Chapter Title:

Aggressive Management of Severe Traumatic Brain Injury

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Key words:

LEARNING OUTCOMES: After completing this e-chapter you will be able to:

1. Review key concepts related to the physiology of intracranial hypertension

2. Discuss the classifications of traumatic brain injury (TBI)

3. Identify priorities in the critical care management following TBI

4. Distinguish primary brain injury from secondary brain injury

5. Explain the nurses role in coordinating intracranial pressure (ICP) monitoring with cerebral spinal fluid (CSF) drainage

6. Discuss the role of targeted temperature management protocols in brain trauma management.

Chapter overview:

This chapter differentiates brain trauma by etiology and type including blunt versus penetrating brain trauma as well as primary versus secondary brain injury. Clinical analysis and case study explore intracranial pathophysiology, risk of secondary brain injury and modulating intracranial contents (brain, blood and CSF volumes) in critical care management of brain trauma as well as the role of temperature management in traumatic brain injury. Discussion examines cardiopulmonary physiology and multisystem consequences of injury on intracranial physiology, ICP control and recovery as well as implications for critical care nursing worldwide in the assessment and monitoring of patients.

Abstract:

Blunt or penetrating brain trauma alters intracranial physiology immediately as primary brain trauma. From that moment onward, intracranial pathophysiologic changes begin the cycle of secondary brain injury. Secondary injury evolves from consequences including brain edema, cerebral blood flow/blood volume alterations and/or changes in cerebrospinal fluid (CSF) hydrodynamics. Secondary injury may be consequent to global complications or multisystem trauma such as chest/abdominal trauma. Aggressive management of brain trauma must address intracranial consequences and include selective manipulation of brain tissue, blood and/or CSF volumes. Effective management must also account for multisystem dysfunction, oxygenation/ventilation and fluid/electrolyte balance because of the intimate relationships among cardiopulmonary and intracranial physiology. Multidisciplinary collaboration, the role of the intensive care unit (ICU) nurse in neurologic surveillance, rapid intervention and effective communication among all team members as well as meticulous attention to family needs and developing trust are vital aspects of overall care and optimal outcomes.

Introduction

Globally, traumatic brain injury (TBI) is a leading cause of death and disability in patients less than 45 years old, carrying with it a significant societal and personal burden (Decuypere & Klimo, 2012; Pangilinan, 2014). The overwhelming majority of patients following mild to moderate TBI have neurologic consequences 3 months post-injury with many requiring rehabilitation (Badgiata, Carney, & Crocco, 2007; Decuypere & Klimo, 2012; Pangilinan, 2014). Additional human costs include loss of employment, altered family dynamics, low self-esteem and lost potential. Severe TBI is defined as a Glasgow Coma Scale Score of 3-8/15 (Dawodu, 2015; Decuypere & Klimo, 2012; Haddad & Arabi, 2012). Mild TBI is defined by a GCS of 13-15 and moderate TBI is defined by a GCS of 9-12. ***Review of the GCS is found in table one*** (Dawodu, 2015; Decuypere & Klimo, 2012; Haddad & Arabi, 2012; Teasdale & Jennett, 1974). ***Comparison of mild, moderate and severe TBI is listed in table 2*** (Dawodu, 2015; Decuypere & Klimo, 2012; Haddad & Arabi, 2012). The purpose of this chapter is to review pathophysiology and aggressive management of TBI. Scope includes pathophysiology, clinical evaluation, neurodiagnostics and monitoring as well as clinical management and nursing care implications. Optimal patient and family care is illustrated by case study.

Physiology of Intracranial Hypertension:

TBI affects all three components of the contents within the intracranial space. **ICP physiology is illustrated in figure 1.** Salient events in ICP elevation and onset/progression of secondary brain injury are alterations in the relative volume of these 3 components contained within the intracranial vault. Multiple interventions may modulate one or more components of intracranial pathophysiology. Osmotherapy with mannitol and/or hypertonic saline creates an osmotic gradient between edematous

brain tissue and circulating blood volume, facilitating water movement out of swollen brain tissue. Increased brain blood volume may be modulated by titrating controlled ventilation and facilitating venous drainage from the head. Hydrocephalus may be modulated by ventricular drainage coordinated with ICP monitoring. Brain metabolic state and related ICP/blood flow elevations may be modulated by drug therapies such as barbiturates or propofol. Therapeutic hypothermia, though controversial, may be utilized on a case-by-case basis to modulate brain metabolism, blood flow and ICP. Aggressive normothermia protects the brain from consequences of fever and may prevent ICP elevations consequent to increased cerebral blood flow and hypermetabolic state. Decompressive hemicraniectomy may be used on a case-by-case basis for refractory ICP elevations pending resolution of severe brain edema.

Sedation may decrease anxiety and brain arousal. Analgesia may decrease response to pain and brain arousal. Brain arousal may increase cerebral blood flow and complicate ICP control. Neuromuscular blockade (NMB) can be used to decrease global metabolic load by skeletal muscle paralysis as well as eliminate patient-ventilator dyssynchrony and coughing, both of which elevate intrathoracic pressure and ICP. The overall plan of care for TBI must also include avoiding hypoxemia, electrolyte/acid-base imbalances and preventing ICP progression to brain herniation syndromes. Terminal brainstem herniation is an end-stage and fatal outcome of refractory ICP elevations.

TBI Pathophysiology and trajectory

One classification of TBI is closed head injury where the brain is injured from trauma to the skull or a sudden, severe force applied to the skull causing brain trauma from hard contact against the inner table of the skull (Dawodu, 2015; Decuypere & Klimo, 2012; Ling & Marshall, 2008; L Rangel-Castilla, 2014). ***Figure 2 illustrates examples of closed head injury versus penetrating brain injury.*** A second

classification is penetrating brain trauma, injury resulting from a projectile or sharp object (generally) penetrating the scalp, cranial vault, meninges and brain tissue itself, exposing the intracranial cavity to the environment (Griffin & Hickey, 2012; Santiago, Oh, Dash, Holcomb, & Wade, 2012).

TBI further differentiates between primary and secondary brain injury (Chen et al., 2008; Dawodu, 2015; Greve & Zink, 2009; Haddad & Arabi, 2012; Ling & Marshall, 2008; L Rangel-Castilla, 2014; Sahuquillo & Vilalta, 2007; Werner & Engelhard, 2007). Primary, at the moment of injury, occurs consequent to depressed skull fracture, closed head injury, penetrating brain trauma, subdural/epidural hematoma and/or traumatic intracerebral hemorrhage as well as brain contusion or laceration (Dawodu, 2015; Greve & Zink, 2009; Ling & Marshall, 2008; Pangilinan, 2014; L Rangel-Castilla, 2014; Santiago et al., 2012; Werner & Engelhard, 2007). Diffuse injury may be consequent to rapid acceleration/deceleration leading to diffuse axonal injury and/or brain edema (Dawodu, 2015; Pangilinan, 2014; L Rangel-Castilla, 2014; Werner & Engelhard, 2007). Secondary injury follows the immediate trauma and includes tissue ischemia, auto-regulatory failure, anaerobic metabolism, increased tissue lactate, cellular energy failure, release of excitatory amino acids and loss of cell membrane integrity (Greve & Zink, 2009; Ling & Marshall, 2008; L Rangel-Castilla, 2014; Sahuquillo & Vilalta, 2007; Werner & Engelhard, 2007). Loss of membrane integrity allows sodium and calcium influx into the cells, lipid peroxidation and loss of structural integrity, allowing cellular/tissue water influx resulting in further brain edema (Dawodu, 2015; Greve & Zink, 2009; Ling & Marshall, 2008; Pangilinan, 2014; L Rangel-Castilla, 2014; Sahuquillo & Vilalta, 2007; Werner & Engelhard, 2007). Loss of membrane integrity activates the coagulation cascade risking small-vessel clot formation and brain ischemia (Chodobski, Zink, & Szmydynger-Chodobska, 2011).

TBI Case study: Initial injury and presentation

A 21-year-old white female was found unconscious outside late at night. Emergency medical system (EMS) was activated and she was transported to the emergency department (ED) of a large regional trauma center. She had apparently fallen and sustained traumatic brain injury, multiple skull fractures and multisystem trauma. During transport, full cervical-spine precautions, intravenous (IV) access and ventilation support were initiated. Upon ED arrival, airway, breathing and circulation (ABC's) were prioritized. Controlled ventilation was maintained through an oral endotracheal tube. Early airway management and controlled ventilation is vital to avoid hypoxemia, hypercarbia and slow progression of secondary brain injury (Harris, Davenport, Hurst, & Jones, 2012). She was initially hypotensive and tachycardic. Multiple large-bore peripheral IV accesses were inserted for administration of crystalloid, medications and blood products. The patient had a GCS of 4/15, indicating severe TBI. Following volume resuscitation, her blood pressure was stabilized, ventilation was controlled and she was transported for emergent head CT for evaluation of intracranial injury. **Figure 3** illustrates head CT obtained immediately following admission and stabilization in the ED. Clinical neurological examination is the standard for evaluation of the potentially injured brain. With severely depressed consciousness, immediate evaluation for structural brain injury by obtaining stat head CT is paramount (Schimpf, 2012; Tsang & Whitfield, 2012).

Following heat CT results as noted, the patient was hyperventilated in the short-term pending and during transport to the operating room (OR) for neurosurgical intervention to modulate presumed severe ICP elevations. Hyperventilation ($PaCO_2$ below 35 mm Hg) can result in brain ischemia, increased morbidity and mortality. Hyperventilation is appropriate for the shortest duration possible pending definitive intervention (Brain Trauma Foundation et al., 2007j). Operative intervention included

aggressive craniotomy/craniectomy with evacuation of subdural hematoma and insertion of a ventricular drainage catheter incorporating a fiberoptic transducer for ICP measurement. Immediate postoperative CT and appearance of ICP monitor/drainage insertion site are found in **Figure 4.**

TBI case study: ICU management in immediate postoperative phase.

Upon ICU arrival post-craniotomy and ICP monitor/drain placement, the patient received fentanyl and propofol for analgesia and sedation, to decrease cerebral responses to stimulation and treat pain. Neuromuscular blockade was initiated to promote synchrony with controlled ventilation, preventing surges in intrathoracic pressure consequent to cough responses and patient/ventilator dys-synchrony. She was managed with hyperosmolar therapy. Mannitol was titrated to a serum osmolality of 315-320 mOsm/L and she received hypertonic saline (3%) by continuous infusion. Her controlled ventilation was titrated to maintain normocarbia ($PaCO_2$ approximately 35-40 mm Hg). Ventilator-associated pneumonia (VAP) protocol was in place.

Critical Care Management Following TBI:

Postoperative critical-care management is guided as goal-directed therapy based on ICP monitoring and clinical/neurological assessment data. ICP monitoring may be effectively done by means of an intraventricular catheter, enabling CSF drainage and providing excellent ICP waveforms facilitating ICP pulse wave analysis and assessment of intracranial compliance. Other ICP monitoring options include fiberoptic catheters within the brain parenchyma or incorporated within ventricular catheter placement. Goal-directed therapies include metabolic suppression, sedation/analgesia, neuromuscular blockade (NMB), osmotic diuresis, titration of controlled ventilation as well as targeted

temperature management and therapeutic hypothermia in select cases. Each therapy has specific implications for nursing care, and while variations in resources exist internationally priority areas for nursing care include focused monitoring and reporting of neurological changes and administration of indicated therapies per country specific, national, or international guidelines.

ICP monitoring and waveform analysis

Secondary brain injury may be a direct consequence of intracranial hypertension. ICP and cerebral perfusion pressure (CPP) are immediate priorities as appropriate following TBI (Arbour, 2004; Vender, Waller, Dhandapani, & McDonnell, 2011). ICP monitoring is paramount in a patient with GCS 3-8 and abnormal head CT. ICP monitoring may be appropriate in TBI in a patient with a normal head CT if two of the following are present: age greater than 40 years, decorticate or decerebrate posturing and hypotension (Arbour, 2004; Brain Trauma Foundation et al., 2007j). ICP monitoring in context with clinical evaluation, neuroimaging and goal-directed management significantly improves outcome (Feyen, Sener, Jorens, Menovsky, & Maas, 2012). For more benefit versus risk in clinical application, ICP monitoring devices used, should be easy to use, accurate, interpreted within clinical context, rapidly acted upon in a reproducible manner and guide therapy (Mendelson et al., 2012; Schimpf, 2012).

The most commonly utilized options for ICP monitoring include ventriculostomy and intraparenchymal device placement (Brain Trauma Foundation et al., 2007d; Vender et al., 2011). Ventriculostomy placement is considered the reference standard for ICP monitoring, giving good quality ICP waveforms and accurate, reproducible pressure measurements (Arbour, 2004; Brain Trauma Foundation et al., 2007d; Feyen et al., 2012; Schimpf, 2012). Ventriculostomy placement allows for

CSF drainage as part of mechanism-based care and coordinated for managing intracranial hypertension (Arbour, 2004; Brain Trauma Foundation et al., 2007e; Mendelson et al., 2012; Schimpf, 2012; Vender et al., 2011). ICP treatment threshold is generally 20 mm Hg (Brain Trauma Foundation et al., 2007f; Schimpf, 2012).

Monitoring cerebral perfusion pressure (CPP) is also integral in managing severe TBI. CPP is determined by the following formula: CPP = mean arterial pressure (MAP) – ICP (Arbour, 2004; Feyen et al., 2012; Schimpf, 2012). Optimal monitoring of ICP and MAP are vital in managing severe TBI due to risks of hyperemia versus oligemia. Hyperemia consequent to hypertension may result in cerebral blood flow (CBF) surges and ICP elevation. Oligemic CBF states consequent to hypotension may result in brain ischemia. One management guideline includes a general CPP range of 50-70 mm Hg (Brain Trauma Foundation et al., 2007c). Other authors advocate goal-directed therapy for CPP between 60-75 mm Hg (Schimpf, 2012). CPP and ICP should be very closely monitored. For example, with CPP trending lower than 60 mm Hg, identifying possible causes and intervening appropriately intervention are vital. Management may be 2-fold and be directed toward ICP reduction as well as directed towards supporting blood pressure by administering crystalloid, blood products or vasoactive versus inotropic agents.

Additional information is obtained by detailed analysis of the ICP pulse waveform, waveform changes over time and in response to stimulation. Pulse waveform amplitude reflects changes in CBF consequent to the cardiac cycle, cerebrovascular compliance and reactivity. While requiring additional validation, this may be an additional approach to monitoring and yield further, actionable information from ICP pulse waveforms and concurrent MAP (Aries et al., 2012). Additional directions for research include analysis of complexity and responsiveness of ICP trends over time and in response to

stimulation providing feedback on reactivity of brail blood flow. Initial studies suggest that more responsive and complex ICP is predictive of better outcome (Lu et al., 2012).

Close ICP waveform analysis indicating elevated P-2 component of ICP pulse waveform may also indicate compromised intracranial compliance and higher predictive value for more significant ICP elevation in response to stimulation (Arbour, 2004). Stimulation may include airway manipulation/suctioning, repositioning or invasive procedures such as peripheral venipuncture or thoracostomy. ***Figure 5 illustrates ICP pulse waveforms as exemplars, indicating degree of compliance at baseline and relationship between degree of intracranial compliance and ICP elevation in response to stimulation.***

TBI case study: Coordinating ICP monitoring with CSF drainage:

Ventricular CSF drainage was utilized and coordinated with ICP monitoring. The ventriculostomy/transducer system was closed at intervals and CSF was to be drained if ICP remained above 20 mm Hg for greater than 5 minutes. ICP monitoring via ventriculostomy yielded good quality ICP waveforms and ability to assess intracranial compliance by waveform analysis and ICP responses to stimulation with time to resolution. The patient continued to receive mannitol for hyperosmolar therapy, sedation, analgesia and neuromuscular blockade. Protocol for prevention of ventilator-associated pneumonia (VAP) was in place.

Hyperosmolar therapy

Hyperosmolar therapy is among the mainstays of ICP control following brain trauma (Decuypere & Klimo, 2012). The two main options for hyperosmolar therapy are mannitol (considered first-line) and hypertonic saline (Brain Trauma Foundation et al., 2007a; Decuypere & Klimo, 2012; Griffin & Hickey,

2012; Haddad & Arabi, 2012; Helmy, Vizcaychipi, & Gupta, 2007; Honeybul, 2011; Ling & Marshall, 2008; Protheroe & Gwinnutt, 2011; Ropper, 2012). **Table three outlines specific agents utilized for hyperosmolar therapy and includes dosing, cardiovascular/clinical effects, goals of care and nursing considerations** (Brain Trauma Foundation et al., 2007a; Decuypere & Klimo, 2012; Griffin & Hickey, 2012; Haddad & Arabi, 2012; Helmy et al., 2007; Honeybul, 2011; Kerwin et al., 2009; Ling & Marshall, 2008; Oddo et al., 2009; Protheroe & Gwinnutt, 2011; Rockswold et al., 2009; Ropper, 2012; Sakellaridis et al., 2011).

Pulmonary management and severe traumatic brain injury

Pulmonary management following severe TBI is extremely challenging for multiple reasons. One reason is arterial CO_2 , which must be closely monitored and managed by frequent, close ventilator titration to avoid extremes of hyper versus hypo-capnia, avoiding cerebral blood flow extremes and decreasing risk of hyperemia versus ischemia. A second reason is optimal pulmonary care including head-of-bed (HOB) elevation and protocol-directed care to prevent ventilator-associated pneumonia (VAP). This includes frequent mouth care as well as deep airway suctioning. Mouth care and deep airway suctioning stimulate strong gag and cough reflexes, raising intrathoracic and intracranial pressures. A third reason is ventilator management in the setting of severe respiratory failure such as acute respiratory distress syndrome (ARDS) or concurrent chest/lung trauma. Maintaining oxygenation may require positive-end-expiratory-pressure (PEEP) and non-physiologic ventilation modes which, with elevated intrathoracic pressures, may make ICP more difficult to control. Maintaining oxygenation and tissue oxygen delivery is paramount in preventing secondary brain injury.

Titrating arterial carbon dioxide

While the use of hyperventilation may vary based on clinical guideline recommendations, it is usually reserved for emergent management of increased ICP unless there is the ability to monitor brain tissue oxygenation. Hyperventilation may be indicated for aggressive care immediately following TBI because aggressive hypocapnia in the short term (arterial CO_2 approximately 25 mm Hg), ICP can be rapidly reduced. Hypocapnia reduces ICP due to cerebral vasoconstriction, increasing risk of brain ischemia in a CBF state already likely compromised (Brain Trauma Foundation et al., 2007j; Decuypere & Klimo, 2012; Griffin & Hickey, 2012; L. Rangel-Castilla et al., 2010). Long-term hyperventilation is not recommended but may be effective in the short-term to control ICP elevations pending other definitive, mechanism-based therapeutics (Brain Trauma Foundation et al., 2007j; Decuypere & Klimo, 2012; Griffin & Hickey, 2012; Haddad & Arabi, 2012; Honeybul, 2011). If available, measures to monitor brain oxygen levels may be appropriate to titrate therapy (Brain Trauma Foundation et al., 2007j; Honeybul, 2011). Long-term ventilation should be titrated for a $PaCO_2$ approximately 35-40 mm Hg.

Pulmonary management and Traumatic Brain Injury

Integral to managing a patient following brain trauma is aggressive pulmonary care. This mandates meticulous attention maintaining airway patency, appropriate pulmonary hygiene and initiation/maintenance of VAP protocols. VAP protocols include mouth care at appropriate intervals, HOB elevation >/= 30 degrees and stress ulcer as well as deep vein thrombosis prophylaxis.[10] Due to possible risk of cough or gag-induced surges in ICP consequent to deep airway or pharyngeal

suctioning, sedation/analgesia and neuromuscular blockade may be indicated to modulate risk of additional injury.

Ventilator management, respiratory failure and severe TBI.

Pulmonary complications following severe TBI may have multiple causes including pneumonia, concurrent pulmonary contusion or chest trauma, ALI/ARDS and pulmonary edema. In ALI/ARDS, lung recruitment maneuvers may be of particular concern with concurrent brain trauma with higher levels of PEEP and non-physiologic ventilation modes utilized (Lee & Rincon, 2012). Altered thoracic pressure dynamics may cause ICP elevations and mandate close attention of ventilator status and effects on ICP, MAP and CPP (Lee & Rincon, 2012; Zhang, Yang, Wang, & Fan, 2011). Close monitoring and incremental ventilator titration appropriate due to the individualized nature of ICP, MAP and CPP responses (Zhang et al., 2011).

Pain and Agitation Management in Severe TBI

Patient positioning, ventilation, airway suctioning, mouth care, concurrent injury and clinical states including drug/alcohol intoxication versus withdrawal may cause pain and agitation (Haddad & Arabi, 2012). Agitation and ventilator sys-synchrony can increase cerebral metabolic rate of oxygen ($CMRO_2$), ICP, blood pressure and systemic oxygen consumption, decreasing oxygen availability to brain tissue, risking secondary brain damage (Brain Trauma Foundation et al., 2007g). Clinically appropriate care for agitation must differentiate and address the cause. If agitation is due to alcohol withdrawal, replacement therapy with benzodiazepines may be effective. If agitation is due to pain, opioids such as fentanyl or morphine would be appropriate. If hypercarbia or progressive intracranial

pathology is the cause, ventilation management or mechanism-based intervention for intracranial pathophysiology is most appropriate (Ling & Marshall, 2008).

Sedation/analgesia may decrease overall metabolic demand, $CMRO_2$, cortical arousal and patient/ventilator dys-synchrony, contributing factors to intracranial hypertension (Brain Trauma Foundation et al., 2007g; Griffin & Hickey, 2012; Helmy et al., 2007). While pharmacological agents vary internationally, midazolam is one commonly used short-acting benzodiazepine sedative/hypnotic which may also provide anti-convulsant effects. Short-acting opioids such as fentanyl citrate are appropriate, well-tolerated hemodynamically and have a shorter duration of action (Helmy et al., 2007; Ling & Marshall, 2008). Propofol may be superior as a sedative/hypnotic to benzodiazepines due to its more pronounced metabolic suppression and short, more predictable duration of action (Brain Trauma Foundation et al., 2007g; Griffin & Hickey, 2012; Haddad & Arabi, 2012; Helmy et al., 2007). Propofol has the potential risk of propofol infusion syndrome (PRIS), reported in patients following severe TBI, clinically associated with a pronounced inflammatory state. PRIS is characterized by a temporal relationship between hemodynamic instability and initiation or upward titration of propofol. Clinical findings of PRIS include significant hemodynamic instability, metabolic (lactic) acidosis, hyperkalemia, rhabdomyolysis and renal failure (Brain Trauma Foundation et al., 2007g; Diedrich & Brown, 2011; Griffin & Hickey, 2012; Haddad & Arabi, 2012; Helmy et al., 2007; Ilyas, Balacumaraswami, Palin, & Ratnatunga, 2009; Ling & Marshall, 2008; Zaccheo & Bucher, 2008). There are many superb references available addressing dosing, titration and coordinating bolus versus infusion dosing of sedation/analgesia following severe TBI (Brain Trauma Foundation et al., 2007g). Optimal care and best nursing practice mandates identifying the specific clinical state, utilizing appropriate drug classes, individualizing dosing and monitoring patient tolerance as well as vigilance for side effects.

Metabolic suppression following severe TBI.

Metabolic suppression therapy is utilized to control refractory ICP elevations. Barbiturate therapy, in a patient-specific, dose-related manner is utilized for this purpose. Agents utilized for this purpose include pentobarbital sodium. A listing of these agents including dosing, cardiovascular consequences, goals of care, clinical effects/side effects and nursing considerations is found in table 4, however it is acknowledged that pharmacologic therapy varies internationally (Brain Trauma Foundation et al., 2007g; Diedrich & Brown, 2011; Griffin & Hickey, 2012; Haddad & Arabi, 2012; Helmy et al., 2007; Ilyas et al., 2009; Ling & Marshall, 2008; Zaccheo & Bucher, 2008). **Figure 6** compares and contrasts normal EEG tracing with EEG tracing illustrating appropriate level of burst suppression (4-6 bursts/min or as directed per provider) during drug-induced coma for ICP control.

Temperature management following TBI

Aggressive temperature management may have two applications. One is maintaining normothermia. A second, on a case-by-case basis, therapeutic hypothermia. Hyperthermia or a febrile state is defined as an increase in core body temperature above 38.0^0C and in TBI may be consequent to thermoregulatory failure, such as direct damage to the hypothalamus, excessive vasoconstriction limiting heat loss to the environment, autonomic hyperactivity and increased sweating threshold (Sessler, 2009). Inflammatory response may also contribute to fever post-TBI. Fever increases neuronal hyperactivity, cerebral blood flow, oxygen consumption and ICP. Significantly, brain temperature may exceed core body temperature by as much as 2^0C (Badjatia, 2009; McIlvoy, 2012). Fever has a strong relationship with poor outcomes following TBI and should be aggressively treated and prevented when

possible (Badjatia, 2009). Higher mortality, longer length-of-stay and greater disability are associated with fever post-TBI (McIlvoy, 2012).

Treatment options include pharmacological interventions such as acetaminophen and non-steroidal anti-inflammatory agents (Badjatia, 2009; Haddad & Arabi, 2012; Ling & Marshall, 2008; McIlvoy, 2012). Non-pharmacological interventions include surface cooling measures such as water-circulating cooling blankets/gel pads, intravascular cooling devices and ice-water application to skin as well as gastric lavage and IV infusion of chilled fluids (Badjatia, 2009; McIlvoy, 2012).

TBI Case study: Brain trauma and fever prevention.

Normothermia was maintained in this patient by use of water-circulating gel pads, decreased ambient room temperature and administration of acetaminophen. Increasing the temperature gradient between the patient and environment balanced heat production with heat loss and maintained normothermia. In the short-term, ICP reduction was maintained with the cooling device automatically adjusting water temperature based on core body temperature. ***Figure 7 illustrates relationship between prevention of ICP elevations and aggressive fever prevention.***

Therapeutic hypothermia and brain trauma.

Therapeutic hypothermia (TH) is a management option post-TBI on a case-by-case basis for refractory intracranial hypertension and is defined as controlled temperature depression to a range between 32.0^0C-35.0^0C (Decuypere & Klimo, 2012; Helmy et al., 2007; Rupich, 2009). Routine hypothermia following severe TBI is not supported by strong evidence (Brain Trauma Foundation et al., 2007b) In select circumstances of refractory intracranial hypertension TH has been demonstrated to reduce ICP, CBF and mortality/severe disability six months post-injury (Helmy et al., 2007; Kramer et

al., 2012). Refractory ICP elevations post-TBI are associated with poor clinical/neurological outcomes and effective ICP control improves survival (Sadaka & Veremakis, 2012).

TH produces primary neuroprotection effects by decreasing $CMRO_2$, glucose utilization and lactate production. Brain oxygen consumption during TH may decrease between 5-7 % per 1^0C decrease in temperature (Faridar et al., 2011; Varon & Acosta, 2008). TH may also preserve high-energy phosphates, modulate gene expression, facilitate anti-inflammatory/anti-apoptotic pathways and significantly reduce ICP (Faridar et al., 2011; Jiang, 2009; Meyer et al., 2010; Rupich, 2009; Sadaka & Veremakis, 2012). In addition, TH may stabilize the blood-brain barrier, inhibit production of free radicals and reduce mobilization of excitatory neurotransmitters such as glutamate (Faridar et al., 2011; Jiang, 2009; Meyer et al., 2010; Rupich, 2009; Sadaka & Veremakis, 2012).

Methods of controlled reduction on body temperature are multiple and include internal and external cooling devices. TH may be produced by multiple techniques including by conduction with devices such as cool-water circulating blankets and gel pads applied to large skin surface areas have been utilized in addition to gastric lavage with iced water, ice-water application to skin, ice-pack applications and forced-air cooling devices (Faridar et al., 2011; Jiang, 2009; Meyer et al., 2010; Polderman & Herold, 2009; Varon & Acosta, 2008). Rapid IV infusion of chilled IV fluids such as normal saline at 3-4 degrees C has been utilized in hypothermia initiation (Jiang, 2009; Polderman & Herold, 2009; Varon & Acosta, 2008). Intravascular devices utilizing circulation of cold water through a catheter placed within a high-flow blood vessel such as the femoral vein have been utilized for rapid cooling (Polderman & Herold, 2009; Varon & Acosta, 2008).

TH has potentially harmful side effects and risks versus potential benefits must be analyzed. Side effects include shivering, which may increase metabolic rate and interfere with TH induction, hypokalemia, decreased drug metabolism/elimination, dysrhythmias, bradycardia, decreased cardiac output/hypotension, increased systemic vascular resistance (SVR), Q-T prolongation and hyperglycemia (Jiang, 2009; Polderman & Herold, 2009; Rupich, 2009; Sadaka & Veremakis, 2012; Varon & Acosta, 2008) Coagulopathy may occur secondary to effects on platelet count, platelet function and possibly dilutional coagulopathy consequent to crystalloid administration (Polderman & Herold, 2009; Sadaka & Veremakis, 2012; Varon & Acosta, 2008). Risk of pneumonia and wound infection is increased with TH. GI motility may be significantly impaired, impacting feeding protocols, wound healing, physiologic reserve, muscle wasting and recovery (Jiang, 2009; Polderman & Herold, 2009; Rupich, 2009; Sadaka & Veremakis, 2012; Varon & Acosta, 2008). Multiple aspects of TH in management of severe TBI remain to be refined by controlled study with larger sample sizes including timing, duration of therapy, best monitoring parameters and endpoints. Some patients may have maximal benefit with temperature reductions to $35\text{-}36^0$C (Tokutomi et al., 2009).

Decompressive hemicraniectomy and timing in trajectory of care:

Intractable intracranial hypertension is one of the most dangerous secondary insults following severe TBI and a significant source of mortality and morbidity (Bao et al., 2010; Cianchi et al., 2012; Haddad & Arabi, 2012; Helmy et al., 2007). For refractory intracranial hypertension, progressive injury including terminal herniation can occur. Decompressive craniectomy (DC) as rescue for refractory, progressive intracranial hypertension is an option (Bao et al., 2010; Cianchi et al., 2012; Meyer et al., 2010; Olivecrona, Rodling-Wahlstrom, Naredi, & Koskinen, 2007). In DC a large area of the skull is surgically removed and the dura is opened which allows the brain to expand by increasing available

space and controlling ICP (Bao et al., 2010; Cianchi et al., 2012; Haddad & Arabi, 2012; Helmy et al., 2007; Meyer et al., 2010; Olivecrona et al., 2007). Evidence is conflicting regarding survival and clinical outcomes following craniectomy (Cianchi et al., 2012; Cooper et al., 2011; Eberle et al., 2010; Olivecrona et al., 2007). DC in has also resulted in sustained improvement in brain oxygenation and decreased ischemic burden (Weiner et al., 2010). Timing and patient selection are significant. Patients with reactive pupils and without terminal brainstem dysfunction have more potential to benefit (Bao et al., 2010; Yatsushige et al., 2010). There are therapeutic risks and as with any invasive procedure, risk/benefit analysis must occur. Complications reported post-DC include brain herniation through the skull defect, subdural effusion, infection, brain contusion/hemorrhage at edge of craniectomy defect, hydrocephalus, seizures and ventricular enlargement (Honeybul, 2010; Honeybul & Ho, 2011; Stiver, 2009). Late complications may include cognitive dysfunction and failure of cranioplasty (Stiver, 2009). In the patient for this case study, immediate decompressive craniectomy was life-saving and clinically appropriate in her continuum of care from the initial ED management >>> CT scan >>> directly to OR and then followed by ICU admission for postoperative critical care management. She was young, had few comorbidities and still had neurological function at time of surgery.

Brain Tissue Oxygen Monitoring

All therapeutic interventions including osmotherapy, craniectomy and metabolic suppression as well as sedation/analgesia are goal-directed therapeutics to improve oxygen delivery and modulate the effects of ischemia at the tissue level. Mechanism-based modalities do effectively improve brain tissue oxygenation (Chen et al., 2008; Oddo et al., 2009; Pascual et al., 2011; Rockswold et al., 2009; Spiotta et al., 2010; Weiner et al., 2010).

Brain tissue oxygenation ($PbtO_2$) is measured following placement of a small oxygen-sensing probe into brain tissue. One device in common practice, the LICOX monitoring system (Integra Neurosciences, Plainsboro, New Jersey, USA) uses a small electrode with both temperature and oxygen sensing capability and is placed approximately 25-35 mm into white matter, usually the frontal lobe (Bader, 2006; Barazangi & Hemphill, 2008; Littlejohns, Bader, & March, 2003; Stewart et al., 2008). There are multiple outstanding references with additional technical detail on direct measurement of $PbtO_2$ including catheter placement, calibration and imaging (Bader, 2006; Barazangi & Hemphill, 2008; Littlejohns et al., 2003; Stewart et al., 2008). Comprehensive discussion of all these aspects is beyond the scope of this chapter. Clinical management of severe TBI using $PbtO_2$ –directed therapy is being increasingly used globally. $PbtO_2$ is the product of CBF, cerebral arteriovenous oxygen difference and is a focal measurement of tissue oxygenation (Haddad & Arabi, 2012). $PbtO_2$ values below 15-20 mm Hg may be considered a treatment threshold for goal-directed therapies to increase cerebral oxygen delivery (Bader, 2006; Haddad & Arabi, 2012; Littlejohns et al., 2003; Spiotta et al., 2010).

Systemic hypoxemia can reduce brain tissue oxygenation if oxygenation/ventilation needs are not met. Brain tissue oxygenation may be improved by titrating ventilation and/or inspired oxygen. Other interventions include administration of packed red blood cells (PRBC) to increase oxygen-carrying capacity; metabolic suppression to decrease cerebral oxygen utilization; repositioning; fever control; hypertonic saline; CPP augmentation; repositioning/kinetic therapy; NMB; craniectomy (Bader, 2006; Bader, Littlejohns, & March, 2003; Chen et al., 2008; Haddad & Arabi, 2012; Littlejohns et al., 2003; Pascual et al., 2011; Rockswold et al., 2009; Spiotta et al., 2010). ***Responsiveness of $PbtO_2$, ICP and MAP to physiologic interventions is found in figure 8.***

The patient reflected in the collected data had severe TBI consequent to a severe fall down 15 steps in his home. She underwent aggressive, mechanism-based therapy for deteriorating neurological examination including hemicraniectomy. Following $PbtO_2$-directed therapy she recovered to in-patient rehabilitation.

TBI Case Study-Conclusion and Recovery:

With ICP stable during monitoring in the postoperative period and remaining stable, and intracranial compliance improving and serial head CT's showing improving intracranial physiology multiple steps toward recovery and ventilator liberation became possible. One step was downward titration of neuromuscular blockade to off with recovery of neuromuscular function as determined by clinical examination (cough, gag reflexes) initially and train-of-four evoked responses of 4/4 at 50 Ma current output. A second step was downward titration and discontinuation of CNS depressants (fentanyl and midazolam). Clinical response was a marginal increase in responsiveness to stimulation with patient-triggered ventilations.

Follow up head CT revealed initial resolving brain edema, ventricular system remained compressed but not deviated away from midline, as well as additional detail in sulci. ***Head CT representative images and results summary are found in figure 9.***

The patient became increasingly responsive to family members. Ventilator weaning proceeded as clinically appropriate, ventilator liberation was achieved and she progressed dramatically with physical therapy in the critical care unit. This continued through bedside work with therapy professionals through increasing activity and ambulating with assistance around the unit. With high motivation as well as encouragement from her family and caregivers and significant hard work she was discharged to home

after in-patient rehabilitation. Just 22 days after her traumatic brain injury, the patient was ambulating around the unit (with supervision), able to communicate and expressed thanks to the team of caregivers who "saved her life" and rescued her from a "close call with death."

Nursing considerations:

Care of any patient following severe TBI remains among the most challenging in critical care practice. Severe brain trauma affects all body systems and can stimulate a hypermetabolic state, complicating nutritional support. Patient risk may be due to therapeutic interventions such as airway management and invasive lines/drains risking hospital-acquired infections such as VAP, bloodstream infections or meningitis. Aggressive measures to attenuate these risks include aggressive surveillance of signs of infection, meticulous care of any invasive lines such as central venous catheters and site rotation for peripheral IV catheters. Careful and frequent assessment of operative sites (craniotomy/craniectomy), ICP monitoring/wound and CSF drain sites is imperative. Assessment and documentation of CSF and other drainage for color, amount, character and condition of any drain sites are vital to early identification and intervention for complications.

Surveillance of the clinical neurological examination, trends in ICP over time and in response to stimulation as well as detailed ICP waveform analysis if this technology is available and used. These assessments are paramount in determining progression of injury, response to therapeutic interventions, intracranial compliance and intracranial responses to stimulation and nursing care activities such as pulmonary care, repositioning and tactile as well as auditory stimulation in a critical care area. Aggressive pulmonary care including detailed lung assessment, maintaining patient-ventilator synchrony and monitoring oxygenation and ventilation are critical. Pulmonary physiology and intrathoracic

pressure dynamics alter intracranial physiology and ICP due to risks associated with hypoxemia, hyper/hypo-capnia and surges in intrathoracic pressure being transmitted to the intracranial cavity through the jugular venous system. Careful determination of actual intake/output (including potential insensible fluid losses) and judicious fluid management can maintain adequate circulating blood volume and modulate risk of fluid/electrolyte imbalances. Aggressive feeding protocols are needed to match caloric intake with metabolic needs particularly following severe trauma and subsequent hypermetabolic state. Early nutrition support is recommended, is associated with improved survival and decreased degree of disability and enhances immune function (Helmy et al., 2007). Maintaining close control of blood glucose levels by titrating insulin therapy is also appropriate(Helmy et al., 2007). Hyperglycemia is associated with progression of secondary brain injury and worse outcomes (Brain Trauma Foundation et al., 2007h; Helmy et al., 2007). Deep vein thrombosis (DVT) prophylaxis appropriate. Non-pharmacological interventions such as sequential compression devices and pharmacological interventions such as unfractionated or low-molecular-weight heparin are options (Brain Trauma Foundation et al., 2007h; Helmy et al., 2007; Ling & Marshall, 2008). Seizure risk may be reduced post-TBI by administration of anticonvulsant agents such as levetiracetam, carbamazepine or valproic acid as clinically appropriate due to risk of secondary brain damage (Brain Trauma Foundation et al., 2007i; Ling & Marshall, 2008).

Nursing considerations and family needs.

Global nursing considerations include care directed at patients' families. The patient experience of severe TBI produces a cascade of effects within the family system. The family may experience almost unendurable stress, anticipatory grief and significant fear seeing someone they love so critically ill and vulnerable. Providing regular updates at an appropriate level of understanding establishes and maintains

trust as well as lessens anxiety. Families consistently need information, professional support from the team and may benefit from some involvement in care and experience significant uncertainty during a family member's critical illness (Keenan & Joseph, 2010). Nursing implications for families include education, caring behaviors, involving families in care as appropriate, being aware of their own anxiety and how it may affect families as well as maintaining open communication and not avoiding families (Yetman, 2009).

Summary:

Worldwide, patients following severe TBI are among the most challenging and vulnerable populations in critical care practice. Primary brain injury typically begins the cycle of secondary brain injury which, if progressive and refractory to therapy, can prove fatal. Secondary brain injury may arise from evolving intracranial pathophysiology as well as other body systems including pulmonary, cardiovascular, neuroendocrine and GI dysfunction as well as hospital-acquired infections. For these reasons, optimal care of the patient following severe TBI must include aggressive, mechanism-based therapeutics for intracranial pathophysiology, focused surveillance of neurological assessment data and meticulous assessment and care for all body systems. Multidisciplinary collaboration and effective communication is key to rapid recognition of clinical changes quickly coupled with optimal clinical management in pursuit of neurologic recovery. Family needs are also key to long-term recovery and family communication, involvement in care as clinically appropriate and updates help significantly build trust which can only help with family interaction during critical illness.
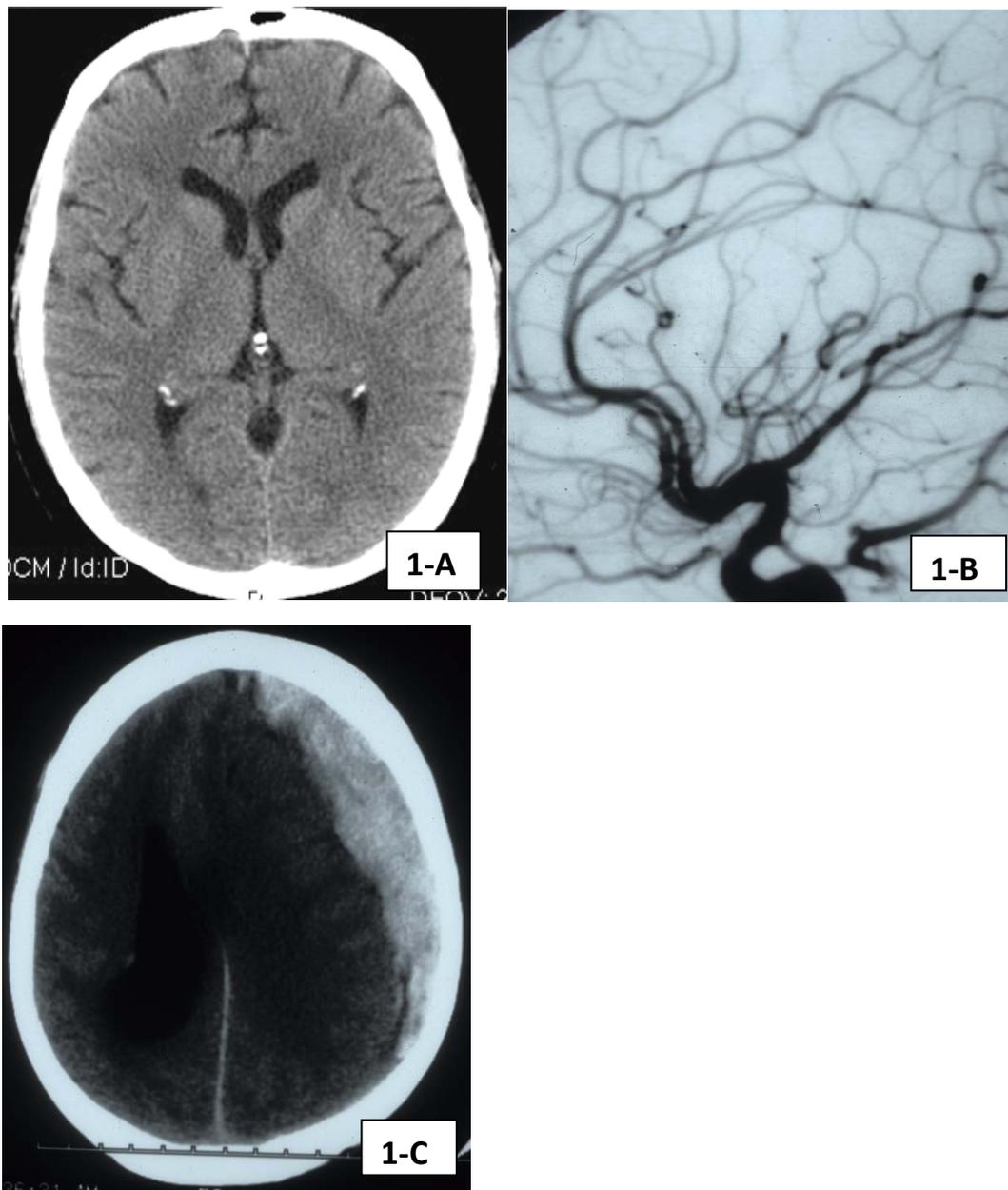
Figure 1: Illustration of ICP physiology. Figure 1-A illustrates normal CSF dynamics and brain bulk. Ventricular system normal and generally symmetrical and normal detail/no effacement of sulci/cerebral cortex. Figure 1-B illustrates normal cerebral arterial supply/distribution. In the smaller vessels, blood flow is at risk from compression due to edema and/or mass lesion. When ICP approaches/meets MAP, global brain blood flow is compromised, risking ischemic injury. These may be consequent to autoregulatory failure, hyperemia and/or compromised venous drainage. Cerebral blood flow extremes of hyperemic and oligemic flow states risk ICP increases and brain ischemia respectively. In figure 1-C (traumatic subdural hematoma), brain bulk (approx. 80 %) increases due to water influx. Cerebrospinal fluid (CSF) dynamics (approx. 10 %) may be altered due to obstructive or communicating hydrocephalus and ventricular system is significantly distorted. Brain blood volume (approx. 10 %) is affected due to compression/distortion of cerebral vessels.

Initial ICP readings immediately following monitor insertion were significantly elevated (45-50 mm Hg) requiring immediate intervention.
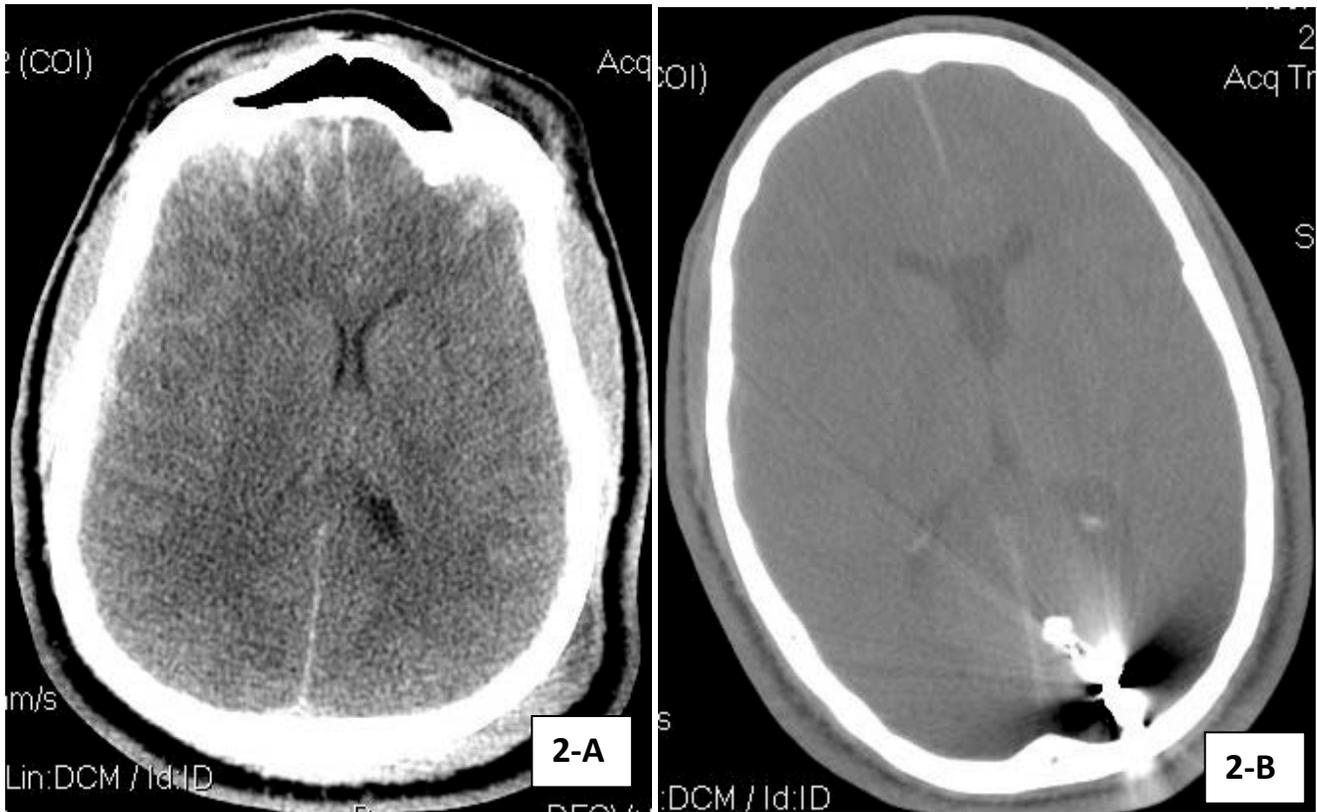

Figure 2: Comparison between head CT of closed head (blunt) injury versus penetrating brain injury. Figure 2-A illustrating post-motor vehicle collision. Brain edema, effacement of sulci, compression/distortion of ventricular system and frontal lobe contusions are evident. Vascular injury may also result from closed head injury and cause epidural or subdural hematoma. Figure 2-B illustrates penetrating brain injury (gunshot wound at close range). Image shows brain edema/effacement of sulci, initial distortion of ventricular system penetrating injury (bullet fragment/missile) within brain parenchyma. Small cross-sectional area of missile allows maximal delivery of force to small point of contact and maximal penetration.
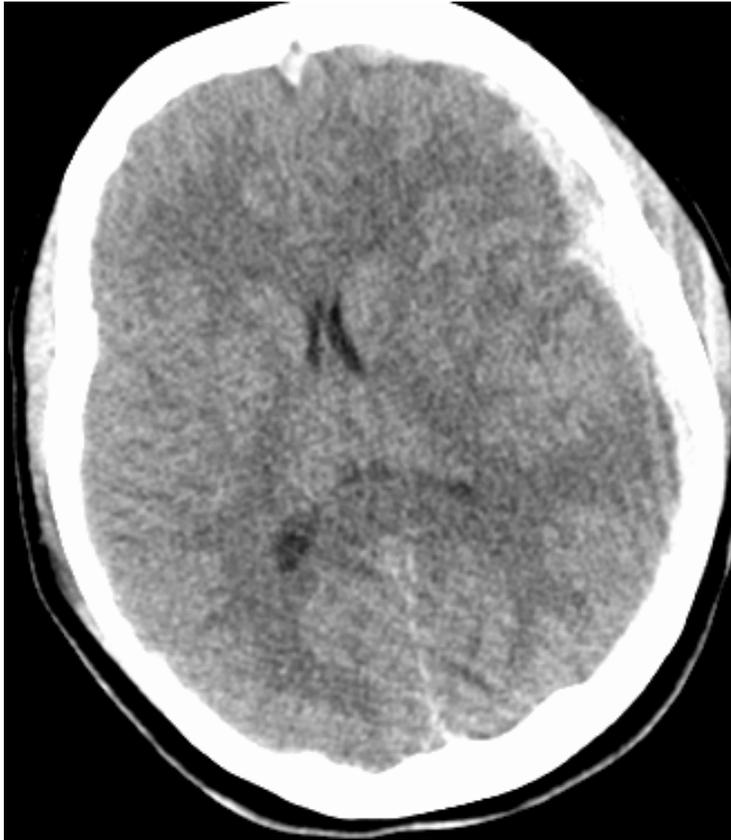
Figure 3: Immediate head CT obtained following initial stabilization in ED of a large, regional medical center. Imaging revealed left-sided subdural hematoma, beginning left frontal contusion, near-total effacement of the sulci, midline shift and compression/displacement of the ventricular system on the left side.
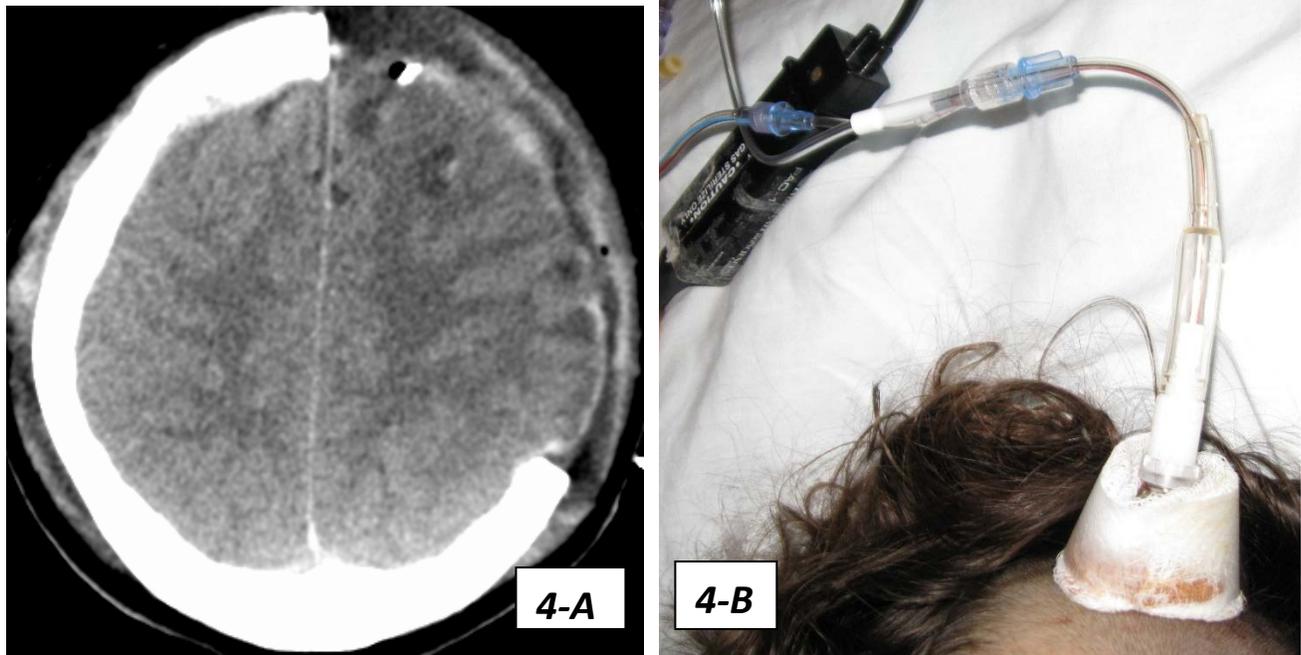
Figure 4: Figure 4-A illustrates immediate postoperative head CT showing decompressive hemicraniectomy and evacuation of left subdural hematoma. Brain edema/sulci effacement remains present but midline shift resolved. Small right frontal subdural hematoma is visible and was to be monitored. Figure 4-B illustrates ICP monitor/drain insertion site.
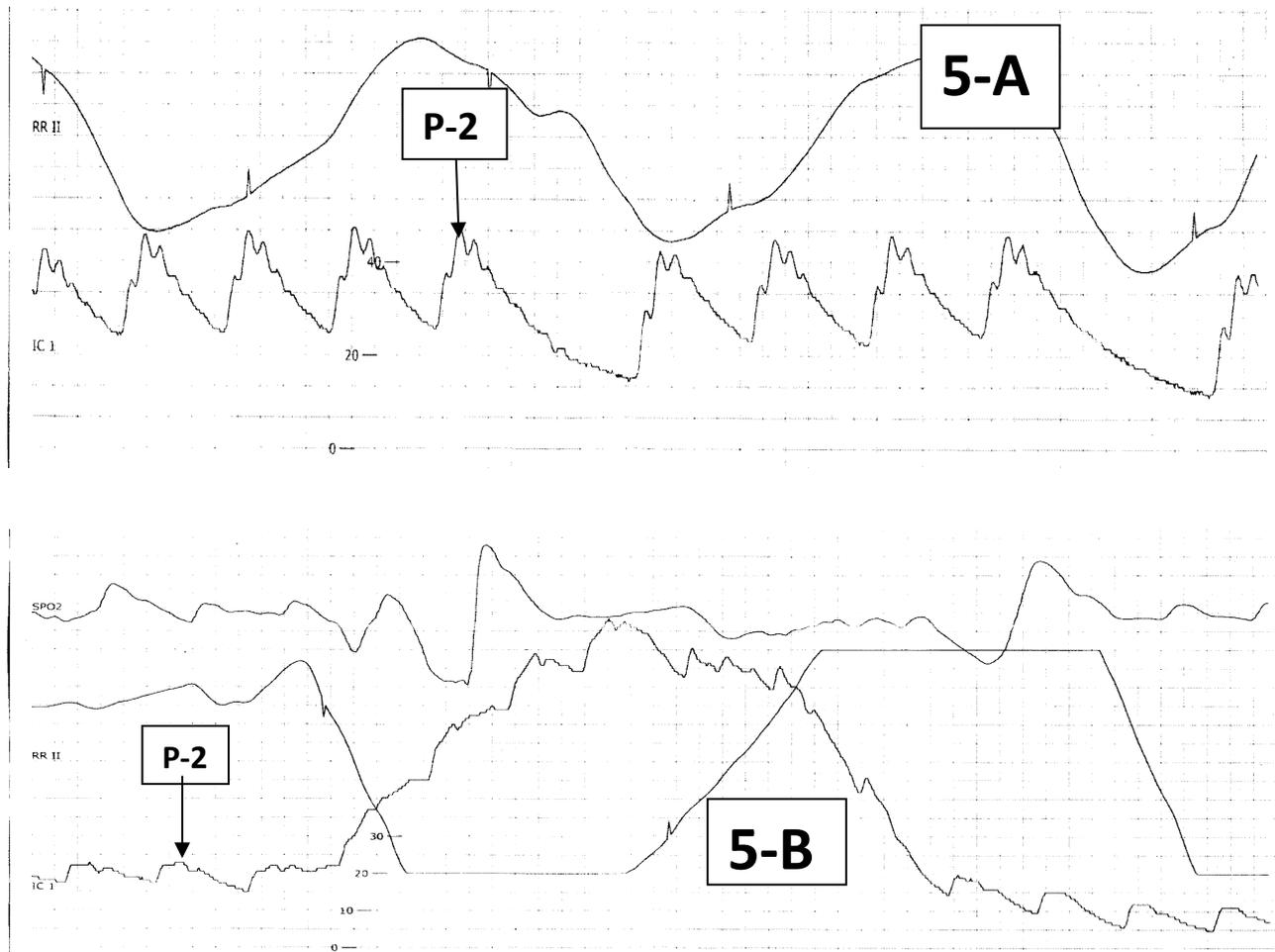
Figure 5: ICP waveforms illustrated at patient baseline and in response to stimulation. **Figure 5-A** illustrates ICP pulse waveforms consistent with pressure elevations (mean ICP of 35-43 mm Hg) and poor compliance (dramatic elevation of P-2 waveform component). This elevated ICP and evidence of poor compliance are highly predictive for far more dramatic ICP elevations in response to stimulation and increased risk of herniation syndromes. **Figure 5-B** illustrates ICP in response to stimulation, significant pressure increase beyond the measurement scale from an already elevated baseline ICP/poor compliance (P-2 elevation) consequent to short-term ventilator dys-synchrony. This monitoring data, in context with intracranial pathophysiology must be taken into account when executing the plan of care. For example, minimizing stimulation or avoiding "grouping" of activities due to risk of more dramatic and hazardous ICP elevations.
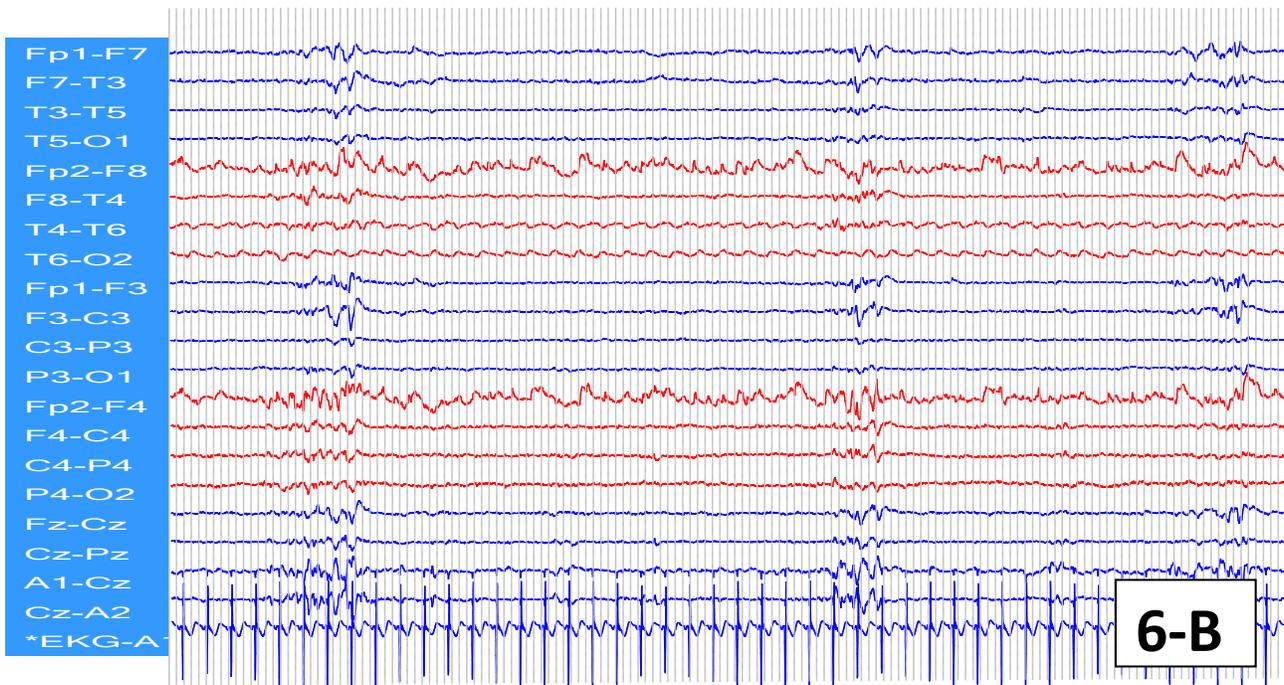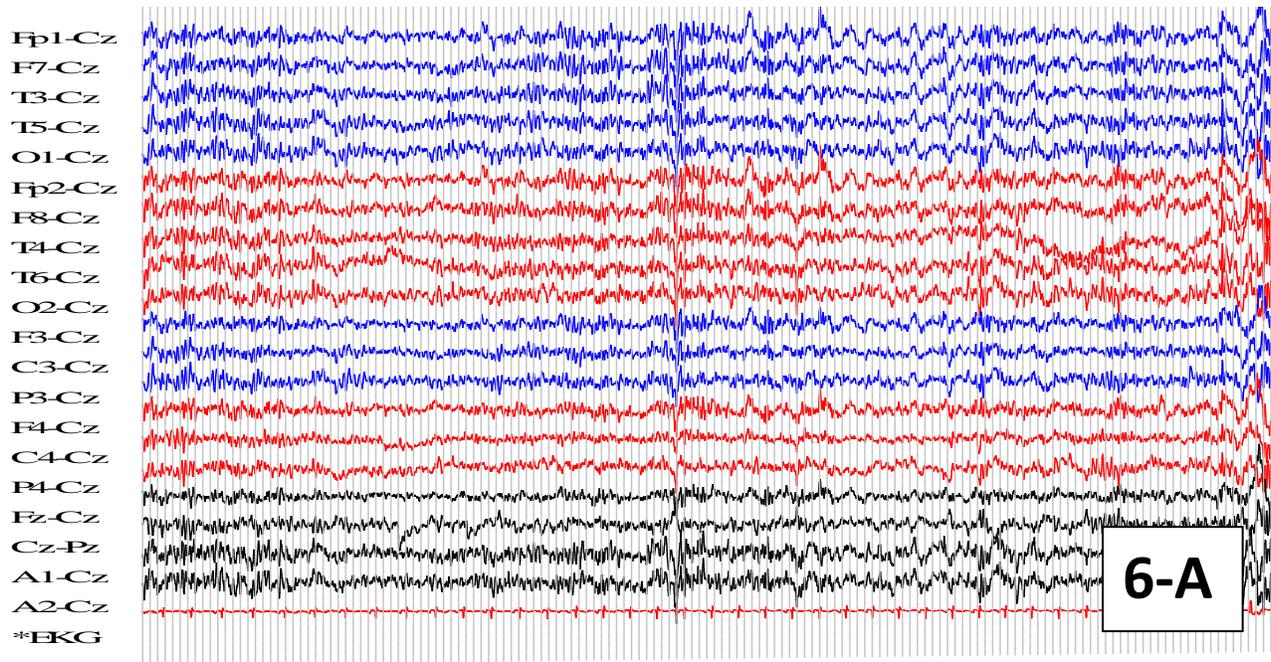
**Figure 6**: Diagnostic EEG tracings differentiating between normal diagnostic tracing (clinical correlation is an awake, interactive patient: **Figure 6-A)** and EEG tracing consistent with appropriate level of burst-suppression in response to metabolic suppression therapy. Level of burst-suppression is 4-6 bursts/minute **(Figure 6-B).** Sensitivity set at 7 uV/mm and each EEG tracing contains 30 seconds of collected data.

ICP	15	19	20	13	15	11	11	11	12	12	11	11

2223 0923

7-A

ICP (mm Hg)	10	11	11	11	11	9	10	10	12	10	13
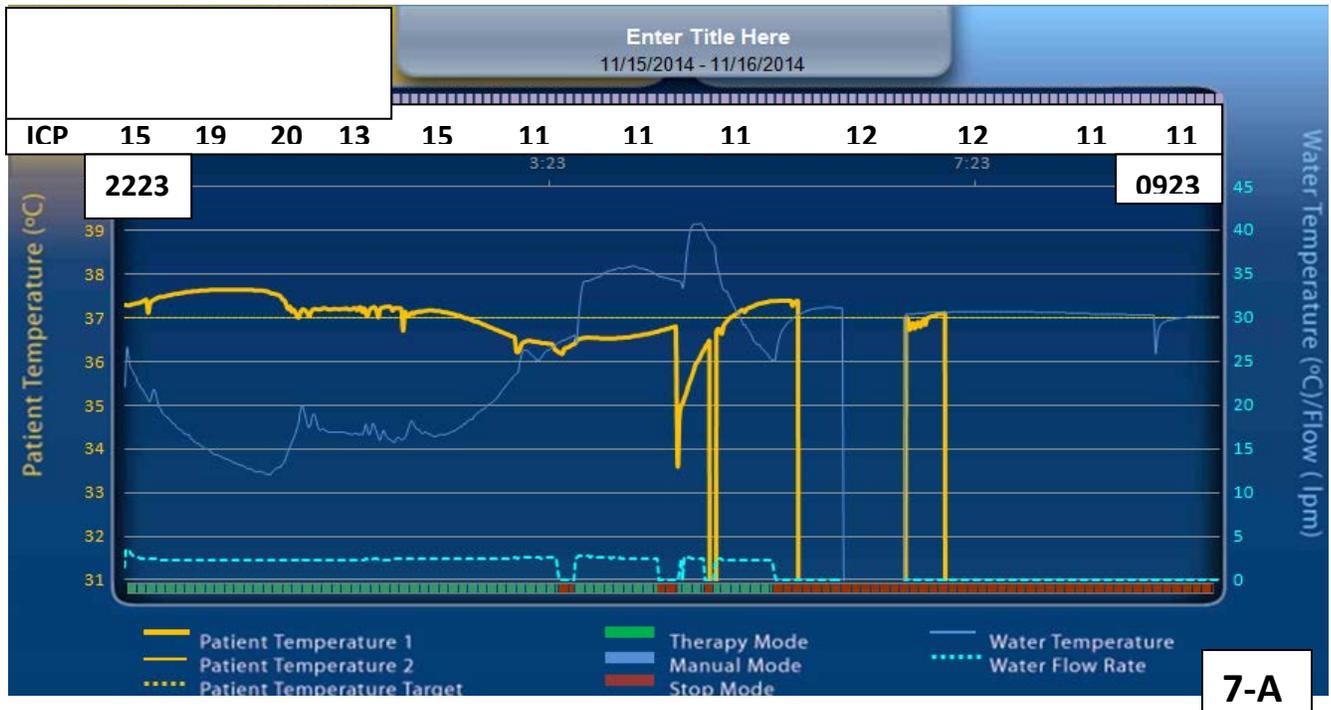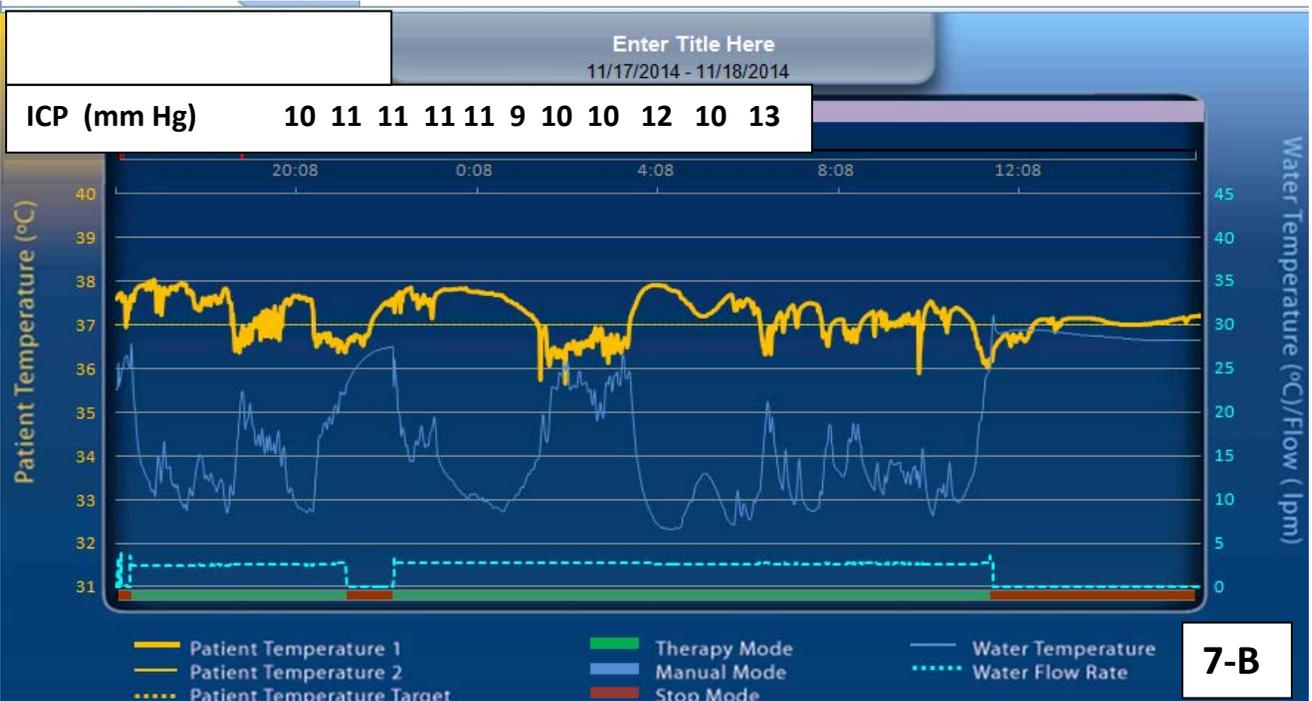
7-B

**Figure 7:** Temporal relationship between ICP reduction and decrease in core body temperature/fever prevention. Patient body temperature maintained afebrile, making ICP easier to control over long-term. **Figure 7-A** illustrates immediate ICP control in postoperative period (2223 on 11-15-14) through 0923 on 11-16-14. **Figure 7-B** illustrates maintenance of normothermia until ICP monitoring discontinued on 11-18-14.
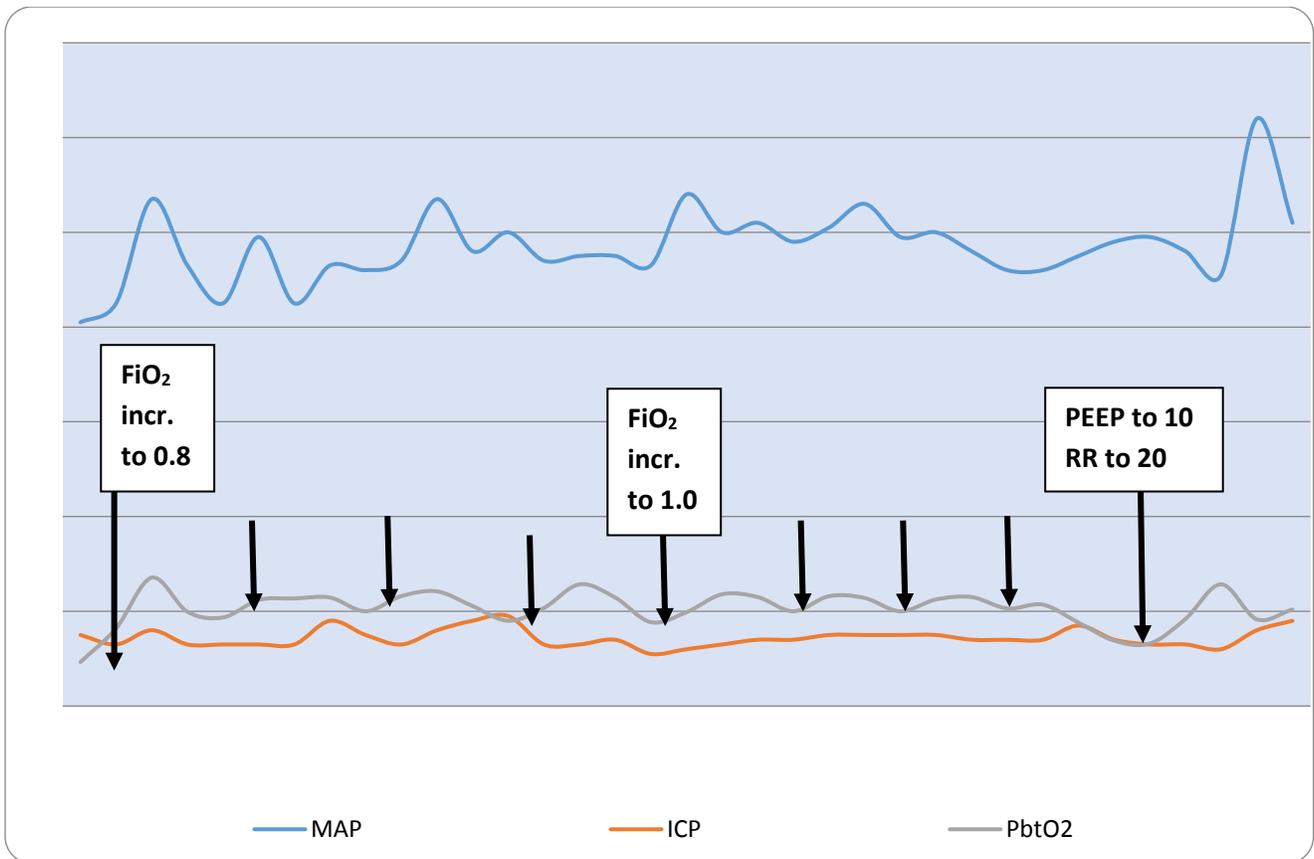
Figure 8: Trending of $PbtO_2$, ICP and MAP in patient as exemplar to illustrate responsiveness of PbtO2 to global physiologic interventions including ventilation/oxygenation titrations as noted which produced increases in $PbtO_2$. Remaining temporary decreases in $PbtO_2$ (arrows) correspond with patient repositioning and time-limited increases in global oxygen consumption.
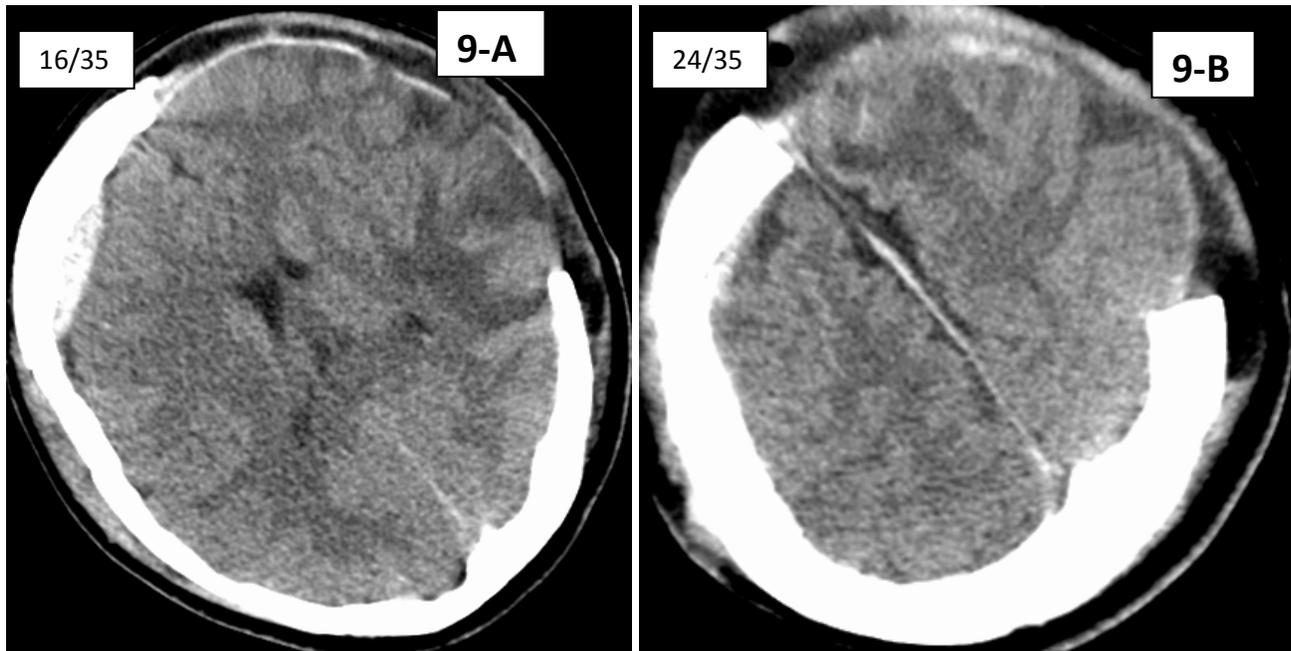
Figure 9: Follow up head CT (figure 9-A/9-B) revealing initial resolution of brain edema/recovery of detail at cerebral cortex, ventricular system and resolved midline shift (9-B). Ventricular system remains compressed but not displaced away from midline. Hypodensity remains in left frontal/temporal lobes and diffuse swelling is evident. Invasive monitoring catheter has been removed and extensive craniectomy defect on left side remains.

Table 1: Glasgow Coma Scale Score (Dawodu, 2015; Decuypere & Klimo, 2012; Haddad & Arabi, 2012; Teasdale & Jennett, 1974).

Motor Response (M)		Verbal Response (V)		Eye Opening (E)	
Follows commands-	*6*				
Localizing to stimulation-	*5*	*Oriented-*	*5*		
Withdrawal to painful stimulation-	*4*	*Confused, appropriate-*	*4*	*Spontaneous-*	*4*
Flexion (decorticate) posturing-	*3*	*Disoriented, inappropriate-*	*3*	*Eye opening to voice-*	*3*
Extensor (decerebrate) posturing-	*2*	*Incomprehensible sounds-*	*2*	*Eye opening to stimulation-*	*2*
No response-	*1*	*No response-*	*1*	*No response-*	*1*

Table 2: Comparison of mild, moderate and severe traumatic brain injury (Dawodu, 2015; Decuypere & Klimo, 2012; Haddad & Arabi, 2012).

Index	Mild TBI	Moderate TBI	Severe TBI
Glasgow Coma Scale Score	13-15	9-12	3-8
Loss of consciousness	< 30 minutes	30 min-24 hours	Greater than 24 hours
Post-traumatic amnesia	0-1 day	1-7 days	Greater than 7 days

Table 3: Hyperosmolar agents utilized in managing brain edema, cerebral hemodynamics following

TBI (Brain Trauma Foundation et al., 2007a; Decuypere & Klimo, 2012; Griffin & Hickey, 2012; Haddad & Arabi, 2012; Helmy et al., 2007; Honeybul, 2011; Kerwin et al., 2009; Ling & Marshall, 2008; Oddo et al., 2009; Protheroe & Gwinnutt, 2011; Rockswold et al., 2009; Ropper, 2012; Sakellaridis et al., 2011).

Agent	Dosing	Cardiovascular consequences	Clinical effects	Goals of care	Nursing considerations
Mannitol	**Low-dose:** 0.25 gm/kg IV bolus. **High-dose:** 1.0 gm/kg in 20% sol'n over 20 min.	Plasma volume expansion. Increased blood pressure	Osmotic gradient between circulating blood volume and swollen brain, net water loss. Decreased blood viscosity and hematocrit. Increased CBF, O2 delivery.	Decreased brain bulk and ICP. Guide and titrate therapy to ICP and serum osmolality 320 mOsm/L. May use prior to ICP monitoring with progressive neurologic decline or pre-terminal herniation.	Close monitoring: After D/C, risk of rebound ICP increase. Monitor electrolytes: Risk of renal injury, dehydration, electrolyte depletion. Appropriate isotonic volume replacement.
Hypertonic Saline	1.9 to 29.2 % concentration. Variable volumes administered. Acute/emergent use: 30 ml 23.4 % saline,	Improved blood pressure, volume expansion.	Brain water reduction across blood-brain barrier. Dehydrates vessel endothelium. Reducing blood viscosity. Improved CBF.	Decreased brain bulk. Reverse pre-terminal herniation.	Administer through central access (higher concentrations) or large-bore peripheral site. Monitor neurologic

reverse pre-terminal herniation.		Improved brain oxygenation.		status, ICP, cardiovascular response. Monitor electrolytes (sodium).

Table 4: Selected metabolic suppression/CNS depression therapies in clinical management of severe TBI (Brain Trauma Foundation et al., 2007a, 2007g; Decuypere & Klimo, 2012; Haddad & Arabi, 2012; Helmy et al., 2007; Honeybul, 2011; Ling & Marshall, 2008; Marshall et al., 2010; Stocchetti et al., 2008)

Agent	Dosing	Cardiovascular consequences	Clinical effects/side effects	Goals of care	Nursing considerations
Pentobarbital Sodium	**Load**: 5 mg/kg bolus over 30 minutes. **Maintenance:** 1-3 mg/kg/hr. **High-dose:** 1-mg/kg over 30 minutes. **Infusion:** 5 mg/kg/hr over 3 hrs 1 mg/kg/hr	Hypotension: • Vasodilation. • Negative inotropic effect. • Brainstem depression (dose-related). Altered thermoregulation.	• Modulating $CMRO_2$, CBF and ICP reduction. • Prolonged duration of action (esp. with hypothermia). • Immune suppression. • Infection risk. • Decreased vasomotor tone. • Bradycardia.	• ICP reduction to clinical endpoint. • Goal-directed titration to burst-suppression on EEG, EEG-derived parameters.	• Monitor ICP. • Monitor EEG to endpoint (4-6 bursts/min or as directed per provider). • Multiple large-bore IV accesses. • Central venous access (consider CVP monitoring). • Vasopressor/inotropic support as indicated. • Neurological assessment. • Neuro assessment in clinical context: Consider prolonged duration of action in TH.
Propofol	**Infusion:** Up to 80-90 mcg/kg/min.	Hypotension: • Vasodilation. • Negative inotropic effect.	• Modulating $CMRO_2$, CBF and ICP reduction. • Infection risk. • Decreased vasomotor tone. • Bradycardia. • Hypotension.	• ICP reduction, agitation resolution to clinical endpoint. • Goal-directed titrations.	• Monitor ICP. • Monitor degree of agitation vs resolution. • Multiple large-bore IV accesses. • Central venous access (consider CVP monitoring).

					• Vasopressor/inotropic support as indicated. • Neurological assessment. **Risk of PRIS:** • Monitor temporal relationship with propofol initiation, upward titration and hemodynamic instability. • Monitor acid-base balance, electrolytes, CPK.

Note: The agents listed in the table above are selected, commonly used agents for cerebral metabolic suppression (pentobarbital) versus ICU sedation (propofol), but it is acknopwledged that pharmacologic therapy varies internationally. Country specific or international guidelines should be consulted.

CHECK YOUR PROGRESS: Assess your understanding of key points from this e-chapter.

1. Mild TBI is defined by a Glasgow Coma Scale Score of what level?
   A. 9-12
   B. 13-15
   C. 8-11
   D. <10

   Answer: B

2. Which of the following designates an elevated intracranial pressure?
   A. 35-40 mm Hg
   B. 15-20 mm Hg
   C. 5 -10 mm Hg
   D. 10-15 mm Hg
      Answer: A

3. Which of the following are causes of secondary brain injury?
   A. Auto-regulatory excitability
   B. Aerobic metabolism
   C. Entrapment of excitatory amino acids
   D. Loss of cell membrane integrity

   Answer: D

4. Therapeutic hypothermia has potentially harmful side effects including which of the following?
   A. Hyperkalemia
   B. Increased drug metabolism/elimination
   C. Increased systemic vascular resistance
   D. Increased cardiac output

   Answer: C

5. Which of the following is accurate regarding the use of routine hypothermia following severe TBI
   A. It is supported by strong evidence
   B. It is supported by clinical trial data
   C. It is supported by limited clinical trial data
   D. It is not supported by strong evidence

   Answer: D

6. True or False:
   Patient/ventilator dys-synchrony can contribute to intracranial hypertension
   Answer: True

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