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“The Banged Up Brain!”

An Approach to Cranio-Cerebral Trauma and Brain Dysfunction

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Head Trauma and Traumatic Brain Injury

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Head trauma and traumatic brain injury are relatively common consequences of many types of injury in dogs and cats, including road traffic trauma, dog attacks and other accidental injury. Head trauma in itself can be potentially devastating to an animal if it is not managed appropriately. However, with timely and appropriate management, many animals that present with severe brain injury can make good neurological recovery, and regain good quality of life. The aim of this presentation is to provide a short over-view of the normal physiology of the brain, the response of the brain to injury, and the latest recommendations on management of brain trauma. Furthermore, the principles of management of brain trauma management can also be applied to other causes of abnormal brain function, including seizure management and CNS management of excitable toxicosis. Let’s begin by looking at normal brain function...

Physiology of the Normal Brain

Normal neuronal function is essential to ongoing life. The loss of normal neuronal function in the course of injury or illness therefore represents a major loss. Neurological damage from any cause may result in the development of elevated intracranial pressure, resulting in a reduction in cerebral perfusion pressure, and ultimately compromising cerebral blood flow sufficient to produce permanent neuron loss.

In the normal animal, the brain receives 14-15% of resting cardiac output, and uses 15-20% of the body's oxygen consumption. Blood flow to gray matter is higher than to white matter. The brain has a high resting energy requirement, and no energy or oxygen stores. This makes the brain extremely susceptible to injury following events resulting in cellular damage, or disruption to normal oxygen delivery and metabolism within the cranial vault.

Cerebral blood flow is determined by five factors

1. **PCO**₂ - A change in cerebral CO₂ is the main and most sensitive regulator of cerebral blood flow. Carbon dioxide is a potent cerebral vasodilator, regulated by changes in cerebral pH, and leads to an increase in cerebral blood volume
2. **PO**₂ - normal oxygen tension in cerebral circulation maintains vascular tone in cerebral blood vessels
3. Blood pressure autoregulation – The cerebral circulation is regulated in such a way that a constant total cerebral blood flow is maintained under varying conditions. This is called autoregulation. Autoregulation maintains cerebral blood flow at a constant level between a systolic arterial blood pressure of between 50-150mmHg, outside of which, cerebral blood flow becomes linearly related to blood pressure. Autoregulation is less efficient in states of ischaemia, hypoxia, hypercapnia, and increasing blood viscosity, as may be encountered in patients suffering severe dehydration and haemoconcentration, or polycythaemia Vera.
4. The level of neuronal stimulation - Increasing neuronal activity and hence metabolic rate will increase cerebral blood flow, for example, with seizures, hyperthermia etc. As with autoregulation,
this relationship is uncoupled with in conditions of trauma, infarction, subarachnoid hemorrhage, and cardiac arrest.

5. Systolic blood pressure

From the above, it may be seen that disruption to cerebral blood flow will be altered under conditions of head trauma, traumatic brain injury, and also during seizures and periods of uncontrolled neuronal activity, as these conditions will alter cerebral metabolic rate, cerebral carbon dioxide concentrations, oxygen concentrations, blood pressure autoregulation, the level of neuronal stimulation, and systolic blood pressure. In addition, the presence of haemorrhage, shock, and loss of colloid oncotic pressure and electrolyte imbalances will also alter normal brain perfusion and brain oxygen delivery, further affecting neuronal function. The aim of much of our treatment of brain trauma therefore, concentrates on restoring and maintaining cerebral blood flow.

Pathophysiology of Brain Trauma

Brain injury may be conceptually divided into primary and secondary injury. Primary brain injury occurs immediately following brain tissue impact, and initiates multiple cascades that result in secondary brain injury. Primary and secondary processes associated with brain injury in dogs and cats are outlined in the table below.

<table>
<thead>
<tr>
<th>Primary and Secondary Processes Associated with Brain Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Brain Injury</strong></td>
</tr>
<tr>
<td>• Direct damage to brain parenchyma</td>
</tr>
<tr>
<td>• Direct damage to blood vessels</td>
</tr>
<tr>
<td><strong>Secondary Brain Injury</strong></td>
</tr>
<tr>
<td>• ATP depletion</td>
</tr>
<tr>
<td>• Intracellular accumulation of sodium and calcium</td>
</tr>
<tr>
<td>• Increased cytokine production</td>
</tr>
<tr>
<td>• Elevated extracellular glutamate</td>
</tr>
<tr>
<td>• Oxygen free radical production</td>
</tr>
<tr>
<td>• Lactic acidosis</td>
</tr>
<tr>
<td>• Nitric Oxide accumulation</td>
</tr>
<tr>
<td>• Arachadonic acid, kinin, complement, coagulation and fibrinolytic pathway activation</td>
</tr>
</tbody>
</table>

The progression from primary to secondary brain injury is described below.

1. **Trauma induced neuronal damage** – neuronal damage in head trauma results from contusions or concussive injury. Neuronal damage is damage directly cause by trauma includes physical damage to neurons, including axons, cell body injury, damage to supporting structures (Perkinje cells, blood vessels), compression from hematomas (epidural, subdural, subarachnoid, parenchymal), and damage to blood vessels. Neuronal damage from seizures usually is the result of excessive neuronal activity inducing cerebral hypoxia and subsequent secondary neuronal damage, as described below.
1. **Ischemic damage** – neuronal and vascular damage in the brain leads to a cascade of reactions that result in ongoing tissue damage and inflammation. Brain trauma resulting in cell and vascular damage ultimately cause brain oxygen deprivation. Oxygen deprivation leads to anaerobic glycolysis and ATP depletion. ATP depletion produces a host of changes in cellular function. ATP depletion results in intracellular flux of calcium, sodium and water, and intracellular loss of potassium. The increase in intracellular calcium results in activation of intracellular phospholipases, proteases, xanthine oxidase, and nitric oxide synthase, which lead to cell protein and phospholipid degradation, arachidonic acid and free radical production and cell death. Anaerobic glycolysis also results in production of lactic acid, which lowers intracellular pH. Cellular acidosis compromises cell functions, including mitochondrial ATP production and may enhance free radical formation. Ischemia of brain tissue is significant in most patients during the first 24 hours following traumatic brain injury, and has a significant impact on neurological outcome.

2. **Cerebral Oedema** - Both of these mechanisms can lead to oedema of the brain parenchyma, which peaks at 24-48 hours post trauma. Brain oedema may be classified as vasogenic, cytotoxic, and interstitial.

   i. **Vasogenic oedema** – Vasogenic oedema occurs secondary to increased vascular permeability, or increased intravascular pressures – both common findings following trauma and inflammation. This leads to compromise of the blood-brain barrier through disruption of endothelial tight junctions.
   
   ii. **Cytotoxic oedema**, which as outlined above, will occur secondary to hypoxia and impaired cellular function and metabolism as outlined above.
   
   iii. **Interstitial oedema** occurs when fluid shifts from the ventricles into the peri-ventricular interstitium due to obstruction of cerebrospinal fluid outflow (obstructive hydrocephalus)

**So what does all of this mean for my patient?**

Ultimately, the result of tissue injury, cell death and inflammation resulting in cerebral oedema causes an increase in intra-cranial pressure

**Increased Intracranial Pressure**

Following head trauma, the primary and secondary events involved in brain injury – direct trauma, ischaemia, inflammation and oedema, all result in disruption to normal blood flow, oxygen delivery and cell function within the brain. These things are often combined with alterations in carbon dioxide, oxygen, and blood flow dynamics in the head trauma patient, and lead to an elevation in brain volume, and increased intracranial pressure.

Most patients with head trauma will develop increased intracranial pressure. Interestingly – and somewhat frustratingly, the clinical signs of increased intracranial pressure will often-times complicate early measures to localize and monitor the degree of brain injury.

The Monro-Kellie doctrine states that within the confines of the inelastic skull, blood (10%), cerebrospinal fluid (10%), and brain parenchyma (80%) normally exist in equilibrium with each maintaining a stable volume and pressure. Sudden increases in brain parenchyma, blood or cerebrospinal fluid pressure or volume do not allow time for equilibrium and adjustment, leading to increased intracranial pressure. If
severe enough, increased intracranial pressure can even result in herniation of the falx cerebri, tentorium, cerebellum; or skull fractures. Most cases of parenchymal herniation are fatal.

**Causes of increased intracranial pressure**

- Haemorrhage
- Cerebral oedema
- Arterial and venous dilatation - increasing tissue carbon dioxide will increase arteriolar dilatation
- Increasing cerebral metabolic rate – which results in increased brain production of carbon dioxide, which results in cerebral vasodilatation.
- Fever, seizures and some anesthetic agents (halothane will cause vasodilatation)
- Concurrent disease states such as pulmonary disease, hemorrhage, cardiac disease etc. alter gas exchange

In summary, elevated carbon dioxide concentrations, decreased oxygen concentrations, and increased cerebral metabolic rate are all present following head trauma, and will all increase cerebral blood volume. In addition, cerebral oedema, haemorrhage and inflammation also lead to an increase in brain parenchymal mass. The net result is a rapid rise in intracranial volume, and elevated intracranial pressure.

When intracranial pressure becomes elevated, the cerebral blood flow reduces due to compression of blood vessels within the cranial vault. The resultant ischaemia stimulates the vasomotor centre of the brain, which raises systemic blood pressure, the so-called “Cushing reflex”. However, when intracranial pressure exceeds the arterial pressure, cerebral circulation ceases.

**Treatment of the Patient with Head Trauma**

As can be seen, there are several key aspects of the physiology of the normal brain, and in the pathophysiology of head trauma, that are potentially able to be manipulated in order to minimise secondary brain injury and the help offset the development of severe cerebral oedema. The following algorithm has been developed in accordance with the “Lund Concept” principles of management of severe head trauma, which focus on normalizing physiological values of blood pressure, haemoglobin concentration, colloid oncotic pressure, carbon dioxide concentration and glucose concentration, in order to provide optimum conditions for brain healing, whilst minimizing potentially harmful effects of under- or over-treatment.

1. **First Aid Recommendations**
   First aid recommendations in head trauma or neurological patients are similar to those for any patient with trauma, and fall into basic assessment of airway patency, breathing ability and control of obvious external haemorrhage. Thereafter, specific recommendations are sometimes a little difficult to make, as each patient will likely respond to handling and manipulation in a different way. However, there are a couple of principles to encourage owners to follow to minimise the chance of worsening injury to the patient whilst transporting to the veterinary clinic:
   - Minimize patient movement during transport – this is critical. Brain-injured patients may become frantic or violent during handling or transport. Cats should be confined in a cage with soft bedding. The cage should be covered with a towel or similar covering to reduce arousal level during transport. Dogs may need physical restraint if they are disoriented, because they may
become frantic during transport. Having a person in the back seat of the car with the dog during transport is ideal. Cloth muzzles may be applied for aggressive dogs prior to handling and transport to prevent injury to handlers. Patients who are recumbent or unable to move may benefit from placing on a board or on a stretcher for transport. Animals may be secured to the stretcher with belts or blankets wrapped around the animal and stretcher to prevent excessive movement.

On arrival at the veterinary clinic, the animal should be assessed in a calm and logical manner so that an accurate and precise treatment plan may be instituted, and so that vital components of patient evaluation are not missed. These two points also help to ensure that every chance possible is given for the patient to show signs of improvement in response to treatment.

2. **Airway - Ensure the patient has a patent airway**
   - Airway protection is vital. Early onset pneumonia due to aspiration of foreign material, mucous, blood and regurgitated contents worsens neurological outcome. Early intervention to protect an airway is essential to minimize the risk of aspiration and pneumonia.
   - Provide oxygen by cage, flow past, mask or ET tube. The aim is to supply 100% oxygen on presentation
   - Avoid nasal oxygen as sneezing increases intracranial pressure, (and also the possibility of basilar skull fractures!)
   - Assess oral and nasal cavity for the presence of fractures, palatine defects, and haemorrhage. Control hemorrhage using pressure, topical adrenaline or cautery
   - Intubation and mild elevation of the head reduces chance of aspiration of gastric and oral secretions, blood and debris. If the patient requires intubation, let head lie on table, and elevate maxilla only to avoid occlusion of the jugular veins, and elevation of intracranial pressure. Hyper-extension of the head during intubation can cause injury to blood vessels at the base of the brain, and can cause intracranial haemorrhage.
   - If an anaesthetic induction agent is required to facilitate intubation, propofol is the agent of choice. Propofol does not disrupt brain metabolism – blood flow coupling, thereby minimizing the risk of additional neurological damage. Alternatively, alfaxalone may be used, as this drug causes less depression of cardiovascular and respiratory systems than propofol, and is associated with reasonably quick induction times. Drugs to avoid would include morphine and methadone – both of which reduce the sensitivity of the brain to carbon dioxide, as well as reduce respiratory rate, both of which will likely result in elevated blood carbon dioxide concentrations, cerebral vasodilatation and cerebral oedema.

3. **Breathing**
   - If the patient is comatose, or semi-comatose, induce anesthesia with propofol (if required), intubate, and provide assisted ventilation. Ventilate the patient to achieve an end-tidal CO₂ of between 35 and 40 mmHg. This aids in prevention of excessive carbon dioxide associated vasodilatation in the brain, as well as avoiding excessive vasoconstriction in the brain associated with hypocapnea. The patient should remain on 100% oxygen at all times for up to 2 hours post presentation. If capnography is not available, a normal end-tidal carbon dioxide concentration may be assumed if the patient is ventilated at 1 breath per 4-5 seconds (12-15 breaths per minute) at a tidal volume of 15 ml/kg.
   - If the patient is conscious and ventilating adequately - provide oxygen. If the patient is not ventilating adequately, as determined by blood gas analysis (if available) showing elevated PaCO₂
above 45 mm Hg, or by clinical evidence of poor chest wall movement and/or inadequate respiratory rate (less than 15 breaths per minute), anesthetize the patient and provide ventilatory assistance. Provide 1 breath every 45 seconds (12-15 breaths per minute) at a tidal volume of 15 ml/kg.

- Avoid excessive hyperventilation, as this can lead to hypcapnea, which causes intense cerebral vasoconstriction, which has been shown to induce harmful decreases in cerebral blood flow, potentially worsening neurological outcome.
- Oxygenation assessment using pulse oximetry can be misleading; the following table is used as a guide

<table>
<thead>
<tr>
<th>Interpretation of Pulse Oximetry Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SaO₂</strong></td>
</tr>
<tr>
<td>&gt;95%</td>
</tr>
<tr>
<td>&lt;89%</td>
</tr>
<tr>
<td>75%</td>
</tr>
</tbody>
</table>

4. Circulation

- Treat hypovolaemic shock or intravascular volume deficits using an isotonic crystalloid solution such as Hartman’s, using a technique of small volume resuscitation, to avoid excessive fluid accumulation in the brain. The small volume resuscitation protocol involves administering boluses of Hartman’s at 10ml/kg intravenously over 10 minutes, followed by patient reassessment for ongoing rapid fluid administration, using heart rate, respiratory rate, blood pressure and mucous membrane characteristics. Boluses of fluid are administered in the same manner until the patient is haemodynamically stable. Once the patient is haemodynamically stable, shock rates of fluid therapy should cease, and the patient should be placed on isotonic fluid therapy at between 3-5 ml/kg/hr.

- The aim of all circulatory support is to maintain cerebral perfusion pressure at least above 60mmHg (which means maintaining a mean arterial pressure above 70mmHg) - below this level, brain blood flow is inadequate, and results in cerebral hypoxia and ischemia. In humans, sustained systolic blood pressures below 90 mmHg are associated with neurological outcome that is two times worse, than in patients with normal systolic blood pressure following intravascular volume resuscitation. Therefore, it is vital that we re-examine our patients to ensure they have cardiac indices (heart rate, blood pressure, mucus membrane color and refill) within normal limits to minimize the chances of worsening neurological outcome.

- What about other fluid types?
  - **Isotonic crystalloids** are widely used and are currently recommended as the fluid of choice. There is no significant difference in survival rates when isotonic crystalloids are used in volume resuscitation when compared to hypertonic saline or colloid administration
  - **3% sodium chloride** is associated with more rapid fluid shift from interstitial to intravascular spaces during immediate fluid resuscitation, and has a theoretical benefit in early patient management. However, long-term recovery studies show no benefit to its administration
  - **Colloid fluid therapy** with hydroxy-ethyl starch (HES) in treatment of head trauma is controversial. Human studies on the use of albumin and hydroxy-ethyl starch in high volumes
(up to 50 ml/kg/day) are associated with worse neurological outcome over crystalloid alone. Yet other human studies suggest that low to moderate infusions of colloids in acute resuscitation assist maintenance of colloid oncotic pressure and an improvement in brain tissue oxygen delivery, and a favorable outcome. In dogs and cats, use of synthetic colloids at dose ranges of 10-20 ml/kg/day is an accepted “safe” range, and has not been associated with adverse outcomes. In experimental studies in dogs, colloid use, of synthetic colloids at doses of 10-30 ml/kg/day is associated with improved tissue oxygen delivery and improved wound healing following injury. At this point in time, the use of synthetic colloids such as hydroxy-ethyl starch is recommended in the Lund Principle guidelines, to normalize colloid oncotic pressure, as part of a balanced fluid therapy strategy, including the use of isotonic crystalloids, haemoglobin (blood) and synthetic colloids. Doses for use in dogs and cats have not been established – however, as an adjunct to crystalloid fluid therapy using the small bolus resuscitation protocol described above, a single dose of 3-5 ml/kg HES given over 10 minutes may be given to increase the duration of action of crystalloid fluid boluses.

5. **Control cerebral metabolic rate** – cerebral metabolic rate has a profound influence on the development of secondary brain injury, in head trauma. Elevated cerebral metabolic rate increases tissue oxygen demand, lactic acidosis, and perpetuates a cycle of cerebral metabolic dysfunction. Patients who are anxious or stressed, painful, or who are showing symptoms of seizures should be managed using sedatives and anti-epileptic medications. Interestingly the presence of seizures is strongly suggestive of intracranial hemorrhage. Note that the presence of nausea is also supportive of intracranial hemorrhage. Early recognition of symptoms such as nausea, vomiting, and seizures permits early detection of patients at risk for rapid deterioration. Administration of anti-epileptic medications and anti-nausea medications early in head trauma may reduce the risk of worsening neurological injury.

6. **Perform and Initial Neurological Examination** –

   - Perform a neurological evaluation using the Small Animal Coma Scale to determine the severity of neurological deficits on presentation.
   - Evaluation of the Small Animal Coma Scale can aid in identifying patients that will require intubation and ventilatory support, and those patients that may require additional therapies during
re-institution of feeding. Trends in coma scale can also be an aid to predicting neurological recovery in a broad sense – although the extent of full neurological recovery may not be apparent for several weeks.

- The small animal coma scale is presented below for reference, and has been adapted from the Glasgow Coma Scale developed for humans with head trauma.

### Small Animal Coma Scale

#### Motor Activity

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal gait, normal spinal reflexes</td>
<td>6</td>
</tr>
<tr>
<td>Hemiparesis, tetraparesis, or decerebrate rigidity</td>
<td>5</td>
</tr>
<tr>
<td>Recumbent, intermittent extensor rigidity</td>
<td>4</td>
</tr>
<tr>
<td>Recumbent, constant extensor rigidity</td>
<td>3</td>
</tr>
<tr>
<td>Recumbent, constant extensor rigidity with opisthotonos</td>
<td>2</td>
</tr>
<tr>
<td>Recumbent, hypotonia of muscles, depressed/absent spinal reflexes</td>
<td>1</td>
</tr>
</tbody>
</table>

#### Brain Stem Reflexes

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pupillary light reflexes, and oculocephalic reflexes</td>
<td>6</td>
</tr>
<tr>
<td>Slow PLR, with normal to reduced oculocephalic reflexes</td>
<td>5</td>
</tr>
<tr>
<td>Bilateral miosis, normal to reduced oculocephalic reflexes</td>
<td>4</td>
</tr>
<tr>
<td>Pinpoint pupils, reduced to absent oculocephalic reflexes</td>
<td>3</td>
</tr>
<tr>
<td>Unilateral unresponsive mydriasis, reduced/absent oculocephalic reflexes</td>
<td>2</td>
</tr>
<tr>
<td>Bilateral unresponsive mydriasis, reduced/absent oculocephalic reflexes</td>
<td>1</td>
</tr>
</tbody>
</table>

#### Level of Consciousness

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occasional periods of alertness, responsive to environment</td>
<td>6</td>
</tr>
<tr>
<td>Depression/delirium, capable of responding to environment but response may be inappropriate</td>
<td>5</td>
</tr>
<tr>
<td>Semi-comatose, responsive to visual stimuli</td>
<td>4</td>
</tr>
<tr>
<td>Semi-comatose, responsive to auditory stimuli</td>
<td>3</td>
</tr>
<tr>
<td>Semi-comatose, responsive only to repeated noxious stimuli</td>
<td>2</td>
</tr>
<tr>
<td>Comatose, unresponsive to repeated noxious stimuli</td>
<td>1</td>
</tr>
</tbody>
</table>

- A patient having a coma score less than seven is deemed as having severe neurological injury.
- A coma score between seven and twelve is deemed to have moderate neurological injury.
- A patient with a score above twelve as having mild neurological injury.

Importantly, an improving coma score indicates response to therapy, whereas a static or decreasing score may dictate further therapy is required, such as ventilation therapy.
Prognosis should be based on the results of several neurological examinations, localization of the neurological abnormalities, and the presence of concurrent medical and surgical problems with the patient. A single coma score should not be used as justification for euthanasia.

7. **Relieve anxiety and pain.** Drugs used to relieve anxiety and pain in patients with head trauma may include sedatives, and narcotic agents. The most widely used include a combination of butorphanol and diazepam, or fentanyl and midazolam. These drugs can facilitate intubation during the provision of ventilatory support, aid in reducing sustained activation of the neuro-hormonal response to stress, and decrease cerebral oxygen demand. Opiates can decrease brain sensitivity to carbon dioxide, which results in cerebral vasodilatation, and increasing brain volume. Ventilatory effort and effectiveness therefore need to be closely monitored following sedation with opiates. Provision of supplemental oxygen, endotracheal intubation and ventilatory assistance is recommended if the patient respiratory or neurological status deteriorates following analgesic therapy, and possible reversal of the opiate. Non-steroid anti-inflammatory drugs should be avoided.

8. **Diuretics** have been advocated in the management of head trauma, but their use is not without controversy due to uncertainty regarding their effectiveness and safety. Indications for consideration of diuretic administration include the following...

   - Deteriorating neurological status following appropriate therapy in as described above (points 1-7)
   - Pinpoint pupils that are poorly responsive to light
   - Dilated, poorly responsive pupils
   - The development of seizures
   - The development of coma

Diuretics are administered once the patient is hemodynamically stable, as indicated by normal heart rate, respiratory rate, pulse quality, mucous membrane characteristics and urine output. The use of drugs such as urea, glycerol and mannitol have not shown conclusive benefit in the management of head trauma in people, and no studies on their effectiveness in dogs and cats have been conducted. Their use may also be associated with a rebound effect – resulting in increased brain water content. The use of constant rate infusions over time may prove more beneficial in time.

   - **Mannitol** is a small molecular weight substance that is present in a hypertonic solution. It is large enough, that, in the normal brain, it does not cross the blood-brain barrier, and therefore, when administered intravenously, exerts a strong osmotic stimulus for movement of fluid from the intracellular and interstitial spaces within the brain, into the systemic circulation. In addition, the small particle size of mannitol decreases blood viscosity, and increases blood flow through the brain, assisting oxygen delivery to the tissues. This in turn, results in improvement in blood vessel tone in the brain, and decreased intracranial pressure. Mannitol also reduces CSF production, scavenges free radicals, and produces an osmotic transfer of fluid from the interstitial and intracellular compartments to the intravascular space. Osmotic shift effects are seen approximately 15 minutes following administration, resulting in a clinical effect being observed usually within 15-30 minutes. The effect persists for approximately 4 hours. Current evidence supports the use of furosemide over mannitol.

   - Give mannitol following correction of hypovolemia
   - Dose: 0.25 gm/kg, up to 2 ml/min (20% solution) q 4 hrs; give no more than 3 doses in any 24 hr period to avoid hyperosmolar syndromes.
Indications include deteriorating neurological status, depressed LOC on presentation.

If patients’ neurological status deteriorates following mannitol administration, repeated doses should be withheld, as this may indicate intracranial loss of mannitol.

Precautions: significant diuresis may ensue, resulting in hypovolaemia and dehydration. Intravenous fluid rates may need to be increased to replace losses induced by diuresis.

Furosemide is a potent diuretic acting on the sodium-potassium co-transporter in the thick ascending loop on Henle in the kidney. Furosemide has been used in both human and veterinary medicine in the management of increased intra-cranial pressure. Furosemide administration in head trauma is associated with reduction in intracranial water content. Furosemide may be used in conjunction with mannitol, or without mannitol. Current experimental and clinical evidence supports CRI furosemide use over mannitol.

Dose: 0.2-0.5 mg/kg/hr administered by constant rate infusion.

Precautions: significant diuresis may ensue, resulting in hypovolaemia and dehydration. Intravenous fluid rates may need to be increased to replace fluid losses induced by diuresis.

Corticosteroids are of no proven benefit patients with traumatic brain injury. They may cause hyperglycemia, and gastrointestinal ulceration. Currently, they are not recommended.

Monitoring the Patient with Head Trauma – The First 24 Hours

Patients with traumatic brain injury following head trauma are critical patients that require frequent monitoring and reassessment. Treatment plans frequently need to be re-evaluated in light of the findings of serial clinical examinations, including TPR assessment, neurological assessment, coma score, and the presence of concurrent medical and surgical conditions associated with trauma.

In general, the following rules apply to the monitoring of the patient with traumatic brain injury:

1. Repeat primary survey q 10-30 minutes, depending on the patient status, until the patient is stable.
2. Monitor PCV/TP and glucose q 30-60 minutes until the patient is stable.
3. Perform secondary survey/thorough clinical evaluation of the patient q 30-60 minutes as for any patient with trauma.
4. Perform coma scale evaluation q 30 minutes, until the patient is showing signs of continued improvement.
5. Re-evaluate the treatment plan following each clinical and neurological assessment to ensure the most appropriate treatment is being given.
6. Fluid therapy – should continue following initial volume resuscitation at a rate of 1.5 x maintenance levels (3-4 ml/kg/hr). The fluid of choice for the first 24 hours is LRS, with addition of hydroxy-ethyl starch @ 20 ml/kg/day (dog) or 10 ml/kg/day (cat) if total plasma protein concentration is below 50 g/L. Monitoring of systolic blood pressure is preferred, in order to better tailor a fluid therapy plan. Maintain systolic blood pressure above 90 mmHg, and preferably in the normal range (110-140 mm Hg).
7. Nursing care includes turning the patient q 2 hrs, nutritional support, enemas, and assisted bowel function. Physiotherapy, limb massage, and passive limb flexion should also be used to minimize muscle contracture and wasting, and ischemic damage to gravity dependant limbs.
8. Nutrition – In head trauma, the functional gut-brain link is altered, causing gastric dysrhythmias, nausea, vomiting and intolerance to feeding. Administrations of prokinetic drugs such as
metoclopramide are advised in all patients with head trauma. Begin nutrition with a semi-liquid diet via syringe, or esophagostomy or gastrotomy tube within 12-24 hrs of trauma.

**The Deteriorating Patient – What To Do**

Continued evaluation of the patient with head trauma and traumatic brain injury is an essential component of therapy. If the patient continues to show signs of neurological deterioration despite therapy, it is necessary to follow a methodical plan in an effort to determine the cause of the deterioration, and to put into effect a timely therapeutic plan for intervention.

- **Assess the patients’ respiratory function** – ensure the patient has a patent airway; establish a patent airway. Assess respiratory rate, effort, and effectiveness by visual examination, mucus membrane color, and blood gas and pulse oximetry if available. Provide ventilatory assistance by oxygen supplementation and manual ventilation as previously described if required respiratory function is abnormal or insufficient.

- **Assess the patients’ cardiovascular function** – as outlined above, poor tissue perfusion is a major contributing factor in poor neurological outcome. Assess mucous membrane color and refill time, pulses, blood pressure (if available), heart rate, and body temperature. Symptoms of persistent hypovolemia include elevated heart rate, poor pulse quality, low peripheral blood pressure, poor capillary refill time, and low body temperature. These symptoms may be present due to:
  - Inadequate volume resuscitation – treat by administering intravenous fluid therapy in a pulsatile, low-volume manner as described above. It is important to remember that administration of diuretics such as mannitol and furosemide can result in blood volume depletion. Frequent evaluation of the patient is required following diuretic therapy in order to prevent this complication
  - The presence of pleural space disease – perform a thoracentesis (chest tap) on both sides of the chest to rule out the presence of a pneumothorax, haemothorax, or tension pneumothorax. Manage as required
  - The presence of blood loss into the abdominal cavity, thoracic cavity, or long bone fracture sites. Perform abdominocentesis, thoracocentesis (if lung sounds dull) etc. to evaluate pleural and abdominal third spaces. Manage as required – drain pleural fluid if present; place an abdominal compression bandage to control abdominal haemorrhage; splint and immobilize fractures. Administer whole blood or packed red blood cells if the PCV falls below 20-25% to ensure adequate haemoglobin is available for tissue oxygen delivery.
  - The presence of pain – manage with opioid analgesia and/or sedation
  - The presence of hypothermia – decreases vascular tone (see below)

- **Evaluate neurological status** – deteriorating neurological status despite adequate airway, breathing and circulation is an indication for further administration of diuretic therapy with mannitol and/or furosemide. Failure to respond to further diuretic therapy should prompt the clinician to consider ancillary therapy.

A summary of the therapeutic interventions currently recommended in the management of patients with head trauma or seizures is presented below. It is important to remember that frequent patient assessment is key to ensuring that the therapeutic plan is appropriate to the patient at any given time. Deteriorating neurological status is an indication to re-work the patient’s problems – beginning with airway and respiratory assessment.
In humans, surgery or cranial decompression, including durotomy may be used to relieve intracranial pressure in patients not responsive to medical therapy. Neurosurgical therapy aims to minimize secondary brain damage through evacuation of an intracranial space occupied by a blood clot or hemorrhage, and the reduction of intracranial volumes and pressure. The prognosis after decompression depends on the clinical signs and symptoms on admission, the patients’ age, and the existence of major extra-cranial injuries. Patients having brainstem injury, and patients having sustained trauma greater than 48 hours prior to intended surgery are poor candidates. Interestingly, the presence of skull fractures is associated with improvement in neurological outcome - presumably by allowing brain expansion through the movement of fracture fragments in response to increasing intracranial pressure following brain injury.

The following table presents the key clinical applications in the management of head trauma according to the Lund Concept in point form.
## Clinical Application of Therapies in the Management of Head Trauma/Traumatic Brain Injury

1. Ensure the patient has a patent airway
2. Mechanical ventilation to achieve end-tidal carbon dioxide of 35-40 mm Hg
   - 12-15 breaths per minute
   - 15 ml/kg tidal volume
   - Avoid hyperventilation
3. Achieve normovolaemia, normal haemoglobin concentrations and normal colloid oncotic pressure
   - Intravenous isotonic crystalloid (LRS) @ 10 ml/kg IV over 10 minutes and repeated until symptoms of shock resolve, then administer at 3-4 ml/kg/hr to maintain euvoalaemia, and systolic arterial blood pressure of above 100 mm Hg, and urine output of greater than 2 ml/kg/hr
   - Transfuse patient if PCV falls below 20-25%. End-point for transfusion is PCV above 30%
   - Administer hydroxy-ethyl starch @ 3-5 ml/kg to assist treatment of shock with crystalloids if crystalloids alone are ineffective in resolving symptoms of shock within 20 minutes. Administer hydroxy-ethyl starch @ 10 ml/kg/day (cat) or 20 ml/kg/day (dog) to maintain colloid oncotic pressure if total plasma proteins fall below 50 g/L
4. Reduce stress and excessive neurological activity
   - Opiate medication with butorphanol or fentanyl CRI is preferred. Avoid morphine and methadone due to sedation and hypoventilation
   - Sedatives such as diazepam (bolus) midazolam (bolus + CRI), propofol (CRI) or thiopentone (low dose only) may be used to control excessive neurological activity
5. Maintain normothermia – maintain body temperature above 37°C, and below 39°C
6. Postural support and nursing care
   - Elevate head no more than 20° by placing animal on board and raising the anterior animal. Avoid kinking the neck
   - Enema q 24 hrs
   - Urinary catheter to facilitate urine evacuation
   - Provide nutritional support (via feeding tube if required)
   - Reduce nausea – metoclopramide, maropitant citrate, dolasetron
   - Soft bedding, passive range of motion physical therapy etc.
7. Other therapies showing promise – but as yet unproven
   - Lidocaine CRI
   - Beta-1 antagonists e.g. metoprolol have been used in humans to reduce cerebral hypertension
   - Magnesium
   - Insulin-like growth factor

## Prognosis of the Patient with Head Trauma

Obviously, not all patients with head trauma suffer the same magnitude or location of injury. In addition, injuries sustained to different regions of the brain are also associated with different prognosis for recovery. For these reasons, it is important to attempt to localize the region(s) of the brain that have been affected by neurological dysfunction, so that owners can be informed of prognosis/likely outcome and recovery time.
In general, the following rules can be applied to patients with head trauma regarding recovery and prognosis:

- Cerebral, cerebellum injuries carry a better prognosis than brainstem lesions
- Clinical progress may take up to 4-8 weeks

In terms of localizing the lesion(s) following head trauma, some difficulty can be experienced – particularly as some of the signs and symptoms of neurological dysfunction of one brain region can overlap with those of other brain regions, and also the fact that some animals can have injury in more than one area of the brain. The following summary outlines symptoms that may be expected in the 5 major brain regions…

a. **Telencephalon – cerebral cortex, cerebral white matter, basal nuclei**
   - Abnormal behavior, depression, seizures, head pressing, pacing
   - Posture normal
   - Gait normal, mild ipsilateral hemiparesis
   - Contra-lateral postural deficits
   - Cranial nerves normal, possible contra-lateral vision impairment (cortical blindness, with normal pupillary light reflexes (PLR)

b. **Diencephalon - thalamus, hypothalamus**
   - Altered mental status, aggression, disorientation; disordered endocrine and autonomic functions
   - Posture normal
   - Gait normal to hemi- to tetra-paresis (UMN signs)
   - Contra-lateral postural deficits
   - Cranial nerve deficit CN II (Optic) no PLR, menace ipsilateral side

c. **Mesencephalon (midbrain), Metencephalon (pons), Myencephalon (medulla oblongata)**
   - Altered mental status – depression, stupor, coma
   - Posture normal; possibly turning and falling
   - Gait – ipsilateral hemiparesis (unilateral lesion) or spastic tetraparesis (bilateral lesion), ataxia, grossly abnormal gait
   - Ipsilateral or contra-lateral postural deficits
   - Cranial nerve deficits may be present in CN III-XII
   - Respiratory pattern may vary from bradypnea, hyperventilation, agonal, or Cheyne-Stokes respiration

d. **Metencephalon (cerebellum)**
   - Mental status normal
   - Posture normal
   - Gait – tremors, dysmetria, ataxia
   - Postural reactions normal, possibly dysmetria
   - Cranial nerves normal, possibly reduced menace reaction ipsilateral to lesion, nystagmus

e. **Vestibular**
   - Mental status normal
   - Posture – head tilt
   - Gait – normal to ataxia, hemiparesis if central vestibular
   - Posture – ipsilateral or contra-lateral deficits
   - Cranial nerve deficits may be affected, CN III, V, VII, nystagmus may be present