Chapter 19

Monitoring Anesthetized Patients

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Introduction

The purpose of anesthesia is to provide reversible unconsciousness, amnesia, analgesia, and immobility for invasive procedures. The administration of anesthetic drugs and the unconscious, recumbent, and immobile state, however, compromise patient homeostasis. Anesthetic crises are unpredictable, and tend to be rapid in onset and devastating in nature. The purpose of monitoring is to achieve the goals while maximizing the safety of the anesthetic experience.

The purpose of preoperative monitoring is to determine the existence and magnitude of abnormal processes that might compromise a patient's response to anesthesia and the operative procedure, and to guide the development of the anesthetic plan. The preoperative assessment provides the basis for tailoring drug selection and the intraoperative and postoperative monitoring and support to the specific needs of the patient. Intraoperative monitoring, the subject of this chapter, focuses on insuring an optimum anesthetic depth with minimal physiological impairment. The purpose of postoperative monitoring is to warrant a full and complete recovery from the anesthetic state and to provide adequate analgesia.

Anesthetic Mortality

Anesthetic issues and problems are common, but mortality from them is rare. The difference is in the monitoring, which can lead to the early recognition and correction of the problem. Such events, when they are easily rectified, are seldom even defined as problems. An adverse event that threatens the life or causes the death of a patient is universally defined as a problem. Perioperative cardiac arrest, as opposed to the problem(s) that could potentially cause it, is objective and not likely to be underrecognized. Such mortality analyses may help define when and what should be monitored during anesthesia.

Earlier studies reported a perioperative mortality rate of 20 to 189 per 10,000 patients administered anesthetics.[1–4] Anesthesia contributed to 2.5 to 9.2 deaths per 10,000 patients administered anesthetics. Mortality rates were higher among patients with poorer preoperative physical status and greater age where biological reserves are limited, and among patients undergoing emergency procedures where preoperative planning and preparation are limited, but were still of notable frequency in young, healthy patients undergoing planned procedures. Of the deaths, 1% occurred at induction, 10% to 30% intraoperatively, 10% early postoperatively, and the remainder over the ensuing days.[3,4] Intraoperative causes of death included the primary disease process; aspiration; hypovolemia and hypotension; hypoxia secondary to airway or endotracheal tube problems, or pneumothorax; misdosing of drugs; and hypothermia. Postoperative causes of death included the primary disease process, arrest during endotracheal tube suctioning, aspiration, pneumonia, and heart failure.

Perioperative mortality was reported to be 8.8/10,000 patients administered anesthetics in a recent study of human patients.[5] Deaths attributed entirely to anesthesia were quite uncommon (0.1/10,000), but anesthetic-contributed mortality (anesthesia in combination with surgery and augmented by the underlying disease) was 1.4/10,000. In addition, there was a 0.5/10,000 incidence of postoperative coma 1 day after anesthesia. Of anesthesia-related deaths, 17% occurred in American Society of Anesthesiologist (ASA) classification 1 or 2, 45% in ASA class 3, and 38% in ASA class 4 or 5 patients. Of the deaths, 29% occurred intraoperatively, 6% in recovery, and the remainder postoperatively. No deaths were recorded at the time of induction, which is a notoriously dangerous point in the anesthetic experience. Many problems were noted during induction, but no deaths resulted from them. Of the anesthesia-related deaths, 52% involved cardiovascular problems (hypovolemia and inadequate volume replacement, hypotension and hypertension, ventricular arrhythmias, or heart failure), and 10% involved respiratory problems (inadequate oxygenation, airway problems, aspiration, or ventilatory failure). Metabolic problems were a distant third category.[6] Inadequate preoperative preparation was thought to occur in 25%, and inadequate monitoring in 10%, of the anesthesia-related deaths.

In a survey study reported in 1990, cardiac arrests, 55% of which were fatal, occurred in 2.6 per 10,000 patients administered anesthetics.[7] Anesthesia was thought to play a role in 45% of these cardiac arrests. Of anesthesia-related deaths, 23% occurred in ASA classification 1 or 2, 17% in ASA class 3, and 61% in ASA class 4 or 5 patients. Of the cardiac arrests, 47% were thought to be due to preventable causes, the most common of which were errors in drug administration and hypoxia.

A veterinary study in 1998 cited a complication rate of 2.1% in 8087 dogs and 1.3% in 8702 cats, and an overall mortality rate of 0.1% (10/10,000 anesthetics).[8]

Life-threatening perioperative problems, and therefore the thrust of monitoring, seem to focus on the cardiopulmonary system, although other organ systems and metabolic issues cannot be ignored. Certain patient groups appear to represent greater risk, although anesthesia and operation represent great risk to any patient. Critically ill patients are somewhat advantaged because we know in advance to pay special attention. Healthy patients undergoing routine procedures are perhaps disadvantaged if we let our guard down because we are not expecting a problem. Monitoring encompasses (a) assuring an appropriate anesthetic level and (b) guarding against excessive physiological impairment.

Monitoring Anesthetic Level

The purpose of assuring an appropriate level of anesthesia is to minimize the detrimental effects of excessively light levels of anesthesia (awareness, recall, pain, and movement), as well as those of excessively deep levels of anesthesia (hypoventilation and hypoxemia; reduced cardiac output, hypotension, and inadequate tissue perfusion; hypothermia; and prolonged recovery). The term *anesthetic depth* is somewhat of an anachronism because it is based on the concept that anesthetic agents cause progressive depression of central nervous system (CNS) function. It is clear that anesthetic agents have different mechanisms of action on the CNS, most of which are depressant, but some of which are stimulant.[9] Consciousness might better be represented as a sphere, as opposed to a line. When cortical function is pushed outside the boundaries of this sphere (in any direction) (as opposed to below a line), unconsciousness occurs. Consciousness might be viewed as a state of organized CNS function, and anesthesia as a state of disorganized CNS function produced by facilitated or impaired neurotransmitter release or receptor receptivity. The terms *level of anesthesia* and *anesthetic depth*, however, are familiar and are used in this chapter, but refer to the relationship between anesthetic-induced CNS function and the center of the *sphere of consciousness*.

The state of *general anesthesia* is defined as the lack of awareness of all aspects of one's environment (including pain). Anesthetic drugs, administered in small dosages, may cause sedation, but not anesthesia. There are, of course, degrees of sedation or obtundation between fully awake and anesthetized, but there is no consensus as to what to call them. An animal that is visibly lethargic, sluggish, and depressed, but is spontaneously aware of its environment, might be described as being mildly sedated or obtunded. An animal that is "sleeping" and does not appear to be aware of (or care about) its environment when unstimulated, but that is readily awakened with verbal or light tactile stimulation, might be described as being moderately sedated or obtunded. An animal that awakens only with strong tactile or noxious stimulation might be described as being more sedate or obtunded, whereas anesthetized or comatose patients cannot be awakened even by strong, painful stimulation. Some sedative drugs (e.g., opioids), even in high dosages, do not induce anesthesia reliably. Some sedative drugs administered in small dosages do not even induce sedation, but can decrease a patient's apprehension or anxiety: This is *tranquilization*. Tranquilizers (phenothiazines and benzodiazepines) can never be anesthetics, but they can potentiate the anesthetic effects of anesthetics. Anesthetic drugs, if dosed judiciously, can act as tranquilizers, sedatives, or true anesthetics. Opioids can induce an anesthesia-like state in high dosages, but, if used alone, spontaneous movement in animals and awareness in people are not uncommon.

Analgesia is the lack of awareness of nociceptive stimuli. Some agents (e.g., opioids and nitrous oxide) are good analgesics, but are not particularly good at inducing loss of awareness (anesthesia). Some anesthetic drugs (barbiturates, propofol, etomidate, halothane, and sevoflurane) are good anesthetics but have no analgesic qualities (in subanesthetic dosages). These agents can be used for surgical procedures, however, because, once anesthetized, animals lose their ability to perceive pain. The eminent problems with these agents are the variation in anesthetic depth associated with nociceptive stimulation during the operative procedure and the lack of postoperative analgesia. Some agents (ketamine and isoflurane) are good anesthetics, as well as good analgesics.

There are also levels of anesthesia. In Guedel's classic description of anesthetic depth,[10] loss of consciousness defines the border between stages I and II, and the cessation of spontaneous muscle movement the border between stages II and III (the surgical stage of anesthesia). In the lighter plane of stage III, a hemodynamic response and muscular movement in response to noxious stimuli might still be present, but stage II provided a comfortable margin between these responses and awareness of the noxious stimulus. A hemodynamic response or reflex muscular movement in response to a noxious stimulus proved a light level of surgical anesthesia and yet the patient was far removed from being aware of the noxious stimulus: the ideal anesthetic level. This is an important concept either to accept or to reject because it bears directly upon the philosophy of much of the recent research that equates a hemodynamic response, an electroencephalographic (EEG) response, or a muscular movement response to a noxious stimulus with the conscious awareness of pain.

One of the major goals of anesthesia is that the patient should lack awareness during the procedure. Amnesia is often listed as one of the goals of anesthesia, but it is somewhat of an oxymoron. If the first goal is met, then there is nothing to forget. It would hardly be philosophically acceptable to allow awareness of pain during the operative procedure, as long as the patient forgot about it afterward. It turns out that the first goal (lack of awareness) is not always met, but that awareness, and discomfort and pain, are also not synonymous. There is also a naturally high incidence of amnesia afterward. Awareness probably occurs considerably more frequently than people remember it.[11] In one study, 20 patients were deliberately awoken intraoperatively from propofol anesthesia and asked to perform cognitive tasks, and then were reanesthetized for completion of the surgical procedure.[12] Only 35% of these patients could remember the experience. Awareness, it turns out, is a very difficult thing to study because it can be studied only by asking patients whether they remember anything. There is also the difference between spontaneous, explicit recall of specific events and implicit, nonspecific recall that can be obtained only with extensive questioning or hypnosis. Explicit recall is often better 1 week after surgery than it is after 1 day, so the study results depend on when the question is asked. The incidence of explicit awareness in people is cited to be about 0.2%.[13] Intraoperative awareness is also not always associated with intraoperative pain nor posttraumatic suffering, but when it is, it is a serious problem.[13] Many reports of awareness in people are associated with insufficient dosages of anesthetic; for example, in cesarean section when fetal depression is a concern, and in cardiac and trauma patients where anesthetic-induced cardiovascular depression is a concern.[13] The easiest way to prevent intraoperative awareness is to provide adequate amounts of anesthetic. Preventing movement, hemodynamic, and EEG response to surgical stimulation, although not necessary in most patients, would seem to be the best means of minimizing intraoperative awareness in all patients.

In general, patients lose recall at the lightest levels of anesthesia first, awareness second, movement in response to a nociceptive stimulus third, and a hemodynamic or EEG response to a nociceptive stimulus fourth, with increasing anesthetic depth. For halothane, MAC_{awake} (minimum alveolar concentration [MAC] to prevent response to verbal command in 50% of patients: awareness) is about 0.4%; $MAC_{incision}$ (MAC to prevent muscular movement in response to a strong surgical stimulus) is about 0.9%; and MAC_{BAR} (MAC to block the autonomic response to skin incision) is about 1.1%.[14] The MAC_{awake} and the $MAC_{incision}$ were reported to be 0.39 and 1.3 for isoflurane and 0.61 and 2.0 for sevoflurane, respectively.[15] Patients maintained at an end-tidal anesthetic concentration that is sufficient to prevent movement in response to surgical stimulation, let alone sufficient to prevent a hemodynamic response, have a 2½- to 3-fold anesthetic margin between them and awareness. The *bispectral index* (BIS) is a processed electroencephalogram that quantifies the degree of anesthetic-induced cortical electrical depression. A value below 60 is associated with loss of recall, below 50 with the loss of awareness, below 40 with the loss of muscular movement in response to a noxious stimulus, and below 20 with burst suppression (deep anesthesia). MAC_{BAR} and MAC_{BIS} (the MAC associated with an increase in BIS to 60 in response to nociceptive stimulation) were reported to be about the same in cats.[16] BIS has been used to help ensure that patients are well anesthetized, pain free, and unaware.[13,17]

A hemodynamic or EEG response or movement in response to a nociceptive stimulus does not mean that an animal is consciously aware of the stimulus; the evidence seems to be quite contrary to this assumption. These reactions might represent the ideal anesthetic level (light, but not too light). However, in the clinical practice of anesthesia, since a 100% lack of awareness is the goal, maintaining a depth of anesthesia that is free of hemodynamic, EEG, and movement response to surgical stimuli, as long as the cardiovascular system can handle it, would seem to maximize the likelihood of achieving the lack-of-awareness goal. Spontaneous movement during anesthesia is, however, a characteristic of some anesthetic agents (opioids, etomidate, and propofol) and is not synonymous with inadequate anesthetic depth.

Anesthetic level represents the balance between the amount of drug(s) administered, the amount of surgical stimulation (which tends to awaken patients), and the severity of illness (which tends to synergize the anesthetic). Anesthetic requirements change over time (with an overall decreasing trend) within a single anesthetic experience, because of variations in the magnitude of surgical stimulation, the gradual filling of redistribution sites, and variations in body temperature. It would not be appropriate to maintain initial vaporizer settings or drug infusion rates for the duration of the operative procedure, because animals would invariably be excessively anesthetized by the end of the procedure. Anesthetists should repeatedly try to decrease the amount of anesthetic administered during the course of an anesthetic. Since the dosage of anesthetic required for a patient cannot be predicted, however, the administration of each anesthetic should be considered a clinical experiment. If the signs of anesthetic depth suggest that an animal's anesthesia level is getting too light, then perhaps the anesthetic dose should be returned to its previous setting; unless, of course, one is at the end of the operative procedure: then light is right. The challenge is to keep the animal in a light to medium level of anesthesia; that is, deep enough to abate conscious perception and to provide adequate muscle relaxation, yet light enough that the signs of anesthesia clearly indicated that the animal is not too deeply anesthetized.

Single, point-in-time measurements are meaningful when they are severely abnormal; an animal that is prematurely leaving the operating table of its own will is a problem at the moment, and it does not matter what depth was assessed 5 min earlier. For the most part, though, measurements and evaluations are interpretable only in the context of previous measurements (the palpebral reflex at the moment, compared with what it was 15 min earlier) and with reference to other related parameters. (If an animal is scrambling to leave the table, who cares whether it has a palpebral reflex?) Given the mechanistic differences between anesthetic drugs and interindividual differences in response to them, monitoring of anesthetic level is, at best, very uncertain. It is nevertheless the explicit responsibility of anesthetists to ensure that these drugs are administered in the safest possible way by monitoring the animal's response to them.

Physical Signs of Anesthetic Depth

These depend, for the most part, on the evaluation of muscular tone and muscular reflexes. The signs of anesthetic depth vary from moment to moment, from individual to individual, and between species and anesthetic drugs. No one sign alone defines anesthetic depth. Assess as many signs as possible. They invariably suggest different levels of anesthesia, one sign suggesting a light level, one medium, and one deep, and the anesthetist is left to sort it all out. Observers should prioritize the signs (some are more reliable than others) and then average their findings (medium in the aforementioned example). The presence of a sign is much more meaningful than the absence of it. For instance, in most species and with most anesthetics, the presence of a palpebral reflex is a reliable sign of a light level of anesthesia. The absence of a palpebral reflex suggests that the level is not light. In some individuals, though, the sign is unreliable, and the level is light despite the absence of the reflex. When the signs of anesthetic depth are unclear or contradictory, anesthetic drug administration should be decreased until the animal is clearly at a light to medium level of anesthesia. Lastly, know that there is no obligatory correlation between level of anesthesia and physiological consequence of anesthesia; a light level does not preclude severe hypotension or hypoxemia. These are some points to remember:

1. The recent history of anesthetic dosing is an important component of the evaluation of the depth of anesthesia: Large dosages should be associated with a deep level of anesthesia and vice versa. The vaporizer setting or the drug infusion rate helps define the amount of anesthetic being delivered to a patient. End-tidal anesthetic concentrations and plasma drug concentrations define the amount of anesthetic in a patient. Usual vaporizer settings, drug administration rates, and end-tidal and plasma concentrations that are appropriate for induction (loading) and then maintenance for the various common anesthetics are discussed elsewhere in this text (Chapters 8 through 16). The issue here is that the anesthetic drug dosing is just the beginning of the evaluation of the depth of anesthesia, not the definition of it. "Usual" dosages may cause excessive anesthesia in animals with serious underlying disease and hypothermia. Normal anesthetic drug dosages do not guarantee that an animal will not be overanesthetized. Equally important is that vaporizers and infusion pumps do not always work properly, and normal settings may actually overshoot or undershoot the mark. Knowledge of anesthetic drug dosing and knowledge of the amount of drug "on board a patient" define only what they measure and are not the definition of anesthetic depth in an individual patient. You are going to need more information.

2. Spontaneous movement is a reliable sign of a light level of anesthesia with most anesthetics. Focal muscle twitching has been associated with etomidate and propofol administration and should not be interpreted, per se, to indicate a light level. Spontaneous muscular movement is common with opioid-based anesthetic protocols and also should not be interpreted to indicate a light level. Muscle hypertonus can be a feature of ketamine-based protocols and should not be interpreted to indicate a light level.

3. Reflex movement in response to surgical stimulation is a reliable sign of a light level of anesthesia. It does not, however, mean that an animal is experiencing pain from a nociceptive stimulus.

4. An abrupt increase in heart rate, blood pressure, or breathing rate, specifically in response to surgical stimulation, is generally considered to be a reliable sign of a light level of anesthesia. In general, physiological parameters such as heart rate, arterial blood pressure, breathing rate, and minute ventilation should trend upward as an animal becomes more lightly anesthetized and downward when an animal becomes deeply anesthetized. These are not, however, reliable *premonitory* indicators of anesthetic depth; they are often observed to be quite stable until after an animal abruptly awakes or suffers cardiovascular collapse. There are also many abnormalities that affect these parameters (in either direction) that have nothing to do with anesthetic level. Anesthetic level is only one of the differentials that should be considered when an animal develops a decreased or increased heart or breathing rate.

5. Mandibular muscle tone should be *lots*, *some*, and *none* in light, medium, and deep levels of anesthesia, respectively, in dogs and cats. The descriptors lots, some, and none must be indexed to the species and breed of an animal; one would never expect a cat to have the same muscle tone as a mastiff. Mandibular muscle tone is assessed by the resistance encountered when trying to just open the mandible. Puppies never have any mandibular muscle tone, and this parameter cannot be used to evaluate their depth of anesthesia. Large animals always have much muscle tone and this parameter cannot be used to evaluate their depth of anesthesia. Ruminants and swine exhibit a chewing reflex when they are lightly anesthetized.[18]

6. A change to an abdominal (diaphragm)-first breathing pattern signals a deeper level of anesthesia, as does bradypnea and hypoventilation.

7. The presence of a palpebral reflex is a reliable indicator of a light level of anesthesia. The absence of it suggests a medium or deep level. The goal would be an anesthetic depth where the palpebral reflex is either just barely present or just barely absent. Some individuals fail to exhibit a palpebral reflex even though their anesthesia level is actually light. With ketamine use, the palpebral reflex is always present and the eyelids remain open as opposed to the effect of most other anesthetics on this parameter.

8. The presence of a *pupillary light reflex* (pupillary constriction in response to a bright light shined upon the retina) and the presence of a *dazzle reflex* (a blink in response to a bright light) are reliable indicators of a light to light to medium level of anesthesia. The pupillary light reflex may be minimized or eliminated by parasympatholytics.

9. In small animals, with traditional anesthetics, eyeball position is central (and the pupil size is medium) when the animal's anesthesia level is light, is rotated ventromedially when the level is medium, and is central again (and the pupil is dilated) when the level is deep. The eyeball does not rotate when ketamine is used. In horses, the eyeball can rotate, though not reliably so, but spontaneous nystagmus does occur. A very slow, "roving" eyeball ("one minute it's here; the next it's over there") might represent a medium level of anesthesia, whereas a fast nystagmus represents a very light level in this species. Nystagmus may occur in light levels of anesthesia in ruminants and swine, but disappears at deeper levels. In these species, the eyeball rotates ventrally with deeper levels of anesthesia. Nystagmus does not normally occur in anesthetized small animals.

10. The lack of tear production as noted by a dry-appearing cornea is a sign of a deep level of anesthesia with traditional anesthetics. Lacrimation or "tearing" is seen in horses and is a sign of a light level.

11. The gag and swallow reflexes are reliable indicators of a light level of anesthesia in nearly all species.

EEG: Monitoring of Anesthetic Depth

Typically, the EEG pattern changes from a low-wave, high-frequency pattern during the awake state to high-wave, low-frequency with anesthesia to burst suppression (intermittent periods of electrical silence) and finally persistent electrical silence with deep levels of anesthesia. The raw EEG signals, however, require a considerable volume of recording and considerable specialized training and expertise to interpret subtle changes. Computerized analysis of raw EEG signals facilitates interpretation of those signals. EEG voltage changes (power) as a function of time (time domain) generate such indices as total EEG power, median power frequency, or burst suppression. Interpretational algorithms (by fast Fourier transformation) might also examine signal activity as a function of frequency (frequency domain) and generate such indices as spectral edge frequency (SEF_{95}) (the frequency below which 95% of the total EEG power resides), median frequency (the median EEG power frequency), and the relative power of the delta (0.5 to 3.5 Hz), theta (3.5 to 7.0 Hz), alpha (7 to 13 Hz), and beta (13 to 30 Hz) frequency ranges compared with total EEG power.[19] Such indices have been used to characterize anesthetic depth in people[6,20–22] and animals.[23–26] Other indices[27] and combinations of indices,[28] BIS and Narcotrend (Monitor Technik, Bad Bramstedt, Germany), may represent a more integrated approach to EEG analysis compared with the classic indices[19,22] and may be more user-friendly.

BIS analysis (Aspect Medical Systems, Newton, MA) represents a variably weighted value derived from four subparameters: (a) burst suppression ratio (time domain); (b) a quasi value (time domain); (c) β_2 power ratio in the 30- to 47-Hz range compared with that in the 11- to 20-Hz range (frequency domain); and (d) the bispectral biocoherence ratio of peaks in the 0.5- to 47-Hz range compared with the 40- to 47-Hz range (frequency domain).[17] BIS has been extensively studied in humans primarily as an index of sedation[29,30] or depth of anesthesia.[16,22,26,31–34] It has also been used as an index of brain function in neurological patients.[35,36] The BIS monitor does not require calibration and displays a bar graph denoting signal quality and amount of electromyographic interference. Excessive muscle movement can be a problem.[37] The monitor displays a number between 0 and 100: Values above 90 are compatible with awake and alert, 80 to 90 with anxiolysis, 60 to 80 with hypnotic or moderate obtundation, below 60 with loss of recall, below 50 with unresponsiveness to verbal stimuli, below 20 with burst suppression, and 0 with isoelectric stimuli (Aspect Medical Systems). Not all anesthetics affect BIS in the same way: Propofol, midazolam, and thiopental strongly depress it, inhalational anesthetics have an intermediate effect, opioids have little effect, and nitrous oxide and ketamine tend to increase the BIS value.[17]

Narcotrend analyzes the raw EEG data and then categorizes the levels of sedation as awake (A0), subvigilant (A1 and A2), sedation (B0, B1, and B2), anesthesia (C0, C1, and C2), moderate anesthesia (D0, D1, and D2), deep anesthesia or burst suppression (E), and coma/electrical silence (F).[38]

Auditory evoked EEG responses have been used primarily to assess neurological function in CNS disease, but have also been used to assess anesthetic depth and awareness or recall.[39] Many studies have used sensory (to a noxious stimulus)-evoked EEG or BIS, hemodynamic responses, and movement responses to evaluate nociception.

All EEG indices are subject to large individual and anesthetic drug variation. Depending on the magnitude of the stimulation and the depth of anesthesia, stimulus-induced EEG changes could represent either an arousal pattern or a pattern that suggests a deeper level of anesthesia (the *paradoxical* response).[23,40] The EEG changes do not reflect analgesic properties of an anesthetic drug, per se, but only its hypnotic properties. No EEG index has yet replaced physical evaluation of patients and common sense, although several indices clearly aide the evaluation of anesthetic depth, reduction of anesthetic drug dosages, and shortened recovery times.[38]

Monitoring Perioperative Pain and Analgesia

Nociception is the neural response to a noxious stimulus. *Pain* is the conscious interpretation that the nociceptive stimulus is sufficiently unpleasant to motivate its owner to do something about it. The evaluation of pain is more simple in communicative people (you ask them) than in neonates and animals. The existence of pain in an animal and the need for analgesic therapy depend on the observation of behavioral changes or abnormalities that can reasonably be attributed to pain. Unfortunately, none of the

"pain signs" are specific to pain; many nonpainful situations cause them, as well.

Physical Signs of Pain

It might be helpful to divide pain into levels of magnitude: mild, moderate, and severe. *Severe pain* might be defined as that which is intolerable; the kind of pain where the animal throws itself about its cage in a mindless frenzy because the pain is so severe that it simply cannot deal with it in any other way. Unprovoked vocalizing (crying or whimpering) by an animal that does not have CNS disease and is not recovering from anesthesia, but does have a disease that might be painful, is taken as evidence of severe pain. *Mild pain* might be equated with that amount which one would consider to be a nuisance and not necessarily of such magnitude that its owner would seek out pain-relief medications. Such an animal can tolerate it well and can usually go about its normal daily activity. Since the pain does not interfere with behavior in any fashion, it defies recognition by an outside observer.

Moderate pain may be described as that which starts to interfere with normal behavior, appetite, or activity of an animal that has a disease or that has undergone a surgical procedure or experienced a trauma that is reported to be painful in people. The animal may exhibit an anxious expression and may not rest comfortably, and may be unable to sleep. The animal is less concerned with happenings in its environment. Appetite may be decreased or absent and the animal may lose weight, energy, or productivity. The animal's activity may be decreased (if the animal is trying to minimize pain associated with movement). It may just lie in one spot for extended periods with its eyes open, staring into space without focusing on anything in particular. The animal's activity may become increased (if the animal is trying to find a position wherein the pain is diminished), and the animal may assume abnormal positions. The animal may move, but infrequently, and stiffly, as though to guard and protect the painful area. The attitude may also change to that of an animal that is less tolerant to being handled than normal. The attitude may become more fearful or more aggressive.

The pain may be classified as moderate if an animal develops an anxious expression or tenses when the area in question is about to be touched, or if it cries out or responds aggressively when the area is touched (assuming that these represent inappropriate responses for this particular individual or species to an otherwise innocuous stimulus). Secondary physiological changes that may result from pain are tachycardia, tachypnea, hypertension, arrhythmias, dilated pupils, salivation, and/or hyperglycemia.

EEG: Monitoring of Analgesia

The EEG indices measure brain electrical activity that changes in an approximately consistent pattern with anesthetic depth in such a way that one can predict with some accuracy when a patient loses awareness, recall, and response to a noxious stimulus. EEG changes observed in response to nociceptive stimulation generally reflect a lighter level of anesthesia, although a "paradoxical arousal" response, reflective of a deeper level, is common.[23,40] These EEG indices are not a measure of pain, per se, but of a cortical response to the nociceptive stimulus, in the same way that movement or a change in heart rate may occur in response to a nociceptive stimulus. These responses do not prove that an animal is experiencing pain, but only suggest a cortical electrical response to the nociceptive stimulus; the animal may or may not be experiencing pain.

Most studies use the EEG indices to measure the ability of various drugs to diminish a response to a specifically timed, induced surgical stimulus (such as an incision).[40–43] Although the administration of nitrous oxide did not affect 95% spectral edge frequency or BIS in the absence of surgical stimulation,[44] it was associated with a dose-dependent decrease in these parameters when administered during major lumbar surgery.[45] Although the administration of fentanyl did not affect 95% spectral edge frequency or BIS, per se, it prevented the decrease in these indices (paradoxical response) associated with skin incision.[43] Both results were attributed to the analgesic properties of the drugs. In a novel approach to studying preemptive analgesia, when the spectral edge frequency was maintained within the target range of 8 to 12 Hz, postoperative pain scores and morphine requirements were reduced.[46] There are no analgesia monitors per se, but only monitors of the cortical electrical response to nociceptive stimuli. When a drug diminishes the EEG response to a nociceptive stimulus, it is often presumed to be because of its analgesic qualities (unless, of course, it is because of its hypnotic qualities).

Analgesia assessment in the postoperative period is a different challenge from that of a specific, timed, nociceptive stimulus in the intraoperative period. Postoperatively, pain is pretty much ongoing. The objective might be to return the EEG index and the patient to a state that is relaxed, sedate, and pain free (that is clearly not an arousal nor a paradoxical arousal state) and to maintain them in that state. In EEG terms, this might be an SEF_{95} of 8 to 12 Hz or a BIS value below 60. In physical examination terms, this is represented by behavior which suggests that the animal is comfortable and reasonably pain free. The EEG indices are not likely to be particularly helpful in weaning an animal off of analgesic drugs; that is, in determining when it is okay to withdraw them and allow an animal to return to a normal, aroused, drug-free, pain-free state.

Important Concepts in the Provision of Analgesia

The administration of analgesic drugs prior to the nociceptive stimulus (preemptive analgesia) is thought to reduce the *ramping up* process (amplification of the nociceptive signal) by the modulatory interneurons within the spinal cord. Preemptive analgesia reduces the magnitude of postoperative pain as well as the dosages of analgesics administered.

Animals cannot truly be evaluated for pain during the recovery phase (the reflex phase) of anesthesia. Nevertheless, excessive vocalizing and activity during this time should be subdued with a sedative; they can cause the animal's owner considerable angst. Ensure that the source of the discomfort is not a full urinary bladder (animals typically receive a large volume of fluids during surgery and often do not urinate).

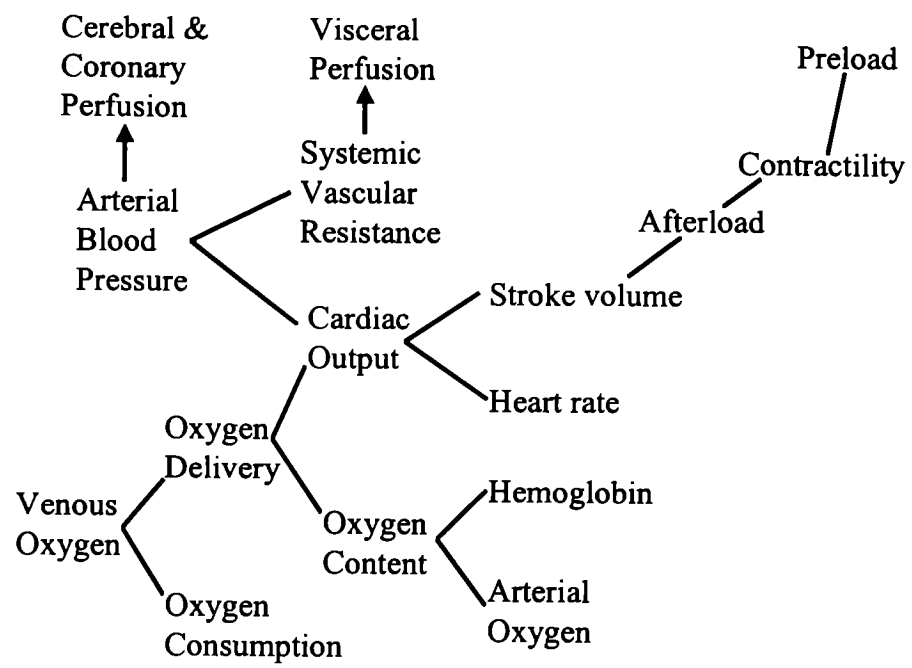

Fig. 19.1. Integration of cardiopulmonary performance.

In the postoperative period, after the evaluation of pain signs, because they are not specific, one is invariably left with doubt as to whether an animal is experiencing pain. In the end, the decision is subjective. Animals should subjectively appear to be comfortable, respond to human interaction normally, sleep, eat and drink, and move about with ease. If they do not present a comfortable picture, something should be done. Analgesic drugs are not without potential adverse effects, and there is sometimes great hesitancy to administer them to treat a problem that one is not sure exists. The relative risks, however, are low and by far outweighed by the potential harm associated with unremitting pain. When it is unclear whether an animal is experiencing undue pain and when it is unclear whether analgesics should be administered, it is appropriate to administer a full dose of an analgesic.

Free nerve endings transduce pressure, heat, or chemical nociceptive stimuli into an electrical signal (transduction) that is then transmitted to the spinal cord, brain stem, and thalamus (transmission). In the dorsal horn of the spinal cord, nociceptive signals can be diminished or augmented by ascending or descending interneuronal pathways (modulation). The somatosensory cortex then integrates, interprets, and quantifies the nociceptive stimulus (perception). Different analgesic drugs affect nociception at different levels of the process, and this justifies the use of drugs with multilevel effects and the use of multiple drugs to take advantage of their differential foci of effect. Transduction can be inhibited by local anesthetics, opioids, and antiprostaglandins; transmission by local anesthetics and α_2-agonists; spinal modulation by local anesthetics, opioids, α_2-agonists, *N*-methyl-D-aspartate antagonists (ketamine), antiprostaglandins, and anticonvulsants; and perception by general anesthetics, opioids, α_2-agonists, and tranquilizers (phenothiazines).[47]

When one or two dosages of an analgesic fail to alleviate the "pain signs," chances are that pain was not the problem in the first case. The use of anxiolytics may be indicated. Acepromazine (0.01 mg/kg) has been remarkably effective; diazepam (0.2 mg/kg) may or may not be effective.

Physiological Consequences of the Anesthetic State

Although the pharmacodynamic effects of the various anesthetic drugs vary, the mechanisms by which they cause morbidity and mortality are the same: excessive bradycardia, arrhythmias, myocardial depression, vasodilation, hypotension, hypoventilation, hypoxemia, or hypothermia. These common problems should be the focus of intraoperative monitoring of organ function. Ongoing, automatic, audible monitors of organ function are the mainstays of intraoperative monitoring and crisis prevention. Single, point-in-time measurements are meaningful when their results are severely abnormal: A heart rate of zero is a problem at the moment, and it does not matter what it was 15 min earlier. For the most part, though, measurements and evaluations are only interpretable in the context of previous measurements (trends) and with reference to related parameters (Fig. 19.1). A dog's heart rate of 50 beats/min may not be a problem if blood pressure and cardiac output are adequate to meet the tissue perfusion needs of the patient, or may even be an appropriate compensation if the arterial blood pressure is high. Some expected cardiopulmonary changes associated with the administration of various anesthetic agents are listed in Tables 19.1 (dogs) and 19.2 (horses).

Cardiovascular Monitoring

Heart Rate and Rhythm

Heart rate and stroke volume are important to cardiac output. Slower heart rates are usually associated with larger end-diastolic

Table 19.1. Cardiopulmonary effects of general anesthesia in dogs.

	Awake[a]	Ketamine[b]	Oxymorphone[c]	Halothane[d]	Pentobarbital[e]
HR	90 ± 21	166 ± 44	72 ± 14	97 ± 13	107 ± 20
CI	4.65 ± 1.09	6.55 ± 2.23	4.13 ± 1.13	3.22 ± 0.62	4.26 ± 0.51
CVP	3 ± 4	2 ± 4	12 ± 4	2 ± 1	NR
PAOP	5 ± 2	NR	15 ± 2	5 ± 2	NR
ABPm	104 ± 12	139 ± 13	112 ± 10	64 ± 9	118 ± 18
PAPm	15 ± 4	17 ± 6	21 ± 4	10 ± 2	17 ± 3
SVRI	(1787)	(1696)	(2166)	(1588)	(2215)
PaO_2	100 ± 6	96 ± 7	81 ± 6	540 ± 46	90 ± 7
PvO_2	50 ± 5	50 ± 5	49 ± 5	81 ± 8	51 ± 3
$PaCO_2$	40 ± 3	41 ± 6	50 ± 2	45 ± 8	43 ± 5
A-aPO_2	10 ± 5	6 ± 3	(14)	(120)	12 ± 5
Ven admix	4 ± 3	3 ± 3	13 ± 6	6 ± 1	7 ± 3
Hb	13.1 ± 1.7	14.9 ± 1.9	16.3 ± 1.8	14.0 ± 2.2	14.0 ± 1.0
DO_2	(801)	(1273)	(854)	(656)	(771)
VO_2	(149)	(230)	(153)	(84)	(126)
O_2 extr	(0.19)	(0.18)	(0.18)	(0.13)	(0.16)

HR, heart rate (beats/min); CI, cardiac index (L/min/m^2); CVP, central venous pressure (cm H_2O); PAOP, pulmonary artery occlusion pressure (mm Hg); ABPm, mean arterial blood pressure (mm Hg); PAPm, mean pulmonary arterial blood pressure (mm Hg); SVRI, systemic vascular resistance index (dynes · s · cm^{-5}); PaO_2, arterial partial pressure of oxygen (mm Hg); PvO_2, venous partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide (mm Hg); A-aPO_2, alveolar-arterial PO_2 gradient (mm Hg); Ven admix, venous admixture (%); Hb, hemoglobin (g/dL); DO_2, oxygen delivery (mL/min/m^2); VO_2, oxygen consumption (mL/min/m^2); O_2 extr, oxygen extraction (%).
Data expressed as mean ± 1 SD. Numbers in parentheses were recalculated from the available data.
[a]In unsedated, calm, recumbent dogs breathing room air
[b]15 min after ketamine (10 mg/kg) administered intravenously.
[c]75 min after 0.4 mg/kg oxymorphone, administered intravenously, followed by 0.2 mg/kg at 20, 40, and 60 min.
[d]30 min after mask induction and intubation with halothane.
[e]40 min after pentobarbital induction.

Table 19.2. Cardiopulmonary effects of general anesthesia in horses[58,59].

	Awake	Isoflurane (1.2 MAC)/ Halothane (1.0 MAC)
HR	37 ± 2	43 ± 5/39 ± 2
CI	69 ± 3	59 ± 8/35 ± 3
ABPm	133 ± 12	92 ± 5/98 ± 9
PAPm	29 ± 2	25 ± 2/26 ± 1
SVRI	333 ± 18	285 ± 28/579 ± 56
PaO_2	507 ± 14	318 ± 46/360 ± 28
PvO_2	52 ± 6	57 ± 4/ND
$PaCO_2$	45 ± 1	73 ± 4/65 ± 2

HR, heart rate (beats/min); CI, cardiac index (L/min/kg); ABPm, mean arterial blood pressure (mm Hg); PAPm, mean pulmonary arterial blood pressure (mm Hg); SVRI, systemic vascular resistance index (dynes · s · cm^{-5}); PaO_2, arterial oxygen partial pressure (mm Hg); PvO_2, venous partial pressure of oxygen; $PaCO_2$, arterial carbon dioxide partial pressure (mm Hg).
Data expressed as mean ± 1 SD.
MAC, minimum alveolar concentration; ND, not done.

ventricular volumes and larger stroke volumes; up to a point, cardiac output is preserved by the larger stroke volumes.[48] Heart rate is too slow when it is associated with low cardiac output, hypotension, or poor tissue perfusion. In lieu of this kind of evidence or a reasonable cause for the bradycardia, values of 60 beats/min for dogs, 90 for cats, and low 20s for horses are common triggers for treatment. Common causes and treatment for bradycardia are listed in Table 19.3. Verify that the problem is truly bradycardia as opposed to a slow pulse rate, which could be caused by ventricular arrhythmias. Excessive vagal tone can be caused by pharyngeal, laryngeal, or tracheal stimulation; by pressure on the eyeball or rectus muscles; or by visceral inflammation, distension, or traction.

Sinus tachycardia is primarily a sign of an underlying problem (Table 19.4). It becomes a problem for patients only when there is not enough time for diastolic filling: Cardiac output decreases. In people, because of coronary artery disease, sinus tachycardia is feared because the increased myocardial oxygen consumption may exceed oxygen-delivery capabilities. In lieu of cardiac output information, the trigger level for specific treatment of sinus tachycardia may be somewhere in the low 200s for dogs, the high 200s for cats, and 80 for horses.

Ventricular arrhythmias, in an animal that did not have them prior to anesthesia, are primarily a sign of an anesthetic-induced complication (Table 19.5). Make sure that the electrocardiographic abnormality is truly of ventricular origin as opposed to a right bundle branch block, which appears similar to a ventricular rhythm except that it is preceded by a P wave. Ventricular arrhythmias may also be caused by intrinsic myocardial disease or arrhythmogenic factors released from various debilitated abdominal organs. Ventricular arrhythmias become a problem for a patient when they interfere with cardiac output, arterial blood pressure, and tissue perfusion, or when they threaten to convert to ventricular fibrillation. Ventricular arrhythmias should be treated when (a) the minute-rate equivalent approaches the trigger point for treating sinus tachycardia, (b) they are multiform, or (c) the ectopic beat overrides the T wave of the preceding depolarization. Total elimination of the ventricular arrhythmia is not necessarily the goal of therapy, because large dosages of antiarrhythmic drugs have deleterious cardiovascular and neurological effects. A simple decrease in the rate or severity of the arrhythmia may be a suitable end point to the titration of antiarrhythmic drugs (Table 19.6).

Table 19.3. Causes of perioperative bradycardia.

Cause	Treatment
Anesthetic overdosage	Lighten the level of anesthesia
Opioids	Administer a parasympatholytic
α_2-Agonists	No treatment
Excessive vagal tone caused by visceral stimulation	Less stimulation; parasympatholytic
Hypothermia	Rewarm
Hyperkalemia	Calcium or insulin-glucose therapy
Sick sinus syndrome	Administer a parasympatholytic or sympathomimetic
Atrioventricular conduction block	Administer a parasympatholytic or sympathomimetic
End-stage metabolic failure	Administer a parasympatholytic or sympathomimetic
Hypoxia	Administer oxygen
Parasympathomimetics (e.g., acetylcholine-sterase inhibitors)	Administer a parasympatholytic
Organophosphates	Administer a parasympatholytic
Digitalis	Administer a sympathomimetic

Table 19.4. Causes and treatment of tachycardia.

Cause	Treatment
Too light a level of anesthesia	Deepen the level of anesthesia
Ketamine	No treatment
Parasympatholytics (e.g., atropine)	Give less or by the subcutaneous or intramuscular route the next time; glycopyrrolate
Sympathomimetics	Decrease the infusion rate
Hypovolemia	Restore blood volume
Hyperthermia	Cool
Hypoxemia	Administer oxygen
Hypercapnia	Improve ventilation or eliminate rebreathing
Individual variation	No treatment
Paroxysmal supraventricular rhythm	Administer verapamil or diltiazem
Recovery phase	No treatment
Postoperative pain	Administer analgesics
Pheochromocytoma	Sypatholytic

Table 19.5. Causes of ventricular ectopic pacemaker activity.

Endogenous release of catecholamines or sympathomimetic therapy
Hypoxia or hypercapnia
Hypovolemia or hypotension
Myocardial inflammation, disease, or stimulation (intracardiac catheters or pleural tubes)
Thoracic and nonthoracic trauma
Certain anesthetics lower the threshold to endogenous or exogenous catecholamines (halothane, xylazine, thiamylal, or thiopental)
Hypokalemia (potentiated by respiratory or metabolic alkalosis, or glucose-insulin therapy)
Hyperkalemia (potentiated by acidosis, hypocalcemia, succinylcholine, or may be iatrogenic)
Visceral organ disease (gastric volvulus and/or torsion)
Intracranial disorders (increased pressure or hypoxia)
Digitalis toxicity (potentiated by hypokalemia and hypercalcemia)

Ventricular arrhythmias can be caused by several mechanisms that are not readily apparent from the electrocardiographic appearance of the arrhythmia: (a) abnormal automaticity characterized by rapid, spontaneous, phase 4 depolarization; (b) reentry of depolarization wave fronts because of unidirectional conduction blocks; (c) early after-depolarizations caused by diminished repolarizing potassium currents prolonging action potentials; and (d) delayed after-depolarizations caused by abnormal oscillations of cytosolic calcium concentrations after myocardial or Purkinje cell repolarization. A given antiarrhythmic may be effective in one mechanism and be ineffective, or even worsen the arrhythmia, in another. Antiarrhythmic therapy is always a bit of a clinical trial. Lidocaine is a first-choice antiarrhythmic because it selectively affects abnormal cells without affecting automaticity or conduction in normal cells.

Vasomotor Tone

Peripheral and visceral perfusion is primarily regulated by vasomotor tone. Vasodilation improves peripheral perfusion, whereas vasoconstriction impairs it. Vasodilation is a potent cause of hypotension, whereas vasoconstriction increases blood pressure. Vasomotor tone is assessed by mucous membrane color (pale = vasoconstriction, whereas red = vasodilation), capillary refill time (<1 s = vasoconstriction, whereas >2 s = vasodilation), toeweb to core temperature gradient (>4°C = vasoconstriction, whereas <2°C = vasodilation). Vasoconstriction may be caused by hypovolemia, heart failure, hypothermia, or the administration of vasoconstrictor drugs. Vasodilation may be caused by the systemic inflammatory response, hyperthermia or the administration of vasodilator drugs. Treatment should be directed to the underlying cause; vasocorrective therapy is only utilized as a last resort (Table 19.7).

Table 19.6. Antiarrhythmic drugs.

Drug	Mechanism	Indication	Intravenous Dosage
Lidocaine	Sodium-channel blocker	VPCs	1–4 mg/kg; 2–6 mg/kg/h
Procainamide	Sodium-channel blocker	VPCs; APCs	1–4 mg/kg; 2–6 mg/kg/h
Quinidine	Sodium-channel blocker	VPCs; APCs	5–15 mg/kg
Amiodarone	Sodium-channel blocker and other effects	VPCs	5 mg/kg over 20 min
Atenolol	ß Blocker	APCs; VPCs	0.2–1 mg/kg
Esmolol	ß Blocker	APCs; VPCs	0.2–0.5 mg/kg; 0.5–10 mg/kg/h
Propanolol	ß Blocker	APCs; VPCs	0.01–0.3 mg/kg
Diltiazem	Calcium-channel blocker	APCs	0.05–0.25 mg/kg; 0.05–0.3 mg/kg/h
Verapamil	Calcium-channel blocker	APCs	0.05–0.25 mg/kg

APCs (atrial premature contractions), supraventricular arrhythmia; VPCs (ventricular premature contractions), ventricular arrhythmia.

Table 19.7. Cardiovascular drugs.

	Indication				
Drug	Contractility	Heart Rate	Vasomotor Tone		Intravenous Dosage
Dobutamine	↑↑↑	↑↑	↓		5–15 µg/kg/min
Dopamine	↑↑↑	↑↑	↑↑		5–15 µg/kg/min
Epinephrine	↑↑↑	↑↑↑	↑↑↑		0.1–1.0 µg/kg/min
Norepinephrine	0	nc	↑↑↑		0.2–2.0 µg/kg/min
Phenylephrine	0	↓	↑↑↑		1–5 µg/kg/min
Vasopressin	0	↓	↑↑		0.5 units/kg
			Art	Ven	
Hydralazine	0	↑↑	↓↓	0	0.5–1.0 mg/kg
Nitroprusside	0	↑↑	↓↓↓	↓↓↓	1–5 µg/kg/min
Acepromazine	0	↑	↓	↓	0.01 mg/kg
Morphine	0	↓	↓	↓↓	0.1–0.5 mg/kg
Diltiazem	↓↓	↓	↓	↓	0.05–0.25 mg/kg; 0.05–0.3 mg/kg/h
Enalaprilat	0	nc	↓	↓	0.01–0.02 mg/kg

Art, arterial; Ven, venous; nc, no change.

Central Venous Pressure

Central venous pressure (CVP) is the luminal pressure of the intrathoracic vena cava. Peripheral venous pressure is variably higher than CVP, is subject to unpredictable extraneous influences, and is not a reliable indicator of CVP. CVP is the relationship between central blood volume and central blood volume capacity. Central blood volume is determined by venous return and cardiac output. Verification of a well-placed, unobstructed catheter can be ascertained by observing small fluctuations in the fluid meniscus within the manometer synchronous with the heartbeat, and larger excursions synchronous with ventilation. Large fluctuations synchronous with each heartbeat may indicate that the end of the catheter is positioned within the right ventricle. Direct observation of the CVP waveform may help identify the proper location of the catheter tip (Fig. 19.2). Measurements should be made during the expiratory pause phase (during either spontaneous or positive-pressure ventilation) because changes in pleural pressure affect the luminal pressure within the anterior vena cava.

The normal CVP in small animals is 0 to 10 cm H_2O. It is 15 to 30 cm H_2O in laterally recumbent horses, and 5 to 10 cm H_2O in dorsally recumbent horses.[49] Low-range or below-range values indicate hypovolemia and suggest that a rapid bolus of fluids should be administered. Above-range values indicate relative hypervolemia and that fluid therapy should be stopped. CVP is a measure of the relative ability of the heart to pump the venous return and should be measured whenever heart failure is a concern. CVP is also a measure of the relationship between blood volume and blood volume capacity and could be measured to help determine the end point for large fluid volume resuscitation. CVP measurements are used to determine whether there is "room" for additional fluid therapy in the management of hypotension.

CVP is not a measure of preload (only of preload pressure) and is a poor predictor of stroke volume or cardiac output.[50] Preload is end-diastolic muscle stretch that, in vivo, is mostly related to end-diastolic volume, which, clinically, is reflected in the measure of end-diastolic diameter. CVP is a filling pressure, not a volume, and will not be representative of preload in diseases associated with decreased ventricular compliance (i.e., hypertrophy, tamponade, and fibrosis). Diastolic performance (relaxation) is also adversely affected by some anesthetics.[51]

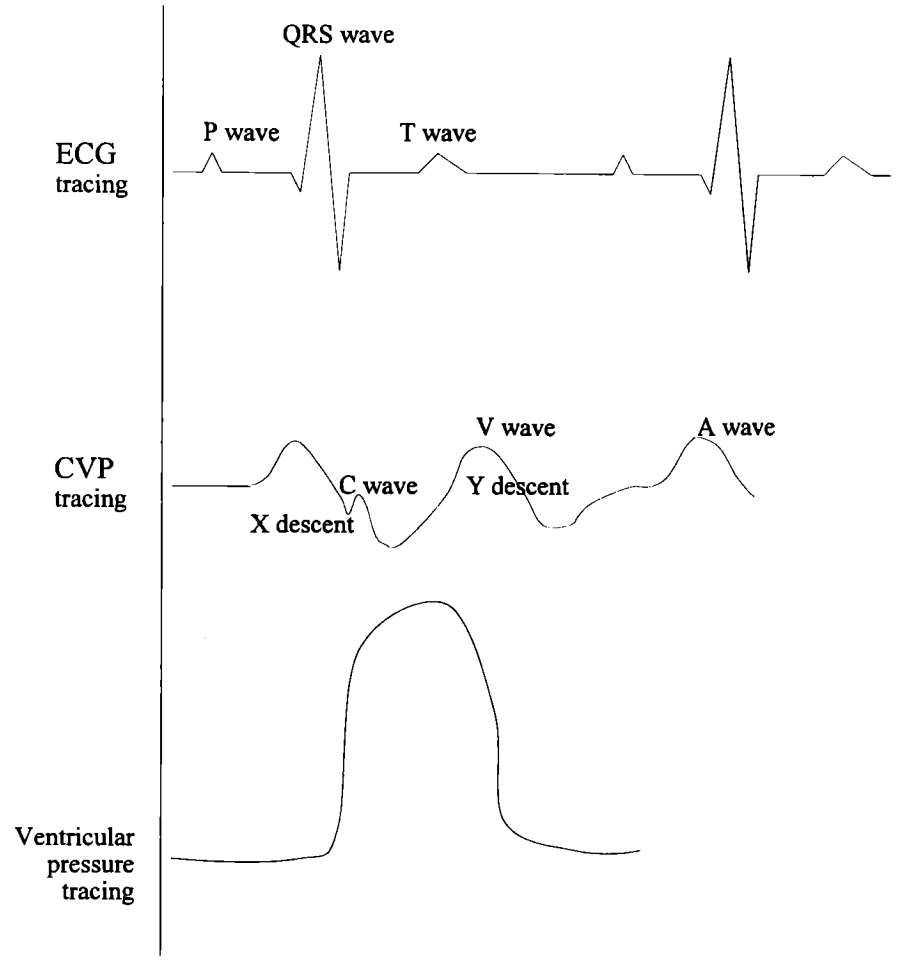

Fig. 19.2. Central venous and ventricular pressure waveforms. CVP, central venous pressure; and ECG, electrocardiogram.

Arterial Blood Pressure

Arterial blood pressure is a consequence of the relationship between blood volume and blood volume capacity. Arterial blood volume is determined by cardiac output and systemic vascular resistance. Arterial blood pressure is a primary determinant of cerebral and coronary perfusion. Systolic blood pressure is primarily determined by stroke volume and arterial compliance. Diastolic blood pressure is primarily determined by systemic vascular resistance and heart rate. Mean blood pressure is the average pressure: one-half of the area of the pulse-pressure waveform. If the pulse-pressure waveform were a perfect triangle, mean pressure would be one-third of the difference between diastolic pressure and systolic pressure. To the extent that the pulse-pressure contour is not a perfect triangle—a tall, narrow pulse-pressure waveform is common—the mean pressure will be closer to diastolic. The mean arterial blood pressure is physiologically the most important because it represents the mean driving pressure for organ perfusion. Many clinical instruments, however, measure only systolic blood pressure. The relationship between systolic blood pressure and mean arterial blood pressure is variable, depending on the shape of the pulse-pressure waveform; systolic blood pressure should always be assessed with this in mind.

Assessment of pulse quality by digital palpation is an evaluation of both the height and width of the pulse-pressure waveform compared with normal. Tall, wide pulse-pressure waveforms are seen in sepsis, whereas tall, narrow waveforms occur with a patent ductus and during cardiopulmonary resuscitation. Small, narrow pulse-pressure waveforms are seen with small stroke volumes and vasoconstriction. A small stroke volume can be seen with hypovolemia, poor heart function from any cause, tachycardia, and ventricular arrhythmias. The pulse-pressure waveform is largely a reflection of stroke volume and vessel size. It is not a measure of arterial blood pressure per se, although, in a species-dependent and very general way, vessels with low pressure are easier to collapse and vice versa. The weak, thready pulse that occurs with hypovolemia is caused by small stroke volumes and vessel constriction; patients with this symptom may be normotensive. Peripheral pulse quality (such as the dorsal metatarsal in dogs) decreases and disappears earlier than it does in larger, more central arteries (such as the femoral) with progressive hypovolemia. The relative pulse quality of more peripheral versus

more central arteries may provide a rough index to the magnitude of the problem.

Arterial blood pressure can be measured indirectly by sphygmomanometry or directly via an arterial catheter attached to a transducer system. *Sphygmomanometry* involves the application of an occlusion cuff over an artery in a cylindrical appendage. The width of the occlusion cuff should be about 40% of the circumference of the leg to which it is applied. The occlusion cuff should be placed snugly around the leg. If it is applied too tightly, the pressure measurements will be erroneously low because the cuff itself, acting as a tourniquet, will partially occlude the underlying artery. If the cuff is too loose, the pressure measurements will be erroneously high because excessive cuff pressure will be required to occlude the underlying artery. Inflation of the cuff applies pressure to the underlying tissues and will totally occlude blood flow when the cuff pressure exceeds systolic blood pressure. As the cuff pressure is gradually decreased, blood will begin to flow intermittently when the cuff pressure falls below systolic pressure. When this occurs, (a) the manometer pressure at which needle oscillations begin to occur on the manometer during cuff deflation (caused by the pulse wave hitting the cuff) corresponds approximately to systolic blood pressure, and (b) the manometer pressure at which one can digitally palpate a pulse distal to the cuff corresponds approximately to diastolic blood pressure. *Doppler ultrasound* involves the application of a small piezoelectric ultrasound crystal over an artery. Some Doppler instruments measure blood flow and are used to measure systolic blood pressure, whereas other instruments generate signals from the movement of the arterial wall and can be used to measure both systolic and diastolic blood pressures. *Oscillometry* analyzes the fluctuation of pressure in the cuff as it is slowly deflated and provides a digital display of systolic, diastolic, and mean blood pressures, and heart rate. Most of these instruments can be set to recycle at discrete time intervals. Small vessel size and motion can interfere with measurements.

All external techniques are least accurate when vessels are small, when the blood pressure is low, and when the vessels are constricted. Direct measurement of arterial blood pressure is more accurate and continuous compared with indirect methods, but requires the introduction of a catheter into an artery by a percutaneous or cut-down procedure. The dorsal metatarsal and ear arteries in dogs and cats, and the facial and metatarsal arteries in horses and cows, are commonly used. The subcutaneous tissues around these arteries are relatively tight, and hematoma formation at the time of catheter removal is rarely a problem. Once the catheter is placed, it is connected to a monitoring device. The catheter must be flushed with heparinized saline at frequent intervals (hourly) or continuously to prevent blood clot occlusion. The measuring device could be a long fluid administration set suspended from the ceiling. Fluid is instilled into the tubing via a three-way stopcock to a very high level and then allowed to gravitate into the artery until the hydrostatic pressure of the column of water is equalized with the mean arterial blood pressure of the patient. Since blood pressure oscillates, leaving the system open between measurements is not advised because that will let blood enter the catheter and clot and occlude it. Alternatively, the measuring device could be an aneroid manometer (Fig. 19.3). Water or blood must not be allowed to enter the manometer.

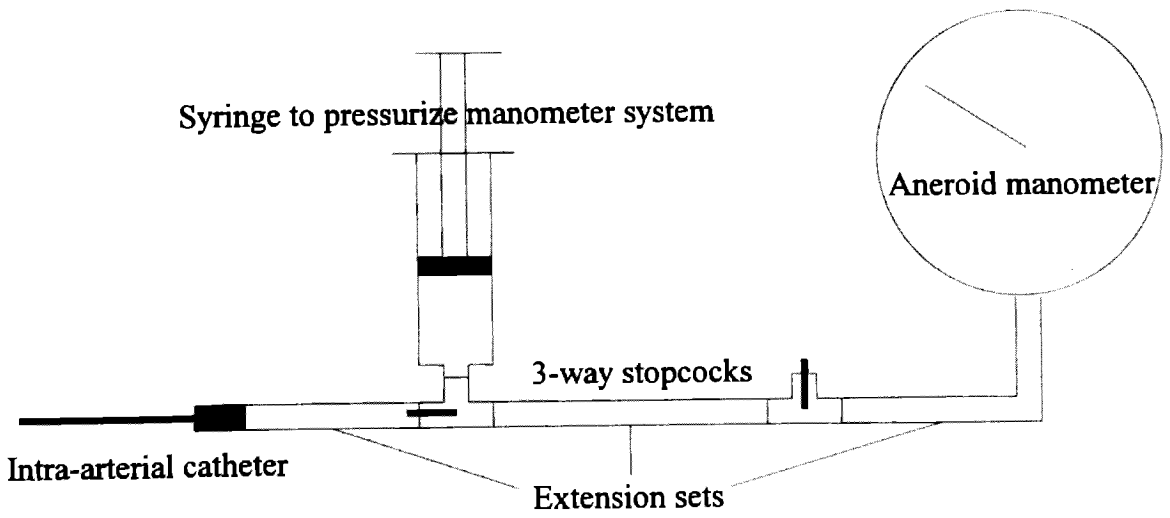

Fig. 19.3. Aneroid manometer system for measuring arterial blood pressure. The intra-arterial catheter is attached to a sterile length of extension tubing (since the system measures only mean pressure, the tubing does not have to be high-pressure, low-compliant tubing); a three-way stopcock; another extension tubing; another stopcock; and a third extension tubing, which is attached to the aneroid manometer. A saline-filled syringe is attached to the first stopcock, which is closed to the patient. Saline is injected into the tubing toward the manometer until the pressure registers at least 150 mm Hg (it needs to be only slightly higher than mean arterial blood pressure). The first stopcock is then closed to the syringe (opened between the pressurized manometer system and the arterial catheter), and the equilibrated pressure equals mean arterial blood pressure. Since blood pressure varies, do not leave the system open between measurements; blood will flow into the catheter and clot. This is an intermittent pressure-measuring device. The second stopcock enables the removal of excess saline from the tubing so that fluid does not get into the aneroid manometer.

Sterile saline is injected into the tubing toward the manometer via a three-way stopcock until the compressed air increases the registered pressure to a level above that of mean blood pressure. The pressurized manometer system is then allowed to equilibrate with the mean blood pressure of the patient. Arterial catheters can also be attached to a commercial transducer and recording system. The extension tubing between the catheter and the transducer should not be excessively long and should be constructed of nonexpansible plastic to avoid damped signals. The transducer should be "zeroed" periodically and calibrated with a mercury manometer to verify accurate blood pressure measurements. The stopcock that is opened to room air for the zeroing process must be at the level of the heart. With modern patient monitors, the transducer can be placed anywhere with reference to the patient (the monitor will compensate internally with an *offset pressure* for any vertical differences between the patient and the transducer). If the relative vertical position between the patient and the transducer changes, the transducer must be rezeroed. With older patient monitors without this offset feature, the transducer and the zeroing stopcock must be placed at the level of the heart.

The fidelity of the reproduction of the pulse-pressure waveform by a fluid-filled measurement system is the result of a rather complex interaction between the frequency response of the measurement system (resonant frequency and damping) and patient factors such as heart rate and systolic vigor. Generally, the intra-arterial catheter should be large; the transducer should be placed close to the patient, with high-pressure tubing connecting the catheter to the transducer; and the measuring system should be free of blood clots or air bubbles (Table 19.8). *Underdamping* occurs when the frequency response of the measuring system is identical to one of the harmonics of the pulse-pressure waveform. The recorded waveform will be exaggerated—the systolic pressure will be erroneously high and the diastolic pressure will be erroneously low; pressure oscillations may override the recorded waveform (Fig. 19.4). *Overdamping* occurs also when the frequency response is less than all of the harmonics of the pulse-pressure waveform. The recorded waveform will be blunted—the systolic pressure will be erroneously low and the diastolic pressure will be erroneously high; the dicrotic notch is diminished or absent (Fig. 19.4).

The frequency response of the measurement system can be assessed by the dynamic pressure response test (Fig. 19.5). This involves the sudden release of pressure on the measurement system, such as is done by flushing the catheter with the continuous-flush device. During the flush procedure, the registered pressure equals that of the pressure bag (>300 mm Hg). When the flushing procedure is abruptly terminated, the pressure should return to baseline after about one to two negative and one to two positive oscillations.[52] Ideally, the measuring system would have a high resonant frequency and low damping. The resonant frequency is calculated as 1 s divided by the length of time of one complete oscillation (peak to peak) (Fig. 19.5). Typical values are 10 to 50 Hz.[52] Damping is calculated as the amplitude reduction ratio: the height of one-half of a complete cycle (peak to trough or vice versa) divided by the height of the previous one-half cycle (Fig. 19.5). Typical values are 0.35 to 0.7.[52] The appropriateness of the frequency response of the measuring system for a particular patient is determined by a combination of the resonant frequency and the damping. Underdamping is caused by the combination of a low resonant frequency and minimal damping. Overdamping is caused by the combination of a low resonant frequency and excessive damping.

If overdamping or underdamping is noted, check for (and remove) blood clots or air bubbles from the measurement system, exchange low-compliant tubes with rigid tubes, shorten the length of tubing between the catheter and transducer, make sure there are no leaks, and eliminate kinks in the tubing or appendage (if a peripheral artery has been catheterized). If the underdamping problem continues, add a damping device (longer tubing, less rigid tubing, and a small air bubble at the transducer).

Normal systolic, diastolic, and mean blood pressures are ap-

Table 19.8. Key features of a high-frequency response measuring system.

Large-inside-diameter catheter
Short (as opposed to long) catheter
Large, more central artery (as opposed to a small, peripheral artery)
Short-catheter-transducer connecting tubing
Noncompliant tubing
No loose, leaky connections
As few stopcocks as possible
No kinks in the tubing
Hyperflexed appendages avoided when the catheter is in a peripheral artery
No air bubbles in the measuring system
No blood clots in the catheter or measuring system (use a continuous-flush device)

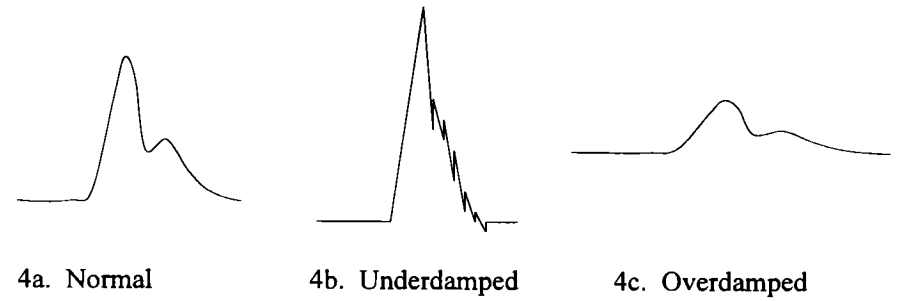

Fig. 19.4. Underdamping and overdamping caused by a frequency response of the measuring system that is the same as one of the harmonics of the original pressure waveform or too low, respectively. **a:** Ideal pressure waveform. **b:** Underdamped pressure waveform. **c:** Overdamped pressure waveform.

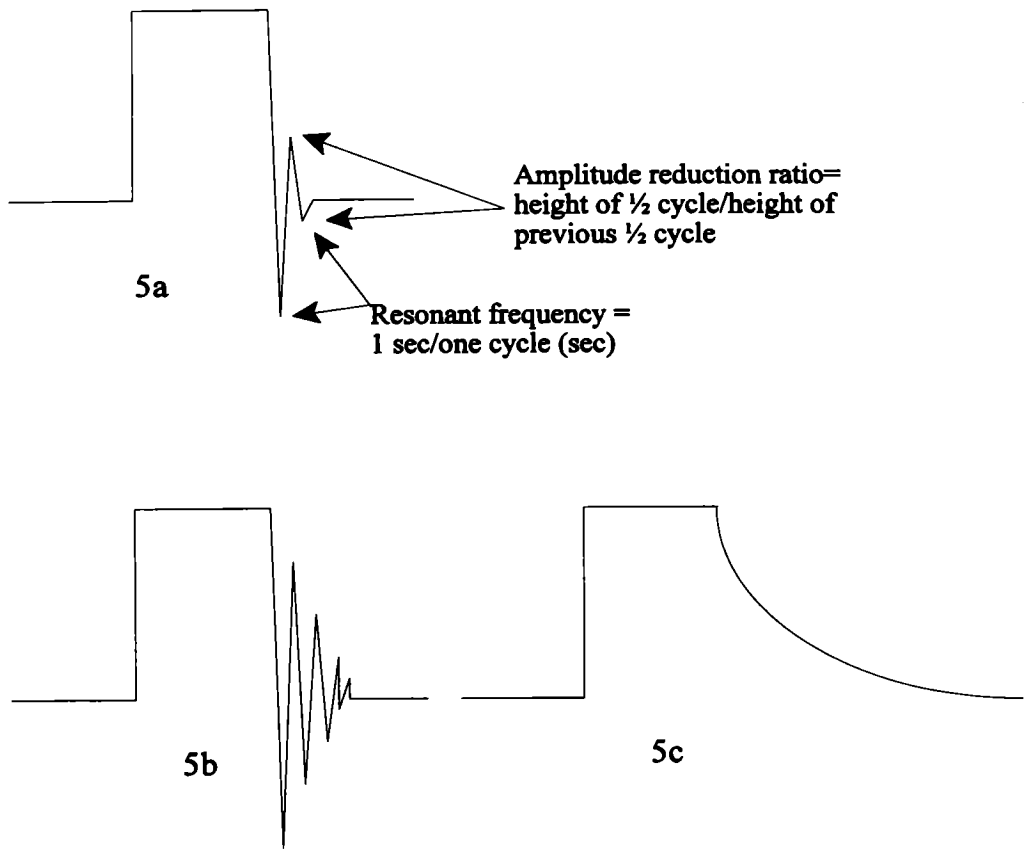

Fig. 19.5. Dynamic pressure response test to determine natural frequency response of a measuring system. The pressure is suddenly released and the fluctuations in pressure recorded. **a:** Optimal: The waveform should oscillate 1 to 1.5 full cycles before returning to baseline. The resonant frequency is calculated as 1 s divided by the duration of one complete cycle (peak to peak or trough to trough). The damping is calculated as the amplitude reduction ratio of the height of one-half cycle (peak to trough or trough to peak) divided by the previous one-half cycle. **b:** Underdamped: The waveform oscillates more than two full cycles. **c:** Overdamped: The waveform oscillates less than 0.5 full cycle.

proximately 100 to 140, 60 to 100, and 80 to 120 mm Hg, respectively. In general, one should be concerned when the systolic arterial blood pressure (ABPs) falls below 100 or when the mean arterial blood pressure (ABPm) falls below 80 mm Hg. In general, one should be very concerned when the ABPs falls below 80 or the ABPm falls below 60 mm Hg. Hypotension may be caused by hypovolemia, poor cardiac output, or vasodilation (Table 19.9). Hypertension (high ABPm) is generally attributed to vasoconstriction. High ABPs, not associated with a high ABPm, is generally attributed to an inappropriate frequency response of the measuring system (for that patient and that time). Hypertension can cause increased hemorrhage, retinal detachment, increased intracranial pressure, and high afterload to the heart, and should be treated when ABPm exceeds 140 mm Hg (Table 19.7). High ABPm may be produced by a light level of anesthesia, hyperthermia, sympathomimetic drugs, hyperthyroidism (thyroxine-catecholamine synergy), renal failure (renin-angiotensin), pheochromocytoma (epinephrine), or increased intracranial pressure. In the latter case, the hypertension is most likely caused by the Cushing's response, to maintain an adequate cerebral perfusion pressure, and should not be treated.

Cardiac Output

Poor cardiac output is implied when preload parameters (CVP, pulmonary artery occlusion pressure, jugular vein distension, postcava distension on chest radiograph, and end-diastolic diameter on cardiac ultrasound image) are high and the afterload parameters (cardiac output, arterial blood pressure, and physical and laboratory measures of tissue perfusion) are low or abnormal. Pulse-quality assessment provides an indirect measure of stroke volume. Cardiac output is a flow parameter and can be low even when arterial blood pressure is normal. Cardiac output in humans is most often measured by thermodilution techniques via the balloon-tipped pulmonary artery catheter. Lithium administration is another indicator-dilution technique that has been used.[53–56] It requires its own detector and computer; cardiac output can be measured only a finite number of times (because of lithium accumulation); the detector probes are fairly expensive; and, of course, pulmonary artery pressure and pulmonary artery occlusion pressure are not measured. Cardiac output can also be measured by esophageal Doppler ultrasonography, thoracic electrical bioimpedance, and pulse analysis.[53,56,57] Cardiac output in normal, awake dogs is 4.42 ± 1.24 L/min/m^2 (165 ± 43 mL/min/kg) and is generally decreased by general anesthetics, except ketamine (Table 19.1). Cardiac output in awake horses is 70 to 90 mL/min/kg and is decreased to 35 to 60 mL/min/kg with general anesthesia.[58–60]

Table 19.9. Causes of hypotension.

Low venous return
Hypovolemia
Preexisting dehydration
Blood loss, plasma exudation, or crystalloid transudation at operative site
Positive-pressure ventilation
Gastric distension
Iatrogenic inflow occlusion
Poor diastolic function
Hypertrophic cardiomyopathy
Pericardial tamponade
Tachycardia
Fibrosis
Poor systolic function (contractility)
Dilative cardiomyopathy
Negative inotropic effect of anesthetic drugs, β_1 blockers, or calcium-channel blockers
Ventricular arrhythmias
Impaired systolic efficiency
Atrioventricular valve insufficiency
Outflow-tract obstruction
Bradycardia
Low systemic vascular resistance
Vasodilating effect of anesthetic or other drugs
Patent ductus arteriosus

Cardiac output may be reduced by poor venous return and end-diastolic ventricular filling (hypovolemia, positive-pressure ventilation, or inflow occlusion); by ventricular restrictive disease (hypertrophic or restrictive cardiomyopathy, pericardial tamponade, or pericardial fibrosis); by decreased contractility; by excessive bradycardia, tachycardia, or arrhythmias; by regurgitant atrioventricular valves; or by outflow-tract obstruction. Poor cardiac output should be improved by correcting the underlying problem when possible. Preload should be optimized. When poor contractility is thought to be the problem, anesthetic dosage levels should be decreased to the least amount that will enable the completion of the surgical procedure. Sympathomimetic therapy (Table 19.7) is indicated when poor contractility is thought to be the problem, and fluid therapy and anesthetic drug reduction have failed to restore acceptable forward-flow parameters.

Oxygen Delivery

Oxygen delivery (DO_2) is the product of cardiac output and blood oxygen content (Fig. 19.1). Some myocardial depression is expected with general anesthesia, and this could be associated with a decrease in cardiac output and DO_2. In fact, DO_2 may be increased or decreased by anesthetic drugs (Table 19.1). A decrease in DO_2 during general anesthesia may not be a problem if oxygen consumption (VO_2) is also reduced by muscular inactivity and hypothermia.[61,62] Oxygen consumption, however, like DO_2, is variably affected by anesthetic drugs[61,62] (Table 19.1). Critical DO_2, the DO_2 below which VO_2 decreases linearly, has been reported to be between 160 and 280 mL/min/m^2 (6 to 11 mL/min/kg) in dogs.[63–66] In critically ill human patients, a minimum oxygen delivery of 550 to 600 mL/min/m^2 has been recommended.[67,68] From our own experiments ($n = 97$), DO_2 in normal dogs is 790 ± 259 mL/min/m^2 (29.5 ± 8.8 mL/min/kg). Optimal DO_2 was thought to be associated with a minimum DO_2 of 600 mL/min/kg because, when DO_2 decreased below this level, oxygen extraction, arteriovenous oxygen content gradient and arteriovenous partial pressure of carbon dioxide (PCO_2) gradient increased, and central venous partial pressure of oxygen (PO_2) decreased. Alternatively, when cardiac output measurements are unavailable, oxygen extraction above 30%, arteriovenous oxygen content gradient above 5 mL/dL, arteriovenous PCO_2 gradient above 5 mm Hg, or central venous PO_2 (PvO_2) below 40 mm Hg may indicate a less than optimal DO_2. Most anesthetics (inhalationals, opioids, and barbiturates, but not ketamine) impair oxygen extraction and increase the critical DO_2 compared with baseline.[69]

Table 19.10. Causes of tachypnea.

Too lightly anesthetized
Too deeply anesthetized
Agonal "gasps"
Hypoxemia
Hypercapnia
Hyperthermia
Hypotension
Sepsis
Atelectasis
Postoperative recovery phase
Postoperative pain
Drug-induced (opioids)
Individual variation

Pulmonary Monitoring

Breathing Rate, Rhythm, Nature, and Effort

The breathing rate can vary widely, and except for extreme values is of limited value as a respiratory monitor. A change in breathing rate, however, is a sensitive indicator of an underlying change in the status of a patient. Bradypnea may be a sign of deep anesthesia or hypothermia. There are many causes of tachypnea, and it is important not to default to the conclusion that its occurrence represents too light a level of anesthesia (Table 19.10). Arrhythmic breathing patterns are indicative of a problem with the central pattern generator in the medulla. A *Cheyne-Stokes breathing pattern* (cycling between hyperventilation and hypoventilation) may be seen in otherwise healthy anesthetized horses and an apneustic breathing pattern (inspiratory hold) may be seen in otherwise healthy dogs and cats anesthetized with ketamine.

Ventilometry

Ventilation volume can be estimated by visual observation of the chest or rebreathing bag or measured by ventilometry. Normal tidal volume ranges between about 8 and 20 mL/kg. A small tidal volume may be acceptable if the breathing rate is fast enough to accomplish normal alveolar minute ventilation. Normal total minute ventilation ranges between 150 and 250 mL/kg/min for dogs. Dead-space ventilation is about 30% to 40% of tidal volume and minute ventilation in a normal patient breathing a normal tidal volume, but may be much higher with shallow breathing, upper-airway dead space, or pulmonary thromboembolism. Arterial PCO_2 ($PaCO_2$) is usually considered to be the definition of alveolar minute ventilation, and the measured minute ventilation should be appropriate. A large minute ventilation in combination with a normal (or high) $PaCO_2$ is indicative of a large dead-space ventilation.

Compliance is calculated as expired tidal volume divided by the change in pressure that it took to generate the tidal volume. A change in airway pressure is easy to measure during positive-pressure ventilation, but to measure the change in transpulmonary pressure during spontaneous ventilation requires the measurement of pleural pressure (which is usually done via the lower esophagus). If, for instance, 10 cm H_2O of pressure was required in order to generate a tidal volume of 10 mL/kg, the compliance would be calculated to be 1 mL/kg/cm H_2O. If the measurements are made during the cyclic breathing process, the value is termed *dynamic compliance*. If the measurements are made after an inspiratory pause, the value is termed *static compliance*. The manner in which these measurements would usually be obtained during general anesthesia would include a component of anesthetic-circuit gas compression and breathing-circuit expansion. Since anesthetic circuits and technique vary, you will need to establish expected values by using your particular equipment and technique. Compliance is decreased by restrictive pulmonary, pleural, or thoracic wall disease.

Partial Pressure of Carbon Dioxide

The $PaCO_2$ is a measure of the ventilatory status of a patient and normally ranges between 35 and 45 mm Hg. $PaCO_2$ values may be slightly higher in anesthetized small animals and is considerably higher (60 to 80 mm Hg) in anesthetized horses[49] (Table 19.2) and cattle.[18] A $PaCO_2$ in excess of 60 mm Hg may be associated with excessive respiratory acidosis and is usually considered to represent sufficient hypoventilation to warrant positive-pressure ventilation in small animals. $PaCO_2$ values below 20 mm Hg are associated with respiratory alkalosis and a decreased cerebral blood flow that may impair cerebral oxygenation.

Venous PCO_2 ($PvCO_2$) is usually 3 to 6 mm Hg higher than $PaCO_2$ in stable states and can generally be used as an approximation of $PaCO_2$. The venous partial pressure of carbon dioxide is variably higher in transition states and during hypovolemia or anemia. $PaCO_2$ may also be estimated by measuring the carbon dioxide in a sample of gas taken at the end of an exhalation (Fig. 19.6). End-tidal PCO_2 is usually 2 to 4 mm Hg lower than $PaCO_2$ in dogs and 10 to 15 mm Hg lower in horses.[70] Capnography enables anesthetists to evaluate adequacy of ventilation, and many other problems, as well (Table 19.11).[71–73]

Table 19.11. Information derived from the capnogram[71–73].

Observed Problem	Possible Cause(s)
No waveform	Apnea; obstructed aspirating tubing
Increased baseline	Rebreathing malfunction or contaminated sample cell
Increased plateau	Hypoventilation or increased rate of carbon dioxide production
Decreased plateau To a new, stable level	Hyperventilation, hypothermia, airway leaks, tachypnea, pulmonary thromboembolism, or capnograph calibration error
Abruptly to zero	Airway obstruction, airway disconnect, apnea, or cardiac arrest
Flattened upsweep (line A in Fig. 19.6)	Small airway narrowing and increase in disparity of alveolar time constants
Flattened downsweep (line C in Fig. 19.6)	Rebreathing
Unstable, fluctuating plateau	Spontaneous breathing during mechanical ventilation

An increased arteriovenous PCO_2 gradient suggests decreased tissue perfusion. A note of caution: Do not contaminate the blood sample with sodium bicarbonate, because that will increase PCO_2 dramatically. The causes of hypercapnia and hypocapnia are listed in Table 19.12.

Partial Pressure of Oxygen

The PaO_2 measures the tension of oxygen dissolved in the plasma, irrespective of the hemoglobin concentration. The PaO_2 is a measure of the oxygenating efficiency of the lungs. The normal PaO_2 is considered to range between 80 and 110 mm Hg when an animal is breathing room air at sea level. When room air is being breathed, the PaO_2 would normally decrease during general anesthesia, because of anesthetic-induced hypoventilation, increased ventilation-perfusion mismatching, and atelectasis. Usually, however, anesthetized animals are attached to an anesthetic machine and breath 100% oxygen. The PaO_2 is usually above 500 mm Hg in small animals and above 200 mm Hg in horses.[49,58,60] Hypoxemia is usually defined as a PaO_2 below 80 mm Hg. Hypoxemia could be caused by low inspired oxygen, hypoventilation while breathing 21% oxygen, and venous admixture (Table 19.13). A PaO_2 below 60 mm Hg is a commonly selected trigger for symptomatic therapy.

PvO_2 reflects tissue PO_2 and bears no correlation to PaO_2. Mixed or central PvO_2 ranges between 40 and 50 mm Hg. Values below 30 mm Hg may be caused by anything that decreases the delivery of oxygen to the tissues (hypoxemia, anemia, low cardiac output, or vasoconstriction) (Fig. 19.1); values above 60 mm Hg suggest reduced tissue uptake of oxygen (shunting, septic shock, or metabolic poisons). Venous blood for such evaluations must be taken from a central vein such as the jugular, anterior vena cava, or pulmonary artery; peripheral PvO_2 values are highly variable and difficult to interpret.

Blood gases are measured at the temperature of the blood-gas analyzer water bath (usually 37°C). Ideally, the animal's body temperature would be identical to that of the water bath, but this seldom occurs. When the animal's body temperature differs from that of the water bath, there will be changes in the measured pH and blood gases associated with the in vitro change in temperature. There is some debate about whether to correct for these temperature changes. If one wants to know what is actually happening in a patient and wants to compare the current measurement with previous measurements, even though there has been a substantial change in body temperature, the temperature-corrected values should be used. If a clinician is contemplating therapy to "fix" an abnormality by using normothermic reference points, then the uncorrected values should be used.[74] "Normal values" for hypothermic or hyperthermic patients are different than those for normothermic patients, but these reference values have not been established for each level of hypothermia or hyperthermia that occurs.

Hemoglobin Saturation with Oxygen

When red to infrared light is transmitted through a blood sample, a certain proportion of it will be absorbed by the various hemoglobins present in the blood sample: oxyhemoglobin, methemoglobin, carboxyhemoglobin, and reduced hemoglobin. A bench-

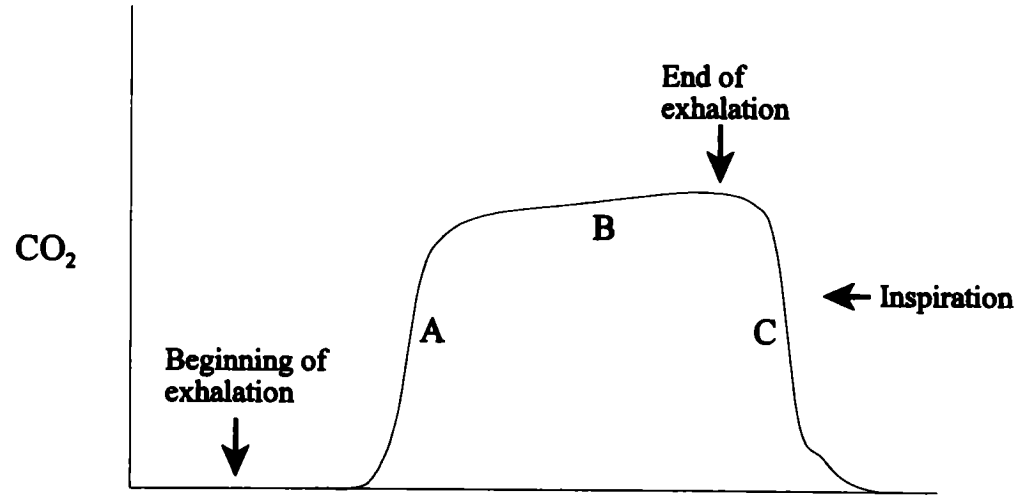

Fig. 19.6. Capnogram. The end-tidal carbon dioxide (CO_2) at the end of exhalation should be only a few mm Hg below arterial CO_2 partial pressure. *Line A* reflects the transition between CO_2-free anatomical and alveolar dead-space gases and functional alveolar gases. The slope of line A reflects variable emptying of fast and slow alveoli (airway disease flattens the slope of line A). *Line B*, the plateau of the capnogram, reflects alveolar gas; the slight upward slope to line B represents an increasing alveolar CO_2 during exhalation. *Line C* represents inspiration; the slope of line C is less steep with rebreathing.

Table 19.12. Causes of hypercapnia and hypocapnia.

Hypercapnia	Hypocapnia
Hypoventilation	Hyperventilation
Neuromuscular: excessive anesthetic depth; intracranial, cervical, neuromuscular	Light level of anesthesia
Airway obstruction: endotracheal tube; large or small airways	Hypoxemia
Thoracic or abdominal restrictive disease	Hyperthermia
Pleural space–filling disorder: air, fluid, or abdominal viscera	Hypotension
Pulmonary parenchymal disease	Sepsis
Inappropriate ventilator settings	Postoperative recovery phase
Malfunctioning/exhausted soda lime	Postoperative pain
Malfunctioning anesthetic machine: dead-space rebreathing	Inappropriate ventilator settings

Table 19.13. Causes of hypoxemia.

Low inspired oxygen
Depleted oxygen supply
Maladjusted flowmeter
Insufficient flow in a Bain's circuit
Anesthetic machine malfunction: dead-space rebreathing
Hypoventilation (when breathing room air)
Venous admixture
Low ventilation/perfusion regions: mild to moderate pulmonary parenchymal disease
Small airway and alveolar collapse (no ventilation but perfused regions): moderated to severe pulmonary parenchymal disease
Diffusion impairment: inhalation injury, oxygen toxicity, or inflammatory lung disease
Anatomic right-to-left shunts

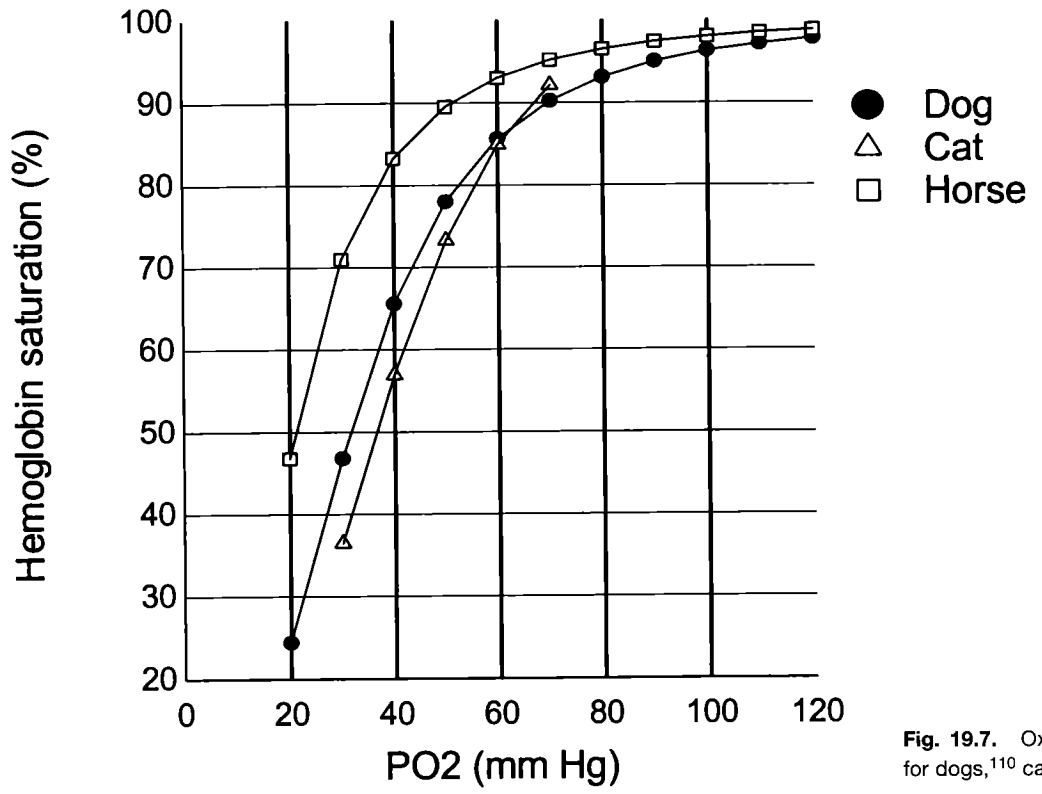

Fig. 19.7. Oxyhemoglobin dissociation curves for dogs,[110] cats,[111] and horses.[112]

top co-oximeter measures and displays values for the first three. The displayed oxyhemoglobin is functional; that is, it is expressed as a percentage of the amount of hemoglobin available for oxygen binding (total hemoglobin minus methemoglobin and carboxyhemoglobin) as opposed to fractional oxyhemoglobin, which is expressed as a percentage of total hemoglobin irrespective of methemoglobin or carboxyhemoglobin. Normal methemoglobin and carboxyhemoglobin levels are normally less than 1% each, and so, usually, functional and fractional oxyhemoglobin levels are quite similar. To the extent that either methemoglobin or carboxyhemoglobin are present in large concentrations, fractional oxyhemoglobin levels will be variably lower than functional oxyhemoglobin levels.

Hemoglobin-oxygen saturation (SO_2) measures the percent oxygen saturation of the hemoglobin and is related to PO_2 by a sigmoid curve. The clinical information derived from the measurement of arterial SO_2 (SaO_2) is similar to that obtained from a PaO_2 measurement in that they both are a measure of the ability of the lung to deliver oxygen to the blood. In this matter, functional oxyhemoglobin is the more meaningful number. The "numbers of concern" are, however, different. In general, a PO_2 of 100 mm Hg is equivalent to an SO_2 of 98%; a PO_2 of 80 mm Hg to an SO_2 of 95%; a PO_2 of 60 mm Hg to an SO_2 of 90%; and a PO_2 of 40 mm Hg to an SO_2 of 75%. Exact quantitative correlation depends on the hemoglobin affinity for oxygen. The P_{50} is the PO_2 at which the hemoglobin is 50% saturated and is commonly used to define hemoglobin affinity. The P_{50} for human hemoglobin is 26 to 28 mm Hg; it is slightly higher for dogs and goats; much higher for sheep, cats, and cattle; and lower for horses. Figure 19.7 and Table 19.14 illustrate representative oxyhemoglobin dissociation curves for horses, dogs, and cats.

Pulse oximeters attach to a patient externally (e.g., tongue, lips, tail, or toenail). For most clinical purposes, most pulse-oximeter readings are sufficiently accurate approximations of oxyhemoglobin saturation, though accuracy should be verified by an in vitro standard if possible. There are substantial bias and precision variations and response times between different commercial products at different levels of saturation.[75] Tissue, venous and capillary blood, nonpulsatile arterial blood, and skin pigment also absorb infrared light. There is a fairly narrow spectrum of wavelengths that passes through skin and yet is absorbed by hemoglobin. A pulse oximeter must differentiate this background absorption from that of pulsatile arterial blood. It does this by measuring light absorbance during a pulse and subtracting from that the light absorbance occurring between the pulses. If the pulse oximeter cannot detect a pulse, it will not measure the oxyhemoglobin level.

The accuracy of a pulse oximeter is greatest within the range of 80% and 95%, and is determined by the accuracy of the empirical formula that is programmed into the instrument.[76] Differences in tissue absorption or scatter of light, different thicknesses of tissue, smaller pulsatile flow patterns and small signal-to-noise ratios, and incompletely compensated light-emitting diodes may account for some inaccuracies. Inaccuracies may also generate from baseline-read errors (motion), differences in sensor location, and electrical or optical interference. When a measurement is obtained, it may either be accurate or inaccurate. When inaccurate, it is usually inaccurately low. When a low measurement is obtained, particularly when it seems incongruous for the patient's condition at the time, it might be wise to retry the measurement in several different locations and then either take the average or the highest reading. If methemoglobin or carboxyhemoglobin were present in high concentrations, they would absorb light and would impact the measurement made by a two-wavelength pulse oximeter designed to measure only oxyhemoglobin. Because of the biphasic absorption of methemoglobin at both the 660- and 940-nm wavelengths, abnormal accumulations tend to push the oximeter reading toward 85% (underestimating measurements when SaO_2 is above 85%, and overestimating it when SaO_2 is below 85%).[77] Carboxyhemoglobin absorbs light like oxyhemoglobin at 660 nm, but hardly at all at 940 nm, and this would increase the apparent oxyhemoglobin measurement.[78] Fetal hemoglobin produces very little effect on measured hemoglobin saturation.[76] Indocyanine green dye and methylene blue dye absorb light and will generate falsely low saturation measurements.[76]

A pulse oximeter is an ideal perioperative monitor in that it is an automatic, continuous, audible monitor of mechanical cardiopulmonary function. It specifically measures pulse rate and hemoglobin saturation, and it requires a reasonable peripheral pulse quality in order to achieve a measurement. One of the common reasons for poor instrument performance is peripheral vasoconstriction. Its value as an ongoing monitor in detecting hypoxemia has been established.[75,76] The pulse oximeter is not discriminating for high PaO_2 values where the oxyhemoglobin curve is flat. The difference between a PaO_2 of 500 and 100 mm Hg in an animal breathing 100% oxygen is very important as an index of lung function; the corresponding decrease in SaO_2, from 99% to 98%, would hardly be noticed.

Table 19.14. Oxyhemoglobin dissociation curve for dogs[110] and horses[112].

PO_2	Dogs	Horses	PO_2	Dogs	Horses
20	24.4	46.8	72	91.0	95.6
22	28.7	52.9	74	91.7	95.9
24	33.2	58.4	76	92.2	96.1
26	37.8	63.2	78	92.8	96.4
28	42.3	67.4	80	93.2	96.6
30	46.8	71.0	82	93.7	96.8
32	51.0	74.2	84	94.1	97.0
34	55.0	77.0	86	94.5	97.2
36	58.8	79.4	88	94.8	97.3
38	62.3	81.5	90	95.1	97.5
40	65.6	83.3	92	95.4	97.6
42	68.5	84.9	94	95.7	97.8
44	71.3	86.3	96	95.9	97.9
46	73.7	87.6	98	96.2	98.0
48	76.0	88.7	100	96.4	98.1
50	78.0	89.6	102	96.6	98.2
52	79.9	90.5	104	96.8	98.3
54	81.6	91.3	106	96.9	98.4
56	83.1	92.0	108	97.1	98.5
58	84.4	92.6	110	97.2	98.6
60	85.7	93.1	115	97.6	98.7
62	86.8	93.7	120	97.9	98.9
64	87.8	94.1	130	98.3	99.1
66	88.7	94.5	150	98.9	99.5
68	89.6	94.9	200	99.5	99.9
70	90.3	95.3	300	99.9	100.0

PO_2, partial pressure of oxygen.

Venous Admixture

Pulmonary dysfunction interferes with the ability of the lungs to transfer oxygen efficiently from the alveoli to the blood, resulting in a lower-than-expected PaO_2. *Venous admixture* is the collective term for all of the ways in which blood can pass from the right side of the circulation to the left side of the circulation without being properly oxygenated (Table 19.13). Several methods are used to quantitate lung-oxygenating efficiency (Table 19.15).

Oxygen Content

This parameter can be measured, but is usually calculated: (hemoglobin concentration × 1.34 [oxygen content of fully saturated hemoglobin] × percent saturation) + (0.003 × PO_2).

Table 19.15. Formulas for quantifying lung-oxygenating efficiency (venous admixture).

Parameter	Formula
Alveolar PO_2 (P_AO_2)	([Barometric pressure − 50] × fractional inspired oxygen) − ($PaCO_2$ × 1.1), where 50 = saturated water-vapor pressure at 38.5°C, and 1.1 = 1/RQ when RQ = 0.9
Alveolar-arterial PO_2 gradient (for any F_IO_2)	Calculated P_AO_2 × measured PaO_2
PaO_2 + $PaCO_2$ (for F_IO_2 = 0.21 at sea level)	Measured PaO_2 + measured $PaCO_2$
PaO_2/F_IO_2 (PF) ratio (for F_IO_2 > 0.4)	PaO_2/F_IO_2, where F_IO_2 is expressed as a decimal fraction between 0.21 and 1.0
Arterial, mixed-venous, and pulmonary capillary oxygen content	(1.34 × Hb × SO_2) + (0.003 × PO_2), where 1.34 is 100% saturated hemoglobin (Hb) oxygen content, SO_2 is hemoglobin saturation, and PO_2 is partial pressure of oxygen in arterial, mixed-venous, or capillary blood
Venous admixture (for any F_IO_2)	(Capillary O_2 content × arterial O_2 content)/(capillary O_2 content × venous O_2 content)

F_IO_2, fraction of inspired oxygen; $PaCO_2$, arterial carbon dioxide partial pressure; PaO_2, arterial oxygen partial pressure; PO_2, partial pressure of oxygen; RQ, respiratory quotient.

Table 19.16. The relationship between partial pressure of oxygen (PO_2), hemoglobin saturation (SO_2), and oxygen content under different clinical circumstances.

	PO_2 (mm Hg)	SO_2 (%)	Hb (g/dL)	O_2 content (mL/dL)
Normal	100	96.4	15	19.7
Anemia	100	96.4	5	6.8
Methemoglobinemia (50%)	100	96.4	15	10.0
Hypoxemia	40	65.6	15	13.3
Hyperoxemia	500	100	15	21.6

The canine oxyhemoglobin relationship was used for determining SO_2. Hb, hemoglobin concentration. Oxygen content was calculated as $(1.34 \times Hb \times SO_2) + (0.003 \times PO_2)$.

Hemoglobin is by far the most important contributor to oxygen content. The PO_2, SO_2, and oxygen content are related, but each measure provides a distinctly different perspective of blood oxygenation, and the difference can be important (Table 19.16). An increased arteriovenous oxygen-content difference (>5 g/dL) suggests increased oxygen extraction, which is usually attributable to decreased oxygen delivery.

Renal Monitoring

Urine flow is used as an indirect measure of renal blood flow, and renal blood flow is used as an indirect measure of visceral blood flow. Urine output can be assessed by serial palpation of the urinary bladder or by actual measurement after the aseptic placement of a urinary catheter. Normal urine output should be about 1 to 2 mL/kg/h. Maintaining visceral blood flow is, of course, an important aspect of any anesthetic plan and is generally achieved by optimizing the circulating blood volume (sufficient, but not excessive, fluid therapy), monitoring and maintaining forward-flow cardiovascular parameters, and monitoring of laboratory indices of tissue perfusion (standard base excess, lactate concentration, and central PvO_2). Oliguria or anuria, per se, can be treated, after ensuring that renal perfusion is adequate, with furosemide (0.5- to 5-mg/kg bolus ± 0.1 to 0.5 mg/kg/h) or mannitol (0.5-g/kg bolus ± 0.1 g/kg/h). Statistically, diuretic therapy does not prevent acute renal failure, but it does facilitate the medical management of the case.

Temperature Monitoring

Hypothermia

Hypothermia during anesthesia may be associated with anesthetic drug depression of muscular activity, metabolism, and hypothalamic thermostatic mechanisms. Heat loss may be augmented by evaporation of surgical scrub solutions from the skin surface, by the infusion of room-temperature fluids, by contact with cold, noninsulated surfaces, and by evaporation of surface fluid from an exposed body cavity. Core temperature can be measured with either esophageal or rectal thermistors attached to a continuously displayed thermometer.

Core body temperatures down to 36°C (96°F) are not detrimental to patients.[79,80] Nonshivering thermogenesis will increase, and there may be some shivering thermogenesis during recovery. Recovery should not be prolonged in any noticeable way. Body temperatures of 32° to 34°C (90° to 94°F) are associated with reduced anesthetic requirements; recovery should be noticeably prolonged. Animals will shiver if they can, but some will not shiver and will have to be artificially rewarmed. Body temperatures of 28° to 30°C (82° to 86°F) have a marked CNS-depressant effect, and usually no anesthetic agent is required. Shivering thermogenesis will not occur, and the animal will have to be rewarmed artificially, at least initially. Atrial arrhythmias may occur. Oxygen consumption is reduced to about 50% of normal, heart rate and cardiac output to about 35% to 40% of normal, and arterial blood pressure to about 60% of normal.[79] Cerebral metabolism is about 25% of normal. These decreases in hemodynamic parameters are secondary to cold-induced hypometabolism. Measurements must be interpreted in this context rather than in comparison with normothermic values. Body temperatures of 25° to 26°C (77° to 80°F) are associated with prolongation of the PR interval and widened QRS complexes, increased myocardial automaticity, and decreased tissue oxygen delivery out of proportion to decreases in oxygen requirement, resulting in anaerobic metabolism, lactic acidosis, and rewarming acidemia. Blood viscosity is about 200% of normal. Body temperatures of 22° to 23°C (72° to 74°F) are usually associated with ventricular fibrillation and death.

Intraoperative hypothermia is usually mild to moderate and, as long as appropriate safeguards are exercised, is seldom detrimental to patients. The largest problem with intraoperative hypothermia is the nonrecognition of it. The continued administration of normothermic amounts of anesthetic to a hypothermic patient can produce a relative anesthetic overdose.

Passive rewarming (minimizing further heat loss and enabling patients to warm themselves metabolically) is usually effective in treating mild hypothermia (temperature above 34°C [94°F]) when a patient is capable of metabolic or shivering thermogenesis. Intraoperative heat loss can be minimized by warm room temperatures, insulating barriers between the patient and table surfaces, and administering warmed fluids. Active rewarming can be achieved by using circulating warm water or warm-air blankets, infrared heat lamps (optimal distance, 75 cm[81]) or radiant-heat warmers; by placing hot-water bottles under the drapes (avoid contact with skin if the water temperature exceeds 42°C); by flushing the abdominal cavity or colon with warm, sterile, isotonic, polyionic fluids; or by extracorporeal techniques.

Aggressive surface rewarming should be avoided in very cold patients[82–84] because peripheral vasodilation may induce excessive hypotension in the face of a cold-depressed heart. Ischemic peripheral tissues may have accumulated various metabolites, which may have deleterious cardiovascular effects when large quantities are washed into the central circulation. The rewarming rate should be limited to about 1°C/h.[80]

Hyperthermia

Fever is a reset thermostat and is caused by the release of endogenous pyrogens (interleukin 1) from monocytes[85] in response to infections, tissue damage, or antigen-antibody reactions. Interleukin 1 stimulates prostaglandin synthesis in the hypothalamic thermoregulatory center. Hyperthermia, without a reset thermostat, is pathological. It not uncommonly occurs in large dogs that are cocooned within many layers of drapes on an operating table. Hyperthermia may be potentiated by surface vasoconstriction, light levels of anesthesia, and ketamine administration.

Mild degrees of hyperthermia are not, per se, harmful to patients and may represent an appropriate response to an underlying disease (fever or infection). Mild hyperthermia (below 40°C [104°F]) does not normally require treatment, per se. Cell damage starts at body temperatures above 42°C (108°F), when oxygen delivery can no longer keep pace with the racing metabolic activity and increased oxygen consumption. Severe hyperthermia causes multiple organ dysfunction and failure: renal, hepatic, and gastrointestinal failure; myocardial and skeletal muscle damage; cerebral edema; disseminated intravascular coagulation; hypoxemia; metabolic acidosis; and hyperkalemia.[86]

Malignant hyperthermia—a rapidly, relentlessly, progressive increase in body temperature—is associated with the metabolic heat production of disturbed intracellular calcium recycling at the sarcoplasmic reticulum.[87,88] Muscle hypertonicity may or may not occur, depending on the calcium concentration in the sarcoplasm. The defect has been identified in families of people and pigs, and a malignant hyperthermia-like syndrome has been reported in dogs,[89,90] cats,[91,92] and horses.[93,94] Aggressive cooling of the animal, by any and all means possible, is indicated. Dantrolene administration (2.5 to 10.0 mg/kg intravenously) is the specific and often effective treatment for this syndrome.

Surface-cooling techniques are most effective with room-temperature fluids. The evaporation of the water from the skin surface causes the cooling. Ice water causes vasoconstriction that impedes heat loss from the core until skin temperature is below 10°C, at which time vessel paralysis and vasodilation occur, and core temperatures decrease precipitously.[95] Convective heat loss can be enhanced with fans. Conductive heat loss can be enhanced with ice packs. The administration of large volumes of cold crystalloid fluids intravenously into the colon or stomach or into a body cavity is an effective internal cooling technique. The administration of antipyretic drugs (antiprostaglandins, dipyrone, or aminopyrine) is generally an effective treatment for fever, but is ineffective for pathological hyperthermia.

Laboratory Monitoring

Hemoglobin

Whether or not animals are anemic prior to the operative procedure, hemoglobin concentrations will be decreased intraoperatively by anesthetic-induced vasodilation and splenic dilation, non-hemoglobin-containing fluid administration, and blood loss. Historically, in humans, the trigger for a hemoglobin transfusion has been a hemoglobin concentration of 10 g/dL (a packed cell volume [PCV] of 30%).[96] Recent studies in humans have suggested that a more relaxed trigger of 7 g/dL (PCV = 21%) is associated with at least as good, and perhaps better, morbidity and mortality statistics.[96] In veterinary medicine, in animals with immune-mediated hemolytic anemia, it is well accepted to withhold blood transfusions until the hemoglobin concentration is below 5 g/dL (PCV = 15%). In human medicine, in Jehovah Witness patients, mortality rate does not increase significantly until the hemoglobin concentration is 5 g/dL (PCV = 15%).[96] There are many examples of human and veterinary patients surviving much greater levels of anemia.

It may not actually be possible to define a minimum hemoglobin concentration, given the complexities of cardiac output and oxygen-extraction compensatory mechanisms. An animal can tolerate greater degrees of anemia if it has the wherewithal to increase cardiac output. If cardiac output were routinely measured, DO_2 could be calculated, which would eliminate some of the guesswork, but cardiac output is seldom measured. Anesthetic agents commonly decrease myocardial contractility and cardiac output (Tables 19.1 and 19.2), and oxygen extraction is often impaired during general anesthesia,[69] so it would be predicted that anesthetized patients require a hemoglobin concentration higher than the bare minimum. Metabolic markers of poor tissue oxygenation, such as a low PvO_2, a high arteriovenous oxygen-content gradient, or a high arteriovenous PCO_2 gradient, may help guide the need for hemoglobin transfusions. Lactic acidosis is a late, after-the-fact (but usually before-the-death) index of inadequate tissue perfusion.

Blood may need to be administered in volumes of 10 to 30 mL/kg, depending on the magnitude of anemia. Cats have a small blood volume (50 to 55 mL/kg) compared with most other species, and bolus dosages of all fluids should be approximately 50% of canine recommendations. The amount of blood to administer can also be calculated: (desired PCV − current PCV) × body weight (kg) × 2 mL whole blood (or 1 mL packed red blood cells).

Oncotic Pressure

Plasma oncotic pressure is an important vascular fluid–retention force. When depleted, there is an increased risk of interstitial edema, but, because of an offsetting decrease in perimicrovascular oncotic pressure, it is not as edemagenic as might be expected. An increased capillary hydrostatic pressure or vascular permeability are, in contrast, potent causes of edema. Colloidal osmotic pressure (COP) can be measured: Values in normal animals are 20 to 25 mm Hg. Values of 15 to 20 mm Hg are common in anesthetized and critically ill patients, but are not thought to be of important concern. Values in the low teens should trigger therapy, and values in the single digits should cause great concern. COP can be qualitatively approximated from an albumin measurement (albumin normally accounts for about 70% of the COP). Albumin values in normal dogs, cats, and horses are 2.9 to 4.2, 1.9 to 3.9, and 2.3 to 3.6, respectively. A 50% decrease in albumin is associated with about a 50% reduction in COP and so on. COP can also be approximated by calculation from albumin and globulin measurements:[97] dogs, $-7.748 + (5.201 \times \text{albumin}) + (4.857 \times \text{globulin})$; cats, $-4.857 + (5.903 \times \text{albumin}) +$

(3.378 × globulin); and horses, −4.3845 + (5.501 × albumin) + (2.475 × globulin).

The cheapest way to augment COP is to administer an artificial colloid such as dextran 70 or hetastarch in bolus dosages (if volume augmentation is also desirable) of 10 to 30 mL/kg or in continuous infusions of 1 to 2 mL/kg/h. Plasma may be indicated if there are concurrent coagulation issues, and whole blood may be indicated if there are concurrent hemoglobin issues.

Bear in mind a note of caution regarding patients with portocaval shunts, which are often presented with single-digit colloid osmotic pressures. Aggressive colloid administration to "get the COP out of the basement" should be avoided because it upsets the COP–capillary hydrostatic pressure balance and causes edema.

Coagulation

Animals bleed perioperatively either because of a cut large vessel or coagulopathy. The latter can be caused by coagulation or platelet problems. Coagulation is assessed by in vitro tests such as partial thromboplastin time (PTT; normal values are laboratory dependent: 9 to 18 s), activated clotting time (ACT; <120 s at 37°C), and whole blood clotting time (<4 min at 37°C; 8 min at room temperature). The PIVKA test assesses for proteins induced by vitamin K antagonists (normal, 15 to 18 s). Elevated fibrin degradation products represent activation of the clotting and fibrinolytic cascades, and an elevated d-dimer level represents fibrinolysis. The results of these tests are usually normal to slightly abnormal in normal animals.[98–100] Decreased antithrombin (normal: dogs, 80% to 140%; and horses, 130% to 220%[100]) may be indicative of a protein-losing "-opathy" and a prothrombotic state or may represent consumption and disseminated intravascular coagulation (DIC). Platelet numbers can be assessed with a platelet count or a platelet screen on a blood smear (normal, 12 to 25 platelets per oil-emersion field, in a good blood smear without platelet clumping; the platelet count is estimated as 15,000 × the number of platelets per oil-emersion field). Platelet function can be assessed by examining for petechia or a buccal mucosal bleeding time (normal, <4 min). Thromboelastography, which provides an integrated assessment of clot formation, can be used to assess for hyper- or hypocoagulopathy.[101,102]

Coagulopathies may or may not need to be treated. If bleeding is minor and not into a vital organ, and blood can easily be replaced by transfusion, specific therapy may not be necessary. Specific treatment with fresh plasma is necessary if platelets are required; fresh-frozen plasma is used if platelets are not required, but labile factors such as von Willebrand's factor, factor 8, or antithrombin are required. For vitamin K antagonist poisoning, any kind of plasma will suffice. The goal of plasma therapy is to stop the bleeding, not to return the abnormal laboratory test to normal. The latter would be very expensive and would probably not even be possible because of concerns about hypervolemia.

Glucose

An adequate level of blood glucose is important for cerebral metabolism. Hypoglycemia might occur during general anesthesia, but is most common as a nonspecific hormonal response to the stress of anesthesia and operation. A blood glucose concentration below 60 mg/dL should be treated with a 2.5% to 5.0% glucose infusion. Severe hypoglycemia should be treated, in addition, with a bolus of glucose (0.1 to 0.25 g/kg). There is growing evidence that persistent moderate hyperglycemia (>200 mg/dL; >11 mM/L) in the intensive care setting is associated with significantly poorer outcomes.[103–105] In this setting, it has been recommended to enforce glycemic control with insulin in quantities sufficient to maintain the blood glucose concentration below 150 to 200 mg/dL (8 to 11 mM/L).[104,105] Whether short-term hyperglycemia, as would occur with a typical anesthetic-surgical experience, is detrimental has not been investigated.

Metabolic Acid-Base Status

Metabolic and lactic acidosis result from inadequate tissue oxygenation. The marker for metabolic acidosis is a decreased bicarbonate concentration (normal: 20 to 24 mEq/L in dogs, 18 to 22 mEq/L in cats, and 24 to 28 mEq/L in horses), a decrease in total carbon dioxide concentration (a value 1 to 2 mEq/L higher than bicarbonate), or an increase in the base deficit (normal: 0 to −4 mEq/L in dogs, −3 to −7 in cats, and 4 to 0 in horses). Lactate is the marker for lactic acidosis (normal, <2 mM/L), which is usually presumed to represent inadequate tissue oxygenation.[106,107] However, the lactate level can also be elevated as a result of catecholamine-stimulated Na-K-ATPase activity.[108] A word of caution: Do not contaminate the blood sample with lactated Ringer's solution because that will cause a proportionate increase in the measured lactate concentration.

Mild to moderate metabolic acidosis does not need to be treated specifically; correction of the underlying problem should suffice. Severe metabolic acidosis (pH < 7.20) may benefit from therapy with sodium bicarbonate: desired base deficit − measured base deficit × body weight (kg) × 0.3. These dosages of bicarbonate should be administered over a period of at least 20 min, and preferably longer.

Sodium

Sodium concentration is important to transcellular fluid flux, and it is important in fluid therapy not to change it too much, too rapidly. Abrupt changes of sodium concentrations of more than about 15 to 17 mEq/L (in either direction) should be avoided because they may be associated with untoward transcellular water shifts and irreversible brain damage.[109] Baseline sodium concentrations below 130 or above 165 mEq/L in dogs must especially be changed slowly (1 mEq/L/h when treating hypernatremia and 0.5 mEq/h when treating hyponatremia). Decreasing the sodium concentration too fast causes immediate intracellular edema (within hours), whereas increasing it too fast causes hemorrhage and central myelinolysis in 3 to 5 days.

Potassium

Hypokalemia is by far the most common electrolyte problem in critically ill animals, but hyperkalemia can also occur. Both are usually preexisting problems. Severe hypokalemia causes hyperpolarization of electrically excitable cells and, eventually, paralysis. Hypokalemia is potentiated by sodium bicarbonate therapy, respiratory alkalosis, and β_2-agonist therapy. Severe hypokalemia should be treated with a potassium infusion (up to 0.5 mEq/kg/h). Severe hyperkalemia causes hypopolarization of electrically excitable cells and myocardial arrhythmias and fibrillation, decreased conduction and contractility, and asystole. Severe hyperkalemia can be treated with either calcium gluconate (0.5 mL of 10% solution per kilogram) or 0.1 to 0.25 units of regular insulin per kilogram, followed by the infusion of 0.5 to 1.5 g/kg of glucose over the next 2 h.

Calcium

Hypocalcemia (ionized) could be a preexisting problem or could result from the administration of citrated blood products. Hypocalcemia can be potentiated by sodium bicarbonate therapy and, for unknown reasons, is commonly observed with hypothermia. Hypocalcemia can decrease myocardial contractility and cause vasodilation. There is no broad agreement as to when hypocalcemia should be treated, but, as a general guideline, ionized concentrations below 0.75 mM/L should perhaps be treated. Calcium gluconate can be administered as a bolus (0.5 mL of the 10% solution [9.3 mg/mL or 0.47 mEq/mL] per kilogram) or as an infusion of 0.5 to 1.5 mL of the 10% solution/kg/h.

Magnesium

Hypomagnesemia is usually a preexisting problem associated with malnutrition or refeeding, diuretic therapy, or diabetic ketoacidosis. It can also result from the administration of citrated blood products. Hypomagnesemia is generally associated with widespread cellular dysfunction manifested by neuromuscular excitability (muscle twitching, fasciculations, and tetany) and eventually paralysis. Hypomagnesemia may also be associated with ventricular arrhythmias and refractory hypokalemia, hypophosphatemia, hyponatremia, and hypocalcemia.

Hypomagnesemia should be treated if the ionized portion is less than 0.2 mM/L (0.45 mg/dL). A dose of magnesium sulfate (0.1 to 0.2 mEq/kg) can be administered slowly intravenously. Magnesium sulfate can then be administered at a daily dosage of 0.25 to 1.0 mEq/kg/day (3 to 12 mg/kg/day) as a continuous-rate infusion.

References

1. Vacanti CJ, VanHouten RJ, Hill RC. A statistical analysis of the relationship of physical status to postoperative morbidity in 68,388 cases. Anesth Analg 40:564–566, 1970.
2. Goldstein A, Keats AS. The risk of anesthesia. Anesthesiology 33:130–143, 1970.
3. Marx GF, Mateo CV, Orkin LR. Computer analysis of postanesthetic deaths. Anesthesiology 39:54–58, 1973.
4. Bodlander FMS. Deaths associated with anaesthesia. Br J Anaesth 47:36–40, 1975.
5. Arbous MS, Grobbee DE, van Kleef JW, et al. Mortality associated with anaesthesia: Quantitative analysis to identify risk factors. Anaesthesia 56:1141–1155, 2001.
6. Mi WD, Sakai T, Singh H, Kudo T, Kudo M, Matsuki A. Hypnotic endpoints vs the bispectral index, 95% spectral edge frequency and median frequency during propofol infusion with or without fentanyl. Eur J Anaesthesiol 16:47–54, 1999.

7. Chopra V, Bovill JG, Spierdijk J. Accidents, near accidents and complications during anaesthesia. Anaesthesia 45:3–6, 1990.
8. Dyson DH, Maxie MG, Schnurr D. Morbidity and mortality associated with anesthetic management in small animal veterinary practice in Ontario. J Am Anim Hosp Assoc 34:325–335, 1998.
9. Winters WD, Ferrar-Allado T. The cataleptic state induced by ketamine: A review of the neuropharmacology of anesthesia. Neuropharmacology 11:303–315, 1972.
10. Guedel AE. Inhalational Anesthesia: A Fundamental Guide. New York: Macmillan, 1937.
11. Kerssens C, Klein J, Bonke B. Awareness: Monitoring versus remembering what happened. Anesthesiology 99:570–575, 2003.
12. Nordstrom O, Sandin R. Recall during intermittent propofol anaesthesia. Br J Anaesth 76:699–701, 1996.
13. Sandin RH. Awareness 1960–2002, explicit recall of events during general anaesthesia. In: Vuyk J, Schraag S, eds. Advances in Modelling and Clinical Applications of Intravenous Anaesthesia. New York: Kluwer Academic/Plenum, 2003:135–147.
14. Stanski DR. Monitoring depth of anesthesia. In: Miller RD, ed. Anesthesia. New York: Churchill-Livingstone, 1990:1001–1029.
15. Katoh T, Suguro Y, Nakajima R, Kazama T, Ikeda K. Blood concentration of sevoflurane and isoflurane on recovery from anaesthesia. Br J Anaesth 69:259–262, 1992.
16. March PA, Muir WW. Minimum alveolar concentration measures of central nervous system activation in cats anesthetized with isoflurane. Am J Vet Res 64:1528–1533, 2003.
17. Vuyk J, Mertens M. Bispectral index scale (BIS) monitoring and intravenous anaesthesia. In: Vuyk J, Schraag S, eds. Advances in Modelling and Clinical Applications of Intravenous Anaesthesia. New York: Kluwer Academic/Plenum, 2003:95–104.
18. Tranquilli WJ. Techniques of inhalation anesthesia in ruminants and swine. Vet Clin North Am Food Anim Pract 2:593–619, 1986.
19. Rampil IJ. A primer for EEG signal processing in anesthesia. Anesthesiology 89:980–1002, 1998.
20. Schwender D, Daunderer M, Mulzer S, Klasing S, Finsterer U, Peter K. Spectral edge frequency of the electroencephalogram to monitor "depth" of anaesthesia with isoflurane or propofol. Br J Anaesth 77:179–184, 1996.
21. Drummond JC, Brann CA, Perkins DE, Wolfe DE. A comparison of median frequency, spectral edge frequency, a frequency band power ratio, total power, and dominance shift in the determination of depth of anesthesia. Acta Anaesthesiol Scand 35:693–699, 1991.
22. Schmidt GN, Bischoff P, Standl T, Lankenau L, Hilbert GD, Esch JS. Comparative evaluation of Narcotrend, Bispectral Index, and classical electroencephalographic variables during induction, maintenance, and emergence of a propofol/remifentanil anesthesia. Anesth Analg 98:1346–1353, 2004.
23. Otto KA, Mally P. Noxious stimulation during orthopaedic surgery results in EEG "arousal" or "paradoxical arousal" reaction in isoflurane-anaesthetised sheep. Res Vet Sci 75:103–112, 2003.
24. Otto KA, Short CE. Electroencephalographic power spectrum analysis as a monitor of anesthetic depth in horses. Vet Surg 20:362–371, 2004.
25. Miller SM, Short CE, Ekstrom PM. Quantitative electroencephalographic evaluation to determine the quality of analgesia during anesthesia of horses for arthroscopic surgery. Am J Vet Res 56:374–379, 2004.
26. Martin-Cancho MF, Lima JR, Luis L, et al. Bispectral index, spectral edge frequency 95%, and median frequency recorded for vari-