the needle help to thread the catheter into the epidural space. If these maneuvers fail, the needle and catheter should be withdrawn together. No attempt should be made to withdraw the catheter back through the needle, because this may sever the catheter. If this does occur, most authorities believe that no attempt should be made to retrieve a severed catheter.[105] Wire-reinforced catheters have been inserted epidurally to the anterior lumbar (L4)[139] or thoracic (T1)[116] vertebrae with minimal resistance and without coiling, turning on themselves, kinking, or knotting.

Tuohy needles have been epidurally placed at the second coccygeal (Co3 to Co2), third coccygeal (Co4 to Co3), or fourth coc-

cygeal (Co5 to Co4) intervertebral space of dogs. A wire-reinforced catheter can then be threaded epidurally for up to 15 cm to reach the thoracic vertebrae.[117] Inserting a catheter for long distances increases the risk that the catheter tip may exit a paravertebral foramen. Fluoroscopy is recommended to facilitate catheter guidance.

A 20-cm-long intravenous catheter can be used to tunnel an epidural catheter subcutaneously if it is left in place for a prolonged period. Poor sterile technique when changing tubing and drugs is the most likely cause of catheters becoming infected. Such an infection is often heralded by radicular pain after bolus injections and decreasing analgesia, which generally precedes any sign of meningitis or systemic infection. The CSF (puncture site at C1-C2 to avoid going through an infected lumbar epidural space), epidural catheter (1-mL sterile 0.9% saline solution injected and withdrawn), and skin-insertion site should be cultured if an infection is suspected. After cultures have been obtained, the catheter is removed, and the patient is treated with systemic antibiotics.

Epidural Opioid Analgesia

Providing long-term analgesia while inducing minimal systemic effects is an important objective in medical care. Epidurally administered opiates (e.g., morphine) provide lengthy analgesia caudal to the umbilicus with very few systemic side effects.[30,32,107,136,138–154] A single epidural injection of 5 mg of morphine before major intra-abdominal surgery consistently relieves intraoperative and postoperative pain in people for at least 3 days.[155]

Preservative-free preparations of morphine (e.g., Duramorph PF [Elkins-Sinn, Cherry Hill, NJ] and Astramorph PF [Astra Pharmaceutical Products, Westborough, MA])[156,157] have not been associated with spinal cord histopathological changes. In contrast, parenterally administered morphine, which contains various preservatives—such as sodium bisulfite, metabisulfite, chlorbutanol, edetate disodium, formaldehyde, or phenol—has neurotoxic effects when placed directly on the spinal cord.[158] Any remaining opioid from single-dose vials that contain no bacteriostatic agents should be discarded.[145] Contraindications to epidural opioid analgesia are primarily associated with the epidural catheterization technique itself.

The presence of a large number of opiate receptors in the substantia gelatinosa of the dorsal horn of the spinal cord suggests that the administration of small doses of opioids into the epidural space should produce effective analgesia.[159] The administration of epidural opioids offers the advantage of producing more profound and prolonged analgesia with significantly smaller doses and less sedation than the analgesia produced by comparable parenterally administered (intramuscular or intravenous) opioids. Epidural opioids relieve somatic and visceral pain by selectively blocking nociceptive impulses without interfering with sensory and motor function or depressing the sympathetic nervous system (selective spinal analgesia).[159–165] Studies using subanalgesic doses of the μ-specific agonist (Tyr-D-Ala-Gly-*N*Me-Phe-Gly-*ol* [DAGO]) and the δ-specific agonist (D-Pen2-5-Enkephalin [DPDPE]) in cats have demonstrated a supra-additive interaction that significantly suppresses noxious stimuli.[166]

Morphine

The major advantages of selective nociceptive blockade by the use of epidural morphine are long-term pain relief without producing muscle paralysis or weakness, or significant hemodynamic effects. For example, a single dose of morphine (1 mg, diluted in 3 to 4 mL of physiological saline solution) administered via a catheter introduced into the epidural space between the lumbosacral vertebrae and advanced to the fourth and fifth lumbar vertebrae in dogs weighing 10 to 15 kg relieved pain caudal to the costal arch for up to 22 h without affecting heart rate, arterial blood pressure, pulmonary arterial pressure, cardiac output, systemic vascular resistance, PaO_2, mixed venous oxygen tension (PvO_2), $PaCO_2$, and arterial pH (pH_a).[139] Similarly, 0.1 mg of oxymorphone/kg in 3 mL 0.9% of sodium chloride solution administered epidurally in dogs via a catheter positioned between the lumbar L5 to L6 or L6 to L7 intervertebral space alleviated postthoracotomy pain for 10 h without affecting heart rate, respiratory rate, systolic and diastolic blood pressure, and PaO_2 and $PaCO_2$.[167]

The effects of epidural and intravenous morphine on analgesic effectiveness, vital signs, and cortisol and catecholamine concentrations in dogs (18 to 26 kg) after experimental thoracotomy have been compared.[168] Dogs were administered either 0.15 mg/kg of preservative-free morphine epidurally in 5 to 6 mL of 0.9% sodium chloride via a catheter 8 to 10 cm cranial to the entrance of the epidural space 30 to 40 min before the end of surgery or 0.15 mg/kg of morphine IV 5 to 10 min before the end of surgery. The efficacy of the opioid was increased if given before onset of pain. Dogs with epidural morphine administration demonstrated lower subjective pain scores and lower serum cortisol concentrations, plasma adrenaline and noradrenaline concentrations, noninvasive systolic arterial blood pressure, heart rates, and respiratory rates than did dogs with intravenous morphine for the first 10 h postoperatively.[168] A single epidural injection of morphine has been shown to be effective for up to 24 h in preventing physiological responses to postthoracotomy pain, one of the most severe causes of stress in the early postoperative period. In contrast, dogs given morphine IV often require supplemental morphine within 4 to 5 h.[143]

Epidural morphine (0.1 mg/kg diluted in 0.26 mL/kg of saline) decreases the minimum alveolar concentration of halothane and improves arterial blood pressure, cardiac index, stroke volume, left ventricular work, and pulmonary artery pressure in dogs.[169] The explanation for morphine's efficacy at such a low dose when given by the epidural route may be related to its low lipid solubility. Epidural administration of morphine (0.1 mg/kg) is typically one-tenth of the systemically administered dose, yet analgesia lasts significantly longer than that provided by other routes.

Postoperative evaluation of dogs undergoing major orthopedic surgery, using either a 100-μg/h transdermal fentanyl patch applied 24 h before surgery or epidural morphine (0.1 mg/kg) after induction of anesthesia, demonstrated a lower pain score with epidural morphine at 6 h after surgery than with transdermal fen-

Table 20.3. Physiochemical properties and doses of opioids for epidural analgesia in dogs.

Opioid	Molecular Weight of Base	pK^a (25°C)	Oil-water Partition Coefficient[a]	Dose (mg/kg)	Approximate Time for Pain Relief (min)	Approximate Duration of Analgesia (h)
Morphine sulfate	285	7.9	1.42	0.05–0.15	30–60	10–24
Meperidine hydrochloride	247	8.5	38.8	0.5–1.5	10–30	5–20
Methadone hydrochloride	309	9.3	116	0.05–0.15	15–20	5–15
Oxymorphone hydrochloride	301	—	—	0.05–0.15	20–40	10–22
Fentanyl citrate	336	8.4	813	0.001–0.01	15–20	3–5

[a]Octanol–pH 7.4 buffer partition coefficient.

tanyl. However, when all periods (6, 18, 30, and 42 h) after surgery were combined, analgesia with transdermal fentanyl was equivalent to that achieved with epidural morphine.[170]

Epidural administration of morphine sulfate (30 mg) in a multivesicular liposome (Depot Foam) formulation has also been evaluated.[171] Epidural morphine (5 mg and 30 mg), but not liposomes without morphine, produced potent analgesia, as measured by latency of thermally evoked skin twitch. The analgesic index (area under the time effect curve) was significantly greater in dogs treated with encapsulated morphine (30 mg) than in those treated with morphine sulfate (3 mg). The epidurally administered encapsulated morphine formulation produced significantly lower morphine concentrations in lumbar CSF and greater residency time than did epidural morphine. This study indicates that the action of epidural morphine can be extended by delivering higher doses of morphine (30 mg) in an encapsulated, persistent-release form.

Pharmacokinetic and Pharmacodynamic Properties

The physiochemical properties of opioids, particularly their lipid solubility, molecular weight, pK^a, and receptor-binding affinity, are important in determining their pharmacokinetic and pharmacodynamic properties and the onset and duration of analgesia (Table 20.3). Relatively hydrophilic morphine (oil-water partition coefficient, 1:42) remains in the CSF for longer periods, allowing rostral spread and analgesia distant from the site of injection (nonsegmental distribution of analgesia). For example, the lumbosacral epidural administration of 0.1 mg of morphine/kg has been reported to produce adequate postthoracotomy analgesia in dogs.[26,32,48,140,146]

Epidurally administered morphine is distributed by at least four different pathways: (a) transdural passage to the CSF and neural axis, (b) vascular uptake by epidural venous plexi and spinal radicular arteries, (c) lymphatic uptake, and (d) deposition into epidural fat.[117,141,172,173] The distribution in CSF, blood, and lymph of lumbar epidurally administered morphine (molecular weight, 285; and p*Ka*, 7.9) into the lumbar area in dogs has been determined.[117] The fraction of morphine crossing the dura after epidural injection of 2 mg into a 30-kg dog has been calculated to be 0.3%.[117] Maximal morphine concentration in lumbar CSF ranged from 5 to 93 ng/mL and was reached 5 to 60 min after injection. Morphine clearance from the CSF was 106 min (mean *t*ß) independent of the dose.[117] In another study, the maximal concentration of a 0.1-mg/kg dose of morphine in cisternal CSF was 102.3 ± 28.0 ng/mL at 180 min after lumbar epidural administration.[141] The maximal concentration of morphine in serum of the same dogs was 95.7 ± 27.0 ng/mL at 31.0 ± 15.2 min.[141]

This large variability in CSF and plasma concentrations is a striking finding that emphasizes the need for adjusting the dose of epidural morphine for each patient. Practically, this can be accomplished by using an epidural catheter while observing the degree of analgesia and the severity of side effects. Pharmacodynamic studies evaluating the degree of analgesia and CSF and plasma drug concentrations of epidurally administered morphine support a spinal mechanism of action. These studies also indicate that rapid but short-lasting serum concentrations and delayed long-lasting CSF concentrations are often achieved with epidurally administered doses of morphine in dogs.

Oxymorphone

Oxymorphone, in comparison to morphine, is a relatively lipid-soluble opioid that binds more rapidly to opiate receptors in the spinal cord and has a smaller area of distribution in the CSF (segmental analgesia) (Table 20.3).

The analgesic and cardiorespiratory effects of epidurally administered bupivacaine (0.5%, 1.0 mg/kg), oxymorphone (0.1 mg/kg) in 0.75% bupivacaine (1 mg/kg), and intravenous oxymorphone (0.05 mg/kg) on halothane requirements have been evaluated.[150] There were no differences in end-tidal halothane requirements for dogs among the three groups. Respiratory depression was increased and heart rate was decreased with epidural oxymorphone-bupivacaine and intravenous oxymorphone treatments. Postoperative requirements of oxymorphone (0.05 mg/kg IV) were significantly less in dogs receiving the epidural oxymorphone-bupivacaine combination.[150]

The postoperative analgesic and cardiopulmonary effects of oxymorphone administered epidurally (0.05 mg/kg) and intramuscularly (0.15 mg/kg) or medetomidine administered epidurally (0.015 mg/kg) have also been evaluated in dogs undergoing pelvic or hind-limb orthopedic surgery.[174,175] The average duration of analgesia obtained with both epidural oxymorphone and medetomidine was 7 h, whereas intramuscular oxymorphone provided approximately 5 h of analgesia. All treatments decreased heart rate. There was no difference in arterial blood pres-

sure with epidural and intramuscular oxymorphone, but pressure was increased with epidural medetomidine.

Butorphanol

Epidural butorphanol (0.25 mg/kg) administration in dogs reportedly reduces the inhalant anesthetic requirement (decreased isoflurane minimum alveolar concentration by 32%) without any cardiovascular and neurological side effects.[176] However, the rather brief analgesic action (80 min), as assessed by dogs not responding to toe-pinch stimulation of the hind limbs and forelimbs, limits the value of epidural butorphanol administration in clinical practice. Pharmacokinetic data from epidural butorphanol (0.25 mg/kg) administration in halothane-anesthetized dogs indicated that the maximum concentration of butorphanol and time to reach this concentration are 42.3 ng/mL at 13.9 min in blood and 18 ng/mL at 30 min in CSF. The authors concluded that the pharmacokinetic data suggest that analgesia is predominantly due to butorphanol's action on supraspinal structures following its vascular systemic absorption.[177]

Buprenorphine

The efficacy of epidural buprenorphine (4 μg/kg) versus epidural morphine (0.1 mg/kg) administered in a total volume of 0.2 mL/kg for postoperative pain relief in dogs undergoing cranial cruciate ligament rupture repair has been compared.[154] Epidural buprenorphine appeared to be as effective as epidural morphine for relief of postoperative hind-limb orthopedic pain in healthy dogs and may offer some advantages over morphine, such as lower abuse potential and reduced cost.[154]

Side Effects of Epidural Opioids

Potential side effects in patients include respiratory depression, dysphoria, urinary retention, delayed gastrointestinal motility, vomiting, rubbing of the face, and catheter-related problems such as catheter displacement, occlusion, and infection from chronic epidural catheterization.[145,158,178]

The analgesic efficacy, duration of action, and adverse side effects of epidurally administered morphine are dose related.[179] The most serious adverse effect is respiratory depression, which is biphasic. Respiratory depression has been attributed to the absorption of morphine into epidural veins and subsequent circulatory redistribution to the brain (early depression), and cephalad movement of morphine in CSF to the brain stem (late respiratory depression).[180] Lumbar epidural administration of excessive doses of morphine (20 mg of morphine sulfate in a 3-mL saline solution) in awake dogs (30 kg) increased $PaCO_2$ by 10 mm Hg at 1.5 to 2.0 h after administration, with no further ventilatory depression thereafter.[163] The maximal concentration of morphine in the CSF of these dogs was 64 ng/mL at 45 min after administration but gradually declined to 50% of maximum concentration at 6 h. The morphine concentration in arterial plasma was maximal at 30 min and declined to 20% of maximal by 6 h.

Administration of increasing concentrations (0.1 to 100.0 ng/mL) of morphine into the fourth ventricle or cisterna magna in awake dogs produced reduced tidal volume but not respiratory rate, suggesting that larger doses (20 mg) of epidural morphine can produce respiratory depression in dogs. This effect is most likely caused by the delivery of morphine to the brain-stem respiratory centers via the blood rather than via the CSF.[163] The time course of ventilatory depression following subarachnoid administration of morphine in dogs corresponded poorly with morphine concentration changes in the CSF.[164] Severe respiratory depression should not occur in dogs when therapeutic doses (0.1 mg/kg) of morphine are administered epidurally.

Preemptively administered epidural morphine with or without bupivacaine given to 242 dogs has produced mild respiratory and cardiovascular depression during anesthesia, whereas urinary retention, pruritus, and vomiting were seen in only seven, two, and six dogs, respectively. Six dogs vomited when a second dose of morphine was given epidurally the day after surgery.[136] Side effects are more common when intrathecal injection is performed as opposed to epidural injection, and side effects can usually be reversed by a low-dose intravenous infusion of naloxone, with minimal effect on the analgesia produced.[181]

Myoclonus[182–184] and neuroexitation[185,186] are very rarely observed complications in human patients after the epidural or intravenous administration of opioids. Similarly, involuntary muscle contractions in dogs, after either epidural or subarachnoid administration of preservative-free morphine, are extremely rare. Myoclonus and urinary retention have been reported in a 5-year-old German shepherd 90 min after subarachnoid injection of preservative-free morphine sulfate (0.15 mg/kg) diluted in 4 mL (0.1 mL/kg) of a sterile isotonic saline solution.[187] Muscle twitches started at the tail and then progressed to the hind limbs, trunk, and even partly the shoulders of the dog, which had just recovered from a 5-h oxymorphone-acepromazine-thiopental-isoflurane-oxygen anesthesia to complete a total hip-prosthesis surgery. The twitches became very strong with time and were not diminished by diazepam (0.2 to 1.0 mg/kg IV) or atracurium injected twice at 45-min intervals (0.2 and 0.1 mg/kg). The spasms were eventually controlled with pentobarbital administration (130 mg IV) and intermittent positive-pressure ventilation for 4 h.[188] The following day, the spasms were absent, but proprioceptive ataxia and hind-limb paresis, with urinary retention, persisted for another day. Bethanechol chloride (5 mg) was given by mouth every 8 h, and the bladder was emptied by catheterization once. The dog recovered over the next few days without further sequelae.[187]

In another report, a dog exhibiting hyperesthesia and extreme neuritis of the pelvic area and tail lasting 24 h slowly resolved over a 4-day period.[189] Overall, the incidence of severe complications was reported to be 0.75% in 365 dogs and 4 cats that received epidural morphine for a wide variety of procedures, including fracture repair or arthrodesis, limb and tail amputation, total hip replacement, thoracotomy, laparotomy, and laminectomy.[189]

Opioid-induced hyperalgesia, myoclonus, and seizures have been reproduced and studied extensively in rats.[182,183,190,191] Direct opioid receptor–mediated and nonopioid receptor–mediated excitatory and inhibitory mechanisms, metabolites (normorphine, morphine-3 glucuronide, and hydromorphone-3 glucuronide), and preservatives (sodium bisulfite) have all been

implicated in these observed neurological side effects. Intrathecal naloxone has also been implicated in the potentiation of intrathecal morphine-induced hind-limb myoclonus and seizure activity in rats.[182]

Nonopioid Epidural Analgesia

Drugs from other classes—such as α-adrenoceptor agonists, *N*-methyl-D-aspartate (NMDA) receptor antagonists (e.g., ketamine), and serotonergic, cholinergic, and γ-aminobutyric acid (GABA) receptor agonists[192]—upon direct spinal administration in laboratory animals, have inhibited behaviors elicited by noxious stimuli.[193,194] With the exception of epidurally administered α_2-adrenoceptor agonists, such as xylazine,[147,148,195–200] medetomidine,[144,153,174,175,200,201] and NMDA receptor antagonist, such as ketamine,[202–207] there is little information on the clinical efficacy of nonopioid spinal analgesic drugs in dogs.

α_2-Adrenoceptor Agonists

Similar to morphine, the administration of α_2-agonists can produce a powerful effect on nociceptive processing by activating a dense population of α_2 receptors (i.e., α_{2A}, α_{2B}, α_{2C}, and α_{2D}) (heteroceptors) in the CNS and periphery.[208–210] In addition, some α_2-agonists can also activate imidazoline receptors (I_1 and I_2) and produce direct effects on sensory transmission (e.g., xylazine). Spinally administered α_2-agonists mediate analgesia by activating presynaptic α_2-adrenoceptors, which are located on primary afferent C fibers terminating in the superficial laminae of the dorsal horn of the spinal cord.[211] This activation induces G_0 proteins that decrease calcium influx, which results in a decreased release of neurotransmitters and/or neuropeptides (e.g., glutamate, substance P, neurotensin, calcitonin gene–related peptide, and vasoactive intestinal peptide), resulting in antinociception.[212,213] Activation of the α_2 heteroceptors, which are located postsynaptically on wide-dynamic-range projection neurons targeted by primary afferent fibers in the dorsal horn, results in hyperpolarization of neurons via G_i protein–coupled potassium channels, producing postsynaptically mediated spinal analgesia.

Epidural Xylazine and Medetomidine

The effects of epidural xylazine on electroencephalogram (EEG) responses to surgical stimuli of varying intensity during experimental orthopedic procedures have been reported.[197,198] After epidural xylazine administration (L7-S1), anesthesia was maintained with isoflurane (end-tidal concentration, 1.5%) in oxygen. The EEG and hemodynamic variables (heart rate and mean arterial blood pressure) were evaluated at prestimulation, skin incision, removal of a bone graft from the dorsoiliac spine, opening and reaming of the medullary canal of the tibia for bone graft installation, and wound closure. Skin incision and removal of bone graft produced a significantly higher increase in α/δ ratio in the EEG in the saline group when compared with the xylazine group. In addition, the prestimulation 80% spectral edge frequency of the EEG in the xylazine group was significantly lower than in the saline group. The results of this study suggest that epidural xylazine (0.25 mg/kg) suppresses responses in the α/δ ratio to surgical stimulation and may exert its antinociceptive effect in dogs in part by a supraspinal action.[198]

The most obvious physiological effects of activating spinal α_2-adrenoceptors, other than their effect on altering nociceptive threshold, are bradycardia and hypotension.[200] Medetomidine (15 μg/kg) or xylazine (0.25 mg/kg) both produced similar cardiovascular and respiratory changes after lumbosacral epidural administration in dogs. Both drugs reduce heart rate, mean arterial blood pressure, and respiratory rate from baseline values. First-degree atrioventricular block was observed more often after xylazine administration (50% vs. 33%), whereas second-degree block was more frequently observed with the use of medetomidine (66% vs. 33%).[200]

Epidural medetomidine administration (0.015 mg/kg) reportedly produces analgesia lasting 7 to 8 h.[174,175] The duration of analgesia is comparable to that achieved with epidurally administered oxymorphone (0.05 mg/kg) for similar procedures. However, all medetomidine-treated dogs developed a decrease in heart rate and a transient increase in arterial blood pressure. Dogs typically develop second-degree atrioventricular block associated with sinus arrhythmia for a brief period during the first 20 min after medetomidine epidural injection.

Epidural Dexmedetomidine

Dexmedetomidine is the pharmacologically active D-isomer of medetomidine, a highly lipid-soluble α_2-receptor agonist[214] and, as such, is rapidly absorbed into the circulation and CNS. A dose-dependent effect of dexmedetomidine on antinociception and effects on respiratory function have been documented.[215] Different dose ranges of dexmedetomidine were used after each route of drug administration, with 4 to 6 days elapsing between the experiments. Dexmedetomidine by intrathecal (1, 3, or 10 μg), epidural (3, 15, and 50 μg), and intravenous (1, 3, and 10 μg/kg) routes produced a rapid dose-dependent increase in the thermal (60° ± 1°C for a maximum of 10 s) skin-twitch response latency at lumbar and thoracic areas and paw withdrawal to mechanical compression of the toes of the front and hind limbs. The dose required to reach 50% of maximal effect for skin-twitch response after intrathecal, epidural, and intravenous administration of dexmedetomidine was 1.8, 10, and 15 μg, respectively. The maximal effective dose produces approximately 90 min of hypoalgesia. The spinal effects do not appear to be associated with changes in behavioral alertness, motor function, or carbon dioxide response. Intravenous dexmedetomidine (1 to 10 μg) also elevates the nociceptive threshold significantly, as measured by thermal or mechanical nociceptive end points. In contrast to the spinal administration, however, intravenous dexmedetomidine produces dose-dependent sedation, significantly reduces heart and respiratory rates, and diminishes response to increased carbon dioxide. The α_2-adrenoceptor antagonist atipamezole (30 to 300 μg/kg IV), but not the opioid antagonist naloxone (30 μg/kg IV), antagonizes all of the observed effects of dexmedetomidine. These results suggest that spinally administered dexmedetomidine produces a powerful antinociceptive effect, mediated via α_2-adrenoceptors at the spinal level, whereas systemic redistribution of the drug produces sedation with significant cardiovascular and respiratory side effects.[215]

Ketamine

Ketamine has an analgesic action at many sites both centrally and peripherally. The mechanism of analgesic action of epidurally and intrathecally administered ketamine has not been clearly defined, and investigation into the contribution of supraspinal and/or spinal sites related to its analgesic and anesthetic action has not provided conclusive results. While reports regarding the efficacy of ketamine as a spinal analgesic are controversial, ketamine may block NMDA receptors and interact with subtypes of opioid, propionate, kainate, γ-aminobutyric acid A receptors,[216] and/or monoaminergic (serotonergic, noradrenergic, and dopaminergic) neural systems.[217] Ketamine also inhibits voltage-gated sodium-ion and potassium-ion channels, thereby suppressing myelinated nerve conduction.[218,219] Ketamine may reverse opioid tolerance by interacting with NMDA receptors, the nitric oxide pathway, and μ opioid receptors.[220] Evidence of the efficacy of ketamine for treatment of chronic pain in human patients has been reviewed and is considered moderate to weak.[221]

The analgesic action of epidurally injected ketamine has been assessed in anesthetized dogs by using cutaneous electrical stimulus (10 V) to the ischial and masseter muscle region.[204,205] The number of dogs responding to cutaneous electrical stimulation was significantly less following epidural ketamine-lidocaine administration than following epidural ketamine-saline administration. Similarly, the lumbosacral epidural injection of ketamine (20 mg/mL) at a dose of 2 mg/kg did not provide significant analgesia in dogs with chemically induced synovitis.[207]

The hemodynamic effects of ketamine when injected into the lumbosacral epidural space typically include increases in heart rate, mean arterial blood pressure, cardiac index, and stroke work index within 15 to 20 min.[205] It is not yet conclusive that epidural ketamine consistently decreases the requirement of inhalation anesthetics. Nevertheless, epidural and intrathecal doses of 1 to 3 mg of ketamine/kg of body weight have shown analgesic efficacy in canine studies.[202,203] Ketamine is rapidly distributed to the plasma and CSF (0.4 and 0.3 h, respectively) from the epidural space of dogs.[202]

Diazepam

Diazepam has been administered epidurally to dogs.[192] With a 2-mg/kg dose, the tail, perineum, anus, sacral, lumbar, abdomen, and hind limbs are desensitized and the hind limbs paralyzed for variable periods (50 to 100 min). Pulse rate is significantly increased, whereas skin temperature, rectal temperature, respiratory rate, mean arterial blood pressure, and central venous pressure are not affected. Neurological damage or toxicity, and inflammatory infiltration in histological preparations of the spinal cord, are not evident.[192] There has been little clinical use of benzodiazepines as analgesics when placed epidurally in dogs or other companion animals.

Ketorolac

Ketorolac (0.4 mg/kg) has been administered into the lumbar epidural space in dogs.[222,223] Gross necropsy revealed gastrointestinal ulceration of varying degrees in dogs administered epidural ketorolac. Histopathological analysis of the spinal cord and meninges revealed minimal focal leptomeningeal phlebitis in 25% of the dogs given this drug. Gastrointestinal ulceration induced by ketorolac is common and limits its use to a single injection. At present, both efficacy and safety need to be further evaluated before epidural administration of ketorolac or any other nonsteroidal anti-inflammatory drug can be recommended for clinical practice.[222,223]

Glucocorticoids

Glucocorticoids (e.g., prednisone, prednisolone, and methylprednisolone) are most commonly administered by systemic routes, either oral or injectable, to relieve pain and reduce inflammation. Perineural injection, either to spinal nerve roots or to peripheral nerves, to alleviate pain caused by nerve root disease or peripheral neuropathies is common in human patients.[224] The beneficial effects of epidurally administered betamethasone in a rat model of lumbar radiculopathy have been reported.[225] However, a series of lumbar epidural steroid injections for chronic back pain has produced life-threatening *Staphylococcus aureus* meningitis and cauda equina syndrome in one person[226] and transient blindness caused by retinal and vitreal hemorrhages from increased intracranial pressure in another person.[227] As of this writing, recommendations or dosages for the use of epidural glucocorticoids in dogs and other small companion animals have not been developed.

Epidural Drug Combinations

Epidural opioids (e.g., morphine or oxymorphone) with local anesthetics (e.g., lidocaine, bupivacaine, or ropivacaine) or α_2-adrenoceptor agonists (e.g., xylazine, medetomidine, or dexmedetomidine) have been administered to dogs before surgery to reduce general anesthetic requirements and provided intraoperative and postoperative pain control.

Local Anesthetics and Opioids

In rats, the combined intrathecal administration of morphine with lidocaine or bupivacaine reportedly produces antinociceptive effects that are more rapid in onset, last longer, and are greater in peak effect than when agents are administered alone at the same dose level.[228] Subsequently, several investigators have reported additive or synergistic effects of epidurally administered opioids and local anesthetics in people,[194,229–232] dogs,[30,107,151] and rats.[228] Although various local anesthetics and opioids have been administered epidurally in dogs, morphine, bupivacaine, and their combination effects have been the most critically evaluated.[93,107,118,140,169,233] For example, the epidural administration of morphine-bupivacaine provided longer-lasting analgesia and required a lower number of supplemental doses of analgesic agent than did morphine or saline alone. The times for rescue-oxymorphone administration in dogs treated with either epidural morphine alone, bupivacaine alone, the morphine-bupivacaine combination, or saline were 5.4, 9.1, 24, and 2.6 h, respectively.[107] Likewise, the coadministration of epidural lidocaine and fentanyl (100 μg in 0.3 mL of 0.9% sodium chloride with epinephrine 1:200,000) produces scrotal analgesia with faster onset

(1.3 ± 0.3 vs. 4.4 ± 0.4 min) and longer duration (143 ± 11 vs. 98 ± 8 min) than does lidocaine with epinephrine alone. The epidural coadministration of lidocaine and fentanyl consistently produces forelimb rigidity in dogs.[234]

α_2-Adrenoceptor Agonists and Opioids

Synergistic antinociceptive interactions have been observed between a variety of α_2-adrenoceptor and opioid receptor agonists.[235–237] The epidural administration of α_2-adrenoceptor agonists (xylazine or medetomidine) alone or in combination with morphine has gained some degree of use in veterinary practice during the last 5 years. A few studies documenting this synergy have been performed.

For example, dogs receiving low-dose epidural medetomidine (5 μg/kg) administration alone did not show evidence of analgesia, as evidenced by response to tail clamping. However, the addition of medetomidine to morphine prolonged the analgesia beyond that achieved with morphine alone (13.1 ± 3.1 vs. 6.3 ± 1.2 h), indicating a supra-additive effect with the administration of both drugs.[238] In another study, postoperative analgesia was assessed in dogs given either preservative-free morphine (0.1 mg/kg) or morphine (0.1 mg/kg) with medetomidine (5 μg/kg) via lumbosacral epidural injection.[153] Based on numerical rating scale, pain scores, posture, vocalization, and facial expression, epidurally administered morphine combined with medetomidine was associated with superior analgesic benefits when compared with morphine alone.

Ketamine and Opioids

In a more recent study, epidural ketamine (40 to 320 μg), morphine (0.6 to 160 μg), or fentanyl (0.16 to 10 μg), and a combination of 80 μg of ketamine with either morphine (2.5 to 80 μg) or fentanyl (0.04 to 10 μg) have all been assessed for analgesic properties.[238] Epidural ketamine produced only limited antinociception, whereas morphine and fentanyl exhibited a dose-related antinociception. Morphine's action was slow in onset and lasted long, whereas fentanyl had a fast onset and briefer action. In combination, ketamine improved maximal possible effect as well as duration of action of morphine-induced, but not fentanyl-induced, antinociception. Moreover, increasing doses of the highly lipophilic ketamine tended to decrease the maximal response of various doses of the highly lipophilic fentanyl. Competition, at least in part, for the same μ receptor or μ receptor subtypes, via P glycoprotein, could have been one mechanism by which higher doses of ketamine decreased the antinociceptive properties of fentanyl. These data indicate that ketamine and perhaps other drugs may actually have antagonistic effects with various opioids when coadministered in the epidural space to induce an analgesic action.[239]

Ganglion Blocks

Anesthesia of the cervicothoracic ganglion and lumbar sympathetic chain in dogs has been described to treat paralysis of the radial, facial, and trigeminal nerves and muscle and joint diseases:[240,241] 5 to 8 mL of 0.5% procaine hydrochloride solution has been administered in close proximity to the cervicothoracic ganglion and lumbar sympathetic chain without ill effects.

Conclusion

Local and regional anesthetic techniques in dogs have been used extensively to relieve the pain related to a variety of medical and surgical procedures. Appropriately selected topical, local, or regional (e.g., epidural) techniques can provide safe, effective, and reliable analgesia with minimal physiological alterations. Similarly, the interpleural administration of local anesthetic drugs or the epidural administration of opioids can provide unparalleled long-term relief of pain while preserving consciousness. Novel systems for the delivery of analgesics and other therapeutic modalities designed to be used with local anesthetics, opioids, and nonopioid analgesics may greatly facilitate the future management of perioperative pain in companion animals.[242]

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