Canine and Feline Anesthesia
and Co-Existing Disease
This book is dedicated to our animal friends and families—many of which have coexisting disease.
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In human anesthesiology, textbooks concerning anesthetic techniques and protocols associated with specific disease states have been published since 1983 (Stoelting’s *Anesthesia and Co-Existing Disease*, 1st edition – currently in its 6th edition). *Canine and Feline Anesthesia and Co-Existing Disease* is the first attempt to compile similar information about our veterinary species into one source and was developed to discuss the most current concepts in the fields of veterinary anesthesia and analgesia, especially with regards to patients with coexisting disease.

No longer is a successful anesthetic procedure defined as one which the patient simply recovers from unconsciousness. The goal of current anesthetic techniques should not just be to have the patient “wake up” from anesthesia but to have them recover from anesthesia with no lasting physiologic or psychologic detrimental effects from the anesthetic procedure itself. To this end, knowledge concerning veterinary anesthesia and analgesia is greatly expanding and continually developing as the breadth and depth of our profession are evolving with the emergence of species- and disease-specific research. Accordingly, changes in case management must also evolve as our cases become more challenging and our patient populations are growing older with more complex disease states. This book was developed to provide foundational information for veterinary professionals to build on (along with their own individual experiences and knowledge) in order to manage each veterinary case safely and successfully.
Introduction

The most critical function of the cardiovascular system is to circulate blood continuously, ensuring the adequate delivery of oxygen and survival of cells and tissues. The body can survive deprivation of food and water far longer than it can survive deprivation of oxygen and lack of perfusion; lack of oxygen delivery can trigger the complicated cascade that leads to temporary, permanent, or irreversible cell death.1 As such, the simplest definition of cardiovascular disease is the decreased ability of this system to ensure adequate oxygen delivery for day-to-day survival.

Nearly all anesthetic drugs compromise cardiovascular function via a single or multiple mechanism(s) and can severely compromise oxygen delivery in patients with underlying cardiac disease.2 Cardiovascular goals during anesthesia include maintenance of oxygen delivery and homeostasis when using drugs that knowingly disturb the system. However, this goal becomes complicated in patients with underlying cardiovascular disease and increasingly more difficult when severe pathology is present. In patients with significant cardiovascular disease, the optimization of oxygen delivery requires a complete understanding of the mechanisms underlying the pathology, as well as the anesthetic drugs, patient support, and monitoring tools available. The most difficult challenge when faced with these patients is how to balance the pathophysiology of disease against the effects of anesthetic drugs and to subsequently individualize an anesthetic plan that minimizes cardiovascular compromise.

It is difficult to predict all possible combinations of patient signalment and temperament, cardiovascular and comorbid conditions, clinicopathologic abnormalities, surgical procedures, and their effects on anesthetic drug choices. Thus, studies have tended to focus more on describing the specific cardiac disease or cardiac effects of specific anesthetics and less on their combinations. This approach leaves the difficult task of knowing how to choose the appropriate anesthetic plan for an individual patient. The goal of this chapter is to provide an overview of cardiovascular physiology and pathophysiology; anesthetic agents; and cardiovascular patient evaluation, monitoring, and support during anesthesia to help the clinician prepare anesthetic plans for patients with mild to significant cardiovascular disease.

Cardiovascular physiology

Tissue perfusion and oxygen delivery

The mathematical definition of oxygen delivery (DO₂) is the product of oxygen content (CaO₂, ml O₂ dl⁻¹ blood) and cardiac output (CO, l min⁻¹; Figure 1.1).³

Figure 1.1 Determinants of oxygen delivery.
Blood pressure and cardiac output

It is critical to monitor blood pressure (BP) during anesthesia and is our best, yet indirect, clinical indicator of perfusion. BP helps determine how anesthesia affects the patients’ ability to perfuse their tissues and, as such, is used as a tool to treat perfusion abnormalities. However, BP is not a component of the mathematical definition of oxygen delivery: \( \text{DO}_2 = \text{CO} \times \text{CaO}_2 \). It is useful to assess BP in an attempt to estimate changes in CO, as CO is rarely measured in nonresearch patients.

Systolic arterial pressure (SAP) is the peak pressure measured in the artery or arteriole during one cardiac cycle and is due to a number of variables, including stroke volume (SV, volume ejected during one ventricular contraction), velocity of left ventricular ejection, arterial resistance, and the viscosity of blood. Diastolic arterial pressure (DAP) is the lowest arterial pressure measured during the cycle and is affected by blood viscosity, arterial compliance, and length of the cardiac cycle. Mean arterial pressure (MAP) is not the arithmetic mean pressure in the vessel and is always a calculated number. Various formulae exist to calculate MAP as follows: (1) \( \text{MAP} = \text{DAP} + \frac{1}{3} (\text{SAP} - \text{DAP}) \) or (2) \( \text{MAP} = (\text{SAP} + (2 \times \text{DAP})/3) \). In regards to perfusion, the most important of these values is MAP, as the time during the cardiac cycle spent at SAP is very short, whereas the time spent at MAP is much longer (Figure 1.2).

Mean arterial pressure and autoregulation

Autoregulation is the automatic adjustment of blood flow through a tissue regardless of the MAP driving blood through the tissue (Figure 1.3). In other words, autoregulation is the unconscious adjustment of arterial and arteriolar smooth muscle tone to maintain a constant blood flow through a tissue across a wide range of pressures. Classically, this is thought to occur between MAPs of \( \sim 60-160 \text{ mmHg} \) and is due to adaptive metabolic, myogenic, and neurogenic feedback mechanisms. Outside of this interval, tissue or organ blood flow is substantially altered, potentially resulting in reduced or nonuniform perfusion patterns.

Hypotension

MAPs \(< 60 \text{ mmHg} \) (or SAP \(< 90 \text{ mmHg} \)) have historically been considered the minimum recommended pressures in small animals associated with adequate tissue oxygen delivery. However, a MAP of \( \sim 60 \text{ mmHg} \) may not actually reflect adequate perfusion for a number of reasons. Firstly, studies investigating autoregulation are routinely performed in nonanesthetized patients. Neurogenic mechanisms for autoregulation depend on sympathetic nervous system (SNS) input. Anesthetic agents depress both the conscious and unconscious (autonomic) nervous systems. Since the SNS tone is substantially reduced during
Cardiovascular disease

Autoregulation

Perfusion is pressure dependent

Blood flow

Mean arterial pressure

Buffer zone

Figure 1.3 Principles of autoregulation. Between mean arterial pressures (MAPs) of ~60 and 160 mmHg, blood flow through a tissue capillary bed is held constant by autoregulatory mechanisms. At MAP > ~160 mmHg and at MAP < ~60 mmHg, autoregulation of blood flow is lost and blood flow through capillary beds becomes pressure dependent; tissues are either overperfused or underperfused.

anesthesia, autoregulatory mechanisms are unavoidably depressed, either partially or completely, and autoregulation is impaired. Secondly, if a MAP of ~60 mmHg is considered the minimum acceptable BP and not hypotension, then treatments for patients assessed as hypotensive (i.e. MAP < 60 mmHg) will not begin until the patient is in a state wherein oxygen delivery is pressure dependent (i.e. to the left of the autoregulatory curve). As all hypotensive therapies are not instantaneously acting, there is concern that the patient may become increasingly hypotensive before treatments are efficacious. Thus, a MAP of 70 mmHg (or SAP of 90 mmHg) should be considered the minimum acceptable BP to build in a buffer zone so that treatments for hypotension can be applied and take effect before tissue perfusion is severely compromised, taking into account both altered autoregulatory mechanisms and the time-dependent treatment effects.

Relationship between mean arterial pressure (MAP) and cardiac output (CO)

When considering the relationship of measured BP to the definition of oxygen delivery, one must understand the components that derive a measured BP. MAP is the product of CO (l min\(^{-1}\)) and SVR (dynes s\(^{-1}\) cm\(^{-5}\)). SVR is considered the degree of vasodilation (which reduces SVR) or vasoconstriction (which increases SVR) present in the systemic circulation. CO is the product of heart rate (HR, beats per minute) and SV (milliliter ejected per heart beat). SV is determined by preload (the venous return during diastole preloading the ventricle before contraction/ejection), afterload (the resistance that ventricular contraction must overcome in order to eject blood), and contractility (the force of contraction of ventricular muscle, independent of preload and afterload; Figure 1.4).

\[
\text{Oxygen delivery} = \text{Cardiac output} \times \text{Oxygen content}
\]

\[
\text{Mean arterial pressure} = \text{Cardiac output} \times \text{Systemic vascular resistance}
\]

\[
\text{Heart rate} \times \text{Stroke volume} = \text{Preload} = \text{Resistance against systolic ejection}
\]

\[
\text{Venous return or circulating blood volume} = \text{Resistance against systolic ejection} = \text{Contractility} = \text{Inotropy or strength of contraction}
\]

Figure 1.4 Determinants of mean arterial blood pressure. Mean arterial blood pressure (MAP) is the product of cardiac output (CO), the volume of blood ejected by the heart per minute, and systemic vascular resistance (SVR), the degree of vasodilation (decreased SVR) or vasoconstriction (increased SVR). Note that MAP is not a component of oxygen delivery. Cardiac output is the product of heart rate (HR) and stroke volume (SV), the volume of blood ejected from the heart per cardiac cycle. Stroke volume is determined by the volume of blood returning to the heart during diastole (preload), the resistance to ejection of blood during systole (afterload), and the strength of cardiac muscle contraction (contractility).
Increases in SVR, SV, preload, and contractility tend to increase BP, whereas increases in afterload tend to decrease SV, CO, and MAP. As MAP is a mathematical product, one cannot definitively determine if a decrease or increase in MAP is due to a decrease or increase in CO or SVR, as CO or SVR are not routinely measured in clinical patients. Choosing which mechanism for hypotension or hypertension is driving the change in pressure for a given patient requires understanding the effects of anesthetic drugs, autonomic physiology, and underlying pathophysiology, among many others.

The four mechanisms based on this algorithm are vasodilation, bradycardia, decreases in cardiac preload, and a decrease in myocardial contractility (Figure 1.4). These mechanisms of hypotension each have a variety of causes (Figures 1.5–1.8) and treatments (Figure 1.9).

For example, vasodilation can be treated either with (1) fluid boluses (crystalloids or colloids) to expand vascular volume to “fill” the vasodilated vasculature or with (2) administration of vasoconstricting agents to “offset” the vasodilation (phenylephrine, vasopressin, norepinephrine, etc.) or a positive inotrope that has vasoconstrictive properties (e.g. dopamine). Bradycardia can be treated with anticholinergics for sinus

**Causes of vasodilation**

(decreased SVR = vasodilation)

- Propofol
- Acepromazine
- Inhalant anesthetics
- Hypothermia
- Cardiac drugs
  - Nitroprusside
  - Nitroglycerine
  - Pimobendan
  - Hydralazine
  - ACE Inhibitors
  - Amlodipine
- Sepsis
- Anaphylaxis
- Hypercapnia

**Figure 1.6** Causes of vasodilation. Example causes of decreased systemic vascular resistance, either via disease, complications of a procedure (e.g. septic shock or anaphylaxis), or via drug side effects. Similar to Figure 1.5, this list can be used not only to treat a cause of vasodilation, but also to predict potential vasodilation from patient comorbidities or diseases for management before or during anesthesia.

**Causes of decreased preload**

- Low total body water (geriatric)
- Dehydration (vomiting, diarrhea)
- 3rd spacing (effusions, ascites, GI fluid)
- Hemorrhage
- Hypovolemia
- Vascular occlusion
- Vascular compression/obstruction
- Positive pressure ventilation
- Vasodilation

**Figure 1.7** Causes of decreased preload. Example causes of decreased venous return (i.e. preload), either via disease or via complications from drug side effects.

bradycardia or second-degree atrioventricular (AV) block or with other antiarrhythmics directed at specific bradycarrhythmias. Decreases in cardiac filling can be treated with blood volume expansion (crystalloid or colloid boluses) or with reversal or removal of
**Causes of decreased or poor contractility**

- Neonates/juveniles/pediatrics
- Dilated cardiomyopathy
  - Secondary cardiomyopathies
- Isoflurane (dose-dependent)
- Propofol
- Hypocalcemia
- Acidosis
- Beta-receptor blocking agents
- Calcium channel blockers

**Figure 1.8** Causes of decreased contractility. Example causes of decreased contractility (or inotropy) via either disease, complications of a disease, or drug side effects. Note that this list can be used not only to treat a cause of decreased contractility, but also to predict potential negative inotropy from patient comorbidities or anesthetics for management before or during anesthesia.

Obstructions or compression of the cranial and caudal vena cava. Lastly, decreases in myocardial contractility from any cause can be treated either by reducing or removing the cause or with positive inotropes that improve contractility. As inhalant anesthetics are moderately to severely depressant on myocardial contractility (depending on dose), reducing the inhaled anesthetic dose (or requirement) of a patient can dramatically improve contractility and improve hypotension.

It is critical to understand that these mechanism(s) and cause(s) exist not only in the anesthetized patient, but also in the patient with preexisting disease or abnormal physiology (e.g. pregnancy, neonates, and geriatrics), and this approach can be used not only in the anesthetized patient, but also in planning ahead for hypotension and other complications under anesthesia.

**Preanesthetic patient assessment**

The presence of underlying cardiac disease necessitates a more extensive patient evaluation compared to noncardiac patients. For example, patient history should include previous cardiovascular diagnoses, medications, and any recent changes in medication dosages. Historical radiographs, electrocardiography (ECG), or Holter monitor evaluation, BP, and echocardiogram findings should be available. Patients with severe disease should be evaluated within 1–2 weeks of a planned anesthetic procedure.

Although a complete physical examination (PE) should be performed before and on the day of anesthesia, particular attention must be paid to the cardiovascular and respiratory systems. The localization and characterization of heart murmurs, changes in lung sounds, increases in respiratory rate and effort, poor color and refill of mucous membranes, presence

<table>
<thead>
<tr>
<th>Mechanism of hypotension</th>
<th>Treatment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Vasodilation</td>
<td>1a. Fluid volume</td>
</tr>
<tr>
<td></td>
<td>1b. Vasoconstrictors or “pressors”</td>
</tr>
<tr>
<td>2. Bradycardia</td>
<td>2a. Anticholinergics</td>
</tr>
<tr>
<td></td>
<td>2b. Antiarrhythmics</td>
</tr>
<tr>
<td>3. Decreased preload</td>
<td>3. Volume bolus, decrease ventilation, relieve obstruction/compression</td>
</tr>
<tr>
<td>4. Decreased contractility</td>
<td>4a. Positive inotropes</td>
</tr>
<tr>
<td></td>
<td>4b. Reduce inspired inhalant levels</td>
</tr>
</tbody>
</table>

**Figure 1.9** Strategies for Management of Hypotension. Suggested treatment options for each mechanism are presented. Vasodilation can be treated with either volume resuscitation or vasoconstrictive agents. Bradycardia can be treated with anticholinergic or antiarrhythmic agents. Decreased preload can be treated with volume boluses or correction of the inciting cause of the loss of preload (i.e. obstruction to venous return). Decreased contractility can be treated with either minimizing the inciting cause (e.g. inhaled anesthetics) or with positive inotropic drugs (e.g. dopamine, dobutamine, etc.)
of jugular pulsations, and pulse irregularities or pulse deficits are obvious indicators of potential heart disease or changes in the patient’s cardiovascular status.

A minimum database for cardiac disease should include assessments of organ function with a blood chemistry panel, electrolytes, and a complete blood count. Patients with cardiac disease should have some combination of preanesthetic ECG, BP, thoracic radiographs, and echocardiogram depending on the type of cardiac disease. Ideally, the entire workup should be completed for patients presenting with a cardiac murmur or arrhythmia and previously unrecognized cardiac disease.

### Functional classification of cardiac disease

Previous texts have established a functional classification of cardiac disease on the basis of clinical signs in an effort to help the clinician recognize which patients may have a higher risk of anesthetic complications and for whom anesthesia should be avoided until the patient has stabilized. If the presenting complaint necessitates anesthesia, this classification alerts the clinician to the high risk nature of such patients for owner counseling, preanesthesia preparation, requirements for intensive patient monitoring, and patient support.

**Classification I** comprises all nonclinical patients with preexisting cardiac disease and can be anesthetized with no preanesthetic stabilization. Classification II includes patients who have preexisting cardiac disease with mild to moderate clinical signs of disease at rest or with exercise. These patients require significant stabilization with medications and/or hospitalization before anesthesia can be considered. If anesthesia is required for a life-saving procedure, immediate stabilization with parenteral medications before anesthesia is required. Aggressive and invasive monitoring is necessary due to their fragile nature. Classification III includes patients with ongoing, fulminant heart failure. Anesthesia is contraindicated until the patient can be stabilized. If anesthesia cannot be avoided due to a life-saving procedure, they carry the highest risk of anesthetic complications, including severe debilitation, morbidity, and mortality.

The American Society of Anesthesiologists (ASA) patient status classification scheme has been adopted by The American College of Veterinary Anesthesia and Analgesia (ACVAA; Table 1.1). The ASA patient status value is not intended to be a risk assessment; however, the assignment of a patient status implies only the presence or absence of disease and that the clinician has evaluated the health status of the patient. The ASA physical status classification has limitations and can be seen as overly vague. However, the ASA does not (and presumably will not, as these definitions were accepted in 1963) expand on these limited definitions. Therefore, assignment of a particular patient to cardiac disease must be determined by the individual clinician (Table 1.1). Some authors have suggested

| Table 1.1 American Society of Anesthesiologists (ASA) physical status. |
|----------------|----------------|---------------------------------|
| Category | Physical status | Clinical examples |
| I | Normal healthy patients | No detectable disease; patients presenting with ovariohysterectomy or castration |
| II | Patients with mild systemic disease | Skin tumor, fracture without shock, uncomplicated hernia, cryptorchidectomy, localized infection, or compensated cardiac disease |
| III | Patients with severe systemic disease | Fever, dehydration, anemia, cachexia, or moderate hypovolemia |
| IV | Patients with severe systemic disease that is a constant threat to life | Uremia, toxemia, severe dehydration and hypovolemia, anemia, cardiac decompensation, emaciation, or high fever |
| V | Morbiund patients who are not expected to survive 24 h without operation | Extreme shock, dehydration, terminal malignancy or infection, severe trauma |

Patient physical status adapted from the American Society of Anesthesiologists (ASA) physical status classification. According to the ASA guidelines, “There is no additional information that will help you further define these categories.” Clinical examples have been suggested by some authors, however, patient classification is highly variable and must be determined by the individual clinician.
classic types of patients who may be categorized into a particular physical status to help guide clinicians in the determination of ASA physical status.13

**Sedation versus general anesthesia**

Sedation is defined as “a state characterized by central depression accompanied by drowsiness. The patient is generally unaware of his or her surroundings but is responsive to painful manipulation.”14 General anesthesia is defined as “drug-induced unconsciousness that is characterized by controlled but reversible depression of the central nervous system (CNS) and analgesia. In this state, the patient is not aroused by noxious stimulation. Sensory, motor, and autonomic reflexes are attenuated.”14 Surgical anesthesia is defined as “the state/plane of general anesthesia that provides unconsciousness, muscular relaxation, and analgesia sufficient for painless surgery.”14 The choice between whether to simply sedate a patient for a procedure or to use general anesthesia is important to consider. The degree of CNS depression that accompanies general anesthesia also depresses autonomic reflexes; the effects of which may be avoided if sedation is an acceptable alternative for the planned procedure. Systemic sedation that is appropriate for the patient’s temperament and underlying disease in combination with locoregional analgesia may be sufficient for surgical analgesia in some cases.15–17

Although sedation may appear to be a universally safer option due to the avoidance of CNS/autonomic depression, sedatives such as alpha-2 agonists and phenothiazines may be absolutely contraindicated with some types of cardiac disease.18 Moreover, the degree of cardiovascular depression may be difficult to treat (particularly in the case of the alpha-2 adrenergic agonists) without reversal of the sedative with an antagonist reversal agent. In some cases, however, sedation may be preferred. However, general anesthesia with cardiovascular-sparing protocols and appropriate patient monitoring and support may be the safer option. There is no single ideal anesthetic agent or anesthetic protocol for all cardiovascular disease; no one plan that will work for all patients and all procedures. All anesthetic plans should be individualized for the patient’s heart disease and coexisting disease. Optimizing the plan requires a complete understanding of anesthetic drug effects and side effects, as well as pathophysiology of disease, so as to combine the two for optimal outcome.

**Anesthetic and analgesic agents**

** Premedications**

Premedication is an extremely important step in the process of anesthetizing patients because it provides sedation, analgesia, and a reduction in induction and maintenance drug doses.2 As the induction and maintenance agents frequently are associated with severely depressant cardiovascular effects (albeit drug and dose-dependent in most cases), a large step toward cardiovascular stability can be provided with good to very good sedation with appropriate premedication.

**Opioids**

Opioids are a mainstay of premedication, induction, and maintenance of anesthesia in patients with cardiac disease, as they have minimal cardiovascular effects.20–23 Bradycardia is the major consequence of opioid use, as opioids have minimal to no effects on cardiac contractility or vascular tone.24,25 Bradycardia can be controlled with treatment or concomitant premedication with an anticholinergic (such as atropine or glycopyrrolate). Differences among the large number of opioids can cause confusion in choosing the most appropriate drug in this class. As a general rule, opioids will produce better sedation in the very young, old, or compromised patient as compared to a normally healthy adult patient. This rule is especially important consider in debilitated patients with cardiac disease.

**Morphine**

Morphine is considered the basis for comparison of all other opioids. Morphine is a full mu-opioid receptor agonist and provides very good sedation, often perceived as the best sedating choice in this class of drugs. It is also the most likely drug to induce vomiting.26 It is absorbed rapidly when given intramuscularly,27 and its duration is ~ 4–6 h. Intravenous (IV) administration is not recommended due to the risk of histamine release.28 Morphine can, however, be delivered by low dose constant rate infusion and provides significant reductions in inhaled maintenance anesthetic requirements.
Hydromorphone/oxymorphone
Hydromorphone and oxymorphone have very similar profiles in small animals. Both are full mu-opioid agonists and provide excellent analgesia. They are moderately sedating opioids and are less likely to induce vomiting compared to morphine. Hydromorphone (as well as morphine) may cause panting in clinical canine patients, which may be undesirable for sedated procedures. Hydromorphone has also been reported to cause postoperative hyperthermia in cats at standard clinical doses; however, the clinical relevance of this is unclear.

Fentanyl
Fentanyl is a synthetic full mu-opioid agonist that is 80–100 times more potent than morphine, implying that an equally effective dose is 80–100 times less than morphine. Owing to its short duration of action (~20–30 min after bolus administration), fentanyl is most useful for IV premedication, induction, or delivery by constant rate infusion. Fentanyl is minimally sedating and is extremely unlikely to induce vomiting. It is very well suited for use as a sole anesthetic induction agent at high doses or as part of a multidrug induction protocol.

Butorphanol
Butorphanol is a mixed opioid agonist–antagonist; it is an agonist at the kappa-opioid receptor and an antagonist at the mu-opioid receptor. Therefore, it is only indicated for mild to weakly moderate pain, as it has analgesic effects only at the kappa receptor and is a very poor analgesic for moderate to severe pain. Although it has a relatively short duration of action (~45–90 min), it can be sedative in small animals and thus used for conscious procedures either as a sole IV sedative or in combination with other more potent sedatives, depending on the requirements. Bradycardia is less likely to occur after butorphanol administration than with full mu-opioid agonists. It is very unlikely to cause vomiting and demonstrates a ceiling effect in which no further sedation or analgesia is seen beyond 0.8 mg kg^{-1}.

Buprenorphine
Buprenorphine is unique among the common opioids in that it is a partial mu-opioid receptor agonist. Buprenorphine has an extremely high affinity for the mu-opioid receptor, such that it outcompetes other opioids for receptor binding, but cannot evoke a full mu-opioid response. Therefore, it is not equally efficacious compared to full mu-opioid agonists. It also demonstrates a ceiling effect in that doses above 0.04 mg kg^{-1} do not provide additional analgesia or sedation. Owing to receptor binding, buprenorphine is poorly reversible to irreversible with opioid antagonists. It is very unlikely to cause bradycardia and vomiting and is a relatively poor sedative.

Phenothiazines
Atropine and glycopyrrolate are parasympatholytic anticholinergic agents used to increase HR associated with vagal-mediated sinus bradycardia and AV block. Atropine has a faster onset time (~1–2 min IV), shorter duration of action (~20–30 min IV), and is more likely to incite tachyarrhythmias. Glycopyrrolate has a longer onset time (~2–4 min IV), longer duration of action (~1 h IV), and may be less likely to cause tachyarrhythmias. Low doses of atropine and glycopyrrolate can initially precipitate second-degree AV block (see the following sections), which may require additional doses of anticholinergic for treatment.

Benzodiazepines
Benzodiazepines (diazepam and midazolam) are good choices for sedation in patients with cardiac disease. They have minimal to no effects on HR, contractility, or vasomotor tone and do not lead to hypotension across a wide range of doses (0.5–2.5 mg kg^{-1} IV). Although respiratory rate decreases, arterial blood gas values do not change appreciably. The major
disadvantage of benzodiazepines is that they are inconsistent sedatives in dogs\textsuperscript{44,45} and may be poor sedatives in cats. For example, IV premedication doses can lead to dysphoria, excitement, ataxia, arousal, and, potentially, violent aggression.\textsuperscript{44} Combinations of butorphanol and midazolam fail to provide sedation in healthy cats.\textsuperscript{45} Although benzodiazepines decrease inhaled anesthetic requirements, this benefit can be achieved when they are combined with induction agents during the induction protocol as opposed to risking excitement when used as premedicants.\textsuperscript{46,47}

**Alpha-2 adrenergic receptor agonists**

Alpha-2 adrenergic receptor agonists (dexmedetomidine, medetomidine, xylazine, etc.) are usually contraindicated in patients with cardiac disease. Alpha-2 agonists cause intense peripheral vasoconstriction and decrease sympathetic outflow from the CNS. The severe increase in SVR leads to a marked increase in BP, a significant increase in myocardial afterload, and a baroreceptor-mediated reflex bradycardia. Some patients may demonstrate a period of vasodilation and arterial hypotension after the initial hypertension. This is commonly seen with xylazine in horses but appears to be less common with longer acting agents such as dexmedetomidine.\textsuperscript{48,49} The initial baroreceptor-mediated bradycardia is exacerbated by a decrease in centrally mediated descending sympathetic tone. Alpha-2 adrenergic agonists can also produce AV block and ventricular escape cardiac rhythms. At sedative doses, these mechanisms will decrease CO by \(\sim 50–60\%\); dexmedetomidine at \(\geq 5\) mg kg\(^{-1}\) IV will decrease CO by \(50–60\%\),\textsuperscript{50} and medetomidine at 20 mcg kg\(^{-1}\) IV will decrease CO by at least \(60\%\).\textsuperscript{51} The increase in afterload from vasoconstriction, increase in left atrial pressure from centralization of blood volume, and decrease in CO are all mechanisms that can be detrimental to the function of a heart with underlying disease. Although alpha-2 adrenergic agonists are extremely reliable sedatives, the cardiovascular side effects are so profound that the depth of sedation may be better sacrificed in the interest of cardiovascular safety.

**Induction agents**

**Propofol**

The main advantage of propofol is a rapid onset (\(\sim 15–20\) s) and short duration of action (\(\sim 6–10\) min of anesthesia) from an IV bolus that allows intubation.\textsuperscript{52} Its main mechanism of action\textsuperscript{53} is stimulation of the gamma aminobutyric acid (GABA, the main inhibitory neurotransmitter in the CNS) receptor away from the binding site for other anesthetics such as thiopental.\textsuperscript{54} Recoveries from propofol administration are extremely smooth. However, propofol is a significant dose-dependent vasodilator\textsuperscript{55} and can precipitate significant hypotension at moderate to doses. While patients with mild cardiac disease may tolerate hypotension associated with propofol, those with more severe disease or in whom a decrease in SVR will worsen cardiac function should be cautiously induced with propofol.

**Dissociative anesthetics**

Dissociative anesthetics such as ketamine and tiletamine produce anesthesia by interrupting neuronal transmission, thus “dissociating” the centers responsible for consciousness and unconsciousness from the peripheral ascending inputs. The cardiovascular effects of dissociative anesthetics result from stimulation of the SNS, increasing HR, contractility and MAP, with little change in SVR.\textsuperscript{56} This leads to an increase in myocardial work and myocardial oxygen demand that is compensated for by increased CO and coronary blood flow.\textsuperscript{57} The increase in oxygen demand in patients with cardiac disease may worsen cardiac function or arrhythmias. Thus, ketamine is contraindicated in hypertrophic cardiomyopathy (HCM) and is frequently avoided in any patient with other forms of cardiomyopathy and valvular cardiac disease (see the following section) or in those with severe systemic illness.\textsuperscript{58}

**Etomidate**

Etomidate is a nonopioid, nonbarbiturate sedative hypnotic drug that works similar to propofol and barbiturates in that it enhances inhibitory GABA effects.\textsuperscript{59} Etomidate has the distinct advantage of having minimal to no cardiovascular depression because it does not significantly change HR, contractility, afterload, or venous return. However, it has several drawbacks. Etomidate has a very high osmolarity (\(\sim 4800\) mOsm l\(^{-1}\)) and can lead to osmolar shifting, causing possible phlebitis, pain at the injection site, red blood cell crenation, and potential hemolysis, as well as adrenocortical suppression.\textsuperscript{60} Etomidate causes a reliable but relatively slow transition to unconsciousness when compared to propofol. Etomidate has poor muscle relaxation and
can stimulate myoclonus and so should be given with a benzodiazepine or fentanyl to facilitate a smooth induction period.\textsuperscript{61}

**High dose opioids**

High dose, full mu-agonist opioids such as fentanyl can be extremely effective in producing general anesthesia with uncomplicated placement of an endotracheal tube. High dose opioids have the disadvantage of moderate to severe respiratory depression and bradycardia; however, both are easily controlled with intubation and anticholinergics, respectively. Unfortunately, transition to unconsciousness with fentanyl appears somewhat less reliable and slower compared to propofol\textsuperscript{62} or etomidate. Patients who are bright and energetic or are stimulated during the induction process by sound, touch, or pain may attempt to “override” the induction process, leading to poorer quality induction. In these cases, a rescue induction agent (typically propofol for speed of onset, but etomidate is an alternative option) can help push such a patient into unconsciousness. Quiet, dimly lit environments with little stimuli are ideal for fentanyl inductions, and fentanyl inductions usually work best in debilitated, older animals. Fentanyl should be given with a benzodiazepine for improved muscle relaxation.

**Anesthetic maintenance**

**Inhaled anesthetics**

Inhaled anesthetics are the most commonly chosen drugs for maintenance of anesthesia. Although injectable protocols for maintenance of anesthesia exist, referred to as total intravenous anesthesia (TIVA) protocols, inhaled anesthetics provide a number of unique advantages. Their pharmacokinetic properties allow for careful titration of and rapid changes in the anesthetic depth. The use of inhaled anesthetics requires the use of an anesthetic vaporizer that requires a carrier gas flow (nearly always 100% oxygen), which supports maximal arterial blood oxygenation. The need for an anesthesia machine requires endotracheal intubation, which allows for more accurate monitoring of ventilation. In addition, ventilation can also be supplemented and/or supported easily with this equipment. The ability to monitor expired gases such as carbon dioxide or exhaled anesthetic concentrations allows for more robust patient monitoring and support. Unfortunately, inhaled anesthetics depress cardiovascular function, leading to dose-dependent CO and BP depression.\textsuperscript{63} This is due to a moderate to severe dose-dependent reduction in myocardial contractility (e.g. negative inotropy) and subsequent decreases in SV and CO.\textsuperscript{63–66} Isoflurane also decreases SVR, resulting in vasodilation, which can incite or predispose to hypotension. Generally, these cardiovascular side effects are managed either by minimizing the dose administered or by counteracting the side effects with interventions aimed at providing cardiovascular support. Many strategies are available to allow reductions (“MAC reduction”) in inhaled anesthetic drug requirements (MAC, the Minimum Alveolar Concentration of inhaled anesthetic required to produce lack of response to a supra-maximal noxious stimulus applied to a patient 50% of the time.) and include use of premedications, induction agents, bolus or infusion-dose analgesics or sedatives, and local/regional anesthesia techniques. The hypotensive effects of inhaled anesthetic agents can be treated by a variety of mechanisms, including optimizing HR and rhythm, judicious use of IV fluids (if not contraindicated by cardiovascular disease), and directly increasing contractility (to oppose the inhaled agents effects) with positive inotropic drugs (Figure 1.9).

**Anesthetic adjuncts**

One major goal of adjunctive techniques or interventions is to increase cardiovascular stability and maximize CO and BP. In practice, this can be generally summarized as applying a technique that has fewer negative cardiovascular side effects as compared to patient management without that particular technique. As an example, fentanyl infusions have been shown to reduce the requirement for enflurane by as much as 65%\textsuperscript{67} and of isoflurane by \(\sim50\%\)\textsuperscript{68} at 0.8 mcg kg\(^{-1}\) min\(^{-1}\) and 0.3 mcg kg\(^{-1}\) min\(^{-1}\), respectively. As the primary cardiovascular effect of opioid infusions is bradycardia, which is easily corrected with anticholinergics, these infusions allow for decreased inspired concentrations of inhalant anesthetics, therefore reducing their cardiovascular compromise. This is presumed to be safer by providing improved cardiovascular stability than using higher doses of inhalants alone. Other anesthetic adjunctive techniques, including nonopioid analgesic constant rate infusions (lidocaine and ketamine) and local and regional anesthesia (epidurals, peripheral nerve blocks, and local anesthetics), are aimed at reducing the requirement of maintenance anesthetics in the interest of cardiovascular stability.
Local and regional analgesia
Local anesthetics have the distinct advantage of blocking peripheral nerve function as compared to other analgesic drug classes (opioids and nonsteroidal anti-inflammatory drugs) that modulate the ascending nociceptive stimuli. If nociceptive stimuli are completely prevented from reaching higher centers, then, theoretically, a patient would not require general anesthesia despite painful surgery or procedures. Although this may not be practical for most procedures, it reminds us that local anesthetics are a powerful tool in preventing pain perception or ascending nociceptive information. For patients under general anesthesia, local or regional anesthesia/analgesia can dramatically reduce systemic and inhaled anesthetic drug requirements. As local anesthetics have minimal cardiovascular compromise at appropriate doses, the reduction in systemic and inhaled anesthetic drug levels can minimize or prevent the cardiovascular depressant effects of these anesthetics, leading to a more stable patient. Numerous studies have shown a significant reduction in inhaled anesthetic requirements due to application of regional anesthesia techniques, including the infraorbital nerve block,69 and methadone epidurals 70 in dogs and morphine/buprenorphine epidurals in cats71 as some examples. However, the use of local anesthetic administration can result in toxicity. For example, the dose of IV lidocaine at which canine patients will develop neurologic signs of toxicity (i.e. convulsions) is \( \sim 22 \text{ mg kg}^{-1} \),72 Bupivacaine has a much lower therapeutic index in that cardiotoxicity and neurotoxicity can be seen at doses between 4.373 and 5.0 mg kg\(^{-1}\) IV,72

Systemic analgesic infusions
Much like local and regional techniques, systemically delivered analgesic infusions have the significant potential for reducing inhaled anesthetic drug doses and responsiveness to painful stimuli. Provided that the cardiovascular side effects of the infusion(s) are not more detrimental than the inhaled anesthetic, the reduction in inhaled anesthetic dose can lead to a significant reduction in their negative consequences, such as negative inotropy, vasodilation, and respiratory depression, thus improving cardiovascular performance. As mentioned previously, IV opioid infusions are particularly beneficial in reducing inhaled anesthetic requirements (Tables 1.2 and 1.3)67,68 and are extremely safe cardiovascular infusions, as their primary side effect is bradycardia, easily treatable with anticholinergics. In horses anesthetized with sevoflurane, an IV lidocaine bolus of 1.3 mg kg\(^{-1}\) followed by a constant rate infusion of 50 mcg kg\(^{-1}\) min\(^{-1}\) reduced sevoflurane MAC by 27%,88 IV lidocaine infusions have been studied in dogs repeatedly for their benefits in reducing both isoflurane and sevoflurane inhaled anesthetic concentrations. Lidocaine at 50 mcg kg\(^{-1}\) min\(^{-1}\) reduced isoflurane MAC by 29%78 and sevoflurane MAC by 22.6%82 in dogs (Tables 1.2 and 1.3). In another study, at 50 and 200 mcg kg\(^{-1}\) min\(^{-1}\), no changes in cardiovascular parameters due to lidocaine infusion(s) were identified, and inhalant MAC was reduced by 15% and 37%, respectively.83

Inotropes and vasopressors
Terminology and definitions confuse these classifications of drugs not only because the term vasopressor is used to refer to both drug categories, but also because of overlapping drug effects. Inotropes or positive inotropes are drugs that increase myocardial contractility by actions on the beta-1 adrenergic receptors and are used to improve SV, CO, and BP. By way of their actions on the beta-1 receptor, these drugs also tend to increase HR, although this is not a positive inotropic effect by the strictest definition. This would be a positive chronotropic effect. Regardless, these drugs are typically referred to by their positive effects on myocardial contractility. Vasopressor is the term applied to drugs that increase SVR via alpha-1 adrenergic or other receptor-mediated vasoconstriction, which subsequently increases BP. Although some drugs are uniquely suited to a single category, an inotrope or a vasopressor, many pharmacologic agents affect multiple receptor subtypes or have varying effects on the basis of dose, and their use in the spectrum of cardiovascular disease is difficult to generalize (Table 1.4).

Dopamine and dobutamine
Dopamine and dobutamine are some of the most commonly applied positive inotropic drugs during veterinary anesthesia. As inhaled anesthetic agents cause dose-dependent suppression of myocardial contractility and decrease SVR, these drugs are highly efficacious for the management of inhaled anesthetic-mediated hypotension.

Dopamine is the immediate precursor to norepinephrine and has dose-dependent positive inotropic
Table 1.2  MAC-reducing effects of common infusions in dogs.

<table>
<thead>
<tr>
<th>Study</th>
<th>Loading dose (mg kg⁻¹)</th>
<th>Infusion dose (mcg kg⁻¹ min⁻¹)</th>
<th>Inhalant</th>
<th>MAC (%)</th>
<th>MAC reduction</th>
<th>MAC-reduction percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fentanyl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ueyama 2009⁷⁴</td>
<td>0.005</td>
<td>0.15</td>
<td>Isoflurane</td>
<td>1.42 ± 0.08</td>
<td>0.93 ± 0.04</td>
<td>−35%</td>
</tr>
<tr>
<td>Hellyer 2001⁸</td>
<td>0.01</td>
<td>0.3</td>
<td>Isoflurane</td>
<td>1.8 ± 0.21</td>
<td>0.85 ± 0.14</td>
<td>−53%</td>
</tr>
<tr>
<td><strong>Remifentanil</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Michelsen 1996⁷⁵</td>
<td>None</td>
<td>1</td>
<td>Enflurane</td>
<td>2.1 ± 0.2</td>
<td>NR</td>
<td>−63 ± 10.4%</td>
</tr>
<tr>
<td>Allweiler 2007⁷⁶</td>
<td>None</td>
<td>0.1</td>
<td>Isoflurane</td>
<td>1.28 ± 0.13</td>
<td>0.78 ± 0.17</td>
<td>−40%</td>
</tr>
<tr>
<td>Monteiro 2010⁷⁷</td>
<td>None</td>
<td>0.15</td>
<td>Isoflurane</td>
<td>1.24 ± 0.18</td>
<td>NR</td>
<td>−43 ± 10%</td>
</tr>
<tr>
<td>None</td>
<td>0.3</td>
<td>Isoflurane</td>
<td>1.24 ± 0.18</td>
<td>NR</td>
<td>−59 ± 10%</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0.6</td>
<td>Isoflurane</td>
<td>1.24 ± 0.18</td>
<td>NR</td>
<td>−66 ± 9%</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0.9</td>
<td>Isoflurane</td>
<td>1.24 ± 0.18</td>
<td>NR</td>
<td>−71 ± 9%</td>
<td></td>
</tr>
<tr>
<td><strong>Ketamine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muir 2003⁷⁸</td>
<td>None</td>
<td>10</td>
<td>Isoflurane</td>
<td>1.38 ± 0.08</td>
<td>1.03 ± 0.07</td>
<td>−25%</td>
</tr>
<tr>
<td>Queiroz-Castro 2006a ⁷⁹</td>
<td>1.0</td>
<td>25</td>
<td>Isoflurane</td>
<td>1.06 ± 0.02</td>
<td>0.73 ± 0.04</td>
<td>−28.7 ± 3.7%</td>
</tr>
<tr>
<td>Doherty 2007⁴  ⁸⁰</td>
<td>1.5</td>
<td>50</td>
<td>Isoflurane</td>
<td>1.11 ± 0.05</td>
<td>0.56 ± 0.04</td>
<td>−49.6%</td>
</tr>
<tr>
<td>Love 2011h  ⁸¹</td>
<td>0.5</td>
<td>6.25</td>
<td>Sevoflurane</td>
<td>2.62 ± 0.21</td>
<td>2.61 ± 0.22</td>
<td>−0.4 ± 4%</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>12.5</td>
<td>Sevoflurane</td>
<td>2.62 ± 0.21</td>
<td>2.06 ± 0.22</td>
<td>−22 ± 4%</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>25</td>
<td>Sevoflurane</td>
<td>2.91 ± 0.21</td>
<td>2.64 ± 0.22</td>
<td>−12 ± 4%</td>
</tr>
<tr>
<td>Wilson 2008⁸²</td>
<td>3.0</td>
<td>50</td>
<td>Sevoflurane</td>
<td>1.9 ± 0.2</td>
<td>1.1 ± 0.1</td>
<td>−40 ± 3.5%</td>
</tr>
<tr>
<td></td>
<td>3.0</td>
<td>100</td>
<td>Sevoflurane</td>
<td>1.7 ± 0.2</td>
<td>0.9 ± 0.1</td>
<td>−44.7 ± 3.5%</td>
</tr>
<tr>
<td><strong>Lidocaine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muir 2003⁷⁸</td>
<td>None</td>
<td>50</td>
<td>Isoflurane</td>
<td>1.38 ± 0.08</td>
<td>0.97 ± 0.04</td>
<td>−29%</td>
</tr>
<tr>
<td>Doherty 2007⁴  ⁸⁰</td>
<td>2.5</td>
<td>100</td>
<td>Isoflurane</td>
<td>1.20 ± 0.04</td>
<td>0.98 ± 0.06</td>
<td>−18.3%</td>
</tr>
<tr>
<td>Matsubara 2009⁸³</td>
<td>2.0</td>
<td>50</td>
<td>Sevoflurane</td>
<td>2.30 ± 0.19</td>
<td>1.95 ± 0.23</td>
<td>−15%</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>200</td>
<td>Sevoflurane</td>
<td>2.30 ± 0.19</td>
<td>1.45 ± 0.21</td>
<td>−37%</td>
</tr>
<tr>
<td>Wilson 2008⁸²</td>
<td>2.0</td>
<td>50</td>
<td>Sevoflurane</td>
<td>2.0 ± 0.2</td>
<td>1.6 ± 0.1</td>
<td>−22.6 ± 3.6%</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>100</td>
<td>Sevoflurane</td>
<td>1.8 ± 0.2</td>
<td>1.3 ± 0.1</td>
<td>−29 ± 3.5%</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>200</td>
<td>Sevoflurane</td>
<td>2.0 ± 0.2</td>
<td>1.1 ± 0.1</td>
<td>−39.6 ± 3.5%</td>
</tr>
<tr>
<td>Valverde 2004⁸⁴</td>
<td>2.0</td>
<td>50</td>
<td>Isoflurane</td>
<td>1.34 ± 0.11</td>
<td>1.09 ± 0.13</td>
<td>−18.7%</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>200</td>
<td>Isoflurane</td>
<td>1.34 ± 0.11</td>
<td>0.76 ± 0.1</td>
<td>−43.3%</td>
</tr>
</tbody>
</table>

aStudy performed in goats.
bStudy evaluated MAC-BAR, the physiologic response to stimulus rather than evaluating for purposeful movement.

effects. The infusion dose of dopamine for beta-1 adrenergic-mediated increases in myocardial contractility, and HR is 5–10 mcg kg⁻¹ min⁻¹. The recommended dose for improvement of CO is 7 mcg kg⁻¹ min⁻¹.⁸⁹ Dopamine actions are unique, as doses above 10 mcg kg⁻¹ min⁻¹ likely stimulate alpha-1 receptors, leading to an increase in SVR. Although this can also be beneficial for BP, it must be noted that this increase in myocardial afterload may, in fact, worsen cardiovascular performance and may be contraindicated in patients with specific cardiovascular diseases such as dilated cardiomyopathy (DCM), HCM, and regurgitant valvular disease. Specific comments regarding positive inotropes and vasopressors are included in the sections of this chapter for each type of heart disease.

Dobutamine is a nonspecific beta-adrenergic agonist, activating both beta-1 and beta-2 receptors and will increase both HR and contractility similar to the beta-1 effects of dopamine. The general recommended dose for dobutamine to achieve beta-1 effects is 1–5 mcg kg⁻¹ min⁻¹. However, it is critically important to understand that dobutamine is also a beta-2 agonist and will induce a decrease in SVR, leading to beta-2-mediated vasodilation. Research has shown that
Table 1.3  MAC-reducing effects of common infusions in cats.

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug</th>
<th>Loading dose (mg kg$^{-1}$)</th>
<th>Infusion dose (mcg kg$^{-1}$ min$^{-1}$)</th>
<th>Inhalant</th>
<th>MAC (%)</th>
<th>MAC reduction</th>
<th>MAC-reduction percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brosnan 200985</td>
<td>Remifentanil</td>
<td>none</td>
<td>0.0625–16</td>
<td>Isoflurane</td>
<td>1.94 ± 0.8</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.125</td>
<td>1.27 ± 0.13</td>
<td>Isoflurane</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferreira 200986</td>
<td>Remifentanil</td>
<td>0.25</td>
<td>0.66 ± 0.08</td>
<td>Isoflurane</td>
<td>1.66 ± 0.08</td>
<td>1.16 ± 0.17</td>
<td>−23 ± 7.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5</td>
<td>1.66 ± 0.08</td>
<td>Isoflurane</td>
<td>1.66 ± 0.08</td>
<td>1.22 ± 0.15</td>
<td>−26 ± 9.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0</td>
<td>1.66 ± 0.08</td>
<td>Isoflurane</td>
<td>1.66 ± 0.08</td>
<td>1.22 ± 0.15</td>
<td>−26 ± 9.4</td>
</tr>
<tr>
<td>Pascoe 200787</td>
<td>Ketamine</td>
<td>2.0</td>
<td>1.51 ± 0.23</td>
<td>Isoflurane</td>
<td>0.84 ± 0.33</td>
<td>−45 ± 17</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0</td>
<td>1.51 ± 0.23</td>
<td>Isoflurane</td>
<td>0.57 ± 0.35</td>
<td>−63 ± 18</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>16.0</td>
<td>1.51 ± 0.23</td>
<td>Isoflurane</td>
<td>0.41 ± 0.35</td>
<td>−75 ± 17</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.4  Inotropes and vasopressors.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Alpha-1</th>
<th>Alpha-2</th>
<th>Beta-1</th>
<th>Beta-2</th>
<th>Dopamine</th>
<th>Vasopressin</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect</td>
<td>Vasoconstriction</td>
<td>Vasoconstriction</td>
<td>Inotropic</td>
<td>Vasodilation</td>
<td>D1 receptor</td>
<td>Vasoconstriction</td>
<td></td>
</tr>
<tr>
<td>Inf: Low</td>
<td>5–10 mcg kg$^{-1}$ min$^{-1}$</td>
<td>Inf: High</td>
<td>10–20 mcg kg$^{-1}$ min$^{-1}$</td>
<td>Inf: 0.01–0.1 mcg kg$^{-1}$ IV</td>
<td>Inf: 0.01–1.0 mcg kg$^{-1}$ min$^{-1}$</td>
<td>Bolus: 0.01–0.1 mcg kg$^{-1}$ IV</td>
<td>Inf: V1++</td>
</tr>
</tbody>
</table>
Canine and feline anesthesia and co-existing disease

the increase in HR and contractility may be offset by the vasodilation, and no change in BP may occur.89

Epinephrine
Epinephrine is a potent alpha- and beta-adrenergic agonist leading to intense peripheral vasoconstriction and increases in HR and contractility, respectively. It dramatically increases myocardial oxygen demand and is highly arrhythmogenic. It is not possible to discriminate effects (i.e. beta effects without alpha effects) with epinephrine and is therefore a poor choice for an inotropic agent, particularly due to the increase in oxygen demand and potential for arrhythmias. Epinephrine should be limited to use for cardiopulmonary cerebral resuscitation (CPCR).

Ephedrine
Ephedrine is similar to an alpha- and beta-adrenergic receptor agonist. However, its effects appear weaker at these receptors. Ephedrine is one of the few inotropic/vasopressive agents that can be delivered by bolus injection, rather than by infusion, as the half-life for activity is longer than most other drugs in this category. Ephedrine bolus leads to increases in BP, cardiac index, and oxygen delivery in dogs anesthetized with isoflurane.90 Onset time is very rapid, and the duration of the increase in BP is shorter than that of the increase in CO. As such, it is useful for short-term treatment of hypotension.

Vasopressin
Vasopressin is the hormone arginine vasopressin (antidiuretic hormone, ADH) and acts as a vasopressor because it increases SVR and has no effect on HR or myocardial contractility. However, it is unique, as it does not affect adrenergic receptors but works through the vasopressin-1 receptor located on peripheral vasculature. Actions at the vasopressin-2 receptor are responsible for the renal effects.91 Since it is not a catecholamine, it is not arrhythmogenic, a significant advantage over other drugs in this group. Vasopressin has been shown to be comparable to phenylephrine for the treatment of hypotension in an endotoxic shock model.92 Although intentionally titrated vasoconstriction can be an important strategy for treatment of refractory hypotension, high levels of SVR may potentially decrease CO and oxygen delivery, particularly in patients with heart disease for which increases in afterload can be severely detrimental such as with DCM.

Phenylephrine and norepinephrine
Phenylephrine and norepinephrine function as vasopressors. Phenylephrine is a pure alpha-1 adrenergic agonist that leads to dose-dependent vasoconstriction and carries the benefits and drawbacks of pure vasoconstrictors as described previously. Norepinephrine has both alpha-1 and beta-adrenergic effects, although in practice, the vasoconstrictive effects predominate, as the beta-2 and beta-1 effects are variable and typically overwhelmed by the alpha response.

Patient monitoring and support

Fluid therapy
As decreases in cardiovascular function and CO are inevitable effects of anesthetics, fluid therapy is recommended to maintain perfusion despite cardiovascular depression. Patients who present with compensated heart disease with no overt clinical signs may tolerate typical rates of IV fluids (balanced electrolyte solutions) during anesthesia, usually in the range of 5–10 ml kg⁻¹ h⁻¹. Patients with evidence of non-compensated cardiovascular disease are often at risk for failure due to poor cardiac function or the cascade of neurohormonal mechanisms that lead to an increase in circulating blood volume such as activation of the renin–aldosterone–angiotensin system (RAAS) and increased secretion of ADH. Patients with a history of heart failure and/or chronic volume overload (mitral, tricuspid, and aortic valve insufficiency, left to right shunts including patent ductus arteriosus [PDA], and ventricular septal defects [VSD]) may be less likely to tolerate high fluid rates during surgery, and so lower fluid rates should be used in these patients. Usually, 3–5 ml kg⁻¹ h⁻¹ is sufficient to meet maintenance metabolic needs but not increase blood volume and risk precipitating heart failure. Furosemide may be used for its’ diuretic effects if the patient receives an excessive amount of IV crystalloid solution. The administration of synthetic colloids (i.e. hetastarch, pentastarch, dextran, and hemoglobin glutamer-200) is often avoided in patients with cardiac disease, as colloids can expand plasma volume for significantly longer periods and are more difficult to treat/reverse with diuretics.
Patient preoxygenation

Most anesthetic premedications and induction agents are respiratory depressants; the most significant of which are the opioids, propofol, and inhaled anesthetic agents. Ketamine is considered a mild respiratory depressant as is etomidate. The onset of respiratory depression can be very rapid, which can result in patient desaturation and cyanosis. The alveolar partial pressure of oxygen (PAO$_2$) is predicted by the alveolar gas equation (Table 1.5).

The following equations are examples of differing conditions during normoxia

\[
\text{PAO}_2 = FIO_2 (Patm - PH_2O) - \frac{PaCO_2}{0.8} \quad (1.1)
\]

\[
\text{PAO}_2 = 0.21(760 - 47) - 40/0.8 = 99.7 \text{ mmHg} \quad (1.2)
\]

\[
\text{PAO}_2 = 0.21(760 - 47) - 60/0.8 = 74.7 \text{ mmHg} \quad (1.3)
\]

and hypoxemia

\[
\text{PAO}_2 = 0.40(760 - 47) - 40/0.8 = 235.2 \text{ mmHg} \quad (1.4)
\]

\[
\text{PAO}_2 = 0.40(760 - 47) - 60/0.8 = 210.2 \text{ mmHg} \quad (1.5)
\]

where FIO$_2$ refers to the inspired fraction of oxygen, Patm is the atmospheric pressure, PH$_2$O is the partial pressure of water vapor, and PaCO$_2$ is the arterial partial pressure of carbon dioxide. In animals that are ventilating normally with a normal PaCO$_2$ of 40 mmHg (Table 1.5, Equation 1.2), the PAO$_2$ is ~100 mmHg. This pressure represents the alveolar pressure of oxygen able to diffuse down the oxygen concentration gradient into pulmonary arterial blood.

As patients hypoventilate, PaCO$_2$ increases which decreases the alveolar partial pressure of oxygen (PAO$_2$) and can result in clinical hypoxemia when PAO$_2$ is less than 80 mmHg. (Table 1.5, Equation 1.3). When providing supplemental oxygen via a tight-fitting facemask (estimated to be a FIO$_2$ of ~40%), PAO$_2$ is subsequently increased (Table 1.5, Equation 1.4), which can blunt the effects of hypoxemia due to hypoventilation (Table 1.5, Equation 1.5). Thus, preoxygenation can be a critical component of maintaining a high PAO$_2$ and arterial partial pressure of oxygen (PaO$_2$) subsequent to anesthetic-related respiratory depression from premedication through the induction process. The general recommendation is to provide oxygen via a tight-fitting facemask for a minimum of 3 min before induction of anesthesia. This can be easily performed as monitoring equipment (ECG, noninvasive BP, capnometry) is placed before induction of anesthesia.

Blood pressure (BP)

BP is the most reliable clinical indicator of perfusion, despite the disadvantage that it is not a clear indicator of CO. BP is a standard monitoring tool for all anesthetized patients and has been the standard of care in humans for decades. The ACVAA Guidelines on Small Animal

<table>
<thead>
<tr>
<th>ETCO$_2$</th>
<th>30</th>
<th>40</th>
<th>60</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIO$_2$ (%)</td>
<td>PAO$_2$</td>
<td>PaO$_2$</td>
<td>PAO$_2$</td>
<td>PaO$_2$</td>
</tr>
<tr>
<td>21</td>
<td>112.2</td>
<td>101.0</td>
<td>99.7$^a$</td>
<td>89.8</td>
</tr>
<tr>
<td>30</td>
<td>176.4</td>
<td>158.8</td>
<td>163.9</td>
<td>147.5</td>
</tr>
<tr>
<td>40</td>
<td>247.7</td>
<td>222.9</td>
<td>235.2$^d$</td>
<td>211.7</td>
</tr>
<tr>
<td>100</td>
<td>675.5</td>
<td>608.0</td>
<td>663.0</td>
<td>596.7</td>
</tr>
</tbody>
</table>

Alveolar partial pressure of oxygen is calculated using the alveolar gas equation: PAO$_2$ = FIO$_2$(Patm-PH$_2$O) – PaCO$_2$/0.8. PAO$_2$ is the alveolar partial pressure of oxygen. FIO$_2$ is the fraction of inspired oxygen. Patm is atmospheric barometric pressure specific to the elevation at or above sea level. PH$_2$O is the vapor pressure of water, which varies by patient temperature but is generally assumed to be ~47 mmHg. PaCO$_2$ is the patient’s current arterial partial pressure of carbon dioxide. PaCO$_2$ divided by 0.8 is the respiratory quotient, which is the ratio of CO$_2$ molecules produced for O$_2$ molecules consumed by the body. The normal alveolar to arterial gradient is ≤10–15% in room air and the PaO$_2$ values calculated in Table 1.5 assume a 10% difference between alveolar and arterial partial pressures. PaO$_2$ is a measured variable with arterial blood gases; the numbers in the above table are calculated as expected normal values on the basis of FIO$_2$ and PaCO$_2$ and measurement at sea level (Patm = 760 mmHg). Refer to equations for values 1.2–1.5 in the body of the text.
Methods of arterial BP monitoring include both noninvasive and invasive techniques. Noninvasive methods include automated oscillometric BP monitors and manual Doppler BP monitoring. Invasive (direct) BP monitoring involves the placement of a catheter into a peripheral artery with connection to a fluid-filled pressure transducer system. All of the techniques have both advantages and disadvantages regarding the ease of placement, frequency and speed of measurement, invasive nature, and technical skill required for measurement and accuracy of measurement.

Invasive BP monitoring is the gold standard with which all other forms of BP measurement are compared. Direct monitoring is the most accurate BP measurement and offers additional benefits of being a continuous, second-to-second monitor for SAP, DAP, and MAP. Acute changes in the patient's hemodynamic status can be appreciated rapidly, and alterations in the arterial pressure waveform can also provide information about patient status. The placement of an indwelling arterial catheter also allows for sampling of arterial blood for arterial blood gas analysis. Invasive BP monitoring has significant drawbacks, including the skill in placing arterial catheters in potentially hypotensive, unstable patients, the requirement for a multiparameter patient monitor with the capability of connecting to a fluid filled transducer system, the understanding of what causes error in the transducer system, and troubleshooting of the system. There is the risk of hemorrhage and reduced perfusion to tissues distal to the catheterization site. Despite these complexities, invasive pressure management is a mainstay of advanced cardiovascular monitoring.

Noninvasive pressure monitoring includes both automated oscillometric monitoring devices and Doppler ultrasound BP monitoring. Oscillometric monitoring devices use the principle of oscillometry to determine BP. An automated cuff is inflated above SAP, occluding arterial blood flow. As cuff pressure is reduced, the arterial pulse begins to generate oscillations in the arterial wall that are transmitted to the cuff. These oscillations increase and then decrease in amplitude as cuff pressure is reduced, and eventually the oscillations are eliminated as blood flow becomes laminar. Although technology and calculation algorithms vary between oscillometric devices, generally, the onset of oscillations is considered SAP, maximal oscillation amplitude MAP, and the cessation of oscillations DAP. Oscillometry carries the advantage of automation and ease of use. However, oscillometric devices are fraught with error, including inappropriate cuff size. The cuff should be ~40% of limb circumference; overlarge cuffs lead to inappropriately low readings, and inappropriately small ones lead to falsely elevated measurements. Other issues with oscillometric devices include motion artifacts and interference from high HRs or potentially cardiac arrhythmias. Studies comparing the accuracy of oscillometric BP cuffs to direct BPs found limited agreement with MAP and DAP in anesthetized dogs: “67% and 95% of readings were within 10 and 20 mmHg of invasive pressure values, respectively.” Another study found poor correlation such that a 25-mmHg bias was identified between invasive and oscillometric pressure in anesthetized cats. Oscillometric BP devices also carry the disadvantages of slow performance compared to continuous arterial catheters.

Doppler BP devices use a BP cuff that is manually inflated over SAP. A Doppler crystal is placed over a peripheral artery, and blood flow is audibly demonstrated with appropriate Doppler sound. Inflation of the cuff occludes flow, and the Doppler signal is lost. As the cuff is manually deflated, blood flow begins to pass through the cuff and is again audible via the Doppler crystal. This is generally interpreted as the peak pressure or SAP. Doppler BPs can be checked manually more frequently than oscillometric devices, carry more confidence for the user in that the user can hear blood flow, provide an audible signal to the anesthetist that there is a blood flow (a comforting sound for many anesthetists), and are simple to use. A Doppler crystal placed over a peripheral artery provides the anesthetist with an audible signal for blood flow, which can be a strong comfort for those moments the anesthetist’s attention cannot be on the patient or patient monitor. The placement of Doppler crystal also allows for a second assessment of BP should an arterial catheter fail. Disadvantages of Doppler crystals include that they are somewhat fragile, require more skill for placement to obtain an audible signal, and show inability to accurately predict SAP. For example, multiple studies have evaluated the assessment of SAP with Doppler noninvasive measurement compared to invasive BPs. In cats, poor agreement was found between invasive SAP and Doppler BPs, such that the Doppler underestimated SAP by ~14 mmHg.
to −25 mmHg.98,99 Doppler BP measurement was not recommended when accuracy is desired. However, in rabbits, direct SAP was found to have good agreement with Doppler BP.107

**Electrocardiography (ECG)**

ECG monitoring allows analysis of the cardiac rhythm. Understanding the components of the cardiac rhythm and how it relates to mechanical function of the heart allows the anesthetist to analyze the rhythm for changes that would indicate abnormalities. These abnormalities might imply that there is asynchrony in mechanical function of the heart and further correction may improve mechanical function, CO, and perfusion. Although ECG monitoring does not “prove the patient is alive,” as there can be dissociation between the electrical and mechanical activity (termed pulseless electrical activity, PEA), it is nevertheless a basic requirement of patient monitoring during anesthesia.

**Pulse oximetry**

Saturation of hemoglobin in arterial blood is an important component of the CaO₂ equation. As the vast majority of oxygen is carried in the hemoglobin molecule, the degree to which hemoglobin is saturated with oxygenated blood is a critical variable in oxygen delivery. The pulse oximeter is a simple tool that measures the oxygen saturation of arterial blood (SpO₂). Hemoglobin saturation of ~90% is correlated with a PaO₂ of ~60 mmHg, well into the hypoxic range. Therefore, a hemoglobin saturation of >93–94% is required to ensure normoxia. Many variables can interfere with the ability of the pulse oximeter to provide an accurate arterial saturation (Table 1.6).110

**Table 1.6  Pulse oximetry: sources of error.**138–140

<table>
<thead>
<tr>
<th>Source of Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motion artifact</td>
</tr>
<tr>
<td>Thickness of tissue</td>
</tr>
<tr>
<td>Tissue hypoperfusion/hypotension</td>
</tr>
<tr>
<td>Vasocostriction</td>
</tr>
<tr>
<td>Hypothermia</td>
</tr>
<tr>
<td>Tissue pigment</td>
</tr>
<tr>
<td>Met-hemoglobinemia (tends to 85% when Met-Hgb ~30%)</td>
</tr>
<tr>
<td>Carboxy-hemoglobinemia (tends toward 90%)</td>
</tr>
<tr>
<td>Intravenous dye injections (indocyanine green, methylene blue)</td>
</tr>
<tr>
<td>Ambient light at 660, 920 nm wavelength(s)</td>
</tr>
<tr>
<td>Severe anemia (hemoglobin &lt; 5 g dl⁻¹)</td>
</tr>
</tbody>
</table>

**Core body temperature**

Hypothermia has varying effects on the basis of the degree of body temperature loss.² Essentially, all patients will become hypothermic to some degree due to the effects of premedication and induction of anesthesia, unless active heat support is provided. Causes of hypothermia include, but are not limited to, opioid, phenothiazine and alpha-2 adrenergic-mediated changes in thermoregulation, high surface area to body mass ratio, high cold-compressed oxygen flow rates, open body cavities, cold surfaces, room temperature IV fluids, cold scrub solutions, and body cavity lavage (especially orogastric lavage with fluids below body temperature). Mechanisms for heat loss include evaporation, conduction, and convection and heat loss from respiration and radiant heat loss.111 Anesthetized patients also have decreased heat production due to central depression and inability to shiver in response to hypothermia. It is far easier to prevent than it is to treat hypothermia, as the peripheral vasoconstrictive effects of hypothermia make external rewarming difficult and inefficient. Consideration of the aforementioned variables for an individual patient or procedure will help the anesthetist generate a robust heat loss prevention or rewarming plan.

The physiologic effects of hypothermia vary with severity and include catecholamine release, decreased cerebral metabolic rate of oxygen consumption and intracranial pressure, and altered electroencephalogram and arterial blood gas results.112,113 At moderate levels, hypothermia decreases inhalant requirements, reduces concentrations of inhalant required to produce apnea, decreases CO and BP, and increases SVR. In addition, moderate hypothermia results in bradycardia, prolonged clotting times, decreased drug metabolism, prolonged nerve conduction and muscle contraction, and a left shift of the oxygen–hemoglobin dissociation curve (which favors hemoglobin loading).114 With these profound physiologic changes, it is clear that body temperature should be controlled in any anesthetized patient and especially in one who may have preexisting cardiovascular compromise, as they may lack the reserves to compensate.

**Capnometry and ventilation**

Capnometry is the assessment of exhaled carbon dioxide as an indicator of ventilatory adequacy. Capnometry refers to the measurement of end-exhalation (end-tidal)
CO₂; a capnograph provides a visual waveform display of the measurement of CO₂ over time. However, the term capnography is often used to imply all of these components. Hypoventilation is defined by an increase in the PaCO₂ with a subsequent increase in end-tidal CO₂ levels. Hypoventilation leads to respiratory acidosis and should be avoided in patients with cardiac disease, as ideal cardiac function occurs at normal blood pH; acute respiratory acidosis has been shown to increase HR and CO but decrease myocardial contractility and SVR. Hypercapnia increases catecholamine release, and can result in tachyarrhythmias from the combination of acidosis, electrolyte changes due to acidosis, and carbon dioxide-mediated increases in catecholamine release. It is possible to roughly estimate the change in pH on the basis of the increase in PaCO₂; for every 10–20 mmHg increase in PaCO₂, arterial pH will decrease by ~0.1 pH unit.

Assisted or controlled ventilation can be helpful in maintaining normoventilation, to optimize oxygenation (SpO₂ or PaO₂) and improve inhaled anesthetic depth. Mechanical ventilation can be provided either with a controlled mechanical ventilator or with intermittent assisted manual ventilation (“bagging”). It is nearly impossible to provide the same consistency, tidal volume, respiratory rate, peak inspiratory pressure, and duration of inspiration with manual ventilation as compared to mechanical ventilation, and the use of mechanical ventilators is strongly recommended to maintain this consistency and allow the anesthetist to attend to other tasks.

However, mechanical ventilation can and very often will decrease BP by one of three mechanisms. Firstly, tidal volume via mechanical ventilation is very likely to be larger than that of a spontaneously taken breath. Therefore, mechanical ventilation represents an increase in anesthetic delivery via a larger number of isoflurane molecules being delivered with a larger tidal volume. Inhaled anesthetics subsequently cause dose-dependent decreases in BP, mediated by decreases in myocardial contractility and SVR. Secondly, increases in intrathoracic pressure during positive pressure ventilation decrease venous return (i.e. preload), leading to reduced SV, CO, and BP. The effects on CO are more pronounced with more frequent respiratory rates, longer inspiratory phase duration, and larger tidal volumes.

Lastly, high PaCO₂ can increase sympathetic tone and improve BP, an effect that is reduced when patients are ventilated to a normal or even low end-tidal CO₂.

**Arterial blood gases**

Arterial blood gas analysis is a useful direct measurement of PaO₂ and PaCO₂ to evaluate pulmonary function and quality of ventilation. Serial monitoring of arterial blood gases can allow the anesthetist to better direct adjustments in ventilation to maintain oxygenation and normal carbon dioxide levels. The availability of arterial catheters allows for continuous invasive pressure monitoring, as well as serial blood sampling for clinical pathology. Normal values for arterial blood gas values are presented in Table 1.

**Central venous pressure (CVP)**

Central venous pressure (CVP) is the intraluminal pressure measured in the intrathoracic vena cava immediately outside the right atrium. CVP is the difference in pressure between the atmosphere and IV at this location. It is often used as an indicator of right ventricular preload and overall patient intravascular volume status, as well as in assessment of right heart function and critical patient care monitoring. However, right ventricular preload is truly defined by the difference between the intracardiac (i.e. right ventricular) and extracardiac transmural pressure gradient. A variety of factors can reduce preload but lead to an increase in measured CVP, which may lead the clinician to erroneously interpret an increase in preload. These include changes in intrathoracic pressure (changes in stage of ventilation, pleural effusion, and abdominal hypertension) and blood volume or cardiac arrhythmias. Decreases in right ventricular compliance also can increase CVP, as end-diastolic filling pressures can be elevated with a “stiff” ventricle, pericardial disease, or pericardial tamponade. Ultimately, CVP represents the balance between volume return to the heart and cardiac function. There are many excellent, in-depth published reviews of CVP monitoring. Although CVP monitoring requires a complete understanding of these variables and the ability to trend values over time, it can be a valuable tool in monitoring patients under anesthesia in select cases.
Anesthetic and pharmacologic recommendations for specific cardiac diseases

Valvular heart disease
Introduction
Valvular heart disease accounts for over 50% of congenital heart disease in dogs; chronic AV valvular disease is the most common cardiac disease in dogs, whereas mitral valve insufficiency is in the top three causes of cardiac disease in cats. The prevalence of valvular disease in small animals necessitates a complete understanding of these comorbidities and how they affect and dictate the perianesthetic plan.

Preanesthetic evaluation
A common misconception is that most heart murmurs do not definitively require complete cardiac evaluation before anesthesia is planned and that all patients with heart disease must be managed similarly when anesthetized. As with any anesthetic patient, patients with underlying cardiac disease should be evaluated with a complete history (detailing both the long- and short-term changes in underlying disease), PE, and minimum database of bloodwork/urinalysis relevant for their signalment. In addition, patients with cardiac disease should be evaluated with thoracic radiographs, ECG, BP, and ECG, which are aimed at not only documenting presence of disease, but also assessing the severity of disease and possible response to previous treatments. As one of the main goals of perianesthetic management is maintenance of homeostasis, especially perfusion and oxygen delivery, preanesthetic cardiac evaluation should include assessments for cardiac pump function.

Degenerative mitral valve disease (dMVD)
Incidence and pathophysiology
Degenerative mitral valve disease (dMVD) is the most common cardiac disease in dogs, found in as much as 30% of the geriatric canine population. dMVD can also be referred to as myxomatous mitral valve degeneration, endocardiosis, degenerative valvular disease, and myxomatous degeneration; all these terms describe the same constellation of pathophysiologic and clinical signs. dMVD is grossly seen as an idiopathic development of nodular irregularities on the free edge of mitral valve leaflets. These nodules consist of deposition of mucopolysaccharides in the layers of the valve leaflet, which can increase in size and number over time. Pathophysiology of dMVD may also include distortion of the chordae tendineae such that they lengthen and/or thicken. When valve changes are severe, this leads to curling of the valve leaflet and subsequent AV valve incompetence. The valve may degenerate to the point at which valve leaflets can prolapse into the left atrium. When valvular changes are sufficient that leaflets do not oppose one another during ventricular systole, regurgitant flow of blood into the left atrium results. Mitral valve regurgitation may be trivial or severe, and volume of regurgitation is dictated by the size of the space between the valve leaflets, the pressure gradient between ventricle and atra, and the duration of systole. Mitral regurgitation leads to a volume overload on the left atrium, as pulmonary venous return is complemented by regurgitant flow. CO suffers as regurgitant flow increases, and the body compensates with renal, neurohormonal, and cardiac remodeling (left ventricular eccentric hypertrophy). High atrial pressures due to volume overload lead to atrial dilation, as well as increases in pulmonary vein pressures and congestion of pulmonary venous flow, which will eventually lead to pulmonary edema. Congestive heart failure (CHF) is the end result of chronic volume overload to the left atrium and pulmonary veins with eventual failure of adaptive mechanisms.

Physical examination findings
Dogs may present with lethargy, cough, exercise intolerance, weight loss, respiratory difficulty, or collapse. Patients may also present with other complaints, and a murmur may be auscultated in a patient with no previous history of cardiac disease. It is these patients who often require a more cautious approach to evaluation and anesthesia planning, a lack of clinical signs may provide a false sense of security with regards to potential anesthetic complications. The classic heart murmur for dMVD is a holosystolic murmur, loudest over the left apex of the heart. The intensity of the murmur tends to be consistent over the duration of
Canine and feline anesthesia and co-existing disease

systole, with no increase or decrease in the loudness of the murmur. Often, the second heart sound is inaudible. The intensity of the murmur is not correlated with the severity of regurgitant flow, but in general, louder murmurs indicate worse regurgitation. Pro-lapse of the mitral valve may result in a midsystolic click.

**Anesthetic management**

Anesthetic management can cover the spectrum from patients with fully compensated, nonclinical disease to those at high risk for heart failure. No consensus statements exist regarding the management of either end of this spectrum. Patients with stable, compensated disease with no left atrial enlargement and no clinical signs of pulmonary edema or heart failure generally do not require intensive management. As a portion of left ventricular ejection regurgitates into the left atrium, CO is compromised, and the patient with dMVD is thought to compensate for this with increases in HR. Normal to high normal HRs are recommended for any particular signalment. Therefore, it is optimal to consider anticholinergics in the anesthesia plan, particularly if opioids are to be administered. Opioids are considered to be extremely safe as part of an anesthesia plan for a patient with dMVD, as the cardiovascular effects are primarily limited to bradycardia, which is easily treated or prevented with the use of anticholinergic. Hypothermia should be avoided by using supplemental heat support to avoid hypothermia-related bradycardia.

Stable patients should tolerate inductions with ketamine and diazepam/midazolam. Alternatively, they should tolerate the dose-dependent vasodilation with propofol induction; however, the dose of propofol should be minimized using preanesthetic sedatives and/or combining propofol with benzodiazepines and/or opioids during induction. The severe negative inotropic effects and mild to moderate vasodilation associated with inhaled anesthetics can be minimized by additional use of local, regional, or systemic sedatives and analgesics. Opioids are well suited for this purpose. Alpha-2 adrenergic agonists are contraindicated due to the severe increase in afterload and the potential for increased regurgitant flow, as well as severe decreases in HR and CO.

Unstable patients, such as those at significant risk for onset of heart failure or a previous history of heart failure, those with arrhythmias, or those with preexisting cardiovascular compromise must be handled with extreme caution. Preinduction stabilization of heart failure, hypotension, and arrhythmias must be attempted. Complete cardiac evaluation (PE, thoracic radiographs, ECG, BP, and echocardiogram) is optimal. Anesthetic management includes all efforts made to minimize or mitigate the cardiovascular compromise due to inhaled anesthetics and reliance on balanced anesthesia. As stated previously, alpha-2 adrenergic agonists are contraindicated. Sedation with opioids and benzodiazepines is recommended, as they have minimal effects on cardiovascular function; opioid-mediated bradycardia can be minimized or prevented with anticholinergics.

Although optimal sedation is ideal, oftentimes, good sedation has to be sacrificed in the name of cardiovascular stability, as induction of anesthesia is approached. Midazolam followed quickly by etomidate is a good induction choice because they have minimal to no cardiovascular side effects. Fentanyl and midazolam may also be used for induction, provided opioid-associated bradycardia (and respiratory depression) are controlled and the patient is sufficiently sedated beforehand or is quite compromised. Alternatively, some patients may require induction with propofol despite the risk of dose-dependent vasodilation and hypotension. In these situations, reducing the dose of propofol with preinduction sedation and/or combining propofol with one (i.e. midazolam) or two (i.e. midazolam/fentanyl) additional induction drugs can minimize propofol doses. Inhaled anesthetic dose should similarly be minimized with additional local, regional, or systemic analgesics and sedatives. Monitoring in patients with severe mitral valve disease should include either Doppler noninvasive BPs or invasive BP monitoring.

**Mitral valve stenosis (MVS)**

**Incidence and pathophysiology**

Mitral valve stenosis (MVS) is a rare finding in dogs, with only 12 reported cases in a 10-year period in one reference. Stenotic lesions may involve the valve annulus, leaflets, chordae tendineae, or papillary muscles and present as a valvular or supravalvular lesion. The heart murmur associated with MVS is a mid-diastolic low frequency murmur and possibly a split S2. The stenotic lesion creates a pressure gradient across the valve and leads to an increase in left atrial pressure, which is transmitted to the pulmonary vasculature and can lead to pulmonary edema with
severe stenosis. Diagnosis of MVS may be made only when a patient presents with left heart failure and the defect is identified with echocardiography. The treatment for MVS is frequently medical, as surgical options are extremely high risk and should only be considered when all alternatives have been exhausted. The goal of medical intervention is to manage signs of left-sided heart failure and to decrease left atrial pressure and signs of left heart failure with diuretics and angiotensin-converting enzyme (ACE) inhibitors. Sodium restriction is recommended in humans and small animals. Additional treatment may be required for supraventricular arrhythmias such as atrial fibrillation or supraventricular tachycardia (SVT).

**Anesthetic management**

Anesthetic management of these patients largely depends on the severity of clinical presentation. The anesthetic goal is to prevent any situation wherein CO is significantly impaired or they are put at risk of development of pulmonary edema. With MVS, CO can be decreased by multiple mechanisms. For example, as MVS worsens in severity, ventricular filling depends increasingly on diastolic filling time and right atrial pressure. Tachycardia or tachyarrhythmias will decrease diastolic filling time and worsen ventricular filling and subsequently CO. Loss of association between atrial depolarization or the atrial kick boosting end-diastolic volume (10–30% of end diastolic volume) and ventricular contraction/ejection will worsen CO. Therefore, arrhythmias affecting AV coordination should be treated rapidly in these cases. Atrial fibrillation and SVTs can develop, while anesthetized and the ECG should be evaluated before and through induction of anesthesia. Acute vasodilatation and decreases in atrial preload may worsen ventricular filling, as the normal response to acute hypotension is tachycardia. Lastly, the pressure overload to the pulmonary vasculature from MVS can precipitate pulmonary edema. Avoidance of increases in blood volume that has the potential for precipitating CHF is strongly recommended.

Patients with mild MVS can likely be managed with any anesthetic plan with the exception of ketamine and tiletamine. Both dissociative agents will increase catecholamine release, which increases sympathetic tone, leading to tachycardia and increases in myocardial contractility. If diastolic filling time decreases significantly, CO can drop precipitously. Similarly, tachycardia from patient stress, anxiety, and pain can decrease CO. Good preanesthetic sedation is optimal to prevent tachycardia. Opioids and benzodiazepines are attractive options, as they do not significantly decrease HR, contractility, or vascular tone. While some opioids are good sedatives, benzodiazepines are inconsistent sedatives in small animals and can precipitate mild dysphoria or excitement in dogs and undesirable behavioral changes including potentially aggression in cats. Anticholinergic agents are controversial in that they can precipitate tachycardia. However, anticholinergics can be indicated if there is a preexisting bradycardia or second-degree AV block. Patients with mild disease can likely tolerate the vasodilation associated with propofol for induction, but combination with an opioid (propofol-fentanyl) or benzodiazepine (propofol-midazolam) is recommended to reduce the total dose of propofol. If patients have severe disease with significant cardiovascular compromise, anesthetic induction can be achieved with etomidate or fentanyl in combination with a benzodiazepine. Monitoring of patients with MVS also depends on their degree of disease and anticipated complications. Patients with mild disease can likely be monitored as for any patient. Patients with advanced disease may require invasive BP monitoring, arterial blood gas assessment to evaluate pulmonary function, and CVPs. Patients with severe disease may warrant referral to specialty centers for consultations with veterinary cardiologists and anesthesiologists for management.

**Tricuspid valve stenosis (TVS)**

**Incidence and pathophysiology**

Tricuspid valve stenosis (TVS) as an independent finding is rare in small animals, and tricuspid valve incompetence is far more often due to tricuspid valve dysplasia or is the result of underlying cardiac disease. Similar to MVS, it may result from abnormalities of the annulus, valve leaflets, or papillary muscles. Labradors or breeds at risk for AV valve disease such as Newfoundlands and Bull terriers may be at higher risk.

**Anesthetic management**

Should TVS be identified as an isolated finding, recommendations for anesthetic management are the same as MVS. Given the rarity of isolated TVS, other causes for tricuspid valve incompetence must be investigated in patients who have suspicion of tricuspid valve disease.
Aortic stenosis (AS)
Incidence and pathophysiology

Aortic stenosis (AS) is the most common congenital cardiac disease of large breed dogs such as Boxers, Great Danes, Rottweilers, Golden Retrievers, German Shepherds, English Bulldogs, and Bouvier des Flandres and has been described as heritable in Newfoundlands. Subvalvular aortic stenosis (SAS) can be due to valvular, supravalvular, and subvalvular lesions; however, SAS is the most common finding in dogs representing more than 95% of lesions identified. The site of SAS is the left ventricular outflow tract (LVOT), which comprises the membranous and muscular portions of the basilar inter-ventricular septum, the cranialateral left ventricular free wall, and the anterior mitral valve leaflet.

AS can be described as fixed or dynamic. Fixed SAS is due to an anatomic abnormality creating the stenotic lesion; the severity of the obstruction does not change with rate or velocity of flow through the area. Fixed SAS has been graded in cadavers depending on the anatomic findings. For example, grade 1 has minor changes (endothelial nodules) in the subaortic endocardial surface, grade 2 has a narrow fibrous band around part of the LVOT, and grade 3 has a complete band of tissue surrounding the entire LVOT. Dynamic SAS is an obstruction in the LVOT that changes on the basis of the rate of flow through the subaortic outflow tract. Increases in HR or cardiac contractility lead to a decrease in intraluminal pressure (on the basis of the Bernoulli principle) and an increase in the degree of LVOT obstruction (LVOTO). Dynamic SAS is most commonly identified in HCM and can be referred to as hypertrophic obstructive cardiomyopathy (HOCM).

The principal hemodynamic consequence of outflow tract obstruction is an increase in resistance to systolic ejection of blood from the ventricle, thereby decreasing flow through the outflow tract, increasing pressure across the stenosis, or both. Left ventricular pressure is increased and results in compensatory concentric hypertrophy to maintain left ventricular output. The ejection of blood through the stenotic area results in turbulence of blood during systole and a resultant systolic murmur, typically described as an ejection murm that increases and then decreases (crescendo-decrescendo) through systole. SAS and LVOTO along with the left ventricular hypertrophy typically do not lead to left-sided heart failure. However, left ventricular hypertrophy, a decrease in capillary density, and increased wall tension predispose to myocardial ischemia. Patients who develop this pathophysiology are at risk for syncope, ventricular arrhythmias, and sudden death, although it is unclear which of these is the definitive cause of death. Another possible explanation for sudden death is exercise-induced increases in left ventricular pressure (in addition to pathologically high resting left ventricular pressure) and activation of ventricular mechanoreceptors that lead to vasodilation and bradycardia; the Bezold-Jarisch reflex. Damage to aortic valve leaflets from high velocity regurgitant jet flow can predispose the valves to bacterial endocarditis associated with bacterial shower from surgical or dental procedures or from concurrent noncardiac infectious causing bacteremia. Prophylactic antibiotics are recommended for all anesthetized procedures to minimize the risk of endocarditis.

Anesthetic management

Anesthetic management in patients with SAS can become very complicated and requires intensive monitoring and antiarrhythmic treatments to maintain normal ventricular filling and optimal CO. Patients should remain in a normal sinus rhythm without sinus tachycardia or bradycardia, and one should be prepared to treat ventricular ectopy or atrial fibrillation. For example, left ventricular CO is dependent on the organization of atrial and ventricular contraction. Thus, AV blocks or atrial fibrillation will lead to loss of the atrial kick and reduction of left ventricular end-diastolic volume. Sinus tachycardia prevents diastolic filling time and should be avoided. Sinus bradycardia leads to poor CO and hypotension, subsequently leading to poor coronary and myocardial perfusion in a thickened left ventricle. Thus, HR should be kept in the normal range to prevent decreased tissue perfusion. Ventricular premature complexes (VPCs) cause contraction before complete ventricular filling and lead to a decrease in CO. Prompt treatment of ventricular ectopy is important, as the presence of ventricular rhythms can be a risk factor for sudden death.

Premedication in patients with moderate to severe AS should provide adequate sedation/analgesia to prevent anxiety, pain, or stress-related tachyarrhythmias. Anticholinergic agents are indicated to prevent bradycardia and AV blocks. The administration of Acepromazine is controversial due to long acting vasodilation but may be tolerated in the minimally affected patient if anxiety is