Chapter 38

Neurological Disease

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Introduction

Veterinary patients frequently require anesthesia for diagnostic evaluation or surgical correction of neurological disorders. Diagnostic procedures that require either general anesthesia or heavy sedation include electroencephalography (EEG), myelography, other imaging techniques, and electrodiagnostic testing. Veterinary neurosurgical anesthesia is more often required in patients with spinal cord rather than intracranial disorders. The most frequently performed neurosurgical procedure in veterinary medicine is used in the treatment of intervertebral disk disease. However, the increased use of advanced imaging techniques, such as computed tomography and magnetic resonance imaging (MRI), has led to a greater frequency of intracranial operative procedures in small animal patients where these imaging modalities are available. In patients with neurological disease, consideration of the dynamics of intracranial pressure (ICP), cerebral blood flow (CBF), and cerebrospinal fluid (CSF) production and flow is important in preventing patient morbidity or death.

Physiology

In normal awake animals, blood supply to the central nervous system (CNS) is controlled by autoregulatory mechanisms. Alteration in CBF can result from a variety of changes in arterial oxygenation, carbon dioxide partial pressure, mean arterial pressure, and venous outflow. The brain and spinal cord are protected by encasement within the bony skull and vertebral column. Increases in blood flow within the noncompliant cranial vault cause an increase in the intracranial volume.[1–3] Once increases in CBF cause the intracranial volume to exceed the limits of effective compliance, ICP increases sharply. When clinical findings suggest ICP is already increased by intracranial masses, trauma, or derangement of autoregulation, extreme care is required, because slight changes in intracranial volume greatly increase ICP.[2] Significant ICP increases may lead to cerebral ischemia and brain herniation.[1]

Autoregulation of Cerebral Blood Flow

Autoregulation of brain blood flow is usually very effective in a systemic mean arterial blood pressure range of approximately 60 to 140 mm Hg. Within this range of blood pressure, many factors—including intracranial tumors, hypercapnia, severe hypoxia, and many anesthetics—interfere with autoregulation and cause changes in ICP (Fig. 38.1).[1,4,5] Blood vessels in the brain supplying diseased or neoplastic tissues may be fully dilated and unaffected by normal autoregulation mechanisms.

The CNS depression of general anesthesia is usually accompanied by a decrease in cerebral metabolic rate and cerebral metabolic requirement for oxygen ($CMRO_2$). This decrease in oxygen requirement is thought to be protective in the possible event of relative ischemia during anesthesia and neurosurgery. There are conflicting reports on the efficacy of various anesthetics in reducing $CMRO_2$, just as there are with regard to the relative effects of the anesthetics on CBF and ICP. Isoflurane, sevoflurane, etomidate, and the barbiturates are generally recognized as contributing substantially to reduction of $CMRO_2$, affording some cerebral protection.[5]

In patients with preexisting elevated ICP, further increases can be caused by gravitational or positional interference with drainage of venous blood from the head. Obstruction by occlusion of jugular veins through surgical positioning of the head, use of a neck leash, or venous occlusion to obtain blood samples or placement of jugular vein catheters can rapidly cause dangerous increases in ICP.[6] For intracranial neurosurgery, a slight elevation of the head above the level of the heart (with the neck in a neutral position) will facilitate venous drainage, lowering ICP. Extreme elevation is avoided to minimize the risk of venous air embolization.[3]

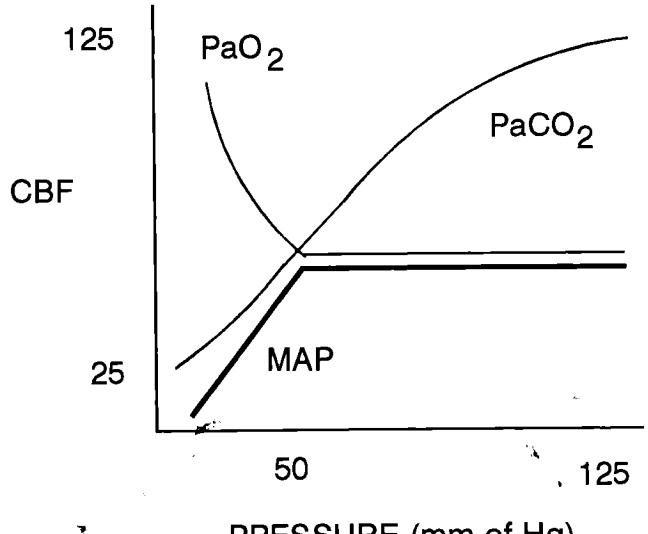

Fig. 38.1. Alterations in cerebral blood flow (CBF), in milliliters per 100 g of brain tissue per minute, caused by changes in arterial tension of oxygen (PaO_2), carbon dioxide ($PaCO_2$), and mean arterial blood pressure (MAP). Redrawn from Shapiro.[1]

Only at very low arterial oxygen tensions does the CBF change in response to oxygen partial pressure. When arterial oxygen partial pressure (PaO_2) decreases below a threshold of 50 mm Hg, CBF increases (Fig. 38.1). The relationship between arterial carbon dioxide partial pressure ($PaCO_2$) and CBF, on the other hand, is linear. CBF increases by about 2 mL · min^{-1} · 100 g^{-1} of brain tissue for every 1-mm Hg increase in arterial carbon dioxide over the range of $PaCO_2$ from 20 to 80 mm Hg.[7] Hyperventilation has been used extensively in neuroanesthesia to reduce CBF (via cerebral vasoconstriction). This maneuver decreases tissue bulk, facilitating intracranial surgery. Although quite effective, this technique is somewhat controversial in some situations, because a potential exists for the diversion of remaining blood flow preferentially to diseased tissues lacking autoregulation at the expense of normal brain tissue.[8] Deliberate hyperventilation to decrease ICP may be risky when mean arterial blood pressure is reduced to less than 50 mm Hg. The ensuing ischemia could be deleterious to normal brain tissues if a "steal" of CBF diverts remaining blood flow.[8,9] The rapid and substantial reduction in CBF and ICP achieved by hyperventilation makes it a valuable tool for the immediate reduction in brain bulk to facilitate intracranial surgery and to reduce acute brain swelling.

Although controversial, restriction of intravenous fluids to only that volume necessary to maintain adequate circulating volume and cardiac output is usually recommended in neurosurgical patients with increased ICP.[10,11] Excessive fluid volume has been associated with increased central venous pressure, decreased venous outflow, and increased risk of compounding cerebral edema. Diuretic therapy is frequently indicated in the medical management of patients with intracranial masses and elevated ICP or cerebral edema.[6] Dextrose administration is somewhat controversial and must be individualized to the situation. Hyperglycemia is associated with adverse outcome in animals with cerebral ischemia, and cerebral edema can be exacerbated by administration of isotonic dextrose. However, intravenous dextrose administration decreases the incidence of seizures in patients after metrizamide myelography and is indicated in hypoglycemic seizures or hypoglycemic coma.[1,12,13]

Glucocorticoids are effective in the treatment of some forms of cerebral edema[14] and have been shown to be effective in reducing the increased ICP that is caused by brain tumors and hydrocephalus. Glucocorticoid therapy may be considered in the management of patients with cerebral edema associated with primary or metastatic brain neoplasia. Since dexamethasone administration has been shown to reduce the rate of CSF formation in dogs, steroid administration may be of some value in the preanesthetic management of hydrocephalic patients considered at risk of further increases in ICP.[14,15] Corticosteroids are now known to be contraindicated in cases of CNS trauma.

Pharmacological Considerations

Sedatives, Tranquilizers, and Analgesics

For many years, the suspected increased seizure activity associated with administration of the phenothiazine (e.g., acepromazine) and possibly butyrophenone (e.g., droperidol) tranquilizers contraindicated their use in seizure-prone patients and in patients for diagnostic EEG.[16] A more recent retrospective study indicates that acepromazine does not potentiate seizure activity.[17] Control of seizures with benzodiazepine tranquilizers (e.g., diazepam or midazolam) is desirable in the management of seizure-prone patients but can obscure characteristic patterns in diagnostic EEGs. In addition, benzodiazepines appear to decrease CBF and ICP.[18]

Use of xylazine in dogs and cats is controversial, yet clinical evidence for or against its use in patients with neurological disease is lacking. In healthy conscious horses, xylazine (1.1 mg/kg IV) decreased CSF pressure measured at the lumbosacral space.[19] Horses anesthetized with pentobarbital and subsequently given xylazine (1.1 mg/kg IV) had no change in either lateral ventricle or lumbosacral CSF pressure.[20] Horses given detomidine (20 μg/kg IV) also had a reduction in CBF.[21] Medetomidine administered to isoflurane-anesthetized dogs had no effect on ICP measured using a fiberoptic transducer, whereas antagonism of medetomidine by using atipamezole was associated with a dramatic transient increase in ICP.[22] Dexmedetomidine, the pharmacologically active stereoisomer of medetomidine, decreased CBF in both halothane and isoflurane anesthetized dogs.[23,24] Thus, although the effects of α_2-agonists on ICP may differ in horses and dogs with head trauma or neurological disease, they appear to be rational choices to provide sedation for examination or as a preanesthetic medication. Venous congestion in the head, when positioned below the level of the heart, may be associated with an increase in ICP. Therefore, the dose of xylazine or detomidine should be titrated to prevent excessive head lowering and possible resultant increased ICP in horses or other species.

Table 38.1. Effects of anesthetics and anesthetic adjuncts on cerebral blood flow (CBF), intracranial pressure (ICP), blood pressure (BP), and cerebral perfusion pressure (CPP).

Agent	CBF	ICP	BP	CPP
Desflurane	↑	↑	↓	↓
Halothane	↑↑	↑↑	↓	↓
Isoflurane	↑	↑	↓	↓
Nitrous oxide	↔	↔	↔	↔
Sevoflurane	↑	↑	↓	↓
Atracurium	↔	↔	↔	↔
Diazepam	↓	↓ or ↔	↓	↔
Droperidol	↓	↓	↓	↔
Fentanyl	↓	↓	↓	↔
Halothane-thiopental	↔	↔	↓	↓ or ↔
Ketamine	↑↑	↑↑	↑	↓
Midazolam	↓	↔	↔	↔
Morphine[a]	↓	↔	↓ or ↔	↔
Propofol	↓↓	↓↓	↓	↔
Thiopental	↓↓	↓↓	↓	↔

[a]Indirectly, respiratory depression caused by morphine (and other opioids) may result in hypercapnia with raised CBF and ICP.

Opioids or neuroleptanalgesic combinations are sometimes used in anesthetic management of patients with increased ICP. The direct effects of opioids on CBF and ICP are minimal. However, opioids may indirectly increase CSF pressure and should be used cautiously in patients with cerebral trauma or space-occupying tumors. Increases in pressure within the cranium may aggravate the underlying condition. The elevation in CSF pressure is caused by accumulation of carbon dioxide, which in turn is caused by opioid-induced hypoventilation. If a patient is ventilated to prevent hypercapnia, the increase in CSF pressure does not occur when opioids are administered.[25] When opioids are used in these cases, the respiratory status must be assessed through arterial blood-gas analysis or end-tidal carbon dioxide levels, and when necessary, the patient should be ventilated to prevent hypercapnia. The judicious use of opioids for pain management in the postoperative period often does not cause as much respiratory depression as does pain itself.[26] Thus, opioid analgesic medication is based on the relative severity of pain in each animal.

Injectable Anesthetics

Most of these cause significant reductions in $CMRO_2$, CBF, and ICP (Table 38.1).[1–3,5,6,12] Recognition of barbiturate-induced reductions in $CMRO_2$, CBF, and ICP has contributed to the concept of *barbiturate coma* therapy for cerebral resuscitation after periods of cerebral ischemia as occurs in near-drowning and in cardiopulmonary resuscitation. The value of barbiturates as a therapy for cerebral ischemia/hypoxia is controversial at best. It is likely that barbiturates are protective if administered prior to the insult but of relatively little value if administered after clinical signs of brain ischemia have developed. Propofol or barbiturates may be of value in avoiding postoperative sequelae to surgical trauma. It must be recognized, however, that barbiturate anesthesia often prolongs anesthetic recovery. In neurosurgical patients, the CNS depression associated with residual barbiturates can seriously obscure postoperative evaluation and prevent meaningful neurological evaluation.

The dissociative anesthetics represent a notable exception to the reduction in CBF, ICP, and $CMRO_2$ characteristic of most injectable anesthetics.[1–3,6,12] EEG activity also increases with dissociative anesthesia. Convulsant activity ranging from muscle twitching to seizures occurs as an infrequent adverse effect of the dissociatives. Patients with a history of seizure-related disorders and those with intracranial masses, closed-head traumatic injuries, and other conditions potentially increasing ICP should not receive dissociative anesthetics. Because benzodiazepine tranquilizers may decrease CBF and ICP, their combination with dissociative anesthetics may attenuate cerebrovascular and neurological effects of the dissociative agent.[27]

Volatile Anesthetics

Inhalant anesthetics increase CBF and alter $CMRO_2$ to varying degrees.[7,10,12,28–31] Since increased CBF and ICP are also highly influenced by carbon dioxide retention, respiratory depression associated with volatile anesthesia can be responsible for increases in ICP that are clinically significant in neurosurgical patients. There is evidence that regional changes in the distribution of CBF result from administration of the volatile anesthetics such that our understanding of cerebrovascular effects may not be accurately based on global estimates of CBF in animals.[4]

Among the volatile anesthetics clinically used in veterinary medicine, halothane dramatically blocks autoregulation, increasing CBF and ICP.[29,30] Methoxyflurane, enflurane, and isoflurane all interfere with autoregulation in a more limited extent than halothane.[3] At 1.1 minimum alveolar concentration levels of anesthesia, CBF increases almost 200% with halothane but by only about 40% with enflurane and is unchanged with isoflurane.[2,28] Higher concentrations of isoflurane cause increases in CBF. The loss of cerebral autoregulation with halothane is implicated in the greater degree of brain swelling noted during neurosurgery with this anesthetic. The increase in CBF occurs rapidly upon halothane administration and is independent of changes in arterial blood pressure, implicating halothane's direct cerebrovascular effects.

Fortunately, modest hyperventilation, reducing arterial carbon dioxide to 30–35 mm Hg, often eliminates the volatile anesthetic-induced increase in CBF.[29] Hyperventilation is rapidly effective in reducing elevated CBF and ICP or in preventing their rise in patients at risk. It is easy, rather cost free, and the safest method available. Excessive hyperventilation should be avoided because cerebral perfusion pressure may decrease, resulting in cerebral ischemia. In light of the respiratory depression of general anesthesia and the potential rise in CBF and ICP, ventilation to prevent hypercapnia should be incorporated into the anesthetic technique for animals with intracranial masses or other disorders of autoregulation. Values between 35 and 40 mm Hg of $PaCO_2$ are recommended in anesthetized patients at risk of increased morbidity associated with raised ICP.

Nitrous oxide has substantial cerebrovascular effects. Although there are conflicting reports and a minority opposing opinion, adverse effects of nitrous oxide have been well documented in animals undergoing neurosurgery.[5,31] Nitrous oxide causes the most profound increase in both CBF and ICP of all the inhalant anesthetics. Owing largely to the limited potency of nitrous oxide in veterinary patients, its use is primarily in combination with other general anesthetics. The combination of volatile anesthetic gases and nitrous oxide can produce greater increases in CBF and ICP. In rabbits, nitrous oxide administration produced a consistent increase in CBF and ICP regardless of whether it was combined with halothane, isoflurane or fentanyl-pentobarbital anesthesia.[16] Furthermore, these potentially adverse effects were not blocked by hyperventilation. In dogs, nitrous oxide increases $CMRO_2$ by 11%. In animal models of regional cerebral ischemia, the use of nitrous oxide worsens the neurological outcome.[5] The disadvantages of nitrous oxide would appear to be substantial for many neurosurgical patients.

Anesthetic Management of Specific Neurological Problems

Myelography and Intervertebral Disk Disease

For the relatively common surgical procedures to decompress cervical or thoracolumbar intervertebral disk herniation, anesthetic management should address (a) protection from possible seizures and other potential complications associated with administration of myelographic contrast agents, (b) perioperative pain relief, (c) maintenance of adequate spontaneous ventilation, and (d) management of concurrent disorders such as urinary incontinence or other factors predisposing patients to adverse recovery.

Radiographic contrast myelography is frequently performed in the immediate preoperative period to localize the lesion(s) and to identify the proper site(s) for surgical decompression. As this procedure is often performed during the same anesthetic period, patient management is designed to optimize conditions for both the diagnostic (radiographic) and the therapeutic (surgical) procedures. Dural puncture for sampling of CSF and/or for administration of myelographic contrast agent requires a depth of anesthesia at less than a surgical plane but adequate to prevent patient movement with subsequent trauma. Considerations for an anesthetic protocol suitable for spinal cord surgery are listed in Table 38.2.

Avoiding the use of potent respiratory depressants and using a light surgical plane of anesthesia will optimally maintain spontaneous ventilation during myelography. Among the less frequent complications associated with myelography are respiratory depression or respiratory arrest and cardiac arrhythmias.[32] Preoperative administration of an anticholinergic will reduce the incidence of bradycardia. Respiratory depression is probably referable to effects of the contrast agent at the level of brain stem and medullary respiratory centers. As such, respiratory effects are most likely to be associated with "high" myelograms, typically those showing contrast agent ascending to the brain and brain stem. The incidence of seizure activity and the other potential adverse side effects of myelography appears to be greatly reduced with use of newer contrast agents such as iopamidol and iohexol rather than metrizamide.[33,34] Hyperflexion of the cervical spine for cisternal CSF collection and for cervical administration of myelographic contrast can easily kink most endotracheal tubes, causing airway obstruction. Endotracheal tubes that are armored or contain spiral wire are quite resistant to kinking. Metal or other radiopaque reinforcement in the armored tubes makes them unsuitable for use in cervical and cranial radiographic studies. Close attention to adequacy of the airway and spontaneous ventilation is of paramount importance when flexing the neck.

Table 38.2. Anesthetic management for intervertebral disk disease.

1. Benzodiazepine tranquilization (e.g., diazepam, 0.2 mg/kg IV)
2. Low-dose opioid (e.g., hydromorphone, 0.2 mg/kg IV or IM)
3. Anticholinergics if needed, especially before myelography (atropine, 0.04 mg/kg IM)
4. Induction with thiopental (15 mg/kg IV) or propofol (3 mg/kg IV) administered to effect
5. Avoid hyperextension of the neck in cases of cervical trauma, instability, or disk disease
6. Maintenance of protected airway during the procedure
7. Judicious fluid therapy
8. Positioning of the patient to avoid venous occlusion
9. Use of intraoperative and postoperative opioids for pain management

IM, intramuscularly; and IV, intravenously.

In addition to the precautions and considerations appropriate for thoracolumbar disk disease, cervical disk disease can be associated with increased risk of cardiac arrhythmias and respiratory arrest.[3] Vagal stimulation during ventral approaches to the cervical spine may increase with retraction of the carotid sheath. Frequently, there appears to be greater postoperative pain with cervical as opposed to thoracolumbar surgical repair, possibly indicating a neuropathic component to the postoperative pain. Patient positioning for a ventral cervical approach often is dorsal recumbency with the neck extended. Patients should be observed carefully during and after positioning, because overextension may lead to respiratory arrest or cardiac arrhythmias.

Patients having lost deep-pain perception are surgical emergencies. Rapid-sequence induction, using intravenous general anesthetics rather than inhalation induction of anesthesia, is indicated if the animal has or may have a full stomach. Additional management related to the emergent nature of their distress may be indicated. The fact that these animals do not feel painful stimuli to the rear limbs suggests that these areas preferentially can be used for placement of injections and intravenous catheters without contributing additional pain to an already highly stressed patient.

Anesthesia for Horses with Cervical Vertebral Instability (Wobbler Syndrome)

The preanesthetic dose of xylazine administered to a horse with wobbler syndrome should be decreased to prevent the horse from becoming recumbent prior to induction of anesthesia. Xylazine should not be administered until the horse is moved to the induc-

tion area. Horses that are severely ataxic prior to drug administration may be anesthetized in the stall and returned there for recovery after the procedure.

Horses with wobbler syndrome may require anesthesia for myelography. For premedication, a low dose of xylazine (0.2 to 0.4 mg/kg IV) can be used. Anesthesia may be induced by using guaifenesin in combination with thiopental. Anesthesia can be maintained with halothane, isoflurane, sevoflurane, or an injectable anesthetic mixture such as guaifenesin-thiopental. Some clinicians prefer to administer guaifenesin alone until the horse becomes unsteady and then administer a bolus of thiopental (2 to 3 g/450 kg body weight). The total dose of anesthetic should be kept to a minimum so that recovery from anesthesia is optimized. As a rule of thumb, a total dose of 2 L of the guaifenesin-thiopental combination is not exceeded (5% guaifenesin with 0.3% thiopental). Horses can be expected to have an acceptable recovery when anesthesia is limited to less than 1 h. Controlled ventilation during the procedure is recommended. Assisted recovery using a tail rope or other method of assistance may be desired; however, experience and extreme caution are required because of the danger of being crushed by an ataxic horse.

Myelography or withdrawal of CSF may precipitate changes in cerebrospinal pressure, which can adversely affect function of the respiratory center in the brain stem.[35] Following administration of a contrast agent, the head should be elevated to minimize the agent's migration toward the brain. In one study, 32% of the horses with significant gait abnormalities that underwent myelography (using metrizamide as the contrast agent) had significant worsening of clinical signs after the procedure.[36] Equine myelography with iopamidol or iohexol as the contrast agent may be associated with less toxicity and fewer side effects than metrizamide.[37,38] Regardless of the contrast agent used, a sudden drop in arterial blood pressure may occur at the time of injection. Monitoring of blood pressure is recommended during the procedure. At the end of the procedure, the horse is returned to spontaneous ventilation and remains anesthetized for at least 30 min after the last injection of contrast agent. Following prolonged lateral recumbency, it is advised to allow the horse to recover with the same side down. Turning horses to the opposite side after long procedures in lateral recumbency does not improve, and may worsen, arterial oxygenation.[39,40] Recovery from anesthesia for myelography is often characterized by several hours of ataxia, which may be more severe than prior to anesthesia. Measures to observe and support recovering horses should be available. Some horses benefit from being placed in a sling for a few hours after anesthesia. To promote a smooth recovery (and possibly to decrease the incidence of postmyelogram seizure or muscle-tremor activity), a low dose of xylazine (25 to 100 mg IV) or diazepam (0.03 mg/kg intramuscularly) may be administered to adult horses. Some clinicians use phenylbutazone to minimize postmyelogram muscle-tremor activity. Because phenylbutazone is highly protein bound and may displace anesthetic from protein-binding sites, it has been recommended that phenylbutazone be administered before anesthetic agents are given. Phenylbutazone administration to horses that already are induced and/or maintained with injectable anesthetics may deepen anesthesia or prolong recovery.

Intracranial Masses and Elevated Intracranial Pressure

Patients with intracranial masses, dysfunctional CBF autoregulation, and/or increased ICP are at risk of rapid decompensation under anesthesia. Preoperative assessment should include measurement of arterial blood pressure, because many patients with elevated ICP will have an accompanying increase in systemic arterial blood pressure (Cushing's response). Systemic hypertension is an attempt to compensate and maintain adequate cerebral perfusion pressure. If mean arterial pressure is significantly elevated prior to drug administration, arterial blood pressure should not be allowed to drop to normally acceptable levels under anesthesia (e.g., a mean arterial pressure of 60 mm Hg), because cerebral ischemia can result despite an "acceptable" mean blood pressure.

Manual or mechanical positive-pressure ventilation should be immediately available and instituted at induction. Mechanical ventilation should be continued until extubation. In some cases, allowing $PaCO_2$ to rise in order to stimulate spontaneous ventilation, before the respiratory depressant effects of the anesthetics wane, may cause serious elevations in ICP and possibly herniation. Anesthetic monitoring should address the physiological variables associated with altered ICP. Venous and arterial blood pressures and airway or arterial sampling for carbon dioxide analysis should be included, if possible. Intravenous mannitol (0.5 to 1.0 g/kg IV slowly) may be useful to reduce ICP before, during, or after anesthesia. Optimal anesthetic management can substantially improve patient status and the outcome of intracranial surgical procedures. A recommended anesthetic technique is summarized in Table 38.3.

Management of Seizures in the Perianesthetic Period

Seizures are most commonly observed in animals with other signs of brain disease. Thus, animals anesthetized for diagnosis or treatment of CNS disease are more likely to exhibit seizure activity during the perianesthetic period. The animal with seizure activity should be medically treated to control standard recom-

Table 38.3. Anesthetic technique for patients with elevated cerebral blood flow and/or intracranial pressure.

1. Preanesthetic critical care management and stabilization
2. Fluid therapy limited to minimize cerebral edema but adequate to support circulation
3. Avoid severe respiratory depression, jugular venous occlusion, and coughing at induction or during recovery
4. Avoid dissociative anesthetics, halothane, enflurane, and nitrous oxide
5. Thiobarbiturate or propofol induction of anesthesia preferred
6. Minimal inhalant anesthetic supplemented with opioids for maintenance
7. Modest hyperventilation to reduce cerebral blood flow and intracranial pressure
8. Postoperative critical care with support of ventilation and circulation as indicated

mendations before anesthesia is attempted. In horses, treatments for status epilepticus include use of anticonvulsants such as diazepam, midazolam, pentobarbital, phenobarbital, phenytoin, primidone, chloral hydrate, and the combination of guaifenesin with a thiobarbiturate.[41] Foals exhibiting seizure activity may be treated with diazepam (5 to 10 mg IV), phenytoin (5 to 10 mg/kg IV, intramuscularly, or orally), or phenobarbital (with plasma-level monitoring).[42] A complication associated with treatment of seizures in neonatal foals is the altered disposition of drugs. Functional hepatic microsomal enzymes and renal function in neonates is immature. Thus, concurrent medication with other drugs may cause unexpected interactions or changes in elimination, necessitating careful patient monitoring and alteration of the anticonvulsant dosage regimen.

Phenothiazine tranquilizers have been shown to augment epileptiform activity on the electroencephalogram of dogs.[43] Intrathecal injection of radiographic contrast agents is frequently associated with seizures.[44] Therefore, the use of acepromazine and other phenothiazine tranquilizers has usually been avoided in animals with preexisting seizures and in animals undergoing myelography (Table 38.4).

Horses sedated with xylazine demonstrate electroencephalographic slowing with irregular waveforms.[45] Xylazine (0.1 to 0.2 mg/kg IV) and diazepam (0.2 mg/kg IV) have both been suggested as effective injectable treatments for seizures in horses recovering from anesthesia.[46] Seizures occurring after myelography that are not controlled by injections of xylazine or diazepam may be treated by reanesthetizing the horse with guaifenesin and a thiobarbiturate. Anesthesia with an inhalation anesthetic may be necessary for up to 1 or 2 h until seizure activity wanes.

In horses, the accidental intracarotid injection of drugs such as xylazine may seriously irritate neural tissues, causing a violent reaction and seizures. Management of this potentially dangerous situation should be directed toward manual and, preferably, chemical restraint to prevent injury. Intravenous injection of thiopental alone or guaifenesin combined with thiopental is recommended as soon as accidental intracarotid injection is recognized. The preplacement of an indwelling intravenous catheter is recommended to help prevent the accidental perivascular injection of any drug. Inspired oxygen should be supplemented, and intravenous fluids should be administered. In the case of intracarotid injection of xylazine, pharmacological antagonism is not recommended. Horses given intracarotid drug injections can be sedated for 30 min by using the combination of guaifenesin and thiopental and often recover uneventfully. The accidental intracarotid injection of larger doses may have severe neurological sequelae (presumably caused by brain edema) requiring additional symptomatic treatment.

Table 38.4. Anesthetic management of seizure-prone patients.

1. Treatment or prevention of hypoglycemia
2. Use benzodiazepines for tranquilization (diazepam or midazolam, 0.2 mg/kg IV) or barbiturate sedation (phenobarbital, 2 to 5 mg/kg, IM)
3. Induction with thiopental (15 mg/kg IV) or propofol (3 mg/kg IV) administered to effect
4. Avoid enflurane for maintenance of anesthesia
5. Prevent hypoventilation and hypercapnia

IM, intramuscularly; and IV, intravenously.

Anesthesia for Electrodiagnostic Techniques

Electrodiagnostic procedures are those that involve recording spontaneous or evoked electrical activity from tissues or organs. Although consistent with the definition, electrocardiography is usually not considered under this rubric. In veterinary medicine, clinical electrodiagnostic techniques are used to record potentials from muscle, peripheral nerves, spinal cord, brain stem, cortex, and retina. In humans, these procedures are performed without the use of general anesthetics, tranquilizers, or analgesics. With adequate instruction, most adults will tolerate some degree of discomfort or boredom to achieve good test results. Some procedures, such as nerve-conduction studies or electromyography, cause some pain, whereas others, such as visual or auditory evoked potentials, may simply require human patients to concentrate or refrain from movement. A fundamental problem encountered in the use of electrodiagnostic techniques in veterinary medicine is that of patient cooperation. Even during those procedures in which the stimulus is innocuous, artifacts caused by movement may render the technique ineffective. Therefore, many of these procedures must be performed in anesthetized or tranquilized animals. This approach is usually less stressful to the animals, insures a minimum of recording artifacts, and often gives the examiner an opportunity to collect more useful data. The obvious trade-off is nervous system function that has been chemically altered to some degree.

The effects of anesthetics on the outcome of electrodiagnostic procedures range from insignificant to dramatic. In some instances, the use of anesthetic agents altogether precludes recording certain types of potentials. The order of increasing anesthetic effects on recordings is peripheral nerve and skeletal muscle, spinal cord and retina, brain stem, and cerebral cortex. Even so, as long as the effects are understood, the benefits of the recordings may still provide valuable diagnostic data and information.

Today, intraoperative monitoring has become standard practice when a physician desires direct and prompt feedback about neural function during surgical procedures. The use of intraoperative electrodiagnostic monitoring in veterinary medicine is not widespread, but many electrodiagnostic laboratories judiciously use anesthetics for their procedures. Certainly, the precautions will vary between animal species and the physical condition of patients. An exhaustive review of anesthetic effects on these diagnostic techniques is not possible here, but some examples from the literature underscore the relevance of this information.

Electroencephalogram and Electromyography

There are two procedures in which electrical activity is recorded from spontaneously, reflexively, or volitionally active tissue. The first is the electroencephalogram (EEG), activity produced by the

cerebral cortex, and the second is the electromyogram, electrical activity produced by skeletal muscle. Most other electrodiagnostic procedures require a stimulus to evoke activity from excitable tissue. The evoking stimulus may be electrical, visual, auditory, or mechanical.

The effects upon the EEG depend on the anesthetic type and depth. Anesthesia initially causes an increase in the voltage and a decrease in the frequency of cortical potentials when compared with the record of an awake alert dog. Spikes and spindles may also riddle the EEG of lightly anesthetized dogs and cats.[47,48] As anesthesia deepens, the overall voltage begins to diminish. A dose-response decrease in cerebral oxygen consumption ($CMRO_2$) accompanies the use of isoflurane in dogs and causes the EEG to become isoelectric at an end-expired concentration of 3%.[49] The same type of cortical alteration in electrical activity, sometimes referred to as *burst suppression*, has been reported in swine.[50] Isoflurane anesthesia may thereby interfere with acquisition of diagnostic information. A recommended anesthetic technique for diagnostic EEG evaluation and for procedures other than EEGs in seizure-prone patients is summarized in Table 38.4.

Dose-dependent CNS depression of EEG activity by most anesthetics is characteristic and has led to the development of EEG-based anesthetic-monitoring techniques.[51] Use of computer-analyzed *quantitative* EEG in isoflurane-anesthetized dogs has been reported.[52] Notable exceptions to the general rule that anesthetics decrease EEG activity include the dissociative anesthetics and the volatile anesthetic enflurane. Enflurane anesthesia can be accompanied by increased EEG activity extending to seizures, particularly if a patient is hyperventilated and hypocarbic.[3,12] Alterations in normal $PaCO_2$ are associated with significant changes in the quantitative EEG of dogs during halothane anesthesia.[53] Methoxyflurane and halothane anesthetics cause a progression of cerebral depression in dogs, with the latter more likely to promote burst suppression than the former.[54] Similar results in dogs have been reported for sodium pentobarbital. In dogs, barbiturate anesthesia is accompanied by reduced EEG amplitude and burst suppression.[55]

Monitoring CNS depression by using EEG during anesthesia has been the focus of study for decades. However, direct interpretation of the EEG has not proven adequately reliable or time responsive for use in operative circumstances. Processed EEG monitoring has evolved as a way to provide immediate feedback to anesthetists in regard to patients' CNS activity. Spectral edge frequency, total power, beta to delta frequency ratios, and other specific parameters derived from computer-processed EEG have been correlated to varying degrees with anesthetic depth, but interpretation can vary depending on the selection of anesthetic agents. Intraoperative EEG processing has been developed with significant improvement in reliability. For example, the bispectral index (BIS) monitor is a proprietary device that provides information related to anesthetic depth and is readily interpreted. In addition, the BIS has proven to be reliable as an indicator of anesthetic depth in people given a variety of anesthetic agents and adjuncts.[56,57] The BIS is a unitless number between 0 and 100 derived from the processed EEG.[58] People undergoing surgery are typically maintained at a depth of anesthesia that yields a BIS value between 40 and 60, which reliably prevents intraoperative awareness.[59–63]

In animals, a few reports have evaluated use of the BIS as an indicator of anesthetic depth. In dogs, isoflurane and sevoflurane anesthetic depth has been correlated to BIS.[64,65] Anesthetized cats had a nonlinear relationship of BIS with increasing multiples of sevoflurane minimum alveolar concentration.[66] The change in BIS values following stimulation in isoflurane-anesthetized cats provided a useful measure of anesthetic depth.[67] In goats anesthetized with isoflurane, BIS values significantly changed in response to intubation and noxious stimulation.[68] One study in unstimulated pigs did not demonstrate reliable correlation between isoflurane anesthetic depth and BIS, whereas others have demonstrated correlation of BIS values to anesthetic depth during surgery or with other noxious stimulation.[69–72]

Nerve-Conduction Studies

Nerve-conduction velocity has been successfully recorded in dogs while using a variety of anesthetic protocols. Because these procedures have not been done in unanesthetized animals, the effects of anesthetics on these procedures are largely unknown. Studies in dogs have been successful using thiamylal sodium and methoxyflurane for assessment of motor and sensory nerve function.[73,74]

Auditory and Visual Evoked Potentials

These may be altered by anesthetic agents, depending on the location of signal generators. Generally, cortical potentials are more likely to be affected than brain-stem potentials. In cats, administration of pentobarbital (20 mg/kg intraperitoneally) was shown to increase latency, area, and amplitude of auditory potentials.[75] In another study, brain-stem auditory evoked potentials recorded from cats were unaffected by sodium pentobarbital, ketamine, halothane, or chloralose administration.[76] Similar results were obtained from rats when ketamine or pentobarbital were used.[77] The use of ketamine in rats does, however, affect photic and field potentials recorded directly from various sensory relay nuclei when using implanted microelectrodes.[78] The use of ketamine and xylazine in cats produces only minimal changes (latency increases) in the brain-stem auditory evoked responses (BAERs) compared to xylazine alone.[79] The use of thiamylal sodium alters the BAER in dogs by increasing the latencies and decreasing the amplitudes of certain peaks.[80] The same dose of thiamylal sodium, however, completely obliterates middle-latency components of the BAER in dogs.[81] Light pentobarbital anesthesia in cats produces an increase or no change in cortical auditory evoked responses (AERs), moderate levels cause some increases in amplitude, and deep anesthesia causes all waves to disappear.[82] Although paraldehyde, ether, and ethyl chloride produce effects similar to those of pentobarbital, chloralose and chloroform are associated with an earlier and more profound period of enhancement.

In rats, the use of halothane (0.25% to 2.0%) affects AERs in a dose-related fashion.[83] These potentials are more sensitive to halothane than are visual evoked responses, especially in the auditory cortex. Pentobarbital, given to rats in sufficiently high doses to cause coma, progressively depresses and then abolishes

all peaks of the auditory brain-stem potential.[84] The use of atropine and xylazine in dogs in combination with ketamine or pentobarbital produces only slight changes in the latency of BAER wave VI when compared with xylazine and atropine alone.[85] When BAER waves in dogs anesthetized with methoxyflurane are compared with those in unanesthetized dogs, all waves have significantly longer latencies.[86] In gerbils, ketamine-xylazine anesthesia induces only minor changes in the low-frequency and high-frequency components of the auditory brain-stem response.[87]

Visual evoked potentials (VEPs) have been successfully recorded in dogs and cats administered halothane, and in cats administered halothane and thiamylal sodium.[88–90] In dogs, a comparison of VEPs from dogs anesthetized with chloralose with VEPs from dogs anesthetized with halothane or halothane and thiopental did not reveal any differences in the waveform.[91]

Electroretinogram and Oscillatory Potentials

These can be recorded from small animals under a variety of anesthetic conditions.[92–94] The effects of clinical anesthetic protocols in animals is not well documented. Methoxyflurane, halothane, enflurane, ether, and chloroform anesthesia retards cone adaptation curves in monkeys.[95] Pentobarbital anesthesia in cats enables visual evoked responses to be recorded with only minor fluctuations over an 80-min period.[96] Barbiturate anesthesia has no effect on the maturation of the visual evoked response during the first 2 weeks of life.[97] Beyond 2 weeks of age, anesthesia causes an increase in the amplitude of early components while eliminating later components altogether.

Somatosensory Evoked Potentials

Somatosensory evoked potentials (abbreviated as SSEPs, SEPs, or SERs [somatosensory evoked responses]) are also affected by anesthesia. Isoflurane at 1% produces a sustained latency change in SSEP in newborn piglets.[98] Halothane administration does not affect peak latencies of lumbar spinal cord evoked potentials, but amplitudes are reduced.[99] In cats, increasing levels of pentobarbital can be used to achieve therapeutic coma levels.[100] The early brain-stem components are relatively unaffected, whereas late brain-stem and initial cortical responses show progressive latency increases. Late cortical waves are abolished at relatively low doses; central conduction is unaffected, and late waves of the visual evoked response are abolished even though a single potential survives massive doses. Components of sheep SSEPs have been shown to be differentially sensitive to barbiturate anesthesia.[101]

Motor Evoked Potentials

The effects of isoflurane on motor evoked potentials (MEPs) in rats has been examined using concentrations ranging from 0.2% to 1.5%.[102] There is a progressive increase in onset latency of the compound muscle action potentials and a decrease in the peak-to-peak amplitude and duration. Spinal cord MEPs have been reported in dogs with the use of a combination of fentanyl, droperidol, sufentanil, and nitrous oxide. Halogenated gas anesthetics raised the stimulus threshold for recording MEPs as compared with narcotic/nitrous oxide anesthesia.[103] Peripheral nerve MEPs have been successfully recorded from dogs when using thiopental sodium, isoflurane, and oxymorphone.[104]

Considerations for Magnetic Resonance Imaging

Anesthetic concerns during MRI examination center on the potentially dangerous environment of a strong magnetic field. Ferromagnetic projectiles have had serious, even lethal, consequences in MRI suites. Anesthetic management of animals undergoing MRI exam can most simply be accomplished by means of injectable agents.[105–107] Inhalant anesthetics have been used in MRI suites by distancing the vital ferromagnetic components of the anesthesia machine from the magnetic field. Use of an extended non-rebreathing circuit, such as the Bain circuit, has been described.[108] One drawback of this technique is the higher fresh-gas flow rates required for larger animals (>50 kg). Another modification of anesthetic technique for MRI involves the use of extended rebreathing hoses with the anesthetic machine placed near the magnet, yet just beyond the critical point of magnetic attraction. For equine MRI, a large animal machine suitable for delivering inhalant anesthetics to horses can be used in this manner. There is anecdotal evidence that prolonged exposure (more than 2 h) in a 3- to 5-gauss magnetic field begins to affect vaporizer (Isotec; Datex-Ohmeda, Helsinki, Finland) output such that higher vaporizer settings are required to maintain adequate anesthesia (S. Greene, personal observation). In human patients, this effect has been reported for Fortec vaporizers (Cyprane, Keighley, U.K.).[109] Although many vaporizers are mainly constructed from nonferrous materials, many do contain components attracted or affected by magnetic fields.[110]

Anesthesia in MRI suites can be monitored by using MRI-compatible equipment to measure the electrocardiograph, blood pressure, pulse oximetry, and airway gases.[111] Less expensive alternatives include use of remotely placed monitors with specialized cabling designed to avoid interference with the magnetic field and induction of electric currents leading to burns. Simple systems can be used to measure direct arterial blood pressure, such as the aneroid manometer placed beyond the magnetic field or several feet of extension tubing placed between the transducer and patient. Some dampening and degradation of the arterial pulse wave may occur, but often direct measurement or arterial blood pressure is invaluable to assure maintenance of adequate cerebral perfusion pressure.

Because the magnetic fields vary considerably among various MRI units in clinical practice, consultation with a knowledgeable biomedical engineer is advised prior to implementing a monitoring system or novel means of anesthetic delivery.

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