

Anesthesia and Perioperative Care

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ASSESSMENT OF RISK

In both medical and veterinary anesthesia, patients are often classified using the American Society of Anesthesiologists Physical Status Classification (ASA-PS), which attempts to give a subjective and relative risk based only on the patient's preoperative medical history (Table 7-1). In this classification ASA 1 is considered a healthy patient with no overt signs of disease, and 5 is considered a moribund patient who is considered likely to die in the next 24 hours with or without surgery. Addition of "E" to the classification indicates emergency surgery.⁶¹

Although anesthetic-related death in cats has decreased over the years, the most recent published mortality rate of 0.24%, or 1 in 453 anesthetics,²⁷ is still up to 10 times that found in human studies.⁴² The "Confidential Enquiry into Perioperative Small Animal Fatalities"²⁶ was undertaken in 117 veterinary practices in the United Kingdom from 2002 to 2004. The study included 79,178 cats with overall risks of sedation and anesthetic-related deaths within 48 hours of procedure of 0.24%. In this study most cats were premedicated (70%), intubated (70%), and breathing spontaneously (92%). Procedures were short (25 to 30 minutes), and fluids were administered to only 26% of cats. Monitoring was rare, with pulse monitored in 38%, pulse oximetry in 16%, and both pulse and pulse oximetry in 25% of cats. Temperature was monitored intraoperatively in 1% to 2% of cats and postoperatively in 11% to 15% of cats. Specifically in cats, factors associated with increased odds of anesthetic-related death were poor health status (ASA-PS classification), increasing age, extremes of weight, increasing

procedural urgency and complexity, endotracheal intubation, and fluid therapy. In this study the greater risk associated with anesthesia in cats compared with dogs was reported to be related to their size (relatively small with a large surface area to volume ratio), which predisposes them to hypothermia and drug overdosage, and a small airway and a sensitive larynx, which predisposes them to upper airway complications. Pulse monitoring and pulse oximetry were associated with reduced odds, related more to patient monitoring than to the specific equipment used. A total of 61% of cats died in the postoperative period, with 62% of those occurring in the first 3 hours after surgery. Factors considered important in reducing mortality risk are listed in Box 7-1.

SEDATION AND PREMEDICATION

Cats often require sedation to allow diagnostic or minor procedures to be performed. Although *sedation* is defined as the induction of a relaxed state, the goals may include decreased stress and anxiety, as well as depression of the central nervous system so that handling is easier, and analgesia. Drugs or drug combinations used for sedation in cats are often similar to those used for premedication before general anesthesia. Ideally, they should have minimal effect on cardiovascular and respiratory function. However, drugs producing moderate to profound sedation in cats produce significant cardiorespiratory effects, and in some cases general anesthesia may be a safer approach, even if only sedation is required for the procedure.

TABLE 7-1 American Society of Anesthesiologists' Physical Status Classification

Class*	Preoperative Health Status	Comments
PS 1	Normal healthy patient	No health problems; excludes the very young and very old
PS 2	Patients with mild systemic disease	Mild, well-controlled systemic disease
PS 3	Patients with severe systemic disease	Severe or poorly controlled systemic disease
PS 4	Patients with severe systemic disease that is a threat to life	At least one disease that is poorly controlled or end stage, possible risk of death
PS 5	Moribund patients not expected to live >24 hours with or without surgery	Imminent risk of death, multiorgan failure

*An E is added to the class to designate emergency surgery.

Adapted from <http://www.asahq.org/clinical/physicalstatus.htm>.

BOX 7-1

Factors Likely to Reduce Mortality

- Better preoperative evaluation of patients
- Better preparation of patients
- Better monitoring of patients both during anesthesia and in the early postoperative period

Premedication before general anesthesia is part of the overall anesthetic plan and should be planned in relation to it. Premedication may aim to produce one or several effects and may require the administration of a single drug or, more often, a combination of drugs. Goals of premedication include the following:

- Sedation to facilitate intravenous catheterization and induction of anesthesia
- Reduction of stress and anxiety
- Analgesia
- Reduction of anesthetic dose for induction and maintenance to reduce adverse effects due to anesthetic agents
- Prevention or treatment of adverse effects of other drugs given for premedication
- Anesthetic induction, or maintenance
- Improvement in quality of anesthetic induction and/or recovery
- Prevention or treatment of specific conditions

This latter effect will not be reviewed here; it would, for example, include the administration of antihistamine drugs in patients with mast cell tumors.

BOX 7-2

Advantages and Disadvantages of Acepromazine

Advantages

- It produces sedation.
- It may prevent the behavioral effects produced by opioids.
- It decreases anesthetic requirements.
- It has minimal impact on ventilation.

Disadvantages

- Sedation appears minimal and variable in cats.
- It produces vasodilation and hypotension.
- It interferes with thermoregulation, leading to hypothermia in most situations.

It is important to consider that premedication is not always necessary and that in some patients only some of the aforementioned effects may be desirable. For example, in the obtunded patient sedation is unnecessary, and agents producing sedation are often contraindicated because of the adverse effects they produce.

Agents used for premedication are usually administered parenterally. Subcutaneous administration is usually easy and causes minimal pain and stress; however, onset of effect is expected to be delayed, and the effect is more variable than after intramuscular or intravenous administration. Some agents may be administered orally (e.g., by the owners before going to the veterinary hospital). This may be advantageous in particularly anxious patients.

Agents commonly used for premedication belong to one of three classes: tranquilizers/sedatives, analgesics, and anticholinergics. The pharmacology of drugs commonly used for premedication is briefly reviewed in **Table 7-2**.

Tranquilizers and Sedatives

Acepromazine

Acepromazine is the prototype tranquilizer and is the only drug in that category commonly used in clinical practice (**Box 7-2**). Acepromazine is a phenothiazine compound. It antagonizes the actions of dopamine as a central neurotransmitter. It also blocks the effects of dopamine at peripheral D₁ and D₂ receptors. Its onset of action is long (15 minutes after intravenous administration, 30 to 45 minutes after intramuscular administration), and it has a long (3 to 6 hours) duration. Acepromazine is sometimes administered orally, but its bioavailability appears poor,⁸⁸ although data in cats are not available. High doses should therefore be used.

TABLE 7-2 Drugs Commonly Used for Sedation and Premedication in the Cat

Drug	Main Desired Effect	Suggested Dose Range and Route
Acepromazine	Sedation	0.02-0.05 mg/kg SC, IM, IV
Diazepam	Sedation	0.1-0.5 mg/kg IV
Midazolam	Sedation	0.1-0.3 mg/kg IM, IV
Xylazine	Sedation	0.5-2 mg/kg SC, IM, IV
Dexmedetomidine	Sedation	5-20 µg/kg SC, IM, IV
Morphine	Analgesia	0.1-0.2 mg/kg SC, IM
Hydromorphone	Analgesia	0.03-0.1 mg/kg SC, IM, IV
Oxymorphone	Analgesia	0.03-0.1 mg/kg SC, IM, IV
Methadone	Analgesia	0.2-0.5 mg/kg SC, IM, IV
Buprenorphine	Analgesia	10-30 µg/kg SC, IM, IV
Butorphanol	Analgesia	0.1-0.4 mg/kg SC, IM, IV
Ketamine	Sedation	5 mg/kg SC, IM; 2-5 mg/kg IV
Telazol	Sedation	3-5 mg/kg SC, IM; 2-3 mg/kg IV
Atropine	Prevention of bradycardia, decreased secretions	0.01-0.04 mg/kg SC, IM, IV
Glycopyrrolate	Prevention of bradycardia, decreased secretions	0.01 mg/kg SC, IM, IV

SC, Subcutaneous; IM, intramuscular; IV, intravenous.

Acepromazine produces sedation. Typically, patients are rousable by stimuli of sufficient intensity. The sedative effect is variable among individuals but may be improved by combining acepromazine and opioids (neuroleptanalgesia). Chlorpromazine, another phenothiazine, was shown to decrease morphine-induced excitement in cats,⁴⁸ and acepromazine is expected to have similar effects. Phenothiazines appear to suppress aggressive behaviors related to dominance rather than fear. Acepromazine is usually not thought to produce analgesia. However, in a recent study in cats, acepromazine produced mechanical antinociception and potentiated the effect of tramadol.²¹¹ Acepromazine has been reported to decrease anesthetic requirements, both for injectable and inhaled anesthetics.^{95,233} In a study in cats, however, acepromazine did not reduce the induction dose of propofol.⁶⁹ Phenothiazines may decrease the seizure threshold,^{57,128} and acepromazine should be used with caution in patients with a history of seizures or during procedures or with drugs that may cause seizures.

Acepromazine produces minimal effects on the respiratory system. Respiratory rate may decrease, but blood gases remain normal, probably because of an increase in tidal volume. Acepromazine produces vasodilation and hypotension.⁴¹ The effect is mainly due to alpha-adrenergic blockade; central sympatholysis, direct vasodilation, and/or stimulation of beta₂ adrenergic receptors may contribute. If a vasoconstrictor is used to treat hypotension in cats receiving acepromazine, an alpha₁ agonist

devoid of beta₂ effect such as phenylephrine or norepinephrine should be used. Heart rate may decrease, but the effect is usually mild. Phenothiazines protect against epinephrine-induced arrhythmias.¹⁵³ They cause splenic sequestration of red blood cells and markedly reduce the hematocrit level.

Acepromazine interferes with temperature regulation. Hypothermia or hyperthermia may result, depending on ambient temperature, although hypothermia is more common. Acepromazine produces antiemetic effects because of its interaction with central dopaminergic receptors at the level of the chemoreceptor trigger zone. Acepromazine reduces gastroesophageal sphincter pressure, possibly increasing the incidence of esophageal reflux and regurgitation.⁹⁰ Acepromazine blocks histamine H₁ receptors and may affect the results of intradermal skin testing.¹⁴ Acepromazine applied topically does not affect intraocular pressure in normal eyes but may reduce it when elevated.⁹⁴ Acepromazine reduces tear production in normal cats.⁷⁰

According to the authors' clinical experience, cats treated with acepromazine appear sedated in the absence of stimulation, but the effects seem to disappear with handling. Acepromazine worsens the hypotensive effect of inhalant anesthetics in cats, and the authors do not commonly use this drug in feline patients.

Benzodiazepines

Three drugs in the benzodiazepine class are used in clinical practice as part of anesthetic management:

BOX 7-3**Advantages and Disadvantages of Benzodiazepines****Advantages**

- They decrease anxiety.
- They produce muscle relaxation.
- They prevent convulsions.
- They may produce sedation.
- They reduce anesthetic requirements.
- They have minimal effects on the cardiovascular and respiratory systems.

Disadvantage

- They may produce dysphoria.

diazepam, midazolam, and zolazepam. Zolazepam is available only in combination with tiletamine (Telazol) and will not be discussed here (Box 7-3).

Benzodiazepines act by modulating GABA_A (gamma-aminobutyric acid) receptors. GABA is the most prominent inhibitory neurotransmitter in the mammalian brain. Benzodiazepines have a short onset of effect, and their duration of action is drug dependent; the effects of diazepam last longer than those of midazolam, as a result of active metabolites with slow clearance.

Clinical effects relevant to anesthesia include sedation or dysphoria, decreased anxiety, inhibition of aggressive behavior, amnesia, muscle relaxation, anticonvulsant effects, and reduced anesthetic requirements. Benzodiazepines do not appear to produce analgesia after systemic administration. In cats 1 mg/kg of diazepam administered intramuscularly caused apparent sedation; however, when cats were restrained for handling, they vigorously objected.⁹³ A study examined the effects of midazolam, administered intravenously or intramuscularly, at various doses ranging from 0.05 to 5 mg/kg.¹⁰⁸ Restlessness was observed initially, followed by sedation, with most cats receiving the higher doses intravenously assuming a lateral recumbency. When cats were restrained, an approximately equal proportion responded more and less than normal, independent of dose and time. It therefore appears that benzodiazepines do not consistently produce sedation in cats, at least when administered alone. Combinations with opioids may improve the consistency of the sedative effect.

Benzodiazepines are commonly used with induction agents to improve muscle relaxation and/or reduce the anesthetic dose. Diazepam and midazolam have been reported to decrease the anesthetic dose of both inhaled and injectable anesthetics.* They are very

effective at preventing and treating convulsions. In humans midazolam is useful in the treatment of status epilepticus refractory to phenobarbital, phenytoin, and diazepam.²²⁷

Benzodiazepines produce minimal cardiovascular and respiratory effects. Diazepam may decrease ventricular arrhythmias resulting from myocardial ischemia.¹⁵² In hypovolemic patients high doses of midazolam may produce hypotension.³ Hypotension, arrhythmias, and asystole have been reported after intravenous administration of diazepam; this is thought to be due to propylene glycol, which is used as a solvent in commercially available solutions.⁷⁹

The main difference between diazepam and midazolam is related to their physicochemical characteristics and pharmacokinetics. Diazepam is highly hydrophobic, and studies in humans suggest that absorption may be poor after administration in some muscle groups. Midazolam is hydrophilic at low pH and lipophilic at higher pH; it may be better suited to intramuscular administration than diazepam. Its bioavailability after intramuscular administration is higher than 90% in humans and dogs. Onset of effect is short for both drugs. Diazepam undergoes oxidation to nordiazepam, an active metabolite, which is eliminated about 6 times more slowly than diazepam. The clearance of diazepam itself in cats is low. Diazepam is therefore expected to have long-lasting effects.⁴³ There are no published data on the pharmacokinetics of midazolam in cats. However, in dogs midazolam is rapidly eliminated, in contrast to diazepam.^{44,126} In the species in which it has been examined, the metabolism of midazolam results in the production of hydroxymidazolams, which have pharmacologic activity but are usually rapidly eliminated. Clinically, the duration of effect of midazolam appears much shorter than that of diazepam.

Acute fulminant hepatic necrosis has been reported in cats following diazepam administration.³⁴ However, it followed repeated oral administration; similar toxicity has not been reported after occasional parenteral administration of the drug.

Clinically, benzodiazepines are sometimes used for premedication before general anesthesia, in combination with opioids, in an attempt to improve the sedation produced by the opioid.

Alpha₂-Adrenoceptor Agonists

Agonists of the alpha₂-adrenergic receptors (alpha₂ agonists) act mainly by modulating noradrenergic transmission in the central nervous system. They also have direct effects on various organs. Drugs in this class commonly used in cats include xylazine and dexmedetomidine (Box 7-4).

Alpha₂ agonists produce sedation; the effect is dose dependent.²¹⁴ At high doses sedation is profound, and patients are unresponsive to most stimuli, although

*References 84, 107, 111, 115, 133, 136, 169, 242, 243.

BOX 7-4**Advantages and Disadvantages of Alpha₂-Adrenoceptor Agonists****Advantages**

- They produce dose-dependent sedation.
- At high doses, they produce profound sedation.
- They produce analgesia.
- They reduce anesthetic requirements in a dose-dependent manner.
- They have minimal effect on the respiratory system.

Disadvantages

- They produce bradycardia and decreased cardiac output.
- They produce vasoconstriction.
- They cause hyperglycemia.
- They cause diuresis.
- They cause hypothermia.

arousal and aggressive behavior is always possible. Alpha₂ agonists also produce analgesia.²²⁸ The duration of the analgesic effect of both xylazine and dexmedetomidine appears short.^{154,208} Alpha₂ agonists reduce anesthetic requirements in a dose-dependent manner. They induce hypothermia through an effect of the hypothalamic thermoregulatory center.

Respiratory effects produced by alpha₂ agonists are considered minimal in cats. Respiratory rate tends to decrease, but blood gases are usually unaffected.^{78,117}

The typical cardiovascular response to the administration of alpha₂ agonists is biphasic. Initially, blood pressure and systemic vascular resistance increase, whereas heart rate and cardiac output decrease.^{74,117,154} The increase in blood pressure may not be seen after intramuscular administration. These effects are followed by a decrease in arterial pressure; heart rate and cardiac output remain lower than normal. Systemic vascular resistance either returns progressively toward normal or remains elevated, depending on the drug and the dose considered. The bradycardia may be accompanied by other arrhythmias. The cardiovascular effects of alpha₂ agonists are usually considered to be dose dependent. The increase in systemic vascular resistance is due to stimulation of alpha₂ receptors on the vascular smooth muscle, resulting in vasoconstriction. The decrease in cardiac output is due to the decrease in heart rate. Myocardial contractility appears unaffected.

Because the decrease in cardiac output appears to be mainly related to the bradycardia, the combination with anticholinergics has been advocated. However, the concomitant use of anticholinergics with alpha₂ agonists is controversial. The effectiveness in increasing heart rate

could depend on the timing of administration of the drugs. When given before the alpha₂ agonist, anticholinergics tend to increase heart rate, which decreases after the alpha₂ agonist is administered. When given simultaneously, there is an initial bradycardia followed by a return of heart rate toward baseline values. In both cases severe hypertension is produced, and cardiac performance further decreases.^{6,50,206}

Alpha₂ agonists inhibit insulin release and cause an increase in glycemia. They also inhibit the release of antidiuretic hormone (ADH) and its effect on renal tubules, resulting in water diuresis. Alpha₂ agonists cause vomiting in cats and have been used for that purpose. The incidence of vomiting is higher after xylazine than after dexmedetomidine administration.

Xylazine is shorter acting, less potent, and less selective for the alpha₂ receptors than dexmedetomidine. Some of the effects following xylazine administration may be related to its action on alpha₁ receptors.

Clinically, xylazine and dexmedetomidine are used mainly for their sedative effect. They are sometimes used to improve analgesia. Combinations with opioids may reduce the dose required to produce sedation.¹⁹⁹ Because of their cardiovascular effects, they should be used with caution in geriatric patients or patients with significant organ dysfunction. The use of medetomidine in cats with hypertrophic cardiomyopathy and left ventricular outflow tract obstruction has been suggested to decrease the obstruction; dexmedetomidine is expected to produce similar effects.¹¹⁸

Dissociative Anesthetics

Ketamine and Telazol are sometimes used as premedication before general anesthesia. Their pharmacology is reviewed in the section on induction agents. Dissociative anesthetics produce dose-dependent effects ranging from mild or moderate sedation to anesthesia. They may be useful in the intractable cat, as long as an injection can be administered. Ketamine should not be used alone because of its effect on muscle tone and the risk for convulsions; it should be combined with acepromazine, a benzodiazepine, or an alpha₂ agonist (Box 7-5).

OPIOIDS

The pharmacology of opioids is reviewed in Chapter 6. Only their use in the context of premedication will be addressed here.

Opioids are used for their analgesic effect (Box 7-6). They are commonly given at the time of premedication to produce preemptive analgesia. Because they are considered to be the first line of treatment for acute (surgical) pain, they should be included in the anesthetic regimen for any procedure likely to cause pain. In addition to their analgesic effect, they reduce the effective dose of sedative and anesthetic drugs. They also produce some behavioral modification. Usually, at the doses

BOX 7-5**Advantages and Disadvantages of Dissociative Anesthetics****Advantages**

- They produce dose-dependent sedation.
- At moderate doses they produce profound sedation.
- At high doses, they produce anesthesia.
- Their effects are consistent.

Disadvantages

- Ketamine can cause convulsions.
- Ketamine increases muscle tone.
- They should always be combined with an agent producing muscle relaxation.

BOX 7-6**Advantages and Disadvantages of Opioids****Advantages**

- They produce analgesia.
- At moderate doses they produce euphoria.

Disadvantages

- They can produce dysphoria and excitement.
- Their efficacy may be variable.

recommended for clinical use, opioids produce euphoria in cats (i.e., cats do not appear sedated but are more playful and resist restraint less). At higher doses dysphoria may be produced, and cats become hyperactive, excitable, and more difficult to handle. Various drugs can be used. Typically, the full agonists (e.g., morphine, hydromorphone, oxymorphone, methadone) are considered to have a higher analgesic efficacy than the partial agonist buprenorphine. The agonists–antagonists such as butorphanol usually have low analgesic efficacy. However, buprenorphine, at the doses commonly used clinically, appears to produce good analgesia in cats.

ANTICHOLINERGICS

Anticholinergics antagonize the effects of acetylcholine at muscarinic receptors, which result in the blockade of transmission at parasympathetic postganglionic nerve terminals. They decrease overall parasympathetic tone (Box 7-7).

Two drugs in this class are used in clinical patients for premedication: atropine and glycopyrrolate. Glycopyrrolate is a quaternary ammonium and does not cross the blood–brain barrier or the placenta. It is therefore devoid

BOX 7-7**Advantages and Disadvantages of Anticholinergics****Advantages**

- They prevent bradycardia due to high vagal tone.
- They decrease secretions.

Disadvantages

- They can cause arrhythmias.
- They decrease gastrointestinal motility.
- Excessive doses of atropine have effects on the central nervous system.

of atropine's effect on the central nervous system, including on pupil size.

At high doses atropine causes central nervous system excitement followed by depression. Atropine causes mydriasis. It increases intraocular pressure in narrow-angle glaucoma and should therefore not be used in patients with this condition.

Anticholinergics inhibit nasal, pharyngeal, buccal, and bronchial secretions. They reduce mucous secretion and mucociliary clearance, sometimes resulting in the formation of mucus plugs. They cause relaxation of the bronchial smooth muscle and therefore bronchodilation.

Anticholinergics increase heart rate. There is sometimes a transient decrease in heart rate after administration of a low dose of atropine. Anticholinergics prevent the effects of vagal stimulation on heart rate. They are effective at treating some forms of second-degree atrioventricular block and sometimes increase ventricular rate in third-degree atrioventricular block.

Anticholinergics decrease salivary and gastric secretions. Gastric pH is increased. These drugs decrease motility of the stomach, duodenum, jejunum, ileum, and colon. They also decrease the tone of the gastroesophageal sphincter, increasing the risk for regurgitation and reflux.

The onset and duration of effect of glycopyrrolate are longer than those of atropine. Glycopyrrolate is considered to decrease the risk of producing tachycardia and may have higher efficacy in decreasing secretions.

The main desirable effects of anticholinergics are to prevent the bradycardia caused by other drugs that increase vagal tone or vagal reflexes and to decrease salivary and bronchial secretions. They are often used to prevent opioid-induced bradycardia and to block dissociative anesthetic-induced increase in secretions. Their use in premedication is controversial; some clinicians prefer to treat bradycardia and increased secretions if needed rather than preventing these effects. At clinical

doses, their undesirable effects appear to be well tolerated in cats.

Induction Agents

The injectable anesthetic agents currently available to induce anesthesia in cats are ketamine, Telazol (a mixture of tiletamine and zolazepam), thiopental, propofol, and etomidate. Alphaxalone is available in some countries but not in the United States. Whereas ketamine and thiopental were the mainstay injectable anesthetic agents in veterinary practice for a number of years, it now appears that propofol is the most commonly used drug, with thiopental reported to have disappeared from the U.S. market by 2010. Telazol is usually restricted for use in feral cats, in which it is administered intramuscularly or subcutaneously, and the use of etomidate as an induction agent is generally restricted to sick or older cats. In countries where it is available, alphaxalone has increased in popularity.

Toxicity studies in cats allowed the therapeutic index of ketamine, thiopental, and alphaxalone to be derived.³⁶ In one study³⁶ the difference between the dose that caused recumbency and the fatal dose was 4 times for thiopental and 5 times for ketamine and alphaxalone.

Calculated intravenous induction doses, reported in Table 7-3, vary depending on the end point and whether the agent is administered after premedication or in conjunction with a benzodiazepine.

Thiopental

Thiopental is the oldest of the injectable anesthetic agents, having been introduced into veterinary practice in the early 1930s. It is a rapidly acting thiobarbiturate with an ultrashort duration of action. It is marketed as the sodium salt in powder form and is reconstituted with 0.9% sodium chloride or water for injection. The usual concentration for clinical use is 2.5%. The drug is a weak acid, and because the unionized form is poorly water soluble, concentrated solutions for administration are alkalinized so that the drug is restricted almost entirely to the water-soluble ionized form. The high pH of the solution is partly responsible for the irritancy of the drug if it is given perivascularly (Box 7-8).

CLINICAL USE

The dose reported in the literature varies from 5 to 20 mg/kg, depending on the desired end point. For induction of anesthesia, after premedication, the calculated dose is 12 mg/kg, whereas administration of adjuvant agents such as diazepam or midazolam, together with premedication, reduces the calculated dose to 10 mg/kg. The usual concentration is 2.5%; however, if the calculated volume is small (<6 mL), a more dilute solution will allow better titration. One quarter of the calculated dose is usually administered over 20 to 30 seconds and the patient observed for drug effects. If more of the drug is required, another quarter of the calculated dose is again administered over 20 to 30 seconds. In a cat with a normal circulation time, 30 seconds is the usual time between administrations of doses.

Generally, induction of anesthesia is rapid, smooth, and excitement-free. Central nervous system activation occurs initially, and this may translate into an excitement phase if insufficient thiopental is administered.

PHARMACODYNAMIC EFFECTS

Although thiopental has been used in veterinary anesthesia for many years, there are few reports concerning pharmacologic effects in cats. Early cardiopulmonary studies reported a decrease in respiratory rate and tidal volume, a fall in blood pressure, and a slowing of heart rate.⁸⁰ A dose of 20 mg/kg produced mild hypotension between 5 and 10 minutes after administration, with little change in heart rate. Approximately 30% of cats developed apnea lasting up to almost 1 minute, and arterial carbon dioxide tension was elevated and arterial oxygen tension decreased at 1.5 minutes.¹⁴³ A more in-depth study undertaken after acepromazine (0.2 mg/kg), meperidine (4 mg/kg), and atropine (0.05 mg/kg) premedication followed by induction with thiopental (10 mg/kg) reported minor respiratory depression but a significant fall in cardiac index with no change in heart rate.⁵¹ Thiopental (6.8 mg/kg) had a negative effect on the cat myocardium, suggesting that the hypotension may be due to direct myocardial depression.⁷⁶

TABLE 7-3 Calculated Intravenous Doses for Induction Agents

Induction Agents	Alone	After Premedication	After Premedication and with a Benzodiazepine
Thiopental	5-20 mg/kg	12 mg/kg	10 mg/kg
Ketamine	10 mg/kg*	5 mg/kg*	
Telazol	1-3 mg/kg		
Propofol	8 mg/kg	6 mg/kg	4 mg/kg
Etomidate	2 mg/kg*	2 mg/kg*	
Alfaxan	5 mg/kg	2-3 mg/kg	

*Must always be administered with a benzodiazepine.

BOX 7-8**Advantages and Disadvantages of Thiopental****Advantages**

- It is a rapidly acting drug, with effects discernible within a circulation time. Thiopental lends itself to titration to effect and is especially useful when an airway needs to be secured quickly, such as in a cat with a full stomach or a history of vomiting.
- It has an ultrashort duration of action (5-10 minutes) depending on administered dose. Thiopental is an excellent induction agent before intubation and maintenance with inhalant agents. It is also suitable for nonpainful procedures of short duration (15-20 minutes), although propofol provides better recovery conditions.
- It decreases intracranial pressure (ICP) in patients with raised ICP and has protective cerebral effects if administered before a hypoxic event. It is an effective anticonvulsant, although its anesthetic and anticonvulsant effects cannot be separated.
- It depresses laryngeal reflexes less than other induction agents, such as propofol and ketamine, and therefore facilitates examination of vocal cords and correct diagnosis of laryngeal paralysis.

Disadvantages

- It is not a suitable drug for maintenance of anesthesia because clearance is slow, leading to accumulation and prolonged recoveries.
- It is an irritant if given perivascularly, and treatment is important to prevent tissue necrosis and sloughing.
- It decreases packed cell volume and white blood cell and platelet counts and may decrease total protein concentration.
- It does not block autonomic responses to noxious stimuli and thus is not suitable for short painful procedures.
- Recovery can be rough, especially if the patient awakes from thiopental alone.
- It is a myocardial-depressant drug that induces tachycardia and an increased incidence of arrhythmias. In healthy animals these arrhythmias are rarely of clinical importance.
- Laryngeal reflexes are active, increasing the difficulty of intubation. Because of this, traumatic intubation may be more likely with thiopental than other agents.

Thiopental induces a dose-related depression of cerebral metabolic oxygen consumption rate and, presumably because of preserved cerebral autoregulation, reduces cerebral blood flow.¹⁴² As a result of the reduced cerebral blood flow and accompanying fall in cerebral blood volume, cerebrospinal fluid pressure is reduced. With thiopental, as with etomidate, cerebral perfusion pressure is not compromised because intracranial pressure decreases more than mean arterial pressure. Thiopental is an effective anticonvulsant, although its hypnotic and anticonvulsant properties occur at similar doses.

No difference in the incidence of gastroesophageal reflux was reported in cats between thiopental and propofol, with an incidence of 16% and 12%, respectively.⁶⁶

PHARMACOKINETIC EFFECTS

The pharmacokinetics of thiopental in cats has not been reported, although that of a very similar thiobarbiturate, thiamylal, has been described.²³⁸ The rapid distribution half-life was 1.91 minutes, and a second, or slower, distribution half-life was 26.51 minutes. The elimination half-life was 14.34 hours. The apparent volume of distribution was 3.61 L/kg, whereas the apparent volume of the central compartment was 0.46 L/kg, and the total clearance was 0.135 L/kg/h. As in other species, initial wake-up is due to redistribution initially into vessel-rich tissues and muscle and later into fat.^{28,29} Although the

drug does not have a high clearance, metabolism does contribute to recovery.¹⁹²

Ketamine

Ketamine is partly water soluble and is prepared in a slightly acidic (pH 3.5 to 5.5) solution. It is formulated for veterinary use as a 10% solution in sodium chloride with the preservative, benzethonium chloride (Box 7-9).

Ketamine is considered a dissociative anesthetic, a term used to describe a state in which there is functional and electrophysiologic dissociation between the thalamoneocortical and limbic systems.²⁴⁰ This unique clinical state of hypnosis and analgesia is characterized by open eyes, dilated pupils, muscle hypertonus, and increased lacrimation and salivation. An anticholinergic drug, atropine or glycopyrrolate, is usually administered as a preanesthetic to decrease salivation.

Ketamine acts primarily through the N-methyl-D-aspartate (NMDA) receptor.^{112,158}

CLINICAL USE

Induction of anesthesia with ketamine alone is unsatisfactory insofar as muscle tone is extreme and spontaneous movement virtually continuous.²⁴⁶ Tranquilizers are often administered before ketamine, whereas the benzodiazepines, diazepam or midazolam, are usually administered in combination with ketamine to eliminate or minimize the deleterious side effects. When ketamine is used as an induction agent, the calculated dose in

BOX 7-9**Advantages and Disadvantages of Ketamine****Advantages**

- Rapidly acting agent without excitement and with a duration of action that allows induction of anesthesia to proceed slowly
- Excellent analgesic agent even at subanesthetic doses with demonstrated preemptive analgesic properties
- Reported to induce less respiratory depression than thiopental or propofol, and respiratory responses to hypoxemia and hypercarbia are better maintained
- Potent bronchodilating drug that is a suitable induction agent in asthmatic patients or patients with reactive airways

Disadvantages

- It increases muscle tone and induces purposeless muscle movements, making it difficult to carry out certain procedures.
- Salivation and lacrimation are present and may be profuse.
- Intraocular pressure may increase, and eyes remain open and are susceptible to corneal abrasion.
- Cerebral blood flow and cerebral oxygen consumption increase, which may have serious adverse effects in patients with raised intracranial pressure.
- Ketamine depresses the myocardium, but central sympathetic stimulation leads to an increase in heart rate, blood pressure, and cardiac output. In diseases such as hypertrophic cardiomyopathy, these cardiovascular effects may prove fatal.

unpremedicated healthy cats is 10 mg/kg IV,⁸⁶ together with diazepam (0.5 mg/kg IV) or midazolam (0.3 to 0.5 mg/kg IV). Premedication reduces the dose of ketamine to 5 mg/kg, and the dose of diazepam or midazolam remains the same. Studies in cats using a calculated dose of 3 mg/kg of ketamine reported that the ED₅₀ (effective dose in 50% of the population) of midazolam required for intubation and to prevent movement in response to a noxious stimulation was 0.286 mg/kg and 0.265 mg/kg, respectively. At that dose recovery to walking with ataxia took 41.50 ± 15.18 minutes and complete recovery 3.6 ± 1.3 hours.¹⁰⁷

One quarter of the calculated dose of ketamine, followed by one half of the calculated dose of diazepam or midazolam, is usually administered over 10 to 20 seconds and the patient observed for drug effects after 1 minute. If more of the drug is required, another quarter of the calculated dose of ketamine and the remainder of the diazepam or midazolam is administered over another minute. Some veterinarians prefer to combine the drugs in the same syringe and then just administer in quarter-dose boluses.⁸⁶

Recovery from ketamine anesthesia can be associated with hyperexcitability, especially in cats. General recommendations are to allow cats to recover in a quiet, dark room with minimal handling.

PHARMACODYNAMIC EFFECTS

Ketamine is reported to have sympathomimetic effects, which increase heart rate, cardiac output, and blood pressure, primarily by direct stimulation of central nervous system structures.²⁴⁰ In the absence of autonomic control, ketamine has direct myocardial depressant properties.^{223,245} The cardiopulmonary effects

of intravenous administration of ketamine have been studied in cats.¹⁴³ At clinical doses (6.6 mg/kg intravenously), both heart rate and blood pressure increased, with peak effects generally occurring 2.5 minutes after administration. Transient respiratory depression was also reported.¹⁴³ In cats anesthetized with halothane, ketamine has been reported to decrease the arrhythmogenic threshold.¹⁷ Respiration has been noted as apneustic, shallow, and irregular immediately after ketamine administration in cats.³⁷

Ketamine has bronchodilating properties¹⁶⁷ and is often recommended as the induction agent of choice in cats with asthma.

Swallow, cough, and gag reflexes are relatively intact after ketamine, and in cats, but not humans, competent laryngeal protective reflexes are maintained, such that material that reaches the trachea is coughed up and swallowed.^{188,221} In cats contrast radiography has been suggested as a diagnostic aid in ketamine-anesthetized cats suspected of laryngeal reflex abnormalities.¹⁸⁸

Care is needed in interpretation of echocardiographic measurements in cats under light sedation doses (1.5 to 2.5 mg/kg intravenously) of ketamine, insofar as significant differences were reported in studies conducted using different drugs or in non-anesthetized cats.⁶⁴

Although there are no specific published studies in cats, in other species ketamine increases cerebral blood flow and intracranial pressure, principally by cerebral vasodilation and elevated systemic arterial pressure.^{200,218} Part of the vasodilation is due to increased arterial carbon dioxide tensions when ventilation is not controlled,¹⁹⁶ and the other most likely results from stimulation of cerebral metabolic rate. Thus the use of ketamine in patients with raised intracranial pressure is not

recommended. Ketamine has been reported to cause seizures in cats,^{15,186} although usually only after intramuscular administration of high doses.

Under ketamine anesthesia, segmental stretch and withdrawal reflexes are preserved even at levels that block electroencephalographic arousal and autonomic changes in response to nociceptive stimulation.²²⁰

Ketamine, compared with thiopental, propofol, and Saffan, had the least effect on gastroesophageal sphincter pressure and barrier pressure in cats.⁸⁹

Administration of ketamine interferes with the results of glucose tolerance tests in cats and thus this test should be performed without chemical restraint.¹⁰²

In cats a slight but significant increase in intraocular pressure occurs with ketamine,⁸² so this agent should be avoided if the cat is at risk for corneal perforation. The increase is thought to be due to increases in extraocular muscle tone induced by ketamine.

Cats induced with ketamine (5 mg/kg intravenously) and diazepam (0.25 mg/kg intravenously) and maintained with halothane anesthesia were found to mount a normal response to an ACTH stimulation test, indicating adequate adrenocortical function.¹⁴⁷

Various sedative protocols, including those containing ketamine, have been reported to produce significant effects on thyroid function and salivary gland uptake of technetium Tc 99m pertechnetate and, as such, may interfere with thyroid scintigraphic image interpretation.¹⁹⁴

Sedation with ketamine results in a lower number of spermatozoa per ejaculate compared with medetomidine when semen was collected after electroejaculation.²⁴⁹

Ketamine has been reported to possess analgesic properties. Induction with ketamine or addition of ketamine to general anesthesia before surgical stimulation decreases postoperative pain and leads to better pain control.^{156,191} It appears that the analgesic properties of ketamine reduce sensitization of pain pathways and extend into the postoperative period. Although ketamine appears to provide good somatic analgesia, its visceral analgesia is weak.¹⁹³

PHARMACOKINETIC EFFECTS

Recovery from ketamine is due to both redistribution and metabolism. Several studies have reported the pharmacokinetic profile of ketamine in cats.^{10,96} Ketamine has a rapid distribution with a brief distribution half-life of 5.2 minutes. The high lipid solubility is reflected in the large volume of distribution (3.21 L/kg). Clearance is also high (37.8 mL/kg/min), which accounts for the short elimination half-life (60.6 min).⁹⁶ Mean total body clearance is very similar to liver blood flow, which means that changes in liver blood flow affect clearance. This has been reported in the cat, where xylazine prolonged the duration of ketamine anesthesia by increasing the elimination half-life.²³² Ketamine is metabolized extensively

in the liver to form norketamine (metabolite I), which has 20% to 30% of the activity of the parent drug. Cats, as a species, are unable to metabolize norketamine further, and elimination of norketamine is dependent on renal excretion. Thus duration of action may be prolonged in cats with severe renal dysfunction.

Telazol

Telazol is a combination of a dissociative anesthetic agent, tiletamine, and a benzodiazepine, zolazepam, and is currently marketed for intramuscular administration in dogs and cats. Once reconstituted for use, the solution contains 50 mg/mL of each compound or 100 mg/mL of the combination. The recommended dose is usually expressed in terms of the combined dose.

CLINICAL USE

Although Telazol is not registered for intravenous use in cats, it is a suitable induction agent. The reported dose is 1 to 3 mg/kg, and administration of an anticholinergic is recommended because salivation can be profuse.¹²⁹ A dose of 3 mg/kg is diluted to 1 mL with saline, and a 1 mg/kg bolus is administered intravenously every 1 minute until intubation is possible.

A dose of 9.9 mg/kg administered intravenously or intramuscularly resulted in a similar duration of anesthesia (20 minutes) and time to walking (174 to 180 minutes).²²⁴

PHARMACODYNAMIC EFFECTS

There is little published data on effects of Telazol, especially in cats, and it is presumed that the effects are similar to ketamine.^{125,129} The cardiovascular and respiratory effects of intravenous administration of Telazol have been reported, although the doses (9.7, 15.8, and 23.7 mg/kg) were higher than those commonly used in practice.⁹⁸ An initial cardiovascular depressor response, with degree and duration depending on the dose, was then followed by a pressor response. In another study Telazol did not alter the arrhythmogenic threshold in cats.¹⁶

The degree of respiratory depression in cats appears to be dose dependent, with higher doses causing more depression. In one study respiratory rate decreased and was often characterized initially by an apneustic respiratory pattern.²⁴⁸ Within 10 to 15 minutes, respiration had returned to a normal pattern.²²⁴ Periods of apnea have been reported after intravenous administration of high doses (15.8 and 23.7 mg/kg), and arterial carbon dioxide tension was elevated.⁹⁸

Telazol is considered a suitable intravenous agent for intradermal skin testing in cats.¹⁴⁹

Telazol carries the same warning as other dissociative agents.¹²⁹ It is not recommended for cats with hypertrophic cardiac disease, hepatic or renal disease may prolong the actions, and dose-dependent respiratory

BOX 7-10**Advantages and Disadvantages of Propofol****Advantages**

- Rapidly acting drug with minimal excitement, even after subanesthetic doses.
- Recovery is rapid, smooth, and complete, making it an ideal outpatient anesthetic.
- It can be used to induce anesthesia before intubation, or anesthesia can be maintained with propofol by either repeated bolus injections or constant-rate infusion.
- It decreases intracranial pressure in patients with raised intracranial pressure and has protective cerebral effects if administered before a hypoxic event.
- It decreases intraocular pressure and is a good induction agent in cats with descemetocles or corneal lacerations.
- It is the induction agent of choice in healthy queens requiring cesarean section if viability of the kittens is important.
- It induces bronchodilation and is a suitable agent in asthmatic patients.
- It is not irritant if administered perivascularly.

Disadvantages

- Apnea is the most common side effect in cats, and cyanosis is often observed during induction.
- Myoclonus sometimes occurs on induction and, if severe, may prevent surgery.
- It has myocardial-depressant and vasodilatory properties without altering heart rate and may cause hypotension, especially in hypovolemic and geriatric patients.
- Bacterial contamination of the solution can increase the incidence of surgical wound infection or cause sepsis.
- Autonomic responses to noxious stimuli are not blocked, and therefore it is not a suitable anesthetic agent for painful procedures.
- Cats have reduced capacity to conjugate propofol, and length of recovery increases with increasing duration of propofol anesthesia.
- Care should be taken if propofol is administered to cats over consecutive days because oxidative injury to feline red blood cells has been reported.

depression is reported when Telazol is administered intravenously with other anesthetic drugs. According to further information on the package insert, use in animals with severe cardiac or pulmonary dysfunction and those requiring cesarean section is not recommended.

PHARMACOKINETIC EFFECTS

The plasma half-life of tiletamine in cats was reported as 2 to 4 hours, with only 5% to 10% of the dose detected in urine, none in feces, and some in bile. Three metabolites were detected in the urine from cats.¹²⁵ The plasma half-life of zolazepam in cats was reported as 4.5 hours, with three metabolites detected in urine.¹²⁵

The package insert recommends against the use of Telazol in animals with renal disease because tiletamine is excreted primarily by the kidneys.

Propofol

Propofol is a substituted isopropylphenol, which is only slightly soluble in water and is formulated as a 1% aqueous solution containing soybean oil, egg lecithin, and glycerol. It has a rapid onset, with a smooth, excitement-free induction (**Box 7-10**).

Patient infections related to the use of propofol have been reported. This is thought to be due to microbial contamination of propofol and has resulted in life-threatening sepsis and postoperative infections of clean wounds in both human and veterinary patients.^{18,97} Propofol was found to be an excellent medium for rapid bacterial growth.²⁰⁹ Current recommendations are to

discard unused propofol 6 hours after a vial or ampule is opened.⁷³

CLINICAL USE

Initial clinical studies in cats reported the induction dose as 6.8 mg/kg in unpremedicated cats and 7.2 mg/kg in premedicated cats.²⁴ In some studies, premedication reduced the dose by up to 60%,^{148,201} while in other studies premedication did not affect the induction dose.^{24,234} In a large clinical trial, the dose in unpremedicated cats was reported as 8.03 mg/kg and in premedicated cats as 5.97 mg/kg.¹⁴⁸ Apnea after induction has been reported in all animal studies and is minimized by slow administration. The time from administration of the last dose to walking was reported as 27 to 38 minutes, depending on premedication and top-up doses. Recovery was rapid and usually excitement free.

Side effects have been reported in all animal studies. In cats an incidence of 14% was reported, with retching, sneezing, and pawing at the eyes and mouth the most prominent effects.²⁴ The incidence was decreased by pre-medication with acepromazine.²⁴

Because of the high incidence of apnea associated with propofol induction, oxygen should be delivered by face mask throughout the induction. If the patient will not tolerate the face mask before propofol administration, it can usually be placed after administration of the first quarter dose. One quarter of the calculated dose is usually administered over 1 minute and the patient observed for drug effects after 30 seconds. If more of the drug is

required, a second quarter of the calculated dose is administered over another minute. When administering propofol to sick patients, the clinician should first administer a very small calculated dose (<0.5 mg/kg) and determine the onset time and effect.

PHARMACODYNAMIC EFFECTS

There are no in-depth studies reporting the cardiopulmonary effects in cats, although in an early clinical study no changes were reported in heart rate or respiratory rate.²³⁴ In other species propofol is depressant, causing a fall in arterial blood pressure and cardiac output. It is not recommended for use in human patients with cardiac disease or hypovolemia. The arrhythmogenic threshold in cats induced and maintained with propofol increased compared with that of cats induced with either thiopental or propofol and maintained with halothane.⁷²

Like thiopental and etomidate, propofol induces a dose-related depression of cerebral metabolic oxygen consumption rate and, presumably because of preserved cerebral autoregulation, reduces cerebral blood flow.²¹⁵ As a result of the reduced cerebral blood flow and accompanying fall in cerebral blood volume, cerebrospinal fluid pressure is reduced. With propofol cerebral perfusion pressure may decrease as a result of a fall in arterial blood pressure, and care is required to minimize the fall so that cerebral perfusion is not compromised.

Propofol, like ketamine, demonstrated bronchodilating properties in the isolated guinea pig trachea¹⁶⁷ and is considered a suitable induction agent for cats with asthma.

Propofol lowers gastroesophageal sphincter pressure and gastric pressure in cats, although this effect was less than reported with Saffan or thiopental.⁸⁹

Propofol was reported to provide good conditions for semen collection by way of ejaculation in cats, in that ejaculation did not induce stress, onset of anesthesia was rapid, and recovery was smooth.³⁵

Care should be taken if propofol is administered to cats over consecutive days because oxidative injury to cat red blood cells has been reported.⁸ Administration of propofol daily for 6 days resulted in an increase in Heinz bodies on day 3. Five of the six cats developed generalized malaise, anorexia, and diarrhea, and two cats developed facial edema.⁸ If anesthesia is restricted to a single induction dose, behavioral effects were not reported after daily administration for 4 weeks, although increases in methemoglobinemia and Heinz bodies were observed.⁷³

PHARMACOKINETIC EFFECTS

Initial studies reported a lower utilization ratio (0.19 mg/kg/min) in cats compared with other species.⁷¹ The utilization ratio was reported as the amount of drug administered divided by the duration of anesthesia. Differences in utilization ratio were likely related to differences in

the rate of biotransformation and conjugation, insofar as the cat has a deficiency in its ability to conjugate phenols.⁷¹ In laboratory animals the initial distribution volume was large and redistribution to other parts of the body was extremely rapid. The total apparent volume of distribution was large, as was metabolic clearance from the body, with elimination half-lives in the range 16 to 55 minutes.² In this study the slowest elimination was found in the cat.² In most species the drug is reported to be noncumulative, making it an excellent drug for maintenance of anesthesia. In cats, when recovery to walking was compared among an induction dose only, an induction and maintenance dose for 30 minutes, and an induction and maintenance dose for 150 minutes, a significant increase in recovery time was reported for the latter dose.¹⁶⁴ This provides further evidence that cats have reduced capacity to conjugate propofol, and thus recoveries will increase with increasing duration of propofol anesthesia.

Pulmonary extraction of propofol has been studied in cats and is substantial.¹³² This uptake is decreased by concomitant administration of halothane or fentanyl.

Etomidate

Etomidate is an imidazole derivative that is soluble in water but not stable, so it is formulated as a 0.2% solution in propylene glycol (35% by volume) with a pH of 6.9 and an osmolality of 4640 mOsm/L. It is more expensive than other induction agents and therefore is not used extensively in veterinary practice. However, in certain circumstances it does offer advantages in cats (Box 7-11).

CLINICAL USE

The initial dose of etomidate is calculated on a body weight basis; however, the drug is titrated to effect. A calculated dose of 2 mg/kg is suitable and should be administered with an adjuvant agent such as diazepam (calculated dose, 0.5 mg/kg) or midazolam (calculated dose, 0.2 to 0.5 mg/kg) to facilitate induction.

One quarter of the calculated dose of etomidate is usually administered over 20 to 30 seconds, followed by one quarter to one half of the calculated dose of a benzodiazepine, and the patient is observed for drug effects after 30 seconds. If more drug is required, another quarter of the calculated dose of etomidate followed by a quarter to half of the calculated dose of benzodiazepine are administered over 20 to 30 seconds. To minimize side effects associated with injection of a solution with a high osmolality into a small peripheral vein, etomidate can be injected at the injection port of a fluid administration set through which a balanced electrolyte solution is being administered.

After 3 mg/kg intravenously, in which half was given rapidly and the remainder over 1 minute, induction of anesthesia was rapid and smooth. Recovery was also

BOX 7-11**Advantages and Disadvantages of Etomidate****Advantages**

- It is a rapidly acting agent, with loss of consciousness occurring in 15 to 29 seconds. In situations in which a rapid sequence induction technique is required, etomidate is a suitable agent.
- It has an ultrashort duration of action, depending on administered dose, with a relatively rapid recovery. It is also suitable for nonpainful procedures of short duration.
- The relatively short elimination half-life and rapid clearance of etomidate make it a suitable drug for administration in a single dose, in multiple doses, or as a constant-rate infusion. Its adrenocortical suppression, however, limits its use to a single dose.
- It is the recommended induction agent when hemodynamic stability is important. It has been recommended in veterinary patients with preexisting cardiovascular disease or cardiac rhythm disturbances. It is a useful induction agent in cats with severe cardiac disease.
- It induces minimal respiratory depression and thus is a suitable agent when ventilatory stability is important.
- It decreases intracranial pressure in patients with raised intracranial pressure and is a good induction agent when there is concomitant cardiovascular disease or hypovolemia from trauma.

- Etomidate is an effective anticonvulsant; however, because it may activate a seizure focus, caution is advised in cats with epilepsy.
- It decreases intraocular pressure and is a good induction agent in cats with descemetoceles or corneal lacerations associated with other systemic trauma.

Disadvantages

- It is the most expensive of the injectable anesthetic agents.
- In the commercially available solution, the diluent is 35% propylene glycol, which can cause hemolysis, pain on injection, and thrombophlebitis.
- Induction and recovery may not be smooth and may include myoclonus and excitement.
- Adrenocortical suppression follows both induction and maintenance doses. Although its use as an induction agent is considered safe, it should not be administered as an infusion for maintenance of anesthesia.
- Some authors suggest that, in animals dependent on corticosteroids, a physiologic dose of dexamethasone or any other short-acting glucocorticoid should be administered if anesthesia is induced with etomidate.

rapid, although a brief period of myoclonia was observed in all cats early in recovery.²³⁹

PHARMACODYNAMIC EFFECTS

There are few reports concerning the pharmacologic effects of etomidate in cats. In all species etomidate has minimal effects on the cardiovascular and respiratory systems. In dogs heart rate, blood pressure, and cardiac output were unchanged after administration of 1.5 or 3 mg/kg of etomidate.¹⁵⁵ Similarly, 1 mg/kg of etomidate induced minimal changes in hypovolemic dogs.¹⁶⁵ It also appears that etomidate has minimal effects on the cardiovascular system in cats.²⁰⁷

Etomidate induces a dose-related depression of cerebral metabolic oxygen consumption rate and, presumably because of preserved cerebral autoregulation, reduces cerebral blood flow.¹⁴⁴ As a result of the reduced cerebral blood flow and accompanying fall in cerebral blood volume, cerebrospinal fluid pressure is reduced. With etomidate cerebral perfusion pressure is not compromised because intracranial pressure decreases more than mean arterial pressure.

Similar to other induction agents, etomidate decreases gastroesophageal sphincter pressure and barrier

pressure and thus may predispose cats to regurgitation under anesthesia.⁸⁹

Etomidate causes hemolysis, even after a single induction dose.²³⁷ The mechanism is thought to be the rapid increase in osmolality caused by the propylene glycol, causing red blood cell rupture. Caution should be exercised in patients with renal insufficiency because of the increased pigment load brought about by hemolysis.¹⁵⁹

Induction of anesthesia with etomidate (2 mg/kg intravenously) in cats caused suppression of adrenocortical function during 2 hours of halothane anesthesia and for 1 hour in recovery. An additional 2 hours were required for cortisol to return to baseline.¹⁴⁷ The impact of adrenocortical suppression after etomidate administration on long-term morbidity and mortality has not been determined. Some authors suggest that, in animals dependent on corticosteroids, a physiologic dose of dexamethasone or any other short-acting glucocorticoid should be administered if anesthesia is induced with etomidate.¹²⁹ Adrenocortical suppression, however, precludes the administration of etomidate as an infusion for maintenance of anesthesia.

BOX 7-12**Advantages and Disadvantages of Alfaxan****Advantages**

- Rapid-acting drug with smooth induction
- Recovery is rapid, smooth, and complete, making it an ideal outpatient anesthetic
- Appears to be noncumulative in the cat at clinical dose rates

Disadvantages

- Currently not available in the United States
- Very little reported on its use in clinical patients

PHARMACOKINETIC EFFECTS

The pharmacokinetics of etomidate in cats has been reported.²³⁹ The drug has a rapid distribution (half-life 0.05 hour); a large volume of distribution at steady state (4.88 L/kg); and rapid clearance (2.47 L/kg/h), which accounts for its short duration of action and rapid recovery.²³⁹

Steroid Anesthetics

The progesterone derivative, alphaxalone, is a neuroactive steroid anesthetic agent (Box 7-12). It was first introduced into veterinary anesthesia in 1971 as a component of the drug Saffan, an anesthetic agent in cats. Alphaxalone was insoluble in water and was mixed with alfadolone acetate to increase its solubility. Alfadolone also had anesthetic properties, with about half the potency of alphaxalone. Saffan is formulated such that the mixture contains 9 mg/mL of alphaxalone and 3 mg/mL of alfadolone, with the solubilizing agent as 20% polyethoxylated castor oil (Cremophor EL). The recommended dose is either expressed as mL of formulated solution/kg or mg of combined steroid/kg. Despite widespread use in other countries, Saffan or its medical counterpart, Althesin, were never available in the United States. Cremophor EL causes histamine release in animals by stimulating mast cell degranulation, and this was responsible for unacceptable adverse events.^{40,49,62} In humans the incidence of anaphylactoid reactions was high, and Althesin was removed from the market.

Recently, an Australian company has reformulated alphaxalone in hydroxypropyl beta cyclodextrin (Alfaxan), and it is commercially available for use in dogs and cats in Australia, New Zealand, South Africa, and the United Kingdom.¹⁵⁰ Two recent publications have reported the pharmacokinetics and cardiorespiratory and anesthetic effects of this drug in cats.^{150,241}

CLINICAL USE

The initial dose of Saffan is calculated on a body weight basis; however, the drug is titrated to effect. The intravenous induction dose is 0.75 mL/kg (9 mg/kg). Generally, one half of the calculated dose is administered over 20 to 30 seconds, and the patient is observed for drug effects. If more drug is required, a quarter of the calculated dose is administered over 20 to 30 seconds, and this is repeated until the desired anesthetic depth is accomplished. Intravenous injection produces unconsciousness in 10 to 25 seconds, and the depth and duration of surgical anesthesia is dose dependent. Return of righting reflex took 7, 17, 44, 75, and 136 minutes after doses of 1.2, 2.4, 4.8, 9.6, and 19.2 mg/kg, respectively.³⁷ After the recommended intravenous dose of 9 mg/kg, relaxation occurs in 9 seconds and surgical anesthesia in about 25 seconds. Anesthesia is usually maintained for about 10 minutes, and recovery is rapid.¹¹⁶

The calculated dose for the newly released, reformulated alphaxalone (Alfaxan) is 5 mg/kg, with premedicants decreasing the dose to 2 to 3 mg/kg.¹¹⁴ After administration of 5 and 15 mg/kg doses, induction of anesthesia was characterized as quiet, uneventful, and relaxed. Time to lateral recumbency was inversely proportional to the dose of alphaxalone administered. The average time to lateral recumbency was approximately 15 to 30 seconds. Recovery scores for the 5 and 15 mg/kg doses of alphaxalone were excellent and not different from each other. Doses 10 times the induction dose were invariably fatal.¹⁵⁰

PHARMACODYNAMIC EFFECTS

Initial cardiovascular and respiratory studies reported a decrease in blood pressure and a tachycardia.³⁷ The decrease in blood pressure was reported to be less than that found with comparable doses of ketamine. Greater cardiovascular depression was subsequently reported, with 9 mg/kg administered as a 12 mg/mL solution at 0.25 mL/sec inducing profound and sustained hypotension with clinical manifestations consistent of histamine release.¹⁴³ An in-depth study undertaken in cats, demonstrated significant depression in cardiac output at 45 and 60 minutes.⁵² Although changes in respiratory pattern were observed, no changes in arterial blood gas tensions were found in the latter two studies.^{52,143}

In primates Althesin induced a fall in cerebral blood flow and a decrease in cerebrospinal fluid pressure.¹⁷⁴

In cats the risk of gastroesophageal reflux was reported to be higher with Saffan than with thiopental, if the lower esophageal sphincter pressure and gastric pressure are used as indicators of likely reflux.⁸⁹

Administration of Saffan was reported to interfere with the results of glucose tolerance tests in cats, and this test should be performed without chemical restraint.¹⁰²

Complications associated with Saffan anesthesia were recorded after 100 administrations of the anesthetic to cats.⁴⁹ Hyperemia or edema of the pinnae or forepaws was recorded in 69% of cats. Other common complications included coughing and partial laryngeal spasm at intubation, cyanosis, postoperative vomiting, and opisthotonus.

Despite the side effects reported for Saffan in cats, the survey undertaken to look at morbidity and mortality in veterinary practice in the late 1980s reported that Saffan seemed to be the safest agent for the induction of anesthesia in cats in veterinary general practice.³⁹

More recently, cardiorespiratory and anesthetic effects of the new formulation have been reported in cats.¹⁵⁰ Alphaxalone produced dose-dependent anesthesia, cardiorespiratory depression, and unresponsiveness to noxious stimulation in unpremedicated cats. Hypoventilation and apnea were the most common side effects, and, other than occasional involuntary muscle movement, other common side effects reported after Saffan were not observed.¹⁵⁰

PHARMACOKINETIC EFFECTS

Initial pharmacokinetic studies in cats reported a mean plasma half-life of 3.5 minutes¹¹⁶ and demonstrated a lack of cumulative effect for Saffan.³⁶ Cats topped up with Saffan for 3 hours took 3 to 4 hours to return to normal behavior.¹¹⁶

More recently, the pharmacokinetic effects of the new formulation have been reported in cats.²⁴¹ In that report two doses were studied, 5 and 25 mg/kg, and the pharmacokinetics of alphaxalone in cats were reported to be nonlinear. Plasma clearance was 25.1 and 14.8 mL/kg/min, and elimination half-lives were 45.2 and 76.6 minutes, respectively. In a second experiment, alphaxalone was administered intravenously at 5 mg/kg followed by four doses each of 2 mg/kg, administered at onset of responsiveness to a noxious stimulus. A regression line through their peak plasma concentrations indicated that there was no clinically relevant pharmacokinetic accumulation. The duration of nonresponsiveness after each maintenance dose was similar at approximately 6 minutes, indicating a lack of accumulation of pharmacodynamic effect. Thus at clinical dose rates neither alphaxalone nor its anesthetic effects accumulated to a clinically relevant extent.

Induction with Inhalant Anesthetics

Some cats are not amenable to intravenous induction agents, and, rather than using drugs administered subcutaneously or intramuscularly, some veterinarians prefer to use inhalant anesthetics administered by way of a chamber. Advantages of inhalant inductions include reduced need to handle the patient, the ability to tailor the anesthetic dose and therefore depth to the individual patient, a relatively fast induction and recovery, and



FIGURE 7-1 An airtight Plexiglas induction chamber that allows input of anesthetic gases; a non-rebreathing circuit, such as a Bain circuit, is attached to the chamber.

little reliance on renal and hepatic systems for removal of anesthetic and thus recovery.²²⁶ Disadvantages of this technique include contamination of the environment with inhalant anesthetics, in some cases greater cost and greater cardiovascular and respiratory depression than some injectable agents. Because of the harmful effects of exposure of personnel to low concentrations of inhalant anesthetics, many recommend that mask or chamber inductions should be avoided whenever possible.^{87,91}

CLINICAL USE

The inhalant agents commonly used in veterinary practice for mask or chamber inductions are isoflurane and sevoflurane.

With chamber inductions the cat is placed in an airtight Plexiglas chamber that allows input of anesthetic gases (Figure 7-1). A non-rebreathing circuit, such as a Bain circuit, is attached to the chamber, and a high flow of oxygen is administered (5 L/min). Generally, the maximum vaporizer setting is used, and the patient is watched carefully until recumbency ensues. At that time the chamber is rocked gently, and when the cat no longer responds, it is removed from the chamber and induction continued using a face mask until intubation is possible. Once induction is continued by face mask, the oxygen flow is decreased to 2 L/min and the vaporizer setting to that required to maintain the desired anesthetic depth.

Mask techniques are not often used in cats given that they require good patient compliance and restraint. Generally, the cat is restrained by the scruff and a close-fitting mask attached to a non-rebreathing circuit is applied to the face. Usually, oxygen alone is administered at a flow of 2 L/min, and then the inhalant concentration is increased at 0.5% increments every 10 seconds until the vaporizer setting is 3% for isoflurane or 4% for sevoflurane. Induction is continued until the cat is at the desired anesthetic depth.

PHARMACOKINETIC AND PHARMACODYNAMIC EFFECTS

No specific studies have been undertaken to measure the pharmacodynamic effects of mask or chamber inductions in cats. Most published studies have determined induction and recovery times and the quality of induction and recovery utilizing different inhalant agents. No difference was reported in the qualitative induction and recovery characteristics when isoflurane and sevoflurane were compared for chamber induction in the cat.¹¹⁰ Time to recumbency and intubation were shorter with sevoflurane compared with isoflurane.¹¹⁰ Similar results were reported after mask induction in cats.¹²⁴ Desflurane administered by way of chamber induction was reported to result in an excellent quality of induction and recovery in cats, with airway irritant effects noticed only during recovery and manifested as a brief period of coughing after extubation.¹² A mask induction technique using sevoflurane with a 2:1 mixture of nitrous oxide has been described in cats.²²⁶

INTUBATION

The onset of unconsciousness produced by general anesthesia is associated with depression of other physiologic systems, such as airway, respiratory, and cardiovascular systems, which can cause immediate threats to the patient. Endotracheal intubation enables maintenance of a patent airway, administration of oxygen, delivery of inhalant anesthetics, protection of the airway from foreign material, application of positive pressure ventilation, and suction of the airway. Although these are all important advantages, endotracheal intubation in cats has been reported to increase anesthetic risk,²⁷ and therefore extra care is needed during endotracheal intubation in this species.

Respiratory complications represent a major cause of perioperative anesthetic-related deaths.²⁵ Problems with airway maintenance and inadequacy of ventilation were the principal factors resulting in death. Endotracheal intubation problems and respiratory obstruction represented a major cause of death in cats in at least three studies.^{27,39,53} In one of these studies, more cats that were intubated died postoperatively than those that were not (63% versus 48%), suggesting that laryngeal trauma, spasm, or edema may have been a more common contributory cause than endotracheal tube obstruction.²⁷

Sensitivity of the larynx and its response to external stimuli vary from species to species. The cat's larynx is reported to be very reactive, and spastic closure is relatively common.¹⁸⁷ For these reasons topical local anesthetics such as lidocaine should always be applied to desensitize the larynx, with at least 60 seconds left from application until intubation.

More recently, tracheal rupture has been recognized as an important clinical entity associated with endotracheal intubation in cats.¹⁴⁵ In all reported cases, incidence was high after procedures in which inadvertent overinflation of the endotracheal tube cuff was likely, such as dental procedures, oral surgery for mass removal, or bronchoalveolar lavage.^{85,145} Clinical signs associated with tracheal rupture included subcutaneous emphysema, coughing, gagging, dyspnea, anorexia, and fever. In all cats that were radiographed, subcutaneous emphysema and pneumomediastinum without pneumothorax were present (Figure 7-2).^{85,145} Medical treatment alone is successful for cats with moderate dyspnea, whereas surgical treatment should be considered for cats with severe dyspnea (open-mouth breathing despite treatment with oxygen) or worsening subcutaneous emphysema. Ruptures that extend into the carina are associated with a poor prognosis.⁸⁵ Prevention of tracheal rupture is considered possible provided that care is taken in endotracheal tube selection and cuff inflation. The largest endotracheal tube that will easily pass through the larynx should be selected (adult cat 3.5- to 4.5-mm internal diameter). Once the tube is placed in the trachea, it should be attached to a non-rebreathing circuit. Positive pressure should be applied to the reservoir bag to a circuit pressure of 10 to 15 cm H₂O for not more than 2 seconds while the clinician listens for escape of audible amounts of air past the endotracheal tube cuff. If escaping air is heard, the cuff should be inflated with 0.5-mL increment of air, and positive pressure again applied to the reservoir bag. This should be repeated until escaping air is no longer audible. In a cat cadaver study, the amount of air required to obtain an airtight seal ranged from 0 to 3 mL (mean \pm SD, 1.6 \pm 0.7 mL; median, 1.5 mL).⁸⁵ It is also recommended that each time a cat is turned under anesthesia, the endotracheal tube be disconnected from the breathing circuit to prevent further tracheal trauma.

MAINTENANCE

Inhalant Anesthetics

Inhalant anesthetic agents are widely used for maintenance of anesthesia in cats. Some advantages include the predictable and rapid adjustment of anesthetic depth along with rapid recovery that is not dependent on metabolism or excretion of drugs by the liver or kidneys. Oxygen is administered along with inhalant anesthetics, and ventilation can be easily controlled if needed. Both these components decrease morbidity and mortality.

Only three inhalant anesthetics are currently available for use in cats: isoflurane, sevoflurane, and desflurane. Of those, only isoflurane and sevoflurane are currently used in veterinary practice. Although nitrous oxide is

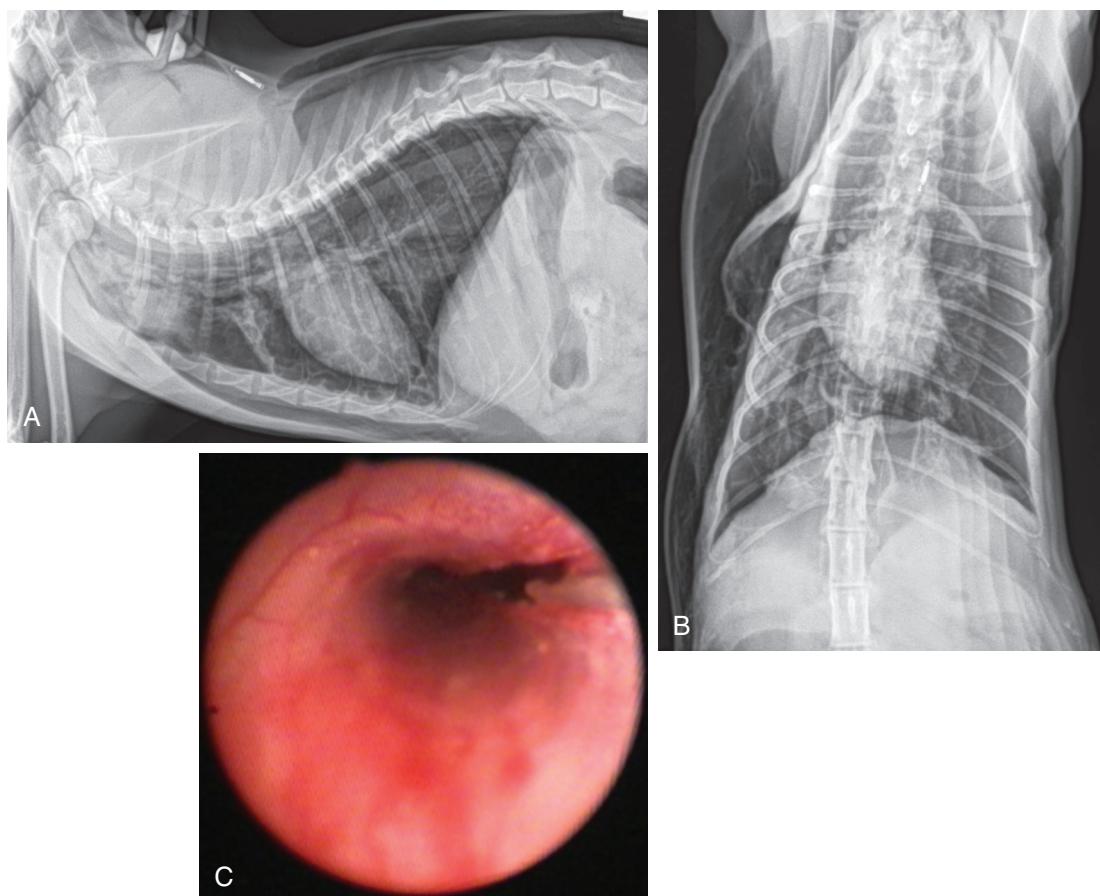


FIGURE 7-2 Lateral (A) and ventrodorsal (B) view of a cat with a tracheal tear showing subcutaneous emphysema and pneumomediastinum; C, bronchoscopic view of a tracheal tear.

still available, it does not induce unconsciousness alone in cats and therefore is used as part of a balanced anesthetic technique.

Isoflurane

Isoflurane is a fluorinated ether released for veterinary use in the late 1980s. It is stable in solution and does not require a preservative. It is easily vaporized (vapor pressure 250 mm Hg) and so is usually delivered through a precision, out-of-circuit vaporizer. It has low blood gas solubility (1.46), resulting in rapid induction and recovery, and undergoes minimal biotransformation (0.2%); thus the potential for toxic metabolites is reduced. It is a potent anesthetic, with a MAC (minimum anesthetic concentration required to prevent a response in 50% of the population) in the cat of 1.63%.²¹³ Cardiopulmonary studies at 1.3 MAC in cats reported minimal cardiopulmonary depression, especially if cats were allowed to breathe spontaneously.¹⁰¹ At 2 MAC isoflurane caused hypotension and hypercapnia; however, cardiac index was maintained. When the hypercapnia was corrected by controlled ventilation, cardiac index decreased. In the cat respiratory rate tends to be maintained as dose is

increased, whereas tidal volume decreases. The alveolar concentration that causes apnea is 2.4 MAC.²¹³ In another study mean arterial blood pressure fell from a conscious value of 95 ± 5 mm Hg to 60 ± 7 mm Hg at 1.5% inspired concentration and 40 ± 2 mm Hg at 2.5% inspired concentration.¹⁷⁵ Isoflurane does not sensitize the heart to catecholamines. It has a strong, pungent odor that many cats find aversive, which may lead to struggling or breath-holding during mask induction.

Sevoflurane

Sevoflurane is also a fluorinated ether released for veterinary use in the late 1990s. It is easily vaporized (vapor pressure 160 mm Hg) and so is usually delivered through a precision, out-of-circuit vaporizer. It has lower blood gas solubility (0.68) than isoflurane, resulting in rapid induction and recovery, and undergoes minimal biotransformation (2% to 5%); thus the potential for toxic metabolites is reduced. It is a potent anesthetic with a MAC in the cat of 2.58%. The cardiopulmonary effects of 1.25, 1.5, and 1.75 MAC of sevoflurane have been reported in cats.¹⁷⁸ Sevoflurane induced dose-dependent cardiovascular depression characterized by decreases in arterial blood

pressure, cardiac index, and stroke index. Arterial blood pressure was better maintained than with isoflurane, thus limiting hypotension despite substantial myocardial depression. Sevoflurane also caused dose-dependent respiratory depression, although it appears less severe than reported in other species. Like isoflurane, sevoflurane does not sensitize the heart to catecholamines; however, it has a pleasant fruity odor, and thus mask inductions are better tolerated than with isoflurane. Compared with isoflurane, it is an expensive inhalant anesthetic.

Desflurane

Desflurane is also a fluorinated ether released only for human use. It is difficult to vaporize (vapor pressure 700 mm Hg) and requires a expensive precision, out-of-circuit vaporizer, which is heated to deliver accurate concentrations. This, together with its very rapid recovery, limits its use in veterinary anesthesia. It has the lowest blood gas solubility (0.42), resulting in very rapid induction and recovery, and because it undergoes minimal biotransformation (0.02%), the potential for toxic metabolites is much reduced. It is the least potent anesthetic, with an MAC in the cat of 9.79%. The cardiopulmonary effects of 1.3 and 1.7 MAC of desflurane have been reported in cats.¹³⁸ Desflurane at 1.7 MAC decreased mean arterial pressure and induced marked hypercapnia, although cardiac index was not affected. When the hypercapnia was corrected by controlled ventilation, cardiac index decreased. In the cat respiratory rate tends to be maintained as dose is increased, and tidal volume decreases. Like isoflurane and sevoflurane, desflurane does not sensitize the heart to catecholamines; however, it appears to be irritant to airways. Compared with isoflurane, it is an expensive inhalant anesthetic.

Balanced Anesthetic Techniques

Balanced anesthesia refers to the use of a combination of drugs, such that the advantages of small amounts of drugs are utilized without the need to contend with the disadvantages of large doses of any one drug. Often, specific drugs can be used for specific effects, such as analgesia. Although balanced anesthetic techniques are the usual maintenance technique in humans and sick dogs, their use in cats is rare, especially in veterinary practice. Doses that have been reported can be found in Table 7-4.

Balanced anesthetic techniques that have been investigated in cats include those discussed in the following sections.

Nitrous Oxide

Although nitrous oxide has been a component of more general anesthetic techniques than any other single inhalant⁵⁵ in human anesthesia, its use in veterinary

TABLE 7-4 Doses of Adjuvants Administered Intravenously as Part of a Balanced Anesthetic Technique

Adjuvant Drug	Loading Dose	Infusion Dose
Fentanyl	2-5 µg/kg	0.4 µg/kg/min
Lidocaine	Not recommended	
Ketamine	0.5 mg/kg	10 µg/kg/min
Dexmedetomidine	0.5 µg/kg	0.5 µg/kg/h

anesthesia is controversial. Its widespread use resulted from many desirable properties, including low blood gas solubility, limited cardiovascular and respiratory depression, and minimal toxicity.⁵⁵ In veterinary anesthesia some report minimal advantages in supplementing more potent anesthetic agents,²¹² whereas others agree that its analgesic properties enable excessive dosage of the more potent agents to be avoided and concurrent cardiopulmonary depression to be minimized.⁸³ More recently, the contribution of anesthetic-released nitrous oxide to global warming, the greenhouse effect, and ozone depletion has led some to call for its elimination from anesthetic practice.

In the cat 50% nitrous oxide has been reported to decrease halothane MAC by 19%, and 75% nitrous oxide decreased halothane MAC by 31%.²¹² In a similar study undertaken with isoflurane, consistent MAC reduction properties of nitrous oxide in cats were not documented.¹⁰⁹ Instead, there were both responder and non-responder groups to the anesthetic-sparing effect of nitrous oxide. A further study comparing the cardiovascular effects of equipotent doses of isoflurane alone versus isoflurane and 70% nitrous oxide in cats demonstrated improved arterial pressure owing to a vasoconstrictive effect.¹⁸² In that study similar isoflurane concentrations were administered with and without nitrous oxide. Despite the lack of reported overall beneficial effects, our clinical impression is that addition of nitrous oxide to isoflurane will often stabilize mean arterial blood pressure within a normal range despite changes in surgical stimulation, especially in critically ill cats.

Because high concentrations of nitrous oxide are administered with oxygen and a potent inhalant, care must be taken to prevent the delivery of a hypoxic mix. Because of an increase in the alveolar to arterial oxygen tension difference under anesthesia, an inspired oxygen concentration of at least 33% is recommended. With a non-rebreathing circuit, such as a Bain coaxial system, accurate measurement of the inspired oxygen concentration requires gas sampling within the endotracheal tube. Inexpensive monitoring devices can be used only to monitor the oxygen concentration at the fresh gas

inflow. Generally, a total gas flow of 200 mL/kg/min is recommended for a Bain circuit, and this gas flow should be split such that oxygen is administered at a flow of 100 mL/kg/min and nitrous oxide at a flow of 100 mL/kg/min. When the nitrous oxide is discontinued, the oxygen flow must be increased to 200 mL/kg/min to avoid rebreathing of expired gases.

Precautions exist with the use of nitrous oxide. Because of the risk of hypoxemia, nitrous oxide should not be administered to patients with respiratory dysfunction unless the arterial oxygen tension can be measured. Potential problems associated with gas spaces can arise when an animal previously breathing air is given a gas mixture containing nitrous oxide. Given that nitrous oxide moves into the space more rapidly than nitrogen moves out, an increase in volume will occur in compliant spaces or an increase in pressure in noncompliant spaces. Thus nitrous oxide should not be administered to patients with pneumothorax or in situations when air embolus could occur (e.g., spinal surgery). At the end of anesthesia, the rapid outpouring of nitrous oxide from the blood into the lung results in a transient but marked decrease in alveolar oxygen tension with a resultant decrease in arterial oxygen tension. To prevent hypoxemia, 100% oxygen, rather than room air, should be administered to the patient during this period. Because nitrous oxide is not absorbed by activated charcoal canisters, active scavenging is necessary to prevent contamination of the environment.

Opioid Infusion

In human anesthesia administration of high doses of opioids, either as primary or sole anesthetics, has become popular because opioids produce or promote stable hemodynamics both in the presence and absence of noxious stimuli. In fact, opioids are said to be superior to most, if not all, other drugs in anesthesia in achieving this goal.²¹⁶ Similar beneficial effects have been documented in cats, in which administration during inhalant anesthesia has been shown to decrease the requirement for inhalant anesthesia and block autonomic responses to noxious stimuli, resulting in better hemodynamic stability.^{104,163}

The most popular method to examine the anesthetic potential of opioids involves their ability to substitute for potent inhaled anesthetics. Variable results are reported, and it appears that the degree of inhalant MAC reduction induced by opioids is dependent on the dose administered, the specific receptor–opioid interaction, and the species to which the opioid is administered. Maximal inhalant MAC reduction is identified as the level where higher plasma opioid concentrations do not induce a statistically significant greater reduction in MAC. The beneficial effect of opioids on MAC reduction, or lack of, was studied initially in cats by screening a number of drugs at both high and low doses. The

reason for this approach was that opioid administration, especially in high doses to cats, had been reported to induce mania, which could increase MAC through central transmitter release. Low and high doses of morphine, butorphanol, buprenorphine, and U50488H (kappa agonist) were found to induce significant MAC reductions of 12% and 28%, 18% and 19%, 11% and 14%, and 4% and 11%, respectively. However, only the MAC reductions induced by morphine (1 mg/kg) and butorphanol (0.08 and 0.8 mg/kg) were considered clinically important.¹⁰⁵ Further studies identified maximal MAC reduction for alfentanil in cats as 35%.¹⁰⁴ From these studies the veterinarian can conclude that when selecting a drug for a balanced opioid technique, a μ -agonist should be chosen. Beneficial cardiovascular effects were reported in cats when isoflurane alone was compared with an equipotent alfentanil–isoflurane MAC multiple.¹⁶³ In that study alfentanil was found to attenuate most of the hemodynamic and metabolic responses to a noxious stimulus. More recently, two studies have published the effect of remifentanil infusions on isoflurane MAC in cats.^{30,58} In the first study, infusion doses of 0.25, 0.5, and 1.0 μ g/kg/min induced significant MAC reduction (23%, 30%, 26%, respectively).⁵⁸ In the other, no significant decrease in MAC was reported.³⁰

To accurately determine loading and constant-rate infusion doses for opioids in cats, pharmacokinetic data is necessary. The pharmacokinetic profiles of fentanyl,¹²¹ alfentanil,¹⁶¹ and the newer opioid remifentanil¹⁷⁷ have been reported in cats. Published pharmacokinetic data for fentanyl¹²¹ predicts a loading dose of 2 μ g/kg (calculated using the volume of the central compartment) with an infusion of 0.4 μ g/kg/min. The authors currently administer a loading dose of 5 μ g/kg followed by an infusion of 0.4 μ g/kg/min. Anesthesia is induced with other agents and converted to a balanced anesthetic technique during maintenance of anesthesia. The infusion is discontinued about 30 minutes before the end of surgery. In cats, unlike in dogs, heart rate does not decrease and administration of an anticholinergic agent is not necessary. Although opioid infusion techniques induce less respiratory depression in cats than in dogs, ventilation is usually controlled. Cats maybe somewhat hypersensitive to touch and sound when awakening, but this is minimized by recovery in a quiet environment with minimal handling.

Epidural/Spinal Opioid

Opioids may be administered by injection into the epidural or subarachnoid (spinal) space to provide regional analgesia. Opioids such as morphine, oxymorphone and fentanyl selectively block pain conduction without interference to motor function. Although opioids are generally administered epidurally to provide post-operative analgesia,¹⁸⁴ their effects will be evident intraoperatively.

Epidural administration of morphine was found to reduce the inhalant anesthetic requirement in cats.⁷⁵ In that study epidural administration of 0.1 mg/kg morphine resulted in 31% isoflurane MAC reduction. More recently, a significant effect of epidural administration of morphine or buprenorphine on the MAC of isoflurane in cats could not be detected.¹⁸³

Transdermal Opioid/Inhalant Anesthesia

Fentanyl administration using a transdermal patch provides postoperative analgesia. However, to be effective in the postoperative period, patches are placed before surgery. Thus plasma fentanyl levels within the analgesic range will also be present during surgery and add a balanced component to standard inhalant techniques.

Pharmacokinetic studies in cats have been reported with sustained plasma concentrations of fentanyl citrate throughout a 5-day period. However, variation of plasma drug concentrations with transdermal absorption for each cat was pronounced.¹²¹

The isoflurane MAC reduction after application of 25 and 50 µg/h patches to cats has been reported.²⁴⁷ Both 25 and 50 µg/h patches reduced isoflurane MAC (17% and 18%, respectively), although the reduction was not different between the two doses.

Lidocaine

Lidocaine is an analgesic agent and in humans has been administered intravenously to provide postoperative analgesia.¹³⁷ When administered intraoperatively, the analgesia has been reported in humans to extend into the postoperative period, decreasing postoperative pain⁴⁷ and the amount of supplemental analgesia.¹³ It also has been reported to reduce the requirement for both inhalant and injectable anesthetic agents.¹⁰⁰ Additionally, small dose of lidocaine administered intravenously are anticonvulsant and induce sedation.

In cats lidocaine was reported to decrease the isoflurane MAC in cats with target plasma concentrations of 1, 3, 5, 7, 9, and 11 µg/mL, linearly decreasing MAC by 3, 14, 24, 33, 40, and 52%, respectively.¹⁸¹ Unfortunately, cardiovascular studies demonstrated that the decrease in inhalant requirements was associated with greater cardiovascular depression than an equipotent dose of isoflurane alone.¹⁸⁰ Oxygen delivery decreased, which could result in poor tissue perfusion. Therefore the administration of lidocaine as part of a balanced anesthetic technique in cats is not recommended.

Ketamine

Ketamine has been reported to decrease isoflurane MAC in cats by 45 ± 17%, 63 ± 18%, and 75 ± 17% at the infusion rates of 23, 46, and 115 µg/kg/min. These infusion rates corresponded to ketamine plasma concentrations of 1.75 ± 0.21, 2.69 ± 0.40, and 5.36 ± 1.19 µg/mL.¹⁶²

In-depth cardiovascular studies have not been reported in cats; however, in the MAC reduction study, both arterial blood pressure and heart rate increased significantly with ketamine infusion. Unfortunately, recovery was prolonged, and therefore further work is needed to better define infusion doses before this can be recommended in cats.

The effect of ketamine when combined with morphine and lidocaine (MLK) has been studied in dogs.¹⁵¹ The MLK solution was prepared by mixing 10 mg (0.8 mL) of morphine sulfate, 150 mg (7.5 mL) of 2% lidocaine hydrochloride, and 30 mg (0.3 mL) of ketamine hydrochloride in the same syringe and injecting the final volume (8.6 mL) into a 500-mL bag of lactated Ringer's solution. The administration rate was set at 10 mL/kg/h, and isoflurane MAC reduction was compared with similar doses of morphine, ketamine, and lidocaine alone. Morphine, lidocaine, ketamine, and MLK significantly lowered isoflurane MAC by 48%, 29%, 25%, and 45%, respectively. The percentage reductions in isoflurane MAC for morphine and MLK were not significantly different but were significantly greater than for lidocaine and ketamine. This mixture has become a very common balanced anesthetic technique in veterinary practice, and its use has spread to cats, although some practitioners do not include lidocaine in the solution.

The effect of ketamine administration on intraoperative and postoperative analgesia has also been reported in dogs.²²⁹ Ketamine was administered intravenously as a loading dose (0.5 mg/kg), 10 µg/kg/min as an infusion during surgery, and 2 µg/kg/min as an infusion postoperatively. Results suggested that perioperative administration of low doses of ketamine to dogs may augment analgesia and comfort in the postoperative surgical period. This technique has become common in veterinary practice, and its use has spread to cats.

Dexmedetomidine

Dexmedetomidine is an alpha₂-adrenergic agonist with sedative, analgesic, and anesthetic-sparing effects.¹³⁵ It also causes cardiovascular depression, characterized by bradycardia, decreased cardiac output, and increased systemic vascular resistance.^{74,117,185} In dogs intravenous dexmedetomidine (0.5 µg/kg loading dose followed by 0.5 µg/kg/h) was reported to decrease isoflurane MAC by about 20% without producing significant cardiovascular depression.^{160,166} Recently, the pharmacokinetics of dexmedetomidine in cats anesthetized with isoflurane has been studied (Escobar, Pypendop, and Ilkiw, unpublished data). Using pharmacokinetic data from that study, dexmedetomidine, at target plasma concentrations between 1.25 and 20 ng/mL, was found to decrease isoflurane MAC in a dose-dependent manner by approximately 25% to 80% (Escobar, Pypendop, and Ilkiw,

unpublished data). In a follow-up study, researchers found that dexmedetomidine at target plasma concentrations of 2.5 ng/mL and higher produced significant cardiovascular depression (Pypendop, Barter, and Ilkiw, unpublished data). On the basis of these studies, it appears that intravenous dexmedetomidine administered to a target plasma concentration of 1.25 ng/mL (corresponding to a loading dose of 0.5 µg/kg followed by 0.5 µg/kg/h) produces about 25% reduction in isoflurane requirements without producing significant cardiovascular depression. However, hemodynamics were not improved compared with an equipotent (i.e., higher) concentration of isoflurane alone. The use of dexmedetomidine for balanced anesthesia in cats is therefore not supported by these data if the goal is to improve hemodynamics. It is nevertheless possible that dexmedetomidine would provide other benefits (e.g., analgesia, better hemodynamic stability).

Total Intravenous Anesthesia

Total intravenous anesthesia (TIVA) refers to induction and maintenance of anesthesia by intravenous agents only. The technique of TIVA anesthesia has gained popularity as a result of the introduction of injectable anesthetic agents that can be infused for long periods of time without resulting in excessively long recovery periods. Injectable anesthetic agents that result in unconsciousness and could be used for TIVA include thiopental, ketamine, propofol, and alphaxalone. Only propofol and alphaxalone offer acceptable recovery quality and times in cats. The drugs can be administered by intermittent bolus administration or as a constant-rate infusion, with constant-rate infusion offering many benefits, such as more stable anesthetic depth, lower total drug administration, and faster recoveries.

Propofol

Initial clinical studies in cats in which anesthesia was maintained by incremental doses of propofol reported a mean maintenance propofol requirement of 0.51 mg/kg/min (confidence limits 0.41 to 0.62 mg/kg/min). After a surgical duration of approximately 30 minutes, mean recovery time was 37.5 minutes (confidence limits 7 to 26 minutes).²⁴ This maintenance rate is much lower than the initial utilization ratio of 0.19 mg/kg/min⁷¹ and may represent the difference between doses required for lateral recumbency versus surgery. Unfortunately, because of the cat's reduced capacity to conjugate propofol, recovery of anesthesia increases with duration of anesthesia.¹⁶⁴

Although propofol provides hypnosis, immobility and muscle relaxation, it does not block autonomic responses to noxious stimuli in other species and must be administered at high infusion rates to induce a surgical plane of anesthesia.¹⁴⁰ Opioids have been

administered with propofol in other species to provide better surgical conditions. Administration of fentanyl (0.1 µg/kg/min), sufentanil (0.01 µg/kg/min), or alfentanil (0.5 µg/kg/min) with propofol in cats was reported to result in satisfactory anesthesia with a reduction in infusion dose of propofol and no greater cardiovascular depression than that associated with infusion of propofol alone. Although the propofol infusion rates were not given in the text, the infusion rate to prevent movement in response to a noxious stimulus was approximately 0.25 mg/kg/min for propofol alone and between 0.1 and 0.15 mg/kg/min during opioid infusions.¹⁴⁰ Ketamine is another drug that can be administered in low doses to block autonomic responses to noxious stimulus. In cats the minimum infusion rate (MIR) required to stop movement in response to a tail clamp was 0.15 mg/kg/min for propofol alone and 0.11 mg/kg/min when either low-dose ketamine (loading dose, 2 mg/kg; constant-rate infusion, 23 µg/kg/min) or high-dose ketamine (loading dose, 4 mg/kg; constant-rate infusion, 46 µg/kg/min) were infused.¹⁰⁶ In this study a linear relationship, depending on the type of stimulus applied, was found between propofol doses and hemodynamic responses, such that as propofol dose increased, the magnitude of the hemodynamic response to stimulus decreased. Follow-up cardiovascular studies also supported that in the cat propofol alone provided stable hemodynamics irrespective of noxious stimuli and addition of ketamine was not beneficial.¹⁰³

Ketamine

Two studies have reported infusion rates for ketamine anesthesia in cats. The first study measured electroencephalographic arousal and autonomic changes in response to tail clamping and reported that these were abolished when ketamine was administered intravenously at infusion rates between 10 and 22 mg/kg/h.²²⁰ In the second study, the MIR in cats to prevent movement in response to tail clamp was reported as 0.41 mg/kg/min (range 0.32 to 0.52) for ketamine.²³⁵

Thiopental

The MIR in cats to prevent movement in response to tail clamp was reported as 0.37 mg/kg/min (range 0.29 to 0.42) for thiopental.¹³⁰

Alphaxalone

The only reported study in cats compared recovery from incremental doses of Saffan and thiopental.¹¹⁶ Cats topped up for 3 hours required 39 to 42 mg/kg of Saffan, which amounts to 0.22 to 0.23 mg/kg/min. Recovery from the last dose to normal behavior was 160 to 233 minutes. This contrasts to thiopental, wherein the total dose administered was 70 mg, amounting to 0.39 mg/kg/min and a recovery from last dose to normal of 45 to 47 hours.¹¹⁶

Anesthetic Options for Feral Cats

Feral cats are domesticated cats that have reverted to a wild state and for safety reasons should be regarded as wild animals. Attempts to reduce overpopulation by trapping and removal have been largely unsuccessful, insofar as the cats remaining in the colonies continue to breed, filling the void left by those that were removed. Feral cat neutering through trap–neuter–return (TNR; castration or spay) programs is a nonlethal method of feral cat population control. TNR programs are an increasingly popular alternative to removal, and veterinarians are frequently called on to participate in feral cat neutering either on an individual-cat basis or large-scale settings. The anesthetic protocol is an important component of these programs if they are to operate effectively.

An ideal anesthetic agent for feral cats would have a wide safety margin; provide rapid and predictable surgical anesthesia and postoperative analgesia; and be reversible, inexpensive, and simple to administer to trapped cats.²⁴⁴ The most commonly reported anesthetic protocol consists of Telazol, ketamine, and xylazine (TKX). Each mL of TKX contains 100 mg of Telazol, 80 mg of ketamine, and 20 mg of xylazine. In a population of almost 7000 cats, the mean initial dose of TKX was 0.24 ± 0.04 mL/cat. The total mean dose of TKX was 0.27 ± 0.09 mL/cat. The drug was injected intramuscularly into either the lumbar or thigh muscles. After surgery yohimbine (0.5 mg) was administered intravenously to adult cats, and 0.3 mg was administered intravenously to kittens. Although total doses between males and females were not different, females received more injections than males. Cats were monitored by assessment of mucous membrane color and respiration and heart rate. Cats were not intubated, breathed room air, and were not supported by fluid administration. In this study the overall mortality was 0.35%, and the death rate attributable solely to potential anesthetic death was 0.23%.²⁴⁴ In another study with almost 100 cats, a dose of 0.25 mL TKX was administered.³⁸ Lateral recumbency occurred in 4 ± 1 minutes, and anesthesia was adequate in 92% of cats to complete surgical procedure. Anesthesia was reversed with yohimbine (0.5 mg IV) at the completion of surgery. Time from anesthetic reversal to sternal recumbency was prolonged (72 ± 42 mins), although all cats recovered.

EQUIPMENT, MONITORING, AND FLUID THERAPY

Anesthesia equipment for use in cats is reviewed elsewhere.^{123,157} Typically, Mapleson (non-rebreathing) systems are used in cats, and high fresh gas flows are

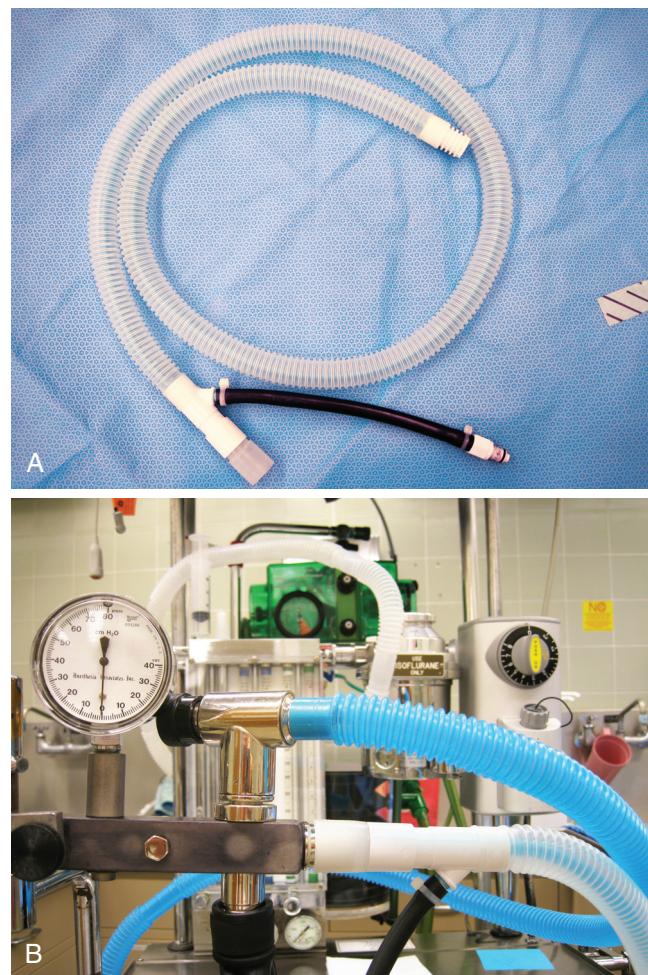


FIGURE 7-3 Bain circuit (A) and Bain circuit adaptor (B) with a low-pressure gauge; this setup helps detect increases in airway pressure if the exhaust system is obstructed for some reason and is also useful for mechanical ventilation.

therefore required. In North America the Bain coaxial system is most popular and offers good efficiency in carbon dioxide removal during both spontaneous and positive pressure ventilation (Figure 7-3). A minimum of 100 to 200 mL/kg/min of fresh gas flow is recommended with this system.¹²³ Higher fresh gas flow is more likely to actually prevent rebreathing of expired gas.

The American College of Veterinary Anesthesiologists (ACVA) recently published Recommendations for Monitoring Anesthetized Patients (<http://acva.org>), and these should be used as a basis to determine the needs for personnel, equipment, and techniques.

Monitoring is directed at assessing vital functions and at detecting changes early so that treatment can be instituted as appropriate. The emphasis is on cardiovascular and respiratory functions. In addition, depth of anesthesia should be assessed so it is maintained at an appropriate level for the degree of stimulation, and body temperature should be measured and maintained as close as possible to normal.

The most critical role of the cardiovascular and respiratory systems is to deliver oxygen to tissues. Oxygen delivery depends on the amount of oxygen carried by arterial blood and cardiac output.^{11,92} Because neither is routinely measured in anesthetized patients, indirect assessment based on observation of the patient and measurement of variables such as blood pressure and packed cell volume is necessary. Nevertheless, the anesthetist should always prioritize maintenance of oxygen delivery to tissues.

A trained, dedicated anesthetist should be available to monitor anesthesia continuously, particularly if the patient is not healthy. Depth of anesthesia requires direct observation of the patient and cannot be automated.⁹² Because anesthetic drugs produce dose-dependent adverse effects, including cardiorespiratory depression, the lowest dose producing the desired effect should always be used. Monitoring of depth of anesthesia mainly relies on assessment of muscle tone and somatic or autonomic responses to stimulation.⁹² The authors have found that the most useful signs for assessing depth of anesthesia are eye position, jaw tone, and palpebral reflex. The palpebral reflex is usually present only at light depth of anesthesia (some individual and drug variations). The eye rotates medioventrally in most individuals and with most anesthetic agents at surgical depth of anesthesia. The eye is central if anesthesia is light or too deep. Jaw tone gives a continuum in the assessment of CNS depression. At light depth of anesthesia, strong jaw tone can be felt; as anesthesia becomes deeper and deeper, jaw tone progressively decreases, to disappear at moderately deep surgical anesthesia. A notable exception is very young animals, which tend to lose jaw tone at light depth of anesthesia. If these signs cannot be used (e.g., surgery of the head), assessment is based on the autonomic response to noxious stimulation (i.e., increase in heart rate, blood pressure, and/or respiratory rate or ventilation), and movement or lack thereof. Clinicians should remember that inhalant anesthetics are not potent at blocking autonomic responses; therefore if anesthesia maintenance relies mainly on these drugs, some degree of response is expected. Lack of autonomic response to noxious stimulation in that situation would mean excessively deep anesthesia.

Pulse rate, respiratory rate, and body temperature should be measured at short intervals and recorded. Normal heart rate in cats ranges from 90 to 240 bpm¹; because anesthesia causes myocardial depression, cardiac output becomes more rate-dependent than in conscious cats, and heart rate should be maintained within that range. Bradycardia is usually caused by excessive vagal tone or hypothermia.⁹² Excessive vagal tone can be prevented or treated with anticholinergics (e.g., atropine 0.01 mg/kg intravenously or 0.02 mg/kg intramuscularly). External heat should be provided as necessary to prevent or treat hypothermia. Means of

providing external heat should allow temperature to be controlled to prevent the risk of skin burns. Warm water-circulating blankets are commonly used, but these have limited efficacy because of the limited area available for heat exchange with the patient. Forced-air systems are more effective.¹²² When these systems are used, caution should be exerted not to cause hyperthermia.

Blood pressure should be routinely measured. Noninvasive techniques are appropriate for most patients. If hemodynamic instability is expected or present, invasive monitoring of blood pressure is preferable. Noninvasive blood pressure measurement relies on the placement of an occluding cuff. Optimal width has been reported to be approximately 40% of the circumference of the appendage on which the cuff is placed.⁷⁷ Two techniques are commonly used: Doppler ultrasound and oscillometric. The Doppler ultrasound technique requires user intervention and can be used only to determine systolic blood pressure (Figure 7-4). It is usually considered to

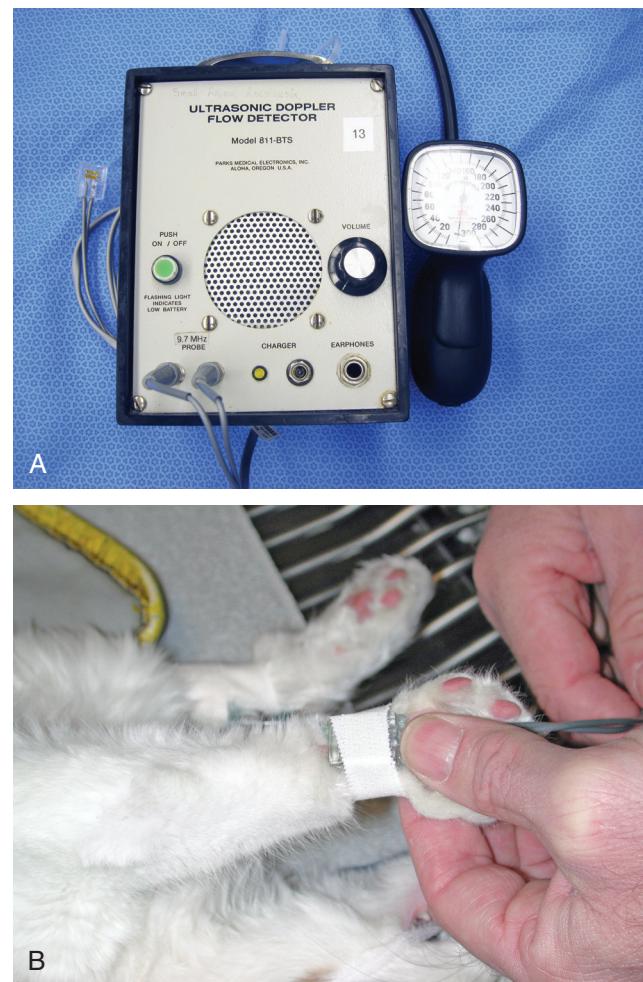


FIGURE 7-4 Doppler ultrasound units can be used only to determine systolic blood pressure but correlate well with invasive measurements. **A**, Parks Medical Ultrasonic Doppler Flow Detector. **B**, Parks Medical infant flat probe in place for blood pressure monitoring during anesthesia.

correlate well with invasive measurements but to underestimate invasive systolic blood pressure.^{33,77} The Doppler ultrasound technique also provides an audible signal corresponding to blood flow, which can be used to count pulse rate and detect arrhythmias. The oscillometric technique allows automated measurement of systolic, diastolic, and mean arterial pressures. The accuracy appears to be highly dependent on the device.^{19,23,33,168} Mean arterial pressure is expected to be the most accurate measurement with this technique. Most devices also measure pulse rate. Oscillometric measurements tend to be inaccurate in cases of movement, arrhythmias, or vasoconstriction. Systolic and mean arterial pressures should be maintained between 100 and 140, and 80 and 100 mm Hg, respectively.⁹² Hypertension is uncommon and usually due to inadequate anesthesia or analgesia. Other causes include excessive treatment of hypotension, drugs causing vasoconstriction (e.g., alpha₂ agonists), and some diseases (e.g., hyperthyroidism, chronic renal failure). The treatment of hypertension is directed to the underlying cause. Hypotension is common, even in lightly anesthetized cats, particularly when there is no noxious stimulation. Treatment includes decreasing anesthetic depth if possible, administration of a fluid bolus (5 to 10 mL/kg, which can be repeated if some improvement is seen), and positive inotropes (dopamine or dobutamine, titrated to effect, starting at 5 µg/kg/min). Vasoconstrictors are preferred to positive inotropes in some disease states (e.g., hypertrophic cardiomyopathy, see relevant section later in this chapter).

Capnography and pulse oximetry may be useful additions to basic monitoring. Capnographs can either sample gas (side-stream) or measure carbon dioxide directly in the respiratory gases flowing to and from the patient, using an adapter connected between the patient and the circuit (mainstream, Figure 7-5). Measurement of end-tidal carbon dioxide partial pressure often yields lower than actual values in cats, particularly if the side-stream method is used, because of small tidal volume, and mixing of inspired and expired gas, in part related to the use of high fresh gas flows. End-tidal carbon dioxide partial pressure closely approximates alveolar carbon dioxide partial pressure,⁶³ which is usually 0 to 5 mm Hg lower than arterial carbon dioxide partial pressure. Capnography therefore allows noninvasive, continuous assessment of PaCO₂. End-tidal PCO₂ should ideally be maintained between 35 and 45 mm Hg. Higher values indicate hypoventilation. If inhalant anesthetics are used, hypoventilation is often related to excessive depth of anesthesia or the use of other drugs causing respiratory depression (or both). The main deleterious effect of high PCO₂ is its effect on pH (i.e., respiratory acidosis). Moderate to severe anesthesia-induced respiratory acidosis (pH < 7.2) is usually treated by mechanical ventilation. However, mechanical ventilation may cause or worsen cardiovascular depression and should



FIGURE 7-5 A mainstream capnograph sensor uses an adapter connected between the patient and the circuit to measure carbon dioxide.



FIGURE 7-6 Pulse oximetry is a noninvasive, continuous assessment of oxygenation that performs variably in cats.

be used with caution, particularly if the patient is deeply anesthetized or hypovolemic.^{65,101}

Pulse oximetry measures the fraction of hemoglobin saturated with oxygen in arterial blood. It is a noninvasive, continuous assessment of oxygenation (Figure 7-6). Pulse oximeters perform variably in cats.¹³⁴ It is not unusual to obtain erroneously low readings. The value of pulse oximetry is somewhat limited in patients receiving a high inspired oxygen fraction. This is due to the shape of the oxyhemoglobin dissociation curve. In normal cats breathing close to 100% oxygen, PaO₂ is expected to be 500 mm Hg or more. Hemoglobin oxygen saturation will be 99% to 100% when PaO₂ is higher than 120 mm Hg. Therefore, in patients receiving a high

inspired oxygen fraction, pulse oximetry will detect only extremely severe deficiencies in oxygenation. This should be taken into account when using this monitor in these conditions. Conversely, a 95% saturation, which corresponds approximately to a PaO_2 of 80 mm Hg, in a patient breathing close to 100% oxygen, if accurate, indicates a serious problem.

Central venous pressure is the pressure measured in the thoracic vena cava. It results from the interaction of blood volume and capacity.⁹² It is a measure of the relative ability of the heart to pump preload and may be helpful to guide fluid therapy, particularly when large fluid volumes are administered. Central venous pressure requires the placement of a catheter, the tip of which lies in the thoracic vena cava. The catheter is usually inserted through the jugular vein. The catheter can be connected to a water manometer or to an electronic transducer and monitor. Normal central venous pressure is 0 to 10 cm H_2O (0 to 7 mm Hg) and should be measured at the end of expiration.⁹² Low values may indicate hypovolemia. High values may indicate excessive circulating volume.

Blood gas analysis is the gold standard for the assessment of oxygenation, ventilation, and acid–base status. Although it requires equipment not commonly available in veterinary practice, it may provide invaluable information in selected cases. Assessment of oxygenation requires the analysis of arterial blood. PaO_2 is normally approximately 5 times the inspired oxygen fraction in % (i.e., approximately 100 mm Hg if breathing room air; 500 mm Hg when breathing 100% oxygen). Lower values may be due to hypoventilation, ventilation–perfusion mismatching, anatomic right-to-left shunting, or impairment of the diffusion of oxygen through the alveolar–capillary membrane. Among these causes, hypoventilation and ventilation–perfusion mismatching are the most common in anesthetized patients. It should be noted that as long as PaO_2 is higher than 80 to 100 mm Hg, hemoglobin is almost fully saturated, and arterial oxygen content will be adequate if hemoglobin concentration is normal, even if PaO_2 is much lower than normal (e.g., if the patient is breathing 100% oxygen). Nevertheless, inadequate oxygen content may arise in these cases when inspired oxygen fraction is decreased (e.g., when recovering from anesthesia and breathing room air). Lower than expected PaO_2 should be treated by addressing the underlying cause or by increasing inspired oxygen fraction. Hypoventilation is managed by decreasing anesthetic depth or by using mechanical ventilation (as previously discussed). Ventilation–perfusion mismatching is treated by increasing inspired oxygen fraction (if possible), mechanical ventilation, and sometimes positive end-expiratory pressure. Alveolar recruitment maneuvers have also been described in humans and may restore better oxygenation.¹¹⁹ Assessment of ventilation relies on the measurement of PCO_2 . Although

arterial PCO_2 is the gold standard, venous PCO_2 is an acceptable alternative, because it is only 3 to 6 mm Hg higher than PaCO_2 in most states. Normal PaCO_2 in cats has been reported to be approximately 33 mm Hg.⁹⁹ Anesthesia depresses ventilation, and normal PaCO_2 is commonly considered to range from 35 to 45 mm Hg in anesthetized patients.

For details on management of fluid therapy, the reader is referred to Chapter 5. Fluid therapy during anesthesia usually relies on the administration of isotonic crystalloids, colloids, or a combination of both. Fluids should be given intravenously or, if this is not possible, intraosseously. Preoperative dehydration or hypovolemia should be corrected before anesthetizing the patient (see Chapter 5). Intraoperative fluid therapy is directed at maintaining effective circulating volume and replacement solutions (i.e., solutions with electrolyte concentrations close to plasma concentrations), or solutions remaining in the vascular space are therefore used. If crystalloids are selected, lactated Ringer's solution or similar preparations or isotonic saline are most commonly used. The rate of administration is often set at 5 to 10 mL/kg/h.¹⁹⁷ The number is arbitrary and usually in excess of actual fluid losses because of metabolism, renal excretion, evaporation in the respiratory tract, and evaporation through open body cavities. However, using that rate rarely causes significant adverse effects in cats with normal cardiac function, and expanding vascular volume may partly compensate for anesthetic-induced vasodilation and surgical blood loss. In cats with abnormal cardiac function or structure, crystalloid administration rate is generally reduced to 3 to 5 mL/kg/h. Acute blood loss can be replaced by administering approximately a volume of crystalloid approximately 3 times that of blood lost. Blood loss of more than 20% of blood volume or hemorrhage in an anemic patient is best addressed by administration of whole blood or packed red blood cells. Colloids remain in the vascular volume longer than crystalloids and usually expand plasma volume in excess of the volume administered. Artificial colloids include dextrans and hetastarch. They increase colloid osmotic pressure and may increase blood pressure more reliably than crystalloids. However, they inhibit coagulation in a dose-dependent manner, may cause allergic reactions (dextrans), and may cause renal injury.⁴⁶ Natural colloids include whole blood, packed red cells, and plasma. Fresh whole blood contains erythrocytes, platelets, and all clotting factors and is the fluid of choice when these components are all needed. Packed red cells only contain erythrocytes. Fresh frozen plasma contains all clotting factors and is a source of albumin. Blood and blood products can cause transfusion reactions. Colloids are usually administered as a bolus (3 to 5 mL/kg) for the correction of hypotension or as an infusion (2 to 5 mL/kg/h) in place of or in combination with crystalloids.

ANESTHETIC CONSIDERATIONS FOR SPECIAL CONDITIONS

Neonatal Patients

There is little information regarding anesthetic considerations for neonatal and geriatric feline patients. Most information regarding the management of these patients is extrapolated from experience with adult animals and information obtained in dogs and humans. Cats are considered neonates from birth to weaning, which is approximately the first 4 weeks of life.⁸¹ During that time many organ systems undergo important changes, which will influence anesthetic management (Box 7-13).

Physiologic Changes

The cardiovascular system is dramatically altered at birth, when the fetomaternal circulation is replaced by the neonatal circulation. Additional changes occur as the neonate ages. The neonatal circulation is characterized by low pressure, low volume, and low resistance.⁴ This results in a high heart rate and low blood pressure. Heart rate progressively decreases, and blood pressure increases to reach values close to those observed in adults around 4 weeks of age.⁴ Sympathetic innervation of the heart is incomplete at birth, while parasympathetic innervation is anatomically mature.¹²⁷ However, anticholinergic administration may have minimal effect on heart rate during the first few days of life, suggesting that the parasympathetic system is not functional yet. In very young animals hypoxemia results in bradycardia and hypotension, a response opposite to that seen in the adult animal. This response appears to be lost at 5 days of age.⁶⁰

Neonates have high oxygen requirements, but their carotid body chemoreceptors are immature at birth. This may increase the risk for hypoxemia. In anesthetized kittens the ventilatory response to hypoxia appears biphasic, with an initial increase in respiratory rate and

tidal volume, followed within 5 minutes by a decrease in respiratory rate below baseline, whereas tidal volume decreases but remains larger than baseline values.²¹

The hematocrit level is comparable to adult values at birth, decreases during the first 4 weeks, then increases to reach adult values around 10 weeks.¹⁴¹ P450 enzyme activity is low at birth and increases over the first few months of life.²¹⁹ Maintenance of normal body temperature largely depends on ambient temperature; because of their high surface-to-volume ratio, neonates are particularly susceptible to hypothermia.⁴⁵

Anesthetic Management

Overall, neonatal and pediatric patients have limited physiologic reserves and are less able to compensate for homeostatic disturbances. Hydration status should be carefully assessed, and any fluid deficit should be corrected before anesthesia. Minimum preanesthetic blood work should include packed cell volume, total proteins, and blood glucose measurements. Additional laboratory work should be performed as indicated by the patient's condition. Preanesthetic fasting should be limited to between 2 and 4 hours in pediatric patients eating solid food. No fasting is indicated in neonatal patients still on a milk diet.

Anesthetic premedication should include an anticholinergic because cardiovascular function is highly dependent on heart rate and the parasympathetic nervous system appears to reach maturity before the sympathetic nervous system.¹²⁷ An opioid can be added for painful procedures. Tranquilizers and sedatives are best avoided because of their prolonged duration of action in these patients and because of the potential for adverse effects. If sedation with an opioid is inadequate, a combination with midazolam can be used, but it may have prolonged effects in neonates compared with adult patients.

Induction of anesthesia is preferably achieved with propofol, insofar as this agent does not rely solely on liver metabolism for its elimination. Nevertheless, duration of action is expected to be longer than in adults.⁷ Alternatively, mask induction with an inhaled anesthetic can be used. Dissociative agents should be avoided because of evidence in rodents that they cause neurodegeneration in the developing brain.¹³⁹ Propofol and inhaled anesthetics produce dose-dependent cardiovascular and respiratory depression and should be carefully titrated to effect.

Maintenance of anesthesia is typically achieved using an inhaled anesthetic. Concurrent administration of analgesics should be performed if indicated. Fluid therapy with a balanced electrolyte solution is administered. Dextrose is added if hypoglycemia is present or if glycemia cannot be measured. Minimum monitoring should include heart rate, respiratory rate, depth of anesthesia, blood pressure, and body temperature. Hypothermia should be prevented or treated

BOX 7-13

Key Points of Neonatal Anesthesia

- Cardiac output is highly dependent on heart rate.
- Sympathetic responses may be immature.
- Blockade of parasympathetic responses is important.
- Blood pressure is lower than in adult patients.
- Preanesthetic fasting should be limited.
- Induction of anesthesia is preferably achieved by using propofol or an inhaled anesthetic.
- Fluids may need to be supplemented with dextrose.
- External heat should be provided from the start of anesthesia.

aggressively because neonates are highly susceptible to large decreases in body temperature.

Normal heart rate is approximately 200 beats per minute in neonatal cats, and bradycardia should be treated with diligence in neonates because cardiac output is highly rate dependent. Normal blood pressure is lower in neonates than adults and increases over the few first weeks of life; appropriate reference ranges should be used.⁴ In canine neonates systolic blood pressure is 61 +/- 5 mm Hg at birth, increasing to 139 +/- 4 mm Hg at 4 weeks of age. Similar values have not been published for neonatal kittens.

Geriatric Patients

The definition of *geriatric* in the context of small animal patients has been debated; it is commonly accepted that an animal that has reached 66% to 75% of its life expectancy is geriatric.³² Aging is a physiologic process characterized by decreasing organ reserve and functional capacity, increasing imbalance of homeostatic mechanisms, and increasing incidence of diseases.²³⁶ However, there is a large variability in health status among geriatric patients. A high index of suspicion for diseases or conditions common in old age should be maintained, and appropriate tests should be performed to confirm or rule out these conditions (Box 7-14).

Physiologic Changes

Major organ systems in elderly animals have decreased functional reserve, which may alter the response to anesthetic drugs. Of particular interest to the anesthetist, the cardiovascular, respiratory, hepatic, renal, and central nervous systems are all affected. Drug dose requirements are usually decreased, and duration of effect is usually increased.²⁰³ Careful consideration as to whether a drug is a necessary part of anesthetic management and cautious titration to effect should therefore be exerted.

Geriatric animals compensate less for cardiovascular changes produced by sedative and anesthetic drugs than younger patients, resulting in greater depression of

normal hemodynamics.²⁰³ Autonomic control is altered, with decreased response to beta-adrenoceptor stimulation and increased sympathetic nervous system activity.¹⁹⁰ Cardiac myocyte number decreases, leading to decreased contractility, decreased ventricular compliance, and increased ventricular filling pressures.¹⁷⁶ Clinically, these changes translate to a higher incidence and severity of hypotension in the anesthetized geriatric patient. The chronotropic response to hypotension is decreased. Geriatric animals are expected to be particularly sensitive to perioperative hypovolemia; however, because of the decreased ventricular compliance, they are also expected to be more sensitive to fluid overload than younger patients.

Drug-induced respiratory depression is increased in geriatric patients.²⁵⁰ Aging causes structural changes in the lung. Loss of elastic recoil is due to collagen and elastin reorganization.²¹⁰ Compliance is increased. Small airway collapse may occur during expiration. Closing capacity increases in relation to functional residual capacity, leading to increased ventilation-perfusion mismatching. Ventilatory responses to hypoxia and hypercapnia are impaired.²⁵⁰ Overall, these changes increase the risk for hypoxemia in the geriatric patient.

Liver mass and liver blood flow decrease with age.¹⁹⁵ This is accompanied by a decrease in the liver's intrinsic capacity to metabolize drugs. Clearance of drugs with both high and low extraction ratios is affected. Drug dose requirements, particularly for maintenance, are decreased.

Renal mass decreases with age, predominantly in the cortex.^{56,131,205} This is related to a decrease in the number of glomeruli. Renal blood flow also decreases. Renal capacity to conserve sodium decreases with age, as is the ability to excrete concentrated urine. Overall, this makes the geriatric patient less tolerant of fluid deficits. In addition, the incidence of renal disease increases with age, and many geriatric cats have some degree of chronic renal disease.

Cerebral mass decreases with aging.^{67,68} The risk for perioperative delirium and cognitive dysfunction is increased in geriatric humans. There may be altered balance between inhibitory and excitatory neurotransmission.²⁰ Brain dopamine concentration decreases with increasing age.¹⁷⁰ Serotonin and brain-derived neurotrophic factor levels also fall.¹⁷⁰ There may be calcium dysregulation, mitochondrial dysfunction, and production of reactive oxygen species. The density of NMDA receptors is decreased, and there are age-related changes in the interaction between glutamate and other neurotransmitters, such as GABA and dopamine.¹⁹⁸

Anesthetic Management

Similar to neonatal patients, geriatric animals have limited functional organ reserve and have limited compensatory responses to homeostatic disturbances. A

BOX 7-14

Key Points of Geriatric Anesthesia

- Functional organ reserve is decreased.
- Geriatric patients tend to be more sensitive to the cardiovascular and respiratory depressant effects of anesthetic drugs.
- Careful titration of the lowest possible dose of anesthetic agent is important.
- Acepromazine and alpha₂ agonists should be avoided whenever possible.
- Balanced anesthetic techniques should be considered.

thorough physical examination, with an emphasis on hydration status and the cardiovascular and respiratory systems, should be performed. Complete blood count, biochemistry profile, urinalysis and total T₄ are usually recommended.

Anesthetic premedication usually includes an opioid and an anticholinergic, unless contraindicated. If additional sedation is desirable, a benzodiazepine can be added. Acepromazine appears to produce more severe hypotension in geriatric than in younger animals and is therefore preferably avoided. Similarly, alpha₂ agonists are better avoided due to their effects on the cardiovascular system and organ blood flow. Dissociative anesthetics may have prolonged effects in geriatric animals because of decreased renal elimination.

Preferred agents for induction of anesthesia include propofol and etomidate. Propofol produces significant cardiovascular and respiratory depression and should be carefully titrated to effect. The quality of induction with etomidate is not great, but this agent produces minimal cardiovascular depression. Etomidate should be combined with a benzodiazepine; a benzodiazepine can also be used with propofol to decrease the dose required for induction of anesthesia.

Maintenance of anesthesia usually relies on the administration of an inhaled anesthetic, such as isoflurane or sevoflurane. Balanced anesthetic techniques may be beneficial in geriatric patients that tolerate the cardiovascular depressant effects of inhalant anesthetics poorly.

Meticulous physiologic monitoring and support is particularly important in geriatric patients to ensure that their limited ability to compensate for changes is not overwhelmed. Minimum monitoring consists of assessments of depth of anesthesia, body temperature, noninvasive blood pressure, pulse rate, and respiratory rate. Additional monitoring tailored to the patient's condition should be used when indicated. External heat should be provided to prevent or limit hypothermia. Fluid therapy, aimed at maintaining extracellular fluid volume and electrolyte balance, should be administered.

Hyperthyroidism

Hyperthyroidism is the most common endocrine disorder in cats.¹⁷³ It is a multisystemic disorder resulting from excessive levels of the thyroid hormones T₄ and T₃. Hyperthyroid cats have increased metabolism, energy requirement, and heat production, resulting in increased appetite, weight loss, muscle wasting, weakness, heat intolerance and slightly elevated body temperature. Thyroid hormones also interact with the central nervous system; in particular, sympathetic nervous system tone is increased, which results in hyperexcitability or nervousness, behavioral changes, tremors, and tachycardia (Box 7-15).

BOX 7-15

Key Points of Anesthesia of the Hyperthyroid Patient

- Good sedation is necessary for handling the animal safely and avoiding sympathetic stimulation.
- If possible, antithyroid medication should be administered for 2 to 3 weeks minimum before anesthesia.
- If the procedure is emergent or urgent, beta-adrenergic blockers should be administered, ideally for 48 hours before anesthesia.
- Arrhythmogenic drugs and drugs causing sympathetic stimulation should be avoided.
- Premedication with an opioid combined with acepromazine or an alpha₂ agonist is indicated.
- Induction of anesthesia with propofol or etomidate is preferred.
- Balanced anesthetic techniques should be considered to blunt autonomic responses to noxious stimulation.
- Caution should be exerted in the treatment of hypotension with catecholamines.

Hyperthyroid cats most often require anesthesia for elective surgical management of hyperthyroidism, but occasionally they require anesthetic management as an emergency for problems unrelated to hyperthyroidism. The pathophysiology of hyperthyroidism is reviewed in Chapter 24; only the aspects directly relevant to anesthesia will be addressed here.

Clinical Signs and Laboratory Findings

Hyperthyroidism causes dysfunction of many organ systems. Of particular concern for anesthesia are the effects on cardiovascular, respiratory, gastrointestinal, and hepatic systems. Handling of hyperthyroid cats may be difficult because of the restlessness associated with the disease. Moreover, hyperthyroid cats may become aggressive when restrained. Good sedation is warranted to avoid excessive sympathetic stimulation. Respiratory distress, weakness, and development of cardiac dysrhythmias may occur when these cats are placed in stressful situations. Weight loss may affect the pharmacokinetics of some anesthetic agents (e.g., by changing the volume of distribution) and will worsen anesthesia-induced hypothermia. When present, muscle weakness may predispose to hypoventilation under anesthesia, which may predispose to dysrhythmias under anesthesia.

The cardiovascular system is affected by hyperthyroidism in important ways.²¹⁷ Heart rate is increased. The sympathoadrenal system appears hyperresponsive. Systemic vascular resistance is decreased, but systolic arterial pressure increases, resulting in systemic hypertension. Cardiac output is increased, as is plasma volume.

Systolic murmurs and gallop rhythms are frequent. Tachypnea is sometimes present but is not necessarily associated with congestive heart failure. Over time, most cats with hyperthyroidism will develop a cardiomyopathy with hypertrophy of the left ventricular free wall and ventricular septum. Dynamic left or right (or both) ventricular outflow tract obstruction is common. These cats are predisposed to cardiac arrhythmias.

Renal blood flow, glomerular filtration rate, and sodium excretion are increased in experimental and naturally occurring hyperthyroidism, possibly as a result of the activation of the renin–angiotensin–aldosterone system.^{146,217} Sodium reabsorption also appears increased, so that blood sodium concentration is usually normal. Polyuria and polydipsia may be prominent signs, and experimental studies in thyrotoxic rats reveal impaired concentrating ability because of the downregulation of aquaporins.^{222,230}

Dyspnea, panting, and hyperventilation have been reported in some cats with hyperthyroidism, often associated with stressful situations.²²² Respiratory muscle weakness has been reported in hyperthyroid humans.²⁰² Pulmonary hypertension may be present.²⁰⁴ Respiratory depression induced by anesthetic drugs is common under general anesthesia, and control of ventilation in hyperthyroid cats is advisable. Dyspnea in cats with congestive heart failure may be caused by pulmonary edema or pleural effusion. If pleural effusion is extensive, thoracocentesis is advisable before induction of anesthesia.

Hematocrit levels may be increased, or hematologic changes may be minimal.^{172,222} The most common serum biochemical abnormalities include elevated serum urea, alkaline phosphatase, lactate dehydrogenase, aspartate aminotransaminase, and alanine aminotransaminase.^{172,222} Avoidance of hypoxemia and maintenance of liver blood flow are important anesthetic considerations.

Anesthetic Management

Thyrotoxic cats are often considered poor anesthetic candidates because they tend to be elderly, cachectic animals with organ system dysfunction. Preparation before anesthesia is important in the hyperthyroid cat to prevent serious complications, such as ventricular dysrhythmias and acute death. Cats not rendered euthyroid before anesthesia appear to be at high risk of perioperative mortality, and untreated cats should therefore be anesthetized only for emergency procedures.¹⁷¹ Elective procedures should be postponed for 2 to 3 weeks and cats started on antithyroid medication. T₄ levels should be rechecked before anesthesia.

Because hyperthyroidism affects multiple organ systems and cardiovascular, respiratory, renal and liver functions may all be compromised, it is important that the laboratory data and other diagnostic tests accurately

define the involvement of these body systems. A complete blood count and serum chemistry profile, an electrocardiogram and serum thyroid hormones are essential in all cases. Cats with cardiac abnormalities on auscultation or electrocardiography should have further cardiac workup, including thoracic radiography and echocardiography. Treatment should be instituted as appropriate.

If anesthesia is required without time to render the patient euthyroid and the cat does not have heart failure with poor contractility, the peripheral manifestations of hyperthyroidism can be dramatically improved within a few days of initiation of therapy with propranolol. The chronotropic and inotropic manifestations of excess hormone secretion are decreased, left ventricular efficiency is enhanced, and the risk of arrhythmias is reduced.

If the cat has been rendered euthyroid, the risk of anesthesia is likely similar to a normal patient, and many drugs can be tolerated if cardiac involvement is minimal. Good sedation is desirable to avoid sympathetic nervous system stimulation. In addition arrhythmogenic drugs should be avoided, and the electrocardiogram should be monitored.

In humans it has been reported that no drug has proved better than any other when outcome is examined.¹⁸⁹ It is therefore likely that preoperative stabilization is more critical than anesthetic drug selection.

An opioid is usually used for premedication. A low dose of acepromazine may be added for improved sedation. Medetomidine or dexmedetomidine may be useful to produce sedation and decrease sympathetic tone. Atropine is generally omitted because it may induce sinus tachycardia and enhance anesthetic-induced dysrhythmias. The authors generally administer glycopyrrolate because it has minimal effects on cardiac rate and rhythm.

Intravenous induction is preferred to mask or chamber induction. In cats without heart failure, a thiobarbiturate may be suitable because it provides a smooth induction without catecholamine release. Diazepam can be administered in combination with thiobarbiturates to decrease the dose of thiobarbiturate and slightly prolong the duration of action. Another possible benefit of thiopental is its antithyroid action.²³¹ However, thiopental is the most arrhythmogenic induction agent currently used in clinical patients. Propofol or etomidate are good alternatives. In particular, in cats with heart failure or dysrhythmias, etomidate combined with a benzodiazepine is expected to have minimal effects on cardiovascular and respiratory function. The dissociative agents ketamine and tiletamine are usually avoided because of the sympathetic stimulation they produce.

Anesthesia is typically maintained with inhalant anesthetics. The larynx should be sprayed with lidocaine to aid intubation and attenuate catecholamine release.

The goals during maintenance of anesthesia are to avoid administration of drugs that sensitize the heart to catecholamines and to provide a level of anesthesia or use a technique that prevents exaggerated responses to noxious stimulation. Isoflurane or sevoflurane are good choices. Because cats under inhalants alone respond to surgical stimulation with increases in heart rate and arterial blood pressure, nitrous oxide can be added to blunt these responses.

Hyperthyroid cats should be closely monitored during anesthesia, with particular emphasis on the cardiovascular system. Before induction, electrocardiogram limb leads and a Doppler crystal and occluding cuff are placed, without causing stress if possible. Hypoxemia should be prevented by oxygenation using a face mask during induction. Additional monitoring can be placed after induction of anesthesia, such as temperature probe, capnograph, and pulse oximeter. If heart failure is present, direct measurement of arterial blood pressure is useful to determine the need for more aggressive management and the response to treatment. In addition, an arterial catheter allows arterial blood to be sampled for blood gas analysis. This enables early recognition and treatment of hypoxemia and hypercarbia, two situations likely to increase the incidence of arrhythmias in hyperthyroid patients.

A balanced electrolyte replacement solution should be administered. The rate of fluid administration will depend on the cardiovascular status of the patient (conservative, 3 to 5 mL/kg/h, if heart failure is present) and the need of the patient (10 to 20 mL/kg bolus if significant blood loss occurs).

Catecholamines for the treatment of hypotension should be used with caution. Hyperthyroid patients may have exaggerated responsiveness to catecholamines, and reduced doses of direct-acting vasopressors such as phenylephrine may be a more logical selection than drugs such as ephedrine, which acts in part by provoking release of catecholamines. Arrhythmias are usually treated by administration of beta-adrenergic blocking agents, such as propranolol or esmolol.

Urethral Obstruction

Disease of the lower urinary tract is common in cats. Urethral obstruction is almost exclusively seen in male cats. Acute urethral obstruction can be life-threatening and can induce acute renal failure, whereas chronic partial obstruction can induce a reduction in renal function. The pathophysiology of urethral obstruction is reviewed elsewhere in this text, and only aspects directly relevant to anesthesia will be addressed here. Male cats presenting with acute urethral obstruction require some form of restraint, usually chemical, to enable urine flow to be restored ([Box 7-16](#)).

BOX 7-16

Key Points of Anesthesia of the Patient with Urethral Obstruction

- Dehydration should be corrected before anesthesia.
- Blood potassium concentration should be measured and hyperkalemia corrected.
- The electrocardiogram should be monitored for signs of hyperkalemia even if it is not present before anesthesia.
- Cardiac output and blood pressure should be maintained to prevent further renal injury.

Clinical Signs and Laboratory Findings

Acute urethral obstruction causes bladder distention with increased bladder wall tension and intravesical pressure. The increased intravesical pressure is transmitted to the renal tubules, where increased intratubular hydrostatic pressure reduces glomerular filtration rate, which persists for some time after relief of the obstruction. With chronic partial obstruction, renal blood flow decreases progressively, and after days to weeks glomerular filtration rate is variably reduced. Depending on the duration and degree of obstruction, renal function may be significantly reduced. Therefore an important anesthetic consideration in these patients is to preserve existing renal function and prevent further loss of function.

Hyperkalemia is the most important abnormality associated with complete obstruction because this electrolyte abnormality may cause life-threatening alterations in cardiac conduction. The first clinical signs of hyperkalemia are usually weakness, absence of reflexes and other neuromuscular dysfunction, eventually leading to muscular and respiratory paralysis. Potassium causes progressive depression in excitability and conduction velocity. The electrocardiographic abnormalities include peaking of the T wave, decreased amplitude and widening of the P wave, prolongation of the P-R interval, eventual disappearance of the P wave, widening of the QRS complex and irregular RR intervals, and sine wave type QRS complexes. Eventually, severe hyperkalemia culminates in ventricular fibrillation or asystole. Prompt recognition and treatment of hyperkalemia are critical. Exposure of hyperkalemic cats to anesthetic agents may further aggravate cardiovascular depression and result in cardiac arrest. An essential part of the preanesthetic preparation is to direct therapy toward normalizing the serum potassium concentration before administration of anesthetic agents.

Cats with urethral obstruction have varying degrees of dehydration. Correction of body fluid deficits before induction of anesthesia is necessary because

anesthetic-induced peripheral vasodilation and myocardial depression accentuate preexisting fluid deficits and may cause profound hypotension.

Acidemia occurs in obstructive uropathy and causes various effects: decreased myocardial contractility, stroke volume, and cardiac output; excitable membrane alterations leading to dysrhythmias; central nervous system depression; dysfunction of metabolic pathways; alterations in transcellular potassium distribution; and changes in plasma protein binding and ionization of pharmacologic agents. Because of its far-reaching effects, acidemia should be corrected before inducing anesthesia.

Elevation of blood urea nitrogen concentration occurs in obstructive uropathy. Uremia causes central nervous system and myocardial depression. The effects of general anesthetic agents are potentiated, and drug dosages should be decreased.

Anesthetic Management

Fluid therapy and restoration of urine flow are the most important components of therapy for cats with urethral obstruction. It appears that relieving the obstruction as sole therapy results in poor outcome, and it is therefore essential also to correct for fluid deficits and electrolyte and acid base imbalances.⁵⁹

Blood should be collected before anesthesia for hematocrit; total protein; blood urea nitrogen; creatinine; serum electrolytes; and, if possible, blood gas and acid-base status. A lead II electrocardiogram should be obtained and continuously monitored for signs of hyperkalemia. Any electrocardiographic sign of hyperkalemia warrants intervention. Calcium gluconate or chloride can be administered to restore normal cardiac excitability; however, the effect is short lived and does not address the primary problem. Insulin, dextrose, and sodium bicarbonate will cause extracellular potassium to move intracellularly. Potassium-free fluids will decrease blood potassium concentration by dilution.

Even in healthy patients, general anesthesia depresses renal function by decreasing renal blood flow, glomerular filtration rate, and electrolyte excretion, at least transiently.³¹ After short uncomplicated anesthesia, renal blood flow and glomerular filtration rate return to normal within a few hours. However, in the obstructed patient in which renal blood flow and glomerular filtration are already decreased, the added depression induced by anesthesia may have profound effects, and every effort should be made to minimize these changes.

An opioid and anticholinergic are usually administered for premedication before general anesthesia. Cats with minimal abnormalities can usually be restrained by intravenous administration of low-dose ketamine and diazepam or midazolam to effect. The administration of the dissociative agents, ketamine and tiletamine, to cats with renal failure is controversial. Pharmacokinetic

studies after ketamine administration to cats found that it is mainly eliminated unchanged by the kidney.¹⁰ This drug should therefore be used with caution in cats with abnormal renal function. However, as for most injectable anesthetics, recovery occurs at least in part because of redistribution rather than elimination. Clinical experience indicates that ketamine, in low doses, is suitable for restraining cats with urethral obstruction, provided they do not have renal failure and that they receive fluids as part of their management. Increased toxicity of thiobarbiturates may be observed in cats with urethral obstruction because of an increase in the nonionized and nonbound portion of the drug from metabolic acidosis, as well as increased permeability of the blood-brain barrier. In addition, barbiturates are arrhythmogenic, and their use may make cardiac abnormalities more prominent. Mask or chamber induction with isoflurane is acceptable for these patients, provided excitement can be minimized.

In critically ill cats the authors prefer to induce anesthesia with a low dose of etomidate and midazolam.

Tracheal intubation is performed, and oxygen is administered. If necessary, isoflurane or sevoflurane is administered to prolong anesthesia. Mechanical ventilation is instituted if necessary. Both hypoxemia and hypercarbia should be avoided insofar as they are likely to increase the incidence of arrhythmias.

Monitoring should be directed toward recognition of arrhythmias and hypotension. As previously mentioned, electrocardiographic monitoring should be started before administration of anesthetic drugs. A Doppler crystal and occluding cuff can also be placed before induction and can be used to monitor systolic arterial blood pressure before and during maintenance of anesthesia. If systolic arterial blood pressure falls below 90 mm Hg, the anesthetic level should be decreased, a fluid bolus should be administered, and administration of an inotropic such as dopamine should be considered. Body temperature should be measured and hypothermia prevented. Measurement of urine production, using a closed technique, provides an index of renal function and should be above 1 mL/kg/h.

Idiopathic Hepatic Lipidosis

Clinical Signs and Laboratory Findings

Cats with hepatic lipidosis usually have significant weight loss. These changes in body weight and composition will make the cats more susceptible to hypothermia under anesthesia and in some cases change the pharmacokinetics of anesthetic agents (Box 7-17).

Many cats with hepatic lipidosis will present with dehydration. Vomiting, diarrhea, chronic anorexia, and reluctance to drink all contribute to the dehydration in these animals. Electrolyte abnormalities, including severe hypokalemia leading to muscle weakness, may

BOX 7-17**Key Points of Anesthesia of the Patient with Hepatic Lipidosis**

- Dehydration should be corrected before anesthesia.
- Fluids should be administered to maintain adequate circulating blood volume.
- Acepromazine, alpha₂ agonists, and benzodiazepines should be avoided.
- Induction of anesthesia is preferably achieved using an inhaled anesthetic.
- Blood pressure should be monitored and hypotension treated aggressively.

be present.⁹ Correction of body fluid deficits before induction of anesthesia is necessary to prevent profound hypotension from anesthetic-induced peripheral vasodilation and myocardial depression.

Many of these patients have a mild to moderate normocytic, normochromic, nonregenerative anemia.⁹ Coagulation disorders may be present.

Cats with severe lipidosis may have hepatic encephalopathy with lethargy, behavioral changes, intermittent blindness, dementia, ptalism, seizures, rage, and coma. Changes in response to anesthetic drugs can occur through changes in receptors such as GABA and opioid, as well as changes in neurotransmitters.

Cats with hepatic lipidosis have varying degrees of hepatic dysfunction. Increased activities of serum alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyltransferase are common. Cats with moderate to severe disease usually are hyperbilirubinemic and appear icteric. These changes cause hepatocyte dysfunction, and drugs that rely heavily on the liver for metabolism or excretion should be avoided.

Anesthetic Management

Blood should be collected for a complete blood count and serum chemistry profile. The coagulation status must be evaluated before a procedure, especially if the patient is icteric. Prolonged clotting times should be corrected by preoperative administration of fresh frozen plasma. If dehydration is present, the patient should be rehydrated before induction of anesthesia by intravenous administration of a balanced electrolyte solution with appropriate potassium supplementation. Serum electrolyte concentrations should be monitored to guide fluid supplementation.

Maintenance of hepatic blood flow during anesthesia is an important goal in these patients. Anesthesia and surgery decrease hepatic blood flow, usually in proportion of the decrease in systemic pressure. Maintenance of an adequate circulating blood volume limits decreases

in hepatic blood flow. Changes in arterial carbon dioxide tension also affect liver blood flow; hypocapnia has been reported to significantly decrease hepatic blood flow, whereas hypercapnia has the opposite effect.

Liver disease alters drug pharmacokinetics. The hepatic elimination of drugs can be affected by either changes in hepatic blood flow or changes in the ability of the liver cells to biotransform or excrete a given drug. Other mechanisms of altered pharmacokinetics in liver disease include changes in protein binding of drugs, as well as changes in volume of distribution.

Owing to alterations in pharmacokinetics and pharmacodynamics (in cases of hepatic encephalopathy), the response of the patient with hepatic disease to anesthetic drugs is virtually unpredictable. Therefore each drug must be carefully selected and, more important, carefully titrated to the desirable effect.

Premedication usually consists of a low dose of an opioid and an anticholinergic. Acepromazine and alpha₂ agonists should be avoided because of their effects on the cardiovascular system and on liver blood flow.^{120,225} The use of benzodiazepines in hepatic encephalopathy is controversial.⁵

Induction of anesthesia is preferably achieved using an inhaled anesthetic such as isoflurane or sevoflurane. Alternatively, propofol or etomidate would be acceptable, although the latter is usually combined to a benzodiazepine to decrease the incidence of myoclonus. Anesthesia is usually maintained using an inhalant anesthetic.

Administration of a balanced electrolyte solution at 5 to 10 mL/kg/h during maintenance of anesthesia will help offset part of the drug-induced decrease in hepatic blood flow. Blood pressure should be monitored, and hypotension should be treated aggressively.

Hypertrophic Cardiomyopathy**Clinical Signs and Laboratory Findings**

Many cats with mild to moderate disease have no clinical signs other than an auscultable gallop rhythm or systolic cardiac murmur. The murmur may be related to either mitral regurgitation or left ventricular outflow obstruction and may vary with changes in heart rate, ventilation, or body position. Audible crackles over the lung fields are suggestive of pulmonary edema. Laboratory tests are usually normal unless there is increased serum potassium or skeletal muscle enzymes caused by aortic obstruction secondary to aortic thromboembolism or unless renal infarction has occurred, resulting in azotemia (Box 7-18).

Anesthetic Management

Before sedating or anesthetizing a cat with hypertrophic cardiomyopathy, a current assessment of the severity of the disease should be obtained. Full hematologic and

BOX 7-18**Key Points of Anesthesia in the Patient with Hypertrophic Cardiomyopathy**

- Acepromazine and anticholinergics should be avoided.
- Dissociative anesthetics, thiopental, and induction with inhaled anesthetics should be avoided.
- Electrocardiography and blood pressure should be monitored.
- Treatment of hypotension with vasoconstrictors may be preferable to the use of positive inotropes.

biochemical evaluation, thoracic radiographs, electrocardiogram, and cardiac ultrasound are recommended. Anemia can be exacerbated by anesthesia and should be corrected. Because of the sensitivity of some of these patients to fluid overload, correction of anemia is best carried out before anesthesia, using slow administration of packed red blood cells and monitoring the patient carefully. Cats on loop diuretics may have electrolyte imbalances that should be corrected before anesthesia. Arrhythmias and pulmonary edema should ideally be treated before anesthesia. Chronically administered medications such as beta-adrenergic blockers and calcium channel blockers should be given as usual on the day of anesthesia. However, it may be preferable to withdraw angiotensin-converting enzyme inhibitors because these drugs have been associated with severe, refractory hypotension in anesthetized humans. A study in cats suggests that enalapril significantly worsens isoflurane-induced hypotension.¹¹³

Cats with hypertrophic cardiomyopathy have poor ventricular compliance, and maintenance of cardiac output requires large ventricular volume and maintenance of (slow) sinus rhythm to improve diastolic filling. The atrial contribution to filling is important. If outflow tract obstruction is a component of the disease, increased myocardial contractility, decreased afterload, and decreased preload are predicted to decrease cardiac output by worsening the obstruction. However, factors that normally decrease cardiac output such as myocardial depression, increased systemic vascular resistance, and ventricular overdistention typically improve systolic function and cardiac output in these cases.

Cats with hypertrophic cardiomyopathy are commonly premedicated with a μ -opioid receptor agonist such as oxymorphone, hydromorphone, or methadone. Glycopyrrolate may be added if heart rate is excessively low. The use of the alpha₂-adrenergic agonist medetomidine has been shown to reduce left ventricular outflow tract obstruction in cats with left ventricular hypertrophy¹¹⁸; however, the effect has not been studied in anesthetized cats, and it is unclear whether the

hemodynamic effects of alpha₂ agonists would prove beneficial during anesthesia in cats with hypertrophic cardiomyopathy. Induction of anesthesia is best performed using an injectable agent because induction with inhalation agents causes excitement and release of catecholamines. Etomidate and a benzodiazepine are preferred, particularly for the severe cases. For mild to moderate cases, propofol, either alone or in combination with a benzodiazepine, is an acceptable alternative, but it does cause systemic vasodilation and decreased afterload. Thiopental and dissociative agents (ketamine, tiletamine) should be avoided, the former because of the tachycardia and ventricular arrhythmias it may induce and the latter because of the sympathetic stimulation produced. Anesthesia is maintained with isoflurane or sevoflurane in oxygen. Sevoflurane may be slightly preferable, because data suggest that it reduces systemic vascular resistance to a lesser extent than isoflurane and that its vasodilatory effect may reach a ceiling at low to moderate concentrations.¹⁷⁸

Balanced anesthetic techniques, most commonly based on utilizing an opioid infusion to reduce the amount of inhalant anesthetic and improve hemodynamics, have often been advocated in these patients. However, opioids decrease inhalant anesthetic requirements only moderately in cats^{58,104,105} or may not even decrease them at all,³⁰ and at the doses required to achieve that effect, significant sympathetic stimulation has been reported,¹⁶³ which would be detrimental to cats with hypertrophic cardiomyopathy. Low doses of opioids could be used, but benefits remain to be demonstrated. Epidural morphine can be used to provide analgesia, but conflicting results on its effect on anesthetic requirements have been published.^{75,183} Alternatives to opioids for balanced anesthesia that have been studied in cats include ketamine, nitrous oxide, and lidocaine. Ketamine and nitrous oxide produce sympathetic stimulation and may therefore not be good choices for cats with hypertrophic cardiomyopathy^{22,54}; lidocaine produces significant cardiovascular depression in normal cats,¹⁷⁹ and caution should therefore be exerted in cats with cardiac disease. Alpha₂-adrenergic agonists at low doses may prove useful for balanced anesthesia in cats with hypertrophic cardiomyopathy; however, no study on their use for that purpose is available to date.

A lead II electrocardiogram, temperature, and blood pressure should be monitored during anesthesia. The electrocardiogram should ideally be assessed during induction of anesthesia as well. Blood pressure can be measured using noninvasive techniques; however, for long or invasive procedures, direct measurement is preferred. A catheter can be inserted in the dorsal pedal or femoral artery. Ventilation can be spontaneous, unless significant hypoventilation occurs, or in cases in which pulmonary edema interferes with oxygenation. In these cases intermittent positive pressure ventilation with or

without positive end-expiratory pressure is usually indicated. Oxygenation should be assessed by blood gas analysis or by the use of a pulse oximeter. Fluid administration and replacement of blood loss must be judicious to optimize preload without causing pulmonary edema. Typically, crystalloids are administered at a slower rate than in the normal cat; however, hypovolemia should be adequately corrected, and large volumes of fluid should be administered if necessary. Treatment of hypotension not related to hypovolemia relies on decreasing the inhalant anesthetic concentration, and, if necessary, on the administration of vasoconstrictors. Phenylephrine may be preferable to norepinephrine in these patients because of the lack of effect on beta₁-adrenergic receptors. Tachyarrhythmias should be treated with a beta-adrenergic antagonist. Esmolol is commonly used in anesthetized patients because of its short duration of action.

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