

Diagnosis and Treatment of Acute Head Injury

Michael Podell, MSc, DVM

Diplomate ACVIM (Neurology)

Associate Professor

Department of Veterinary Clinical Sciences

College of Veterinary Medicine

The Ohio State University

Columbus, Ohio 43210

KEY WORDS

- head trauma
- neurolocalization
- intracranial pressure
- cerebral edema
- medical management

PREVALENCE AND ETIOLOGY

Acute head trauma in small animals may arise from a number of causes, including motor vehicle accidents, bites, direct impact from kicks or other blunt forces, and penetrating projectiles (gunshots). Trauma, particularly traumatic brain injury (TBI), is the most common cause of death in humans under the age of 45 in the United States.¹ Many of these cases are the result of automobile accidents in which the brain goes from a stationary position to a rapid acceleration and deceleration within the cranial vault. The resultant forces create direct contusion at the initial impact site against the skull (coup lesion), rebound contusion against the opposite skull surface from impact (contra coup lesion), and, the worst scenario, diffuse axonal injury of the brain stem due to torsional forces that rotate the overlying cerebrum on the more stationary brain stem. The latter is often rapidly fatal. In this respect, cats and dogs are fortunate in that most of their head injuries are the result of direct impact, with few instances of extreme acceleration and torsional forces on the brain. This factor, coupled with the obvious reduced need for high level cortical function compared to humans, may be a major reason why many small animals can survive a significant head injury.

The prevalence of TBI is poorly documented in veterinary medicine; one study estimated it to be 20% for dogs and 35% for cats presented for acute trauma.² In general, many small animals are presented for multi-system trauma, with either direct involvement of the central nervous system or indirect consequences due to alterations in cerebral perfusion. Since imaging of the brain immediately after injury is not commonly done in veterinary medicine, the nervous system is of-

ten overlooked when overt clinical signs are not apparent. Therefore determination of neurologic impairment is based on historical and clinical signs. Consequently, all animals presented for any acute trauma should be evaluated fully to assess whether the neurologic system is injured. The purpose of this article is to provide current guidelines in the assessment and treatment of small animals suffering from acute head injury. Be aware that rapid advances in our knowledge about the response of the central nervous system to injury dictate the need to periodically reevaluate treatment protocols.

REQUIREMENTS AND GOALS OF MANAGEMENT

Few general requirements exist to treat acute TBI. A proper knowledge base, an assistant, some standard equipment and medications, and a 24 hour monitoring facility are all that are needed. Specific, optimal requirements include appropriate drugs (mannitol, barbiturates, a variety of intravenous fluids), oxygen, radiographic capabilities, indirect blood pressure monitoring, and assisted ventilation. The goals of management focus first on whole body resuscitation, followed by brain resuscitation. Initial body resuscitation is simple in theory but more difficult in practice and has direct bearing on brain resuscitation. First, all hemorrhage must be stopped. Next, organ perfusion must be maintained by proper intravascular volume expansion. Cardiac and respiratory function are supported to maintain proper arterial oxygen tension and perfusion. Finally, renal function is maintained by maintaining perfusion. The goals of brain resuscitation can be broken down into managing the immediate and delayed effects of trauma. Immediate problems to avoid are hypoxia, poor cerebral perfusion, and elevated intracranial pressure. Delayed effects include progressive elevations of intracranial pressure, delayed or recurrent bleeding, delayed cell death due to inflammatory and toxic cellular reactions, and catabolism due to inadequate nutritional support.

PATHOPHYSIOLOGY

The consequences of TBI can be divided into primary and secondary effects of the injury. Primary effects are the direct consequences of hemorrhage, axonal injury, and penetration of objects into the brain. The most critical sequela is elevation of intracranial pressure (ICP). The cranial vault is a relatively closed

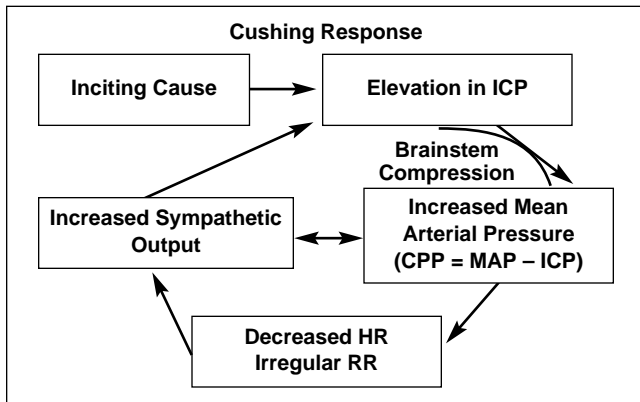


Figure 1. Schematic diagram outlining the recycling pathway of progressive intracranial pressure (ICP) elevation in the face of a mass effect or other inciting cause in the brain after head injury. The initial rise in ICP compresses the pressor region of the floor of the fourth ventricle, resulting in an increase in mean arterial pressure (MAP), which then causes a reduction of the cerebral perfusion pressure (CPP). The cardiac response is to decrease heart rate (HR), which is met with a peripheral response to increase sympathetic output to improve CPP. This increase in sympathetic output can directly raise MAP and ICP. An associated irregular respiratory rate (RR) may also contribute to raising ICP by producing hypocapnia and associated vasodilation, leading to increased cerebral blood volume.

compartment comprising the brain (80%), cerebrospinal fluid (CSF; 10%), and blood (10%). When an existing compartment expands or new ones are introduced, there must be a reciprocal decrease in another compartment to maintain ICP. The brain has a limited threshold to guard against the rise in ICP in cases of impaired CSF absorption, increased cerebral blood flow, or progressive mass effects with cerebral edema. An exponential rise in ICP occurs when intracranial volume goes above this threshold.³ In TBI, increased cerebral blood volume contributes to approximately 70% of the associated ICP elevation. As ICP increases, there is concomitant increase in mean arterial pressure (MAP) as an attempt to maintain cerebral perfusion pressure (CPP; $CPP = MAP - ICP$). Sustained ICP hypertension can lead to the Cushing response (Figure 1) with resultant brain content shifting, leading to brain herniation.⁴ Therefore the major goal of therapy is directed toward maintaining normal CPP by reduction and/or prevention of ICP elevation.

Secondary brain injury after trauma is related primarily to the consequences of cerebral ischemia. Within hours after TBI severe enough to cause loss of consciousness, there is a reduction in cerebral blood flow to levels less than 50% of normal⁵; this is more dramatic in contused brain regions. Two critical cascade mechanisms occur when cerebral ischemia from TBI is present. First, there is an increase in the extracellular excitatory neurotransmitter glutamate, which

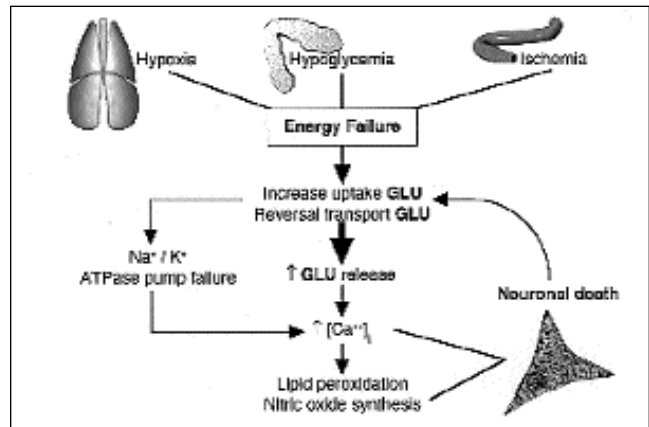


Figure 2. Energy failure via hypoxia, hypoglycemia, or ischemia can all result in secondary neuronal injury via increased release of the excitotoxic neurotransmitter, glutamate (GLU). The net effect is increased intracellular calcium accumulation, lipid peroxidation, and nitric oxide synthesis, all of which contribute to neuronal death. (Adapted from Reference 6.)

is also known as an excitotoxin.⁶ Any cause of cellular energy failure will initiate the excitotoxin cascade that results in intracellular calcium accumulation and neuronal death (Figure 2). The second component of the cascade is the generation of free radical-mediated lipid peroxidation, which leads to progressive secondary brain injury and subsequent neurologic deterioration despite normalization of ICP and CPP.

NEUROLOCALIZATION

The neurologic examination is the critical element in determining the extent of the injury, planning proper therapy, and predicting clinical outcome. Documenting the patient's level of consciousness is the most important initial neurologic determinant in characterizing the functional state of the brain and predicting clinical outcome. The Glasgow Coma Scale is a universally accepted method of classifying the initial extent of head trauma severity based on level of alertness, with high correlation to morbidity and mortality in humans with traumatic head injury,⁷ although accurate prediction of functional outcome is limited.⁸ A modified coma scale that may be helpful in classifying head trauma in small animals has been proposed but has not been evaluated for correlation to functional outcome.⁹ Evaluation of level of consciousness, respiratory patterns, cardiac rhythm, pupillary light reflexes, ocular motility, posture, and motor function will allow the clinician to determine reliably the extent and location of the neurologic injury.¹⁰

Conscious behavior requires an intact functional interaction of the cerebrum and rostral brain stem. Altered consciousness can be graded in a progressively deteriorating state as clouded (confused), obtunded (decreased alertness interspersed with arousable peri-

ods), stupor (unresponsive except to noxious stimuli), and coma (unarousable). Unilateral lesions of the cerebrum blunt level of consciousness proportional to the size of the lesion. Bilateral, but not necessarily symmetric, cerebral lesions are necessary to induce stupor or coma. Caudal brain stem lesions affecting the reticular activating system are more likely to create stupor and coma, as the “switch” can no longer “activate” the cerebrum.

Breathing is a sensorimotor function that is influenced by practically all levels of the brain and rostral spinal cord. The neuroanatomic basis of respiratory abnormalities are summarized in Table 1. Forebrain or deep diencephalic lesions are most readily identified in stuporous or comatose animals as Cheyne-Stokes respirations characterized by periodic hyperpnea followed by apnea. The presence of Cheyne-Stokes respirations implies a bilateral cerebral disease process and may be a valuable sign of impending brain herniation.¹⁰

Table 1
Correlation of Respiratory Pattern Changes and Lesion Location

Lesion	Type	Description
Forebrain or deep diencephalic	Posthyperventilation apnea Cheyne-Stokes	Apnea + hyperventilation Hyperpnea + apnea
Midbrain	Central neurogenic hyperventilation	Involuntary hyperventilation
Lower pontine	Apneustic	Inspiratory cramp
Medulla	Ataxic	Alternating deep to shallow

Table 2
Correlation of Pupillary Light Reflex Changes and Lesion Location

Region	Lesion	At Rest	PLR	Association
Hypothalamus	Ventrolateral hypothalamus	Miosis; ptosis	Normal bilateral	Sympathectomy
Midbrain	Pretectal region Tectal region Cr N III	Midrange Large Large ipsilateral	Fixed; hippus Fixed; hippus Fixed ipsilateral	Periaqueductal gray lesion Transtentorial herniation Uncal herniation
Pons	Tegmentum	Miosis bilateral	Present bilateral	Hemorrhage
Medulla	Lateral medulla	Miosis ipsilateral	Present bilateral	Mass/trauma

Cr N III = oculomotor cranial nerve; PLR = pupillary light reflex.

Cardiac arrhythmias are common with systemic trauma. Imbalances in the central mediation of the autonomic nervous system is the primary mechanism of these changes. Acute prepontine lesions (rostral to the pons) can result in neurogenic cardiac arrhythmias including supraventricular arrhythmias, atrioventricular block, and premature ventricular contractions. As mentioned, the Cushing response results in bradyarrhythmia from pontomedullary compression that affects the pressor area at the level of the fourth ventricle.

Monitoring changes in pupillary light reflex is an invaluable method in assessing location and progression of neurologic deterioration. Moreover, as pupillary pathways are resistant to metabolic insult, the presence of pupillary changes is a potential method of distinguishing metabolic from structural causes of neurologic insult. In general the progression of resting pupillary size from mid-range or large to small is a poor prognostic sign (Table 2); this progression demonstrates the involvement of brain stem structures. Unilateral mydriasis with poor or absent direct response to light is highly suggestive of an ipsilateral midbrain or oculomotor (cranial nerve III) lesion secondary to brain herniation. This finding should alert the clinician to institute immediate therapy to reduce ICP (discussed below).

Ocular motility should be assessed in conjunction with the pupillary examination. Poor prognostic signs include absence of spontaneous blinking (diffuse pontine lesions), failure of the eyes to move rapidly in the direction of a rapid lateral head movement associated with an abnormal vestibulo-ocular response (injury to the white matter tracts of the rostral brain stem), and loss of the corneal reflex (abnormal midbrain and pontine function). If a persistent lateral gaze of both eyes in the direction toward the more normal limbs is present, then a cerebral lesion is suspected.

Posture and motor function abnormalities are common after acute head injuries. Since motor activity may not be readily assessed until the animal is stabilized, the emphasis is placed on identifying postural changes. Three types of postural rigidity may occur, all representing different levels of brain herniation and/or injury:

- *Decorticate rigidity* consists of flexed thoracic and extended pelvic limbs and is the result of altered corticospinal pathway function arising from the cerebrum. Cats, with a more developed corticospinal tract than dogs, are more prone to develop this posture after cerebral injury.
- *Decerebrate rigidity* consists of extended thoracic and pelvic limbs with hypertonus of the cervical extensor muscles resulting in opisthotonic neck posture due to a midbrain injury with compression at the level of the colliculi. This sign usually is associated with herniation of the overlying cerebrum onto the brain stem.
- *Decerebellate rigidity* consists of extended thoracic and flexed pelvic limbs, with hypertonus of the cervical extensor muscles resulting in opisthotonic neck posture due to rostral cerebellar herniation.

MEDICAL MANAGEMENT

General Guidelines

The main goals of medical management are to avoid hypotension and cerebral hypoxia. Studies have shown that a systolic blood pressure less than 90 mmHg or a PaO₂ less than 60 mmHg in the face of head injury are correlated with a poor outcome.¹¹ In this light the first priority for the head-injured patient is complete and rapid physiologic resuscitation. Airway access and maintenance of adequate respiratory function should be confirmed. Circulatory blood volume should be maintained to normalize cerebral perfusion. Finally, the neurologic state of the patient should be assessed via the examination and radiographic studies to determine specific brain-directed therapy. Treatment can then be formulated based on the severity of the head injury¹² (see box at left):

- The *low risk group* includes animals that are asymptomatic, with or without scalp injuries. These patients should be observed serially over the next 24 hours for possible progression of clinical signs. No specific therapy is recommended.
- The *moderate risk group* includes animals that have altered level of consciousness and/or skull fractures. Diagnostic tests should include skull radiographs and computed tomography (CT) scan (if available). Definitive therapy is initiated to reduce

GENERAL TREATMENT GUIDELINES OF TRAUMATIC BRAIN INJURY ACCORDING TO INITIAL NEUROLOGIC CLASSIFICATION

Low Risk Group

Signs: Asymptomatic, with or without scalp injuries

Neurodiagnostic tests: None

Treatment: These patients should be observed serially over the next 24 hours for possible progression of clinical signs; no specific therapy is recommended

Moderate Risk Group

Signs: Altered level of consciousness and/or skull fractures

Neurodiagnostic tests: Skull radiographs and CT scan (if available)

Treatment: Definitive therapy is initiated to reduce intracranial pressure

- Mannitol: 1 g/kg IV over 15 minutes
- Furosemide: 0.7 mg/kg IV 15 minutes after mannitol treatment
- Maintain euvolemia with isotonic fluids
- Treat penetrating skull fractures with appropriate surgical care
- Nutritional support

High Risk Group

Signs: Altered level of consciousness and additional neurologic signs, and/or penetrating skull injuries

Neurodiagnostic tests: Skull radiographs, and CT scan (if available)

Treatment: Definitive therapy is initiated to rapidly reduce intracranial pressure

- Hyperventilation with controlled ventilation for 1 hour to maintain PaCO₂ close to 35 mmHg
- Mannitol: 1 g/kg IV over 15 minutes
- Furosemide: 0.7 mg/kg IV 15 minutes after mannitol treatment
- Maintain euvolemia with isotonic fluids
- Treat penetrating skull fractures with appropriate surgical care
- Nutritional support

ICP and cerebral edema.

- The *high risk group* includes animals that have an altered level of consciousness, additional neurologic signs, and/or penetrating skull injuries. Definitive therapy is initiated to reverse brain herniation by rapid reduction in ICP and cerebral edema.

Definitive Therapy To Treat Intracranial Hypertension

Hyperventilation

Hyperventilation is the most effective method to rapidly reduce ICP. Lowering PaCO₂ to a level close to 35 mmHg will reduce cerebral blood by 40% within 30 minutes due to cerebral vasoconstriction.¹³ The reduction of cerebral blood flow leads to reduced cerebral blood volume and, eventually, decreased ICP. The relative CO₂ vasoreactivity in severe traumatic brain injury is a 3% change in cerebral blood flow (CBF) per torr change in PCO₂.¹⁴ One major consequence of prolonged hyperventilation with a PCO₂ less than or equal to 25 mmHg is profound cerebral ischemia due to dramatic reduction of CBF. Humans suffering from TBI with prolonged (5 days) hyperventilation had a significantly worse prognosis than patients who were normocapneic or who had a short (hours) period of hyperventilation.¹⁵ Thus hyperventilation should be used only in those patients in the high risk group that also have impending brain herniation, at a level to keep PCO₂ near 35 mmHg, and for relatively short periods (1 hour or less).

Hyperosmotic Agents

Hyperosmotic agents should be used when signs of brain herniation or progressive neurologic deterioration are present after head trauma.¹⁶ Hyperosmotic agents are beneficial in reducing ICP by creating an osmotic gradient to draw free water from the brain into the intravascular space. Mannitol is the most widely accepted hyperosmotic agent used to lower ICP by a two-step process.¹⁷ Initially, there is an immediate plasma-expanding effect that reduces the hematocrit and blood viscosity and increases cerebral blood flow and cerebral oxygen delivery. The osmotic effect is delayed for 15 to 30 minutes after administration, with a duration ranging from 90 minutes to 6 hours or more.¹⁸ Concomitant addition of furosemide may prolong the ICP-lowering effect. Potential adverse effects of mannitol center on exacerbation of ICP by three possible mechanisms:

- Increased cerebral edema due to a reversed osmotic shift of fluid caused by mannitol accumulation in the brain
- Worsening of existing intracranial hemorrhage due to blood vessel tearing and osmotic shifts
- Rebound intracranial hypertension due to formation of idiogenic osmoles within brain cells that raise intracranial osmolarity relative to plasma

All of these potential effects can be minimized by us-

ing intermittent boluses of mannitol at a dose of 0.5 to 1 g/kg, not repeating a dose within 1 hour, and limiting the number of doses to three in 24 hours. Euvolemia should be maintained by adequate fluid replacement, and the serum osmolarity should be kept below 320 mOsm to prevent acute renal failure.

Glucocorticoids

The use of glucocorticoids is not recommended in TBI.¹⁹ Definitive evidence exists that no benefit is derived from such treatment to reduce ICP or improve clinical outcome after head trauma.^{20,21} Steroids are extremely helpful, however, in alleviating vasogenic cerebral edema, reducing cerebrospinal fluid production, restoring altered vascular permeability, and attenuating free radical production. Prospective, double-blinded clinical studies in humans with TBI failed to establish any benefit with high or low dose methylprednisone²¹ or dexamethasone.²² Moreover, patients had a higher incidence of the harmful effects of gastrointestinal bleeding and hyperglycemia, the latter of which is associated with a worse neurologic outcome.

High Dose Barbiturates

Barbiturates exert a cerebral-protective and ICP-lowering effect by reducing cerebral vascular tone and cerebral metabolic demand and inhibiting free radical-mediated lipid peroxidation. Pentobarbital is the barbiturate of choice for medically refractory intracranial hypertension in hemodynamically stable patients.²³ This treatment is best used in animals with an initial response to mannitol and/or hyperventilation therapy but that also have a reappearance of signs attributable to recurrence of raised ICP. A loading dose of 5 to 10 mg/kg over 10 minutes to effect to induce a deep plane of sedation, followed by a continuous maintenance intravenous infusion of approximately 1 mg/kg/hr, is recommended. Animals should be intubated with assisted ventilation, and body temperature, heart rate, and blood pressure should be monitored.

Nutritional Support

One of the most important yet commonly overlooked therapies for TBI is adequate nutritional support. The occurrence of hypermetabolism and nitrogen wasting after head injury is well documented. Providing nutritional support greatly reduces morbidity in humans with head injuries.²⁴ The recommended guidelines in humans include using enteral or parenteral formulas (with at least 15% of calories from protein) to replace 140% of resting metabolism by the seventh day postinjury.²⁵ To achieve full caloric re-

placement by 7 days after injury, nutritional replacement should begin within 72 hours of injury. Nasogastric feeding is often well tolerated in the low to moderate risk group, but gastrostomy or jejunal feeding tubes may be better tolerated in the long term.

Novel Therapy

Several advances in treating the sequelae of cell death associated with TBI are under investigation. Two major mechanisms are being targeted: reduction of excitotoxicity and reduction of free radical-mediated lipid peroxidation. Specific pharmacologic blockade of excitatory neurotransmission in the brain improves neurologic function in experimental animal studies of TBI but is problematic due to unwanted, often severe, adverse effects. Recently, the use of magnesium sulfate (600 mg/kg SC) was found to significantly improve neurologic outcome in rats (without adverse effects) by blocking the postsynaptic receptor activity of glutamate and reducing cerebral edema formation.²⁶ Lipid peroxidation is attenuated by blocking the arachidonic acid pathway. Potent nonsteroidal and nonglucocorticosteroid antiinflammatory agents show promise in preventing this deteriorating cellular cascade.²⁷

SURGICAL MANAGEMENT

Animals with severe head injury in the moderate and high risk groups should be evaluated for possible surgical management. Indications for surgical intervention include penetrating skull fractures or objects, uncontrollable skull or scalp bleeding, an obvious brain wound, or an intracranial mass effect. Due to the limitation of the availability of CT scanning for the emergency patient, the latter condition may be presumed to be present in a patient with deteriorating level of consciousness and neurologic lateralization, including unilateral pupillary light reflex changes. Surgical treatment is directed toward removing bone and other objects that penetrate into the brain, recreating a sterile barrier between the brain and the skull, and decompression by removal of mass effects (i.e., hemorrhage) or by selective craniectomy, if possible.

SUPPORTIVE CARE AND MONITORING

After the initial stabilization of the patient, several supportive care measures are helpful for recovery. General guidelines include avoiding jugular vein compression and keeping the head elevated at a 30 degree angle to enhance venous return, avoiding hyperthermia ($\geq 103^{\circ}\text{F}$), and providing a 40% oxygen:air mixture via nasal insufflation or oxygen cage. Around-the-clock monitoring of heart rate, body temperature, seizure activity, and progression of neurologic signs is essential.

PROGNOSIS

No information on the correlation of degree of initial neurologic signs and clinical outcome is available for small animals suffering TBI. Several findings from experimental studies in laboratory animals and clinical studies in humans may serve as useful guidelines to indicate a possible poorer prognosis. Such findings include a PaO_2 less than 60 mmHg, a systolic blood pressure less than 90 mmHg, or loss of brain stem reflexes. Although the brain cannot recover from irreversible cell death, it does possess dramatic plastic properties, especially when cerebral lesions are the predominant region of injury. While time works against the patient and clinician during the immediate phase of the injury, it can work in our favor during the recovery phase.

REFERENCES

1. Baker CC, Openheimer L, Stephens B, et al: Epidemiology of trauma deaths. *Am J Surg* 140:144-150, 1980.
2. Kolata RJ, Kraut NH, Johnston DL: Patterns of trauma in urban dogs and cats: A study of 1000 cases. *JAVMA* 164:499, 1974.
3. Avezatt CJ, van Eijndhoven JH, Wyper DD: Cerebrospinal fluid pulse pressure and intracranial volume-pressure relationships. *J Neurol Neurosurg Psychiatry* 42:687-700, 1979.
4. Fishman RA: *Cerebrospinal Fluid in Diseases of the Nervous System*. Philadelphia, WB Saunders, 1992.
5. Bouma GJ, Muizelaar JP, Stringer WA: Ultra early evaluation of regional cerebral blood flow in severely head injured patients using xenon enhanced computed tomography. *J Neurosurg* 77:360, 1992.
6. Lipton SA, Rosenberg PA: Excitatory amino acids as a final common pathway for neurologic disorders. *N Engl J Med* 330:613-622, 1994.
7. Pal J, Brown R, Fleischer D: The value of the Glasgow coma scale and injury severity score: Predicting outcome in multiple trauma patients with head injury. *J Trauma* 29:746-748, 1989.
8. Zafonte RD, Hammond FM, Mann NR, et al: Relationship between Glasgow coma scale and functional outcome. *Am J Phys Med Rehabil* 75:364-369, 1996.
9. Shores A: Treatment and prognosis in head trauma. Proceedings of the 13th Annual Kal Kan Symposium for the Treatment of Small Animal Diseases. Vernon, CA, Kal Kan Foods, Inc., 1989.
10. Plum F, Posner JB: *The Diagnosis of Stupor and Coma*. Philadelphia, FA Davis, 1982.
11. Chesnut RM, Marshall LF, Klauber MR, et al: The role of secondary brain injury in determining the outcome from severe head injury. *J Trauma* 34:216-222, 1993.
12. White RJ, Likavec MJ: The diagnosis and initial management of head injury. *N Engl J Med* 327:1507-1511, 1992.
13. Raichle ME, Plum F: Hyperventilation and cerebral blood flow. *Stroke* 3:566-575, 1972.
14. Cold GE: Measurements of CO_2 reactivity and barbiturate reactivity in patients with severe head injury. *Acat Neurochir* 98:153-163, 1989.
15. Muizelaar JP, Marmarou A, Ward JD, et al: Adverse effects of prolonged hyperventilation in patients with severe head injury. A randomized clinical trial. *J Neurosurg* 75:731-739, 1991.
16. Brain Trauma Foundation: The use of mannitol in severe head injury. *J Neurotrauma* 13:705-709, 1996.
17. Muizelaar JP, Lutz HA, Becker DP: Effect of mannitol on ICP and CBF and correlation with pressure autoregulation in severely head injured patients. *J Neurosurg* 61:700-706, 1984.
18. Barry KG, Berman AR: Mannitol infusion. Part III. The acute effect of intravenous infusion of mannitol on blood and plasma volume. *N Engl J Med* 264:1085-1088, 1961.
19. Brain Trauma Foundation: The role of glucocorticoids in the treatment of severe head injury. *J Neurotrauma* 13:715-718, 1996.
20. Gudeman SK, Miller JD, Becker DP: Failure of high-dose steroid therapy to influence intracranial pressure in patients with severe head injury. *J Neurosurg* 51:301-306, 1979.
21. Gianotta SL, Weiss MH, Apuzzo MLJ, et al: High dose glucocorticoids in the management of severe head injury. *J Neurosurg* 15:497-501, 1984.
22. Dearden NM, Gibson JS, McDowall DG, et al: Effect of high dose dexametha-

- sones on outcome from severe head injury. *J Neurosurg* 64:81–88, 1986.
23. Brain Trauma Foundation. The use of barbiturates in the control of intracranial hypertension. *J Neurotrauma* 13:711–714, 1996.
 24. Young B, Ott L, Twyman D, et al: The effect of nutritional support on outcome from severe head injury. *J Neurosurg* 67:668–676, 1987.
 25. Brain Trauma Foundation: Nutritional support of brain-injured patients. *J Neurotrauma* 13:721–729, 1996.
 26. Feldman Z, Gurevitch B, Artru AA, et al: Effect of magnesium given 1 hour after head trauma on brain edema and neurological outcome. *J Neurosurg* 85:131–137, 1996.
 27. Marshall LF, Marshall SB: Pitfalls and advances from the international tirilazad trial in moderate and severe head injury. *J Neurotrauma* 12:929–932, 1995.

