Etiologies of elevated ICP:
Increased ICP can occur with any CNS pathology that results in a space occupying mass lesion, edema (osmotic, vasogenic, cytotoxic), or obstruction to CSF flow. Some common etiologies include:
- Trauma: epidural, subdural bleeds, contusion, hematomas, diffuse axonal injury, intraventricular hemorrhage
- Infection: meningitis, encephalitis, cerebritis
- VP shunt malfunction
- Mass lesion: tumors, AVM
- Metabolic: hepatic encephalopathy, DKA
- Vascular or embolic disease, stroke with subsequent edema or mass effect
- Hypoxic/ischemic disease resulting in cytotoxic edema from cell death

Physiology of Intracranial Vault
- Components of intracranial vault
The intracranial vault is comprised of brain (80%), cerebrospinal fluid CSF (10%), cerebral blood volume (10%). The Monroe-Kellie Doctrine states that any individual component of the intra-cranial vault may undergo alterations but the total volume remains fixed since the space within the skull is fixed. The following is a formula of this doctrine with V standing for volume.

\[ V \text{ (intracranial vault)} = V \text{ (CSF)} + V \text{ (brain)} + V \text{ (blood)} + V \text{ (other, i.e. mass)} \]

The brain has certain normal compensatory mechanisms in place to maintain this equilibrium and in turn maintains normal intra-cranial pressure (ICP). For example displacement of CSF or blood will occur to maintain normal ICP. Eventually, the compensatory mechanisms are exhausted and a sharp rise in ICP will occur. The brain has an elastance that is best demonstrated by a pressure-volume curve (see Figure 1). A normal ICP does not indicate where in the pressure volume curve the patient is at and if any compensatory mechanisms are still in tact.
3 types of cerebral edema

- **Vasogenic:** Increased permeability of brain capillary endothelium leads to edema and is usually seen around tumors, abscesses, intracerebral hematomas, encephalitis & meningitis. Neurons are not primarily injured. Reduction of this type of edema can minimize secondary injury.

- **Cytotoxic:** Neuronal swelling occurs secondary to cell injury caused by failure of the ATPase-dependent pump as occurs in diffuse axonal injury. This type of injury is often irreversible.

- **Interstitial:** Edema results from increased CSF hydrostatic pressure and is usually seen in hydrocephalus or decreased CSF absorption by arachnoid villi, e.g. intraventricular hemorrhage.

Regulation of cerebral blood flow (CBF)
The brain maintains CBF via auto-regulation over a wide range of mean arterial pressure (MAP) by altering resistance of cerebral blood vessels. By maintaining a constant CBF, the supply of oxygen and metabolic substrates to the neurons are unaltered. A constant CBF is maintained between MAP of 60mmHg-150mmHg. At a MAP of 60mmHg, the cerebral vessels are maximally dilated; below this MAP, cerebral ischemia will occur. MAP above 150mmHg can lead to ischemia, disruption of the blood-brain barrier, and increased ICP.

Cerebral perfusion pressure (CPP), as determined by the formula below, is directly related to CBF.
CPP = MAP – ICP or CVP (which ever of the two pressures is higher)

A minimum CPP needs to be maintained to prevent cerebral insult. The minimal CPP is age variant and is as follows:
- Infants - 50mmHg,
- Children - 60mmHg,
- Adults - 70mmHg.

CBF is very sensitive to oxygen and carbon dioxide. Hypoxia results in vasodilation therefore increasing CBF and potentially worsening ICP. Hypercarbia likewise results in vasodilation and can alter ICP via effects on CSF pH and increases in CBF.

**Intracranial pressure monitoring**

Maintaining adequate CPP is an important factor in survival for patients with elevated ICP. Several forms of ICP monitors exist.
- Intraventricular monitor is the gold standard. It is accurate and can be re-zeroed. Most importantly, it can withdraw CSF for ICP management. Risks include infection, hemorrhage at time of insertion or removal, and obstruction of the catheter. Insertion of the catheter becomes difficult if the ventricles are small or displaced from shift or mass effect. It is usually positioned at 15cm H2O above the ear. Excessive drainage should be avoided to prevent ventricular collapse.
- Intraparenchymal monitors are generally fiber optic, and are placed directly into brain parenchyma. They can be easily inserted. Although they are fairly accurate initially, they cannot be re-zeroed and will develop drift over time (6mmHg in 5 days). They can’t be used for CSF removal.

**Evaluation of Elevated ICP:**

- **Physical exam** should be done with special attention to vital signs, pupillary response, reflexes, fontanelle, focal deficit, and baseline level of consciousness. Signs and symptoms of concern include:
  - Headache
  - Vomiting or poor feeding
  - Altered level of consciousness: drowsy, combative, agitated, irritable, lethargic
  - Full anterior fontanelle in infants
  - Focal neurologic deficit
  - Posturing, seizures
  - Nuchal rigidity (typically with meningitis, encephalitis)
  - Respiratory symptoms: distress, stridor, hyperventilation, Cheyne-Stokes respiration – particularly seen if brainstem involved and can be mistaken for a pulmonary source of respiration distress
• Cushing’s Triad: hypertension, bradycardia, and abnormal respiration; it is a late and ominous sign of brainstem compression and suggests impending herniation.
• Pupils: unequal, unreactive, sluggishly reactive, pinpoint, or dilated.
• “Sun-setting”: bilateral downward gaze of eyes sometimes seen with shunt malfunction and impending herniation
• Papilledema
• Retinal hemorrhages: seen in non-accidental trauma

❖ **Glasgow Coma Scale (GCS)** is an objective measurement, readily available, and is not dependent on the history of illness. The score is a sum of the best eye, verbal and motor response as listed in the table below.

<table>
<thead>
<tr>
<th>Motor Response</th>
<th>Verbal Response</th>
<th>Eye Opening</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Follows Commands</td>
<td>5 Oriented</td>
<td>4 Spontaneous</td>
</tr>
<tr>
<td>5 Localizes</td>
<td>4 Confused</td>
<td>3 To Speech</td>
</tr>
<tr>
<td>4 Withdraws</td>
<td>3 Inappropriate words</td>
<td>2 To Pain</td>
</tr>
<tr>
<td>3 Abnormal flexion</td>
<td>2 Incomprehensible</td>
<td>1 No response</td>
</tr>
<tr>
<td>2 Extensor response</td>
<td>1 No response</td>
<td></td>
</tr>
<tr>
<td>1 No response</td>
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❖ **Laboratory studies** that may be helpful.
• CBC w/diff (trauma, bleed, infection)
• Coagulation panel (trauma, bleeding)
• Na+, Ca+, Mg+, glucose
• ABG - assess oxygenation and ventilation if patient significantly altered
• BUN/Creatinine (uremia)
• LFTs, ammonia
• Tox screen, Salicylate, tylenol levels
• Thyroid function
• CSF studies if LP is done

❖ **Neuroimaging & other modalities of evaluating ICP**
• **CT scan** is ideal for urgent imaging, and quickly assesses mass effect, shift, edema, and changes in gray/white matter differentiation. It rapidly identifies abnormalities amenable to intervention such as post-traumatic injuries, hemorrhage, tumor, fracture, & hydrocephalus. In trauma patients, the presence of pneumocephalus can be evaluated and bone windows can delineate the location of any skull fractures. A contrast CT is helpful to assess areas of inflammation such as meningitis, vasculitis, encephalitis, and areas surrounding tumors or other lesions (abscess). Decreased enhancement with contrast may indicate infarction, edema or non-enhancing tumors. Acute blood attenuates and is bright, but CSF is
An indirect assessment of ICP and presence of cerebral edema can be accomplished by evaluating the ventricles and the basal cistern.

- **MRI** displays in much greater detail lesions of soft tissue and brain matter. It is the mode of choice for delineating tumors. MRA/MRV are the optimal studies to visualize cerebral blood flow and evaluate for vascular anomalies. It may be used to clarify initial findings seen on CT or that escaped detection on CT, i.e. diffuse axonal injury. Limitations of the MRI include a strong magnetic field making use of equipment more challenging, and longer imaging time. Also, any bony abnormalities are not well visualized on MRI.

- **Lumbar puncture** should also be done if the CT and the patient’s condition do not preclude it. Always obtain an opening pressure (OP), and a closing pressure if fluid is removed; this allows for evaluation of the brain on the pressure-volume curve. Convert cmH2O on manometer to mmHg by dividing by 1.2. For example, an OP of 28 cmH2O is 23 mmHg. The CSF should be sent for usual studies to rule out infectious sources.

**Treatment of intracranial hypertension:**
Patients with a CNS insult have two components: the primary injury, and the secondary injuries that ensue. Once the initial insult has occurred, e.g. head injury or encephalitis, it cannot be reversed. Treatment must therefore focus on either controlling or minimizing the causes of secondary injury. In evaluating the list of secondary injury etiologies, it becomes self evident that if adequate metabolites for recovery are not provided, the pre-existing injury is amplified. The factors associated with secondary CNS injury are hypoxia, hypotension, intracranial hypertension, seizures, fever, and hyperglycemia.

**General principles:** Recall Monroe-Kellie doctrine — volume of rigid skull is fixed; therefore therapy for intracranial hypertension should be directed at reducing space occupied by brain, blood CSF, or new pathology.
- Reduce brain size: osmolar therapy (mannitol, hypertonic saline)
- Reduce CSF: drainage (EVD)
- Reduce blood volume (hyperventilation, avoid hypercarbia, hypoxia)
- Surgical removal of pathology (bleed, tumor)
- Alternatively can expand skull by decompressive craniectomy

1) **ABCs: AVOID HYPOXIA AND HYPOTENSION!!** In traumatic brain injury hypoxia and hypotension have been strongly shown to be associated with increased morbidity and mortality – amplifies secondary insult.
- Monitor oxygenation and apply supplemental O2 as required. If the patient has inadequate respiratory effort, GCS <8, rapid clinical
deterioration (signs of herniation, unequal pupils), or status epilepticus unresponsive to medications, then s/he should be intubated.

- Support blood pressure by fluid resuscitating the patient as required. Always use at least NS for resuscitative efforts and consider 5-10 cc/kg bolus of hypertonic 3%NS in acutely hypotensive head injury patients. PRBCs may be indicated in trauma with ongoing bleeding. Maintain normal blood pressure in order to maintain adequate cerebral perfusion pressure to the injured brain (CPP=MAP-ICP).
- If signs of elevated ICP are present, but an ICP monitor hasn’t placed, one can assume an ICP of at least 20mmHg. Efforts should be made to maintain a MAP that supports the ideal CPP for age.
- Patients should be monitored with an arterial line and may need a CVP as well for infusion of vasoactive drips and other medications.

2) General measures
- **Temperature:** Avoid fever since it increases cerebral metabolic demand and affects ICP.
- **Head position:** Maintain head in midline position at 30 degrees to improve cerebral venous drainage; lower cerebral blood volume (CBV) will lower ICP. In trauma patients, C-spine immobilization must be maintained if concerns until the patient is alert enough for an appropriate exam (even if radiographs and CT of neck are negative).
- **Seizure control & prophylaxis:** Seizures worsen secondary CNS injury by increasing the metabolic requirement and potentially increasing ICP. The incidence of post-traumatic seizures is about 10%. Seizures should be controlled with appropriate therapy. Ativan of 0.05-0.1mg/kg is the initial treatment. A fosphenytoin load of 20mg/kg should also be considered; phenytoin is less likely to interfere with the neuro exam as compared with phenobarbital. The need for seizure prophylaxis should be evaluated on an individual basis and discussed with neurosurgery.
- **Fluid management:** Goal is euvolemia. Maintain adequate cardiac output and filling pressures (CVP 4-10) in order to maintain adequate cerebral perfusion. Use isotonic fluids (NS), never hypotonic solutions, for patients with elevated ICP.
- **Avoid hyperglycemia** since worse neurologic outcomes have been noted with elevated blood sugars. Hyperglycemia appears to amplify secondary injury through ischemic acidosis.
- **Start enteral nutrition** early since head injured patients have increased energy requirements. Stress ulcer prophylaxis should also be initiated immediately.
- **Sepsis** is common, particularly 3-7 days after head injury; don’t delay appropriate antibiotic therapy and consider empiric anti-fungal therapy early.
3) Ventilator management: Avoid hypercarbia and hypoxia. The brain is very sensitive to PaCO$_2$; a 1mmHg decrease in PaCO$_2$ could decrease ICP 2-5 mmHg depending on brain compliance. Ventilate to normal PaCO$_2$ of 35mmHg-40mmHg. Patients with refractory elevated ICP can be hyperventilated to PaCO$_2$ of 28-32mmHg. However, hyperventilation should not be used as a long-term treatment modality since it results in risk of cerebral ischemia to injured areas and its effects of decreasing ICP are only short lived.

4) Sedation: Agitation, pain, and muscular activity increase ICP. Ideally select a drug that provides analgesia, anxiolysis, avoids hypotension, and allows some examination (particularly if ICP not being monitored).

- Fentanyl: safe if patient intubated, may develop hypercarbia if over-sedated and not intubated (Dosing 1-4 mcg/kg/hr)
- Propofol: good sedative, short acting, may actually lower ICP, and has the advantage of allowing periodic assessment of neurologic function. Carries risk of hypotension and fatal acidosis; generally safe at modest doses and not for prolonged periods (i.e. <72hrs). (Dosing 25-80 mcg/kg/min)
- Versed: sedative, anxiolytic, may cause hypotension (Dosing 0.05-0.1 mg/kg/hr)
- Ketamine: not recommended since it may increase ICP.
- Muscle relaxants: Vecuronium or Rocuronium are best for intubation; avoid Succinylcholine since fasciculations may increase ICP. Use paralytics judiciously while the patient is intubated to maintain a physical exam, but also avoid sudden spikes in ICP with sudden cough or valsalva.

5) Osmotic therapy:

- Hypertonic saline (3%NS approx 500meq/L) has osmotic, hemodynamic, vasoregulatory and immunomodulatory effects. 3% NS reduces osmolar swelling by decreasing both intra-cellular and interstitial fluid volume. It also improves and maintains intravascular volume and blood pressure. Other effects may include decreased vascular resistance with improved cerebral blood flow by decreasing vascular endothelial edema. Inhibition of posttraumatic activation of leukocytes also decreases the degree of inflammation. 3%NS has the added advantage over mannitol of maintaining hemodynamic stability by maintaining intra-vascular volume status. A minimum serum sodium of 145 meq/L should be maintained. Higher sodium levels can be achieved as needed to maintain ICP control either by intermittent boluses or by a continuous infusion of 3% NS. A hypothetical risk of central pontine myelinolysis by rapid increase of serum sodium levels also exists, but has not been reported in trials for traumatic brain injury.
- Dosing: 5-10cc/kg boluses over 1hr, not to exceed 500 ml or continuous infusion 0.25-1 cc/kg/hr, not to exceed 30ml/hr
  - Mannitol is an osmotic diuretic that increases serum osmolality. Effects include decreased blood viscosity, maintaining CBF, decreasing CBV and thereby decreasing ICP if cerebral autoregulation is intact. Maximal effect is within 10 minutes, duration of action is 75 minutes, and it is most effective when given in bolus form. Use the minimum amount needed to maintain a goal serum osmolarity generally of 320 mOsm/kg. At high levels, >340 mOsm/kg, a risk of renal insufficiency exists.
- Dosing 0.25-0.5 gm/kg bolus q 4-6hrs

- 6) Barbiturates: Barbiturates decrease cerebral metabolic rate and thereby lower CBV and ICP. Free-radical mediated cell injury may also be limited. Side effects include hypotension and myocardial depression; the use of inotropes (Norepi) is often required to maintain MAP and CPP. Barbiturates may also increase the risk of infections by suppressing neutrophil function.

- 7) Cooling: Induced hypothermia of 32-34°C Celsius may be neuro-protective by decreasing excitatory amino acid levels, and have anti-oxidant plus anti-inflammatory effects. Studies have shown active cooling to be effective in both adult and neonatal patients with hypoxic / ischemic insults. Pediatric trials in traumatic brain injury, however, have not demonstrated any improvements in outcomes with active cooling.

- 8) CSF removal: A surgically placed intraventricular catheter can be used to drain CSF. It improves elevated ICP in patients with decreased intracranial compliance, i.e. small change in intra-cranial volume dramatically reduces intra-cranial pressure. The drain can either be positioned at 10-15cm H2O above the level of ear and left open to drain, or it may be used to monitor ICP and only drained when ICP >20mmHg.

- 9) Surgical decompression is indicated for clear-cut mass lesions amenable to removal, i.e. tumor, epidural bleed, large contusion. For refractory elevated ICP without a surgical lesion, there may be a role for a decompressive craniectomy. Especially if done early after the initial insult, it may improve functional outcomes of patients.

- 10) Corticosteroids: Steroids maybe effective in decreasing vasogenic edema as seen with CNS tumors and abscesses.

**Stepwise approach to ICP Management/Algorithm**

1) Avoid hypoxia/hypotension
   - Supplemental O2 or intubate
- Achieve euvoeemia
- Support BP to maintain CPP

2) Avoid Fever

3) Intubate/sedate

4) Mild hyperventilation/avoid hypercapnia
   - Keep PaCO\(_2\) normal 35mmHg-40mmHg

5) Ventricular Drainage

6) Osmolar therapy to achieve serum Osm 320
   - Mannitol (0.25 to 0.5 g/kg)
   - Hypertonic saline (5 ml/kg of 3%NS) may be given as bolus or continuous 3% infusion checking sodium frequently (q4-6hr)

7) More aggressive hyperventilation - PaCO\(_2\) (28-32 mmHg)
   - Refractory ICP—acute short term therapy

8) Barbiturates (Thiopental/Pentobarbital)
   - Thiopental: initial infusion of 10mg/kg/hr for 4 hours followed by infusion at 4mg/kg/hr
   - Pentobarbital: initial infusion of 10mg/kg over 30 minutes, then 5mg/kg/hr for 3 hours, then 1-2mg/kg/hr
   - Drug levels must be monitored
   - Continuous bedside EEG required for patients on barbiturate infusion; monitor for burst suppression

9) Consider cooling particularly in patients with hypoxic-ischemic injury

10) Decompressive craniectomy has shown promising results for some patients with refractory intracranial hypertension

Any acute change in ICP during any step of therapy should warrant consideration for re-imaging (head CT) and notifying neurosurgery.