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Knowledge of the dimensions and the shape of the pediatric airway are essential for the safe conduct of tracheal intubation in infants and children. It is proposed that the pediatric larynx is conically shaped, with the apex of the cone positioned at the level of cricoid cartilage. The first well-defined description of the pediatric airway dates back to 1897 when anatomical measurements of glottic and subglottic areas were reported. In 1951, Eckenhoff presented a detailed description of the anatomy of the pediatric airway. Both studies used cadavers and airway moulages, and the reported observations were based on small sample size.

Classically, the pediatric airway is believed to be different from the adult airway. Advanced imaging modalities have challenged the historically accepted knowledge. Two recent studies measured the dimensions of the pediatric airway using either magnetic resonance imaging or videobronchoscopy. Data from both studies suggest that the configuration of the larynx of infants and children is more cylindrical than conical and that the shape does not change with age.

The practice of pediatric anesthesia has also shifted from the routine use of non-cuffed tracheal tubes in patients ≤ 6-8 years of age to the more frequent utilization of cuffed tracheal tubes. The traditional use of uncuffed tracheal tubes is based on the argument that the narrowest part of the airway is the cricoid ring. This belief leads to the assumption that uncuffed tracheal tubes that fit through the glottic opening would seal the airway at the cricoid level, eliminating the need for a cuffed tube.

Although different radiological modalities have been used to assess pediatric airway, it is accepted that computed tomography (CT) is the current gold standard for airway measurements as it provides an excellent contrast between the airway wall and the lumen. It is routinely used to evaluate the airway morphology in patients with diseases such as tracheo-bronchomalacia. Furthermore, it provides an excellent method of displaying the cross-sectional anatomy of the growing trachea. Unlike autopsy and bronchoscopy, CT causes no disturbance of tracheal anatomy and allows considerable precision of measurements while minimizing error and distortions.

Studies using CT based measurements have further challenged the funnel shape of pediatric larynx. Airway configuration in infants and children favors an elliptical shape below the subglottis area with a progressive transition to a more rounded shape at the cricoid ring. The subglottis appears to be the narrowest part of the airway in this age group. A narrower subglottis transverse dimension explains the higher resistance upon tracheal intubation and defeats the original belief that the cricoid ring is the limiting area in children.

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Neurosurgery in paediatric patients includes a wide range of procedures which may be either cranial or spinal and may be in neonates, infants and older children. Cranial surgery can be done in various positions, many of which can result in venous pooling causing cardiovascular instability. Complex cranio-facial surgery, as in syndromic craniosynostosis, can result in large replacement fluid losses as well as blood loss. Spinal surgery can range from congenital lesions such as spinal dysraphism to extensive spinal surgery as in scoliosis and these are usually performed in the prone position. These and other neurosurgical operations can be prolonged and may also be associated with large blood losses and fluid shifts.

**Perioperative fluid therapy in children**

Infants and children are sensitive to changes in volume status which can manifest as haemodynamic disturbances and reduced organ perfusion. Newborns, in particular, are more susceptible to dehydration because of the higher water content, large surface to weight area, decreased concentrating capacity of the kidneys, greater insensible losses from thin skin and greater blood flow. There is, therefore, a very limited margin for error in calculating intraoperative fluid requirement. Fluid therapy in these children should be tailored according to the age of the patient, the type and duration of surgery, the position of the patient and on blood loss incurred during surgery, so that adverse consequences due to either inadequate or overinfusion of fluids are prevented.

The goal of perioperative fluid therapy is to maintain cardiovascular stability, ensure adequate organ perfusion and maintain tissue oxygenation. For almost half a century, fluid therapy in children was based on the guidelines set by Holliday & Segar in 1957.

The wisdom of this approach has recently been questioned as it was found that administration of hypotonic fluids leads to hyponatraemia, particularly in view of the fact that in certain situations such as surgical stress, non-osmotic stimuli can lead to increased secretion of anti-diuretic hormone. This has lead to severe hyponatraemia even resulting in encephalopathy and death.

Perioperative fluid therapy in children has been the subject of much debate, but there has been no consensus and there are no practice guidelines till date. In a survey of perioperative fluid management, Way et al found that many responders were using unsuitable and inappropriate fluids in their clinical practice which lead to unfortunate results.

The two issues that need to be discussed with regard to perioperative fluid management in children are the following:

- Should glucose be given intraoperatively?
- What should be the tonicity of intravenous fluids?
- What should be the volume status in children undergoing neurosurgery, cranial or spinal?

**Glucose**

There was a concern whether glucose containing fluids be given to small children to avoid inadvertent hypoglycaemia as, hypoglycaemia, if unrecognized or untreated, can lead to severe and permanent neurodevelopmental deficits. This can not only occur due to severe hypoglycaemia (serum glucose level < 45 mg/dL), but also when severe hypoglycaemia is combined with even mild hypoxia or ischaemia. Severe hypoglycaemia usually occurs when children are fasting for more than 8 hours, which is much beyond the ASA recommended guidelines. Hypoglycaemia is also likely to
occur in neonates, small and premature infants, debilitated children and children with endocrinopathies. This is because they have limited reserves of glycogen and limited gluconeogenesis. In these children continuous infusions of glucose @ 5 to 6 mg/kg/min is given to maintain normal serum glucose levels. Hyperglycaemia, on the other hand, can also have adverse effects. While mild hyperglycaemia may not be harmful, higher blood glucose levels can have adverse effects such as osmotic diuresis, impaired wound healing and less favourable outcome especially if these patients also have a risk of cerebral ischaemia such as during neurosurgical operations. In paediatrics, hyperglycaemia has been linked to poor outcome, but it is not clear if tight glycaemic control offers significant benefits. As even small children can mount a surgical stress response, a number of research groups have shown that glucose-free intravenous fluids can be safely given to children intraoperatively without running the risk of hypoglycaemia. Thus, glycaemic control in the paediatric population is based on the vulnerability of certain groups of children. Till further evidence is available, it is recommended that serum glucose levels be maintained below 180 mg/dL. Intraoperative monitoring of blood sugar levels should be done to avoid both hyperglycaemia and hypoglycaemia.

**Type of Fluids**

Crystalloids is the first choice for volume replacement. Regarding tonicity of the intravenous fluid, it is recommended that isotonic fluids be given intraoperatively. Normal saline is the preferred fluid as it is slightly hyperosmolar (308 mOsm/kg) and this would result in a lax brain and avoid cerebral edema. However, administration of large volumes of normal saline (>60 ml/kg) could result in hyperchloraemic metabolic acidosis. If serum sodium levels are normal, 3% hypertonic saline may also be given to not only replete intravascular volume but also reduce cerebral edema taking care to monitor both osmolarity and serum sodium levels. Children tolerate hypernatraemia and hyperosmolarity better than adults. Lactated Ringer’s solution, on the other hand, is hypoosmolar as it contains 100 ml of free water/L.

**Volume status**

The intravascular volume of children can be quite small and, therefore, it is very important to maintain volume status and correct blood loss so as to avoid haemodynamic instability during surgery. It is recommended that normovolaemia be maintained intraoperatively similar to adults. This is done by correcting volume deficits, providing maintenance requirements as well as correcting losses during surgery so that tissue perfusion is maintained. It involves the correct selection of the amount and composition of fluid depending on the type and duration of surgery.

**Preoperative deficit**

Fluid deficit management involves estimating the severity of deficit, if present, determining the type of deficit and correction of the fluid deficit. Fluid deficits in the paediatric neurosurgical patient can be isotonic, hypotonic or hypertonic depending on the osmolarity and serum sodium concentration. The type of fluid deficit in children presenting for elective surgery is usually isotonic where the serum osmolarity is between 270-300 mOsm/L and the serum sodium is between 130-150 mEq/L. Preoperative deficits are due to insensible losses and urine output. However, based on the new NPO guidelines by the ASA for children for elective surgery, where clear fluids are allowed up to 2 hours prior to surgery, the preoperative deficits assume lesser significance.

**Intraoperative fluid management**

The intraoperative fluid requirement involves replacement of preoperative deficit+ providing for basal metabolic requirements (maintenance fluids) +replacement from the surgical field depending on tissue trauma. While determining the type of fluid for volume replacement, one should consider the following factors:

- type of fluid deficit
• effect of this fluid on intravascular volume
• effect on coagulation cascade
• any allergic reaction

Crystalloids is the initial fluid of choice as it is not expensive. It does not have effect on coagulation cascade, has no allergic reaction and has no risk of transmitting any infections. The choice of fluid is normal saline or Ringer lactate, although we must not use large volumes of the latter in children undergoing craniotomies as it is slightly hypotonic as compared with plasma.

Replacement losses in craniotomies is only 1 to 2 ml/kg over the basal requirement as there is only minimal tissue trauma. However, if a child is undergoing major craniofacial surgery or extensive spinal fusions, the replacement losses are higher. The type of replacement fluid is isotonic crystalloid solution, either normal saline or Ringer lactate.

As stated by the European Society for Paediatric Anaesthesiology (ESPA) and demonstrated recently by various studies, an appropriate intraoperative fluid strategy should include the use of an isotonic solution and a metabolic anion (preferably acetate) as bicarbonate precursor to avoid acid-base imbalances (i.e. hyperchloremic acidosis) and it should also have an osmolarity and acidity close to that of the plasma.

**Summary of perioperative fluid management in children**

1. Prescribing fluid volume and composition appropriately.
2. Consider intravenous fluids as medications.
3. Using isotonic solutions instead of hypotonic solutions during the intraoperative and postoperative period.
4. Replacing ongoing losses with fluids reflecting the electrolyte composition of fluid lost. NaCl 0.9% is appropriate in most cases.
5. Administering isotonic fluids (saline 0.9% or colloids) as a bolus in the event of hypovolemia.
6. Monitor plasma electrolytes, glucose concentrations and serum osmolarity

**Hypertonic saline (HS)**

Hypertonic saline is well tolerated in the pediatric age group – both hyperosmolarity & hypernatraemia are tolerated better. In fact, HS is a level III recommendation in pediatric guidelines. It is given as an infusion 0.1 to 1 ml/kg/hour. Treatment of severe head injury with hypertonic saline has been found to be superior to treatment with lactated Ringer's solution. An increase in serum sodium concentrations significantly correlates with lower ICP and higher CPP. Children treated with hypertonic saline require fewer interventions, have fewer complications, and stay a shorter time in the ICU. Side effects of the use of HS include osmotic demyelination syndrome, rebound rise in ICP & acute renal failure. Although is usually not seen if serum sodium levels are kept below 150 mEq/L.

**Use of Colloids in Paediatric Neurosurgery**

There are very few studies that have compared use of crystalloids versus colloids in the paediatric population. The colloids that are commonly used are natural or synthetic. The natural colloids used are albumin. The synthetic ones are starches, gelatins and dextrans.

**Albumin**

While 5% albumin is isotonic to plasma, 25% albumin is hypertonic and can withdraw fluid from the interstitial compartment and may be useful to decrease brain edema or provide a lax brain during surgery. However, when there is blood brain barrier disruption, one must be careful in administering albumin as it can extravasate into the interstitial compartment and aggravate brain edema. In fact the SAFE study showed that albumin is harmful in patients with head injury and can increase mortality rate. The use of albumin as a plasma expander in neonates & infants is declining.

**Starches**

Recent studies have thrown up a lot of controversy regarding the use of starches for volume replacement in adult patients.
However, moderate doses of HES 130/0.42/6:1 for perioperative plasma volume replacement seem to be safe even in neonates and small infants. The probability of serious adverse drug reaction is lower than 0.3%. Changes in acid-base balance may be decreased when HES is used in an acetate-containing balanced electrolyte solution instead of normal saline.

In a comparison of hydroxyethyl starch (130/4.2) with 5% albumin in children undergoing non-cardiac surgery, it was found that there was no major difference in perioperative haemodynamic stability, coagulation variables, acid-base status and other parameters, although this did not include pre-term infants.

A European, multicentre, post-authorization safety study found that hydroxyethyl starch (130/4.2) had no major effect on coagulation status, acid-base balance and renal function even in small infants and neonates with normal renal function. Overall, with data available, it would seem prudent to use red cell transfusion to replace blood loss when necessary and crystalloid would be a better option rather than colloids for volume replacement when blood transfusion is not indicated. However, colloids may be used to replace blood loss when blood is not readily available.

Transfusion guidelines in Paediatric Neurosurgery

Blood loss during neurosurgical operations is difficult to assess as besides suction bottles, blood is also lost near the head end and on the surgical drapes, cottonoids etc. Use of irrigation fluid further compounds the problem. Therefore, assessment of blood loss should include serial haemoglobin measurement, clinical parameters as well as pulse pressure variation and, if indicated, central venous pressure measurement.

Considerations for blood transfusion in paediatric patients

- Children have a higher oxygen consumption and a higher cardiac output to blood volume ratio than adults
- Neonatal myocardium is operating at full performance and, therefore, is unable to increase cardiac output in the face of decreasing haemoglobin to increase oxygen delivery
- Threshold for transfusion is higher in the neonate as compared to an older child or adult
- Neonates & young infants have higher levels of fetal haemoglobin. As a result, oxygen delivery to the tissues is less and the life span of the RBC is also less
- Administration of RBCs to an infant < 4 months of age need to be only type specific or O negative and cross matching is not required as major haemolytic reactions do not occur. They are unable to produce allo-antibodies to RBC antigens
- Metabolic complications associated with blood transfusion occur more readily in small children, such as hypocalcaemia, hyperkalaemia and hypothermia.

The paediatric neurosurgical procedures which often require blood transfusion include brain tumour surgery especially if they are vascular lesions, spine surgery such as spinal dysraphism & scoliosis surgery and craniosynostosis. Of these there is a lot of literature related to surgery for craniosynostosis with respect to blood loss and blood transfusion.

It is important to estimate the blood volume of children who present for neurosurgical operations. This is given in the table below.

<table>
<thead>
<tr>
<th>Age</th>
<th>Estimated blood volume ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm infant</td>
<td>90-100</td>
</tr>
<tr>
<td>0 to 3 months</td>
<td>80-90</td>
</tr>
<tr>
<td>&gt; 3 months</td>
<td>70</td>
</tr>
<tr>
<td>Very obese infants</td>
<td>65</td>
</tr>
</tbody>
</table>
In addition, the maximal allowable blood loss at which point blood transfusion is indicated should also be estimated.

\[ MABL = \left( \frac{\text{starting haematocrit} - \text{target haematocrit}}{\text{starting haematocrit}} \right) \times \text{EBV} \]

Indications of blood transfusion in children

Red blood cell transfusion is rarely indicated if haemoglobin is > 10 G/dL and should be given if haemoglobin is <6 G/dL. However, in infants < 4 months and in situations of haemodynamic instability and depending on the underlying general condition, the transfusion trigger is higher. A haematocrit of 30% is a reasonable postoperative goal and to that extent an allowable blood loss to a target haematocrit of 30% is recommended. In some institutions, blood transfusion is started with surgical incision, particularly in small babies, as blood loss can be quite rapid during craniotomy and transfusion at that juncture, cannot keep pace with blood loss.

Massive blood loss can occur in paediatric neurosurgical procedures. This can result in dilutional coagulopathy depending on the type and volume of the blood product transfused. Nowadays, whole blood is rarely used and since components are generally used, deficiencies in one or more clotting factors can occur with massive transfusions. In such a situation, platelets, fresh frozen plasma and cryoprecipitate transfusions are indicated particularly if there is microvascular oozing at the surgical site. It is then essential to monitor coagulation parameters. Point of care estimation of coagulation status using thromboelastography is useful in such situations and has been reported in children undergoing brain tumour surgery.

Risks of Massive Blood Transfusion
- Dilutional coagulopathy
- Post-transfusion hepatitis
- Acquired immunodeficiency syndrome
- Haemolytic transfusion reactions
- Transfusion-related acute lung injury
- Leukocyte-platelet allogenic immunization

Rapid blood transfusion in an infant can result in hyperkalaemia and cardiac arrest, primarily because of the high concentration of potassium in stored blood.

Blood Conservation Strategies

Strategies such as pre-operative autologous blood donation & acute normovolaemic haemodilution (ANH) may not be suitable for small children because of their small blood volumes and the fact that infants, in particular, cannot increase their cardiac output following haemodilution like adults. Moreover, only small volumes of autologous blood can be obtained before the target haematocrit of 25% is reached. The benefit of ANH was studied in infants undergoing craniosynostosis surgery over a 4 year period and it was found that ANH neither decreased the incidence or amount of homologous transfusion.

Directed parental blood donations have the potential risks of chimerism and graft versus host disease (GVHD) and it is recommended that all cellular components obtained from parental donations be gamma-irradiated before transfusion.

Perioperative blood salvage using cell saver or continuous autotransfusion system (CATS) has been used as well as studied in children undergoing craniosynostosis, particularly major cranial vault repair surgery. The main aim of this strategy is to reduce the incidence of homologous blood transfusion. The results are controversial, although some authors have reported that the amount of homologous blood transfused is less when CATS is used. However the risks of intraoperative cell salvage include coagulopathy, hemolysis, bacterial contamination and damage to platelets.

Preoperative administration of recombinant human erythropoietin (RHEPO) in children undergoing craniosynostosis surgery has been tried in an attempt to reduce homologous blood transfusion. Administration of erythropoietin along with supplemental iron is started 3 weeks prior to craniosynostosis surgery in children which can result in a higher preoperative haematocrit and results in lesser blood loss.
and lesser volume of homologous blood being transfused.

**Combination of blood sparing strategies**

Erythropoietin administration has also been combined with other blood conservation strategies such as ANH, induced hypotension, preoperative autologous blood donation and intraoperative cell salvage with good results in terms of homologous blood replacement.

There are no transfusion guidelines based on randomized controlled trials for paediatric surgical patients. The ASA Task Force on Blood Component Therapy (1996) have not included children in their guidelines. However, the British Committee for Standards in Hematology Transfusion stated have made the following recommendations for neonates and older children:

1. All components other than granulocytes should be leukocyte depleted
2. Blood transfused in the first year of life should be cytomegalovirus seronegative.
3. A screen filter (170m–200m) or alternative filtration system should be used during transfusion, for all components.
4. Red blood cells stored less than 2 or 3 weeks should be used in young children.

**Summary**

Management of fluid & transfusion requirements in the paediatric neurosurgical patient is very challenging and plays a pivotal role in ensuring a smooth intraoperative course as well as a good postoperative outcome. The neuroanaesthesiologist plays a key role in managing fluid and transfusion requirements. The perioperative management of fluids & blood transfusion practice has undergone paradigm shifts and it is necessary to keep pace with recent guidelines to have a good perioperative outcome in the paediatric neurosurgical patient.

**References**


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Evoked potential monitoring in the operating room. What's new?

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Despite the recent progress in neuroradiological and surgical techniques, post-operative neurological dysfunction including motor deficits and ophthalmologic complications remained to be a critical issue. Patients undergoing craniotomy for cerebral aneurysm and brain tumor are considered to have a risk for postoperative motor and visual dysfunction. In such cases, intraoperative monitoring of motor evoked potentials (MEPs) and visual evoked potentials (VEPs) can provide a method for monitoring the functional integrity of descending motor pathways and visual pathway, respectively, during the operations. In this lecture, I would focus on the techniques and clinical usefulness of myogenic MEP and VEP monitoring during craniotomy under general anesthesia.

Myogenic MEP monitoring

Myogenic MEPs elicited by single pulse stimulation have been shown to be very sensitive to suppression by most the anesthetic agents. To overcome anesthetic-induced depression of myogenic MEPs, multiple-stimulus setups, with a train of pulses for stimulation of the motor cortex have recently come into use. A train of three to six pulses, with an interstimulus interval of 2ms (500 Hz), is the recommended setup for myogenic MEP under general anesthesia (1).

Two stimulation methods, direct cortical stimulation and transcranial electrical stimulation are currently used for MEP monitoring during craniotomy. The latter can be performed without insertion of grid electrodes on the brain surface of the motor area, and is therefore widely performed not only in brain surgery but also spine and aortic surgery. However, some caution is needed when high-intensity transcranial electric stimulation is performed. It may result in stimulation of sites far from the target area. If MEPs were elicited by stimulation of the medulla oblongata, they would not be useful in intraoperative monitoring for surgery of intracranial aneurysms. To avoid false-negative findings, adjustment of stimulation intensity is important. During the craniotomy, we search the threshold level, at which waveform of MEP is elicited from only contralateral abductor pollicis brevis (APB). Then stimulation intensity is set supra-threshold level to stably elicit MEPs at least 30-50μV in amplitude.

Direct cortical stimulation MEP has recently been performed with high sensitivity and reliability. However, installation of specially designed grid electrode strips is required in the subdural space to elicit direct MEPs. This is interfered by subdural adhesions due to previous surgery and might result in injury of bridging veins. In addition, MEPs elicited by direct cortical stimulation can only be recorded during microsurgery, when the brain surface is exposed. On the other hand, transcranial MEP can be performed without insertion of grid electrodes on the brain surface and throughout the course of surgery. To compensate for the weaknesses of transcranial and direct MEP, we have been using transcranial electrical stimulation combined with direct cortical stimulation to elicit MEPs for intraoperative monitoring during craniotomy.

In our series of 48 cases, MEPs were elicited successfully by transcranial electrical stimulation in all cases (100%) (2). On the other hand, direct cortical stimulation elicited MEPs in 44 patients (91.7%). A reduction in MEP amplitude to less than 50% of control was considered significant. There was no postoperative motor paresis in 39 patients in whom transcranial and direct MEPs remained unchanged. The transient MEP changes were observed in 3 patients during...
temporary clipping of the parent artery and in one patient with inadequate clipping of an MCA aneurysm, and were considered due to insufficiency of blood flow. In one patient, direct MEP waves disappeared and did not recover until the end of microsurgical procedures, although transcranial MEP amplitude remained less than 50% of the control level. She developed hemiparesis postoperatively, which recovered within 6 hours. These findings suggest that combined transcranial and direct cortical MEP recording may improve the feasibility and reliability of MEP monitoring during unruptured aneurysm surgery.

**VEP monitoring**

Ophthalmic dysfunction including visual field defects, reduced visual acuity and visual loss can develop after the surgery, in which surgical intervention is performed near the optic pathways or ophthalmic circulation is disturbed. In order to prevent such ophthalmic complications, the attempts to monitor VEPs intraoperatively have been made. However, it had been not successful probably due to the suppressive effects by anesthetic agents and insufficient stimulation. However, recent advances in the technology for stimulation and anesthetic techniques allowed us to monitor VEPs intraoperatively, when new stimulation device was used combined with electroretinography (ERG) under propofol-based anesthesia.

Sasaki et al.(3) reported the new stimulation device consisting of red light-emitting diodes embedded in a soft silicone disc to avoid deviation of the light axis after frontal scalp-flap reflection. The luminosity of device is changeable from 500 to 20,000 Lx. In order to confirm that the light is properly reached to the retina, ERG is simultaneously recorded. Based on the results of EGR, the stimulus intensity can be changed to keep ERG response constant. The results by Sasaki et al. indicated that reproducible EMG and VEP monitoring was feasible in 187 of 200 eyes (95.3%) in patients under propofol and fentanyl anesthesia. The criteria of amplitude changes was defined as a 50% increase or decrease in amplitude compared with the control level. The VEP amplitude decreased without subsequent recovery to 50% of control level in 14 eyes, and all of these developed various degrees of postoperative deterioration of visual function. In a series of our cases, success rate of VEP monitoring was 96% (24/25 patients). Of 6 patients in which VEP amplitude was reduced during the operation, 2 patients developed the postoperative ophthalmic complications. Of 18 patients in which VEP remained unchanged during the operation, 15 patients had unchanged postoperative ophthalmic function. The results indicated that sensitivity and specificity were 67% and 79%, respectively, and negative predictive value was 95%. Further improvement of VEP monitoring may be required and studies in more patients would be required. However, in meantime, intraoperative VEP monitoring may be successfully used to avoid or prevent the postoperative ophthalmic dysfunction.

**References**


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Anaesthetic Management of Intracranial Brain tumors in children

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Anesthetic management of children undergoing procedures designed to cure or palliate intracranial masses can be extremely challenging. In order to facilitate good perioperative outcomes in this patient population, the anesthesiologist must have a thorough understanding of normal pediatric neurocognitive development, normal cerebral physiology and pharmacology, and appreciate newer technologies employed in these procedures. This lecture will briefly review these considerations when caring for such patients. The main focus of this lecture will be to discuss the various aspects of anesthetic management for special circumstances such as use of intraoperative MRI (iMRI), laser thermal ablation of deep brain lesions, and awake craniotomy. The unique considerations of providing an anesthetic for a surgical procedure in the iMRI environment will be explored. Recently, the iMRI environment is being used to facilitate procedures using laser thermal ablation. It is important for anesthesiologists to be aware of such novel uses of iMRI. Awake craniotomies in children present the anesthesiologist with an array of challenges and the lecture will discuss some of these challenges as well as approaches to addressing them. The lecturer has no financial disclosures to make.

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Pediatric Traumatic Brain Injury: The Anesthesiologists Perspective

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Pediatric neurotrauma is the leading cause of death in children > 1 year of age. Children are more susceptible to traumatic brain injury (TBI) because they have a larger head to body size ratio, thinner cranial bones providing less protection to the intracranial contents, less myelinated neural tissue which makes them more vulnerable to damage. Children have a greater incidence of diffuse injury, cerebral edema and increased intracranial pressure (ICP) following TBI than adults. Anatomically, the injury can be extraaxial (eg, epidural hematoma, subdural hematoma, subarachnoid hemorrhage, and intraventricular hemorrhage), intraaxial (eg, diffuse axonal injury, cortical contusion, and intracerebral hematoma), or vascular (eg, vascular dissection, carotid cavernous fistula, arteriovenous dural fistula, and pseudoaneurysm).

Pathophysiology

Primary brain injury is the damage caused by the initial mechanical impact to the brain tissue and skull resulting in skull fracture, brain contusion, intracranial hematoma or diffuse axonal injury. The primary injury then initiates inflammatory process, edema formation and excitotoxicity, resulting in further increase in ICP and reduced cerebral perfusion pressure (CPP), all leading to secondary injury to the brain. Physiological insults after the initial injury, cause further damage to the brain tissue worsening the outcome and are often referred to as the “secondary insults” or “second insults”. Common secondary insults include hypotension, hypoxemia, hypercarbia, hypocarbia, hyperglycemia, hypoglycemia and hyperthermia. Modern management of TBI emphasizes avoidance of primary insult and minimizing secondary insults. Following TBI, cerebral blood flow and cerebral metabolic rate (CMR) may not be matched, resulting in cerebral ischemia or hyperemia. The incidence of impaired cerebral autoregulation is higher following severe compared to mild TBI and impaired autoregulation is associated with poor outcomes.

Anesthetic and Perioperative Management

The cornerstones of modern TBI management are field resuscitation, expeditious triage, emergent surgical evacuation of mass lesions, control of ICP, and support of CPP, multimodal monitoring to optimize physiological environment. The perioperative period is an opportunity for the anesthesiologists to prevent and correct the secondary insults and may be a potential window to initiate interventions that may improve the outcome of TBI.

Initial Assessment

The initial approach involves the primary and secondary surveys with rapid assessment of the airway, breathing, circulation, neurological status and associated injuries. A GCS score (modified for children) of 13-15 signifies mild TBI, 9-12 is moderate TBI, and 3-8 is severe TBI. Signs and symptoms of intracranial hypertension or impending herniation, such as altered level of consciousness, pupillary dysfunction, lateralizing extremity weakness or Cushing’s triad (hypertension, bradycardia, and irregular respirations) should alert the need for urgent interventions to control ICP including possible surgical decompression. Associated thoracic, abdominal, spinal and long bone injuries may be stable or evolve during the perioperative period and must be
considered in differential diagnosis of new onset hypotension, anemia, hemodynamic instability or hypoxemia during anesthesia and surgery.

**Cervical Spine Immobilization**

In infants < 6 months of age, the head and cervical spine should be immediately immobilized using a spine board with tape across the forehead, and blankets or towels around the neck. In infants ≥ 6 months of age, the head should be immobilized either in the manner described above or by using a small rigid cervical collar. Children > 8 years of age require a medium sized cervical collar. The use of rigid cervical collars is essential as it prevents cervical distraction during laryngoscopy. Since children under seven years have a prominent occiput, a pad placed under the thoracic spine provides neutral alignment of the spine and avoids excessive flexion that may occur in the supine position. These two maneuvers are paramount in avoiding iatrogenic cervical spine injury.

**Airway Management**

Children requiring surgery and those with a GCS score < 9 require tracheal intubation for airway protection and management of increased ICP. All TBI patients requiring tracheal intubation must be considered to have full stomach and airway management must account for possible underlying cervical spine injury. The choice of technique for intubation is determined by urgency, individual expertise/skills and available resources and generally incorporates rapid sequence orotracheal intubation with cricoid pressure and manual in-line stabilization. Newer airway devices, particularly the videolaryngoscopes, have gained popularity in recent years for use in trauma victims and may be useful in difficult airway scenarios. Tracheal intubation is a noxious stimulus and can increase ICP. Hence, sodium thiopental (3-5 mg/kg), etomidate (0.2-0.6 mg/kg) or propofol (2-3 mg/kg) are often used to induce anesthesia before intubation in hemodynamically stable patients. These agents decrease the systemic hemodynamic response to intubation, blunt increases in ICP, and decrease the CMR. In addition, administration of lidocaine (1.5 mg/kg intravenous) and short-acting narcotic such as fentanyl (1-2 mcg/kg) can decrease the catecholamine release associated with direct laryngoscopy. However, propofol and thiopental may cause cardiovascular depression leading to hypotension, especially in the presence of uncorrected hypovolemia. Etomidate (0.2-0.6 mg/kg) may be advantageous in patients with unstable hemodynamic status due to little change in blood pressure during induction despite reduction of CMRO₂. Pediatric data on adrenal insufficiency following single dose etomidate in TBI patients are lacking although adrenal depression has been observed following etomidate use in children with sepsis. Ketamine, which causes limited cardiovascular compromise, is often considered relatively contraindicated for intubating patients with risk for or pre-existing increased ICP for the fear of associated increased CBF and increased ICP. However, in mechanically ventilated pediatric patients with intracranial hypertension, ketamine has actually been shown to effectively decrease ICP and prevent untoward ICP elevations during potentially distressing interventions, without lowering blood pressure and CPP. In fact, ketamine may be a safe and effective drug for patients with TBI and intracranial hypertension and it can possibly be used safely in emergency situations. The choice of muscle relaxant for rapid sequence induction is between succinylcholine and rocuronium. While the clinical significance of the effect of succinylcholine on increasing ICP is questionable, increases in ICP secondary to hypoxia and hypercarbia are well documented and much more likely to be clinically important. Hence, in patients with TBI, clinicians may not avoid using succinylcholine if difficult intubation is anticipated.

**Intravenous access and Fluids**

In emergent cases, if peripheral access is unsuccessful after 2 attempts, an interosseous line should be placed. Insertion
of Central venous catheters should not delay evacuation of expanding intracranial hematoma. Isotonic crystalloid solutions are commonly used during the anesthetic. Hypotonic crystalloids should be avoided and the role of colloids is controversial. Non-glucose containing warm, isotonic crystalloids are preferable.

**Monitoring**

The current guidelines for the acute medical management of severe TBI in infants, children, and adolescents provide a level III recommendation for using ICP monitoring in infants and children with severe TBI. Although many advanced technologies including cerebral microdialysis, thermal diffusion probes, transcranial Doppler, and near-infrared spectroscopy are increasingly being used, there are few systematic investigations specific to pediatric TBI, particularly pertaining to their use to guide therapy. If brain oxygenation monitoring is used, maintenance of PbtO$_2$ ≥10 mmHg is advisable. Pediatric patients requiring craniotomy or extracranial surgery for associated injuries should receive the standard ASA monitoring, and invasive arterial blood pressure monitoring, blood gas analysis and blood glucose monitoring.

**Anesthetic technique, Sedation and Analgesia**

The goals of anesthetic management of TBI are to maintain CPP, treat increased ICP, provide optimal surgical conditions, avoid secondary insults and provide adequate analgesia and amnesia. Intravenous anesthetic agents including thiopental, propofol and etomidate cause cerebral vasoconstriction and reduce CBF, CBV, CMRO$_2$ and ICP while opioids have no direct effects on cerebral hemodynamics in the presence of controlled ventilation. All inhaled anesthetic agents (isoflurane, sevoflurane, desflurane) decrease CMRO$_2$ and may cause cerebral vasodilation, resulting in increasing CBF and ICP. However, at concentration less than 1 minimum alveolar concentration (MAC), the cerebral vasodilatory effects are minimal and hence they may be used in low concentrations during craniotomy or extracranial surgery in patients with TBI. Nitrous oxide can increase CMRO$_2$ and cause cerebral vasodilation and increased ICP and should be avoided. Narcotic analgesics are often added to alleviate the pain, stress and the noxious stimuli associated with routine intensive care procedures. Neuromuscular blocking agents may reduce ICP in intubated TBI patients in the intensive care units by reduction in airway and intrathoracic pressure with facilitation of cerebral venous outflow and by prevention of shivering, posturing, or breathing against the ventilator.

**Ventilation**

Ventilation should be adjusted to ensure adequate oxygenation and gas exchange. Inspired oxygen concentration should be adjusted to maintain PaO$_2$ > 60 mmHg. Monitoring arterial PCO$_2$ is recommended. Although controlled hyperventilation is an effective intervention to rapidly decrease elevated ICP, it must not be used indiscriminately because excessive hyperventilation may cause cerebral vasconstriction leading to ischemia. Current guidelines recommend avoidance of prophylactic hyperventilation to a PaCO$_2$ < 30 mmHg in the initial 48 hours after injury.

**Systemic and Cerebral Hemodynamics**

Cerebral autoregulation and coupling between CBF and CMR may be disrupted following TBI, and a decrease in CPP may therefore lead to cerebral ischemia. Hence, continuous monitoring of arterial blood pressure, ICP and CPP with efforts to avoid systemic / cerebral hypotension is desirable. The 2012 Pediatric Guidelines recommend a minimum CPP of 40mmHg in children with TBI. A CPP threshold 40-50mmHg may be considered. SBP < 5$^{th}$ percentile (70 + 2*age mmHg) defines hypotension.

**Management of Intracranial Hypertension**

The 2012 Pediatric Guidelines recommend treatment of ICP at a threshold of 20 mmHg. Intracranial hypertension can be initially managed through elevation of the head, sedation, analgesia and neuromuscular
blockade. Additionally, following therapies are recommended:

**Hyperosmolar Therapy**: The guidelines support the use of 3% hypertonic saline for the acute treatment of severe pediatric TBI associated with intracranial hypertension (6.5-10 mL/kg and as a continuous infusion between 0.1 and 1.0 mL/kg of body weight per hour administered on a sliding scale). The minimum dose needed to maintain intracranial pressure (ICP) < 20 mm Hg should be used and serum osmolarity should be maintained < 360 mOsm/L. There is insufficient evidence to support or refute the use of mannitol, concentrations of hypertonic saline > 3%, or other hyperosmolar agents for the treatment of severe pediatric TBI.

**High dose barbiturate therapy** may be considered in hemodynamically stable patients with refractory intracranial hypertension but volume loading and inotropic support may be needed to counter myocardial depression and hypotension. High-dose barbiturates lower ICP by suppression of metabolism and alteration of vascular tone. Barbiturate therapy improves coupling of regional CBF to metabolic demands resulting in higher cerebral oxygenation with lower CBF and decreased ICP from decreased cerebral blood volume.

**Cerebrospinal Fluid Drainage** is recommended through an external ventricular drain and also the addition of a lumbar drain in case of refractory intracranial hypertension with a functioning EVD, open basal cisterns and no evidence of mass lesion or shift on imaging.

**Decompressive craniectomy for intracranial hypertension** in pediatric patients who are showing early signs of deterioration or herniation or are developing intracranial hypertension refractory to medical management during early stages of treatment. It may consist of uni- or bilateral subtemporal decompressions, hemispheric craniectomies of varying sizes (from relatively small to quite expansive), circumferential craniectomy, or bifrontal craniectomy.

**Therapeutic Hypothermia.** Moderate hypothermia (32–33°C) beginning early after severe TBI for 48 hrs, duration may be considered to reduce intracranial hypertension. Following therapeutic hypothermia, rewarming at a rate of > 0.5°C/hr should be avoided. The rationale for use of therapeutic hypothermia is a reduction in mechanisms of secondary injury resulting from decreased CMR, inflammation, lipid peroxidation, excitotoxicity, cell death, and acute seizures. In any case, fever and hyperthermia should be avoided in patients with TBI.

**Corticosteroids in TBI**
Steroid administration in severe pediatric TBI is not associated with improved functional outcome, decreased mortality, or reduced ICP. Instead, steroid use may cause suppression of endogenous cortisol levels and may increase the risk of pneumonia. Given the lack of evidence for benefit in children and the potential for harm from infectious complications and known suppression of the pituitary adrenal axis, routine use of steroids to lower ICP or improve functional outcomes or mortality is not recommended in children with TBI.

**Glucose and Nutrition**
Hyperglycemia occurs frequently in children with severe TBI and is associated with poor outcome, longer ICU length of stay and higher in-hospital mortality. Yet, there are no proven benefits of intensive glucose control strategies. In the absence of outcome data, the 2012 Pediatric Guidelines do not make any recommendation for glycemic control in pediatric TBI. Importantly, perioperative hyperglycemia is common and intraoperative hypoglycemia is not rare, and regular intraoperative glucose sampling may be needed. It is advisable to maintain glucose in the range of 80-180 mg/dL.

**Antiseizure Prophylaxis**
Early posttraumatic seizures (occurring within 7 days of injury) occur in approximately 10% pediatric patients with TBI. Prophylactic anticonvulsant therapy with phenytoin may be considered to reduce
the incidence of early posttraumatic seizures after severe TBI.

**Summary**

TBI is a major cause of morbidity and mortality in the pediatric age. Modern TBI management emphasizes minimizing secondary insults to the injured brain. The perioperative period is an opportunity to optimize cerebral and systemic physiology, minimize secondary insults and, may be a potential window to initiate interventions that may improve the outcome of TBI. Anesthetic management should be based on the current guidelines for the acute medical management of severe TBI in infants, children, and adolescents.

**References**


Neonatal Anesthetic Neurotoxicity: An Update

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Introduction
The traditional view of general anesthesia is that anesthetics produce a reversible loss of consciousness and that the brain and spinal cord are not structurally or functionally affected by anesthesia. The demonstration that anesthetics can induce structural changes in the neonatal brain that have functional consequences during adulthood necessarily requires a revision of this premise. These structural changes include not only neuronal apoptosis but also alterations in dendritic spines and synapse formation; especially with respect to synapse formation, the induced changes can be persistent for several weeks to months. That anesthetics can alter fundamental properties of the brain has led to widespread concern about the potential adverse impact of anesthetics on the developing brain. In the present discussion, the structural changes induced in the brain and the underlying mechanisms that produce these changes will be reviewed. By necessity, the discussion is focused on pre-clinical studies. Although the relevance of anesthetic induced structural changes in humans is not known, an understanding of the underlying mechanisms is essential for the development of therapeutic interventions to prevent adverse effects of anesthetics.

Pathology of Anesthetic Induced Structural Changes in the Neonatal Brain
A large variety of agents have been shown to increase neuronal apoptosis in the developing brain. These include NMDAR antagonists and GABA-A agonists. Anesthetic agents are primarily agonists at the GABA-A receptor and antagonists at the NMDAR. A number of investigations have now shown clearly that anesthetics induce widespread neurodegeneration in the developing brain. These include isoflurane, sevoflurane, desflurane, thiopental, midazolam, propofol, ketamine and nitrous oxide. Exceptions include dexmedetomidine and xenon. The apoptosis is apparent within the cortex, hippocampus, striatum, cerebellum and other subcortical structures. This neurodegeneration is apoptotic in nature and interference with the apoptosis machinery in neurons reduces cell loss. The susceptibility to apoptosis is age dependent and occurs primarily during the period of synaptogenesis. In rodents, this occurs during the first two weeks of life, with peak susceptibility at 7 days post birth. Anesthetic exposure 2 weeks after birth does not lead to apoptosis.

More recent data indicate, however, that anesthetics induced structural alterations of the brain are not just limited to apoptosis. Anesthetic exposure modulates synaptic plasticity. Isoflurane and propofol dramatically reduce dendritic spines and synapses in the developing brain when exposure occurs at post natal day 5-7. By contrast, propofol, sevoflurane and desflurane all increase dendritic spines and synapses when exposure occurs 2 to 4 weeks after birth. The newly formed spines have functional synapses and importantly, persist for at least 3 months. These data indicate anesthetic induced changes in the brain extend beyond apoptosis and that the nature...
of the change is age dependent. The neurocognitive deficits that have been demonstrated in adulthood after neonatal exposure to anesthetics are probably a combination of neuronal apoptosis as well as modulation of synaptic plasticity.

**Proposed Mechanisms of Neonatal Anesthetic Neurotoxicity**

1) **Excitation – inhibition imbalance.**

The development of synaptic networks in the neonatal brain is dependent upon coordinated excitation and inhibition of neurons within the network. Increased excitation, increased inhibition or a combination of both during critical periods of synaptic development can lead to synaptic involution, and under certain circumstances, can lead to release of cytochrome c from mitochondria and the initiation of the apoptosis cascade 11.

2) **GABA-A receptor mediated excitotoxicity.**

In developing neurons, GABA-A receptor agonism leads to depolarization of neurons. In these neurons, a chloride transporter (NKCC1) increases intracellular concentration of calcium. Upon GABAR activation, there is a net efflux of chloride from the cell, leading to neuronal depolarization. This depolarization also removes the Mg block from NMDAR, opening of the NMDAR and calcium influx into the cell 12,13. Excessive activation of GABAR

Therefore has the potential to induce excitotoxicity. With further development, expression of NKCC1 is reduced and that of a chloride transporter (KCC2) that leads to efflux of chloride from the cell. Upon KCC2 expression, GABA agonism no longer leads to chloride efflux and depolarization but to hyperpolarization that occurs in mature neurons. The switch from GABA-A mediated excitation to inhibition occurs at approximately 10-14 days after birth. Interestingly, this switch correlates with the reduced susceptibility to anesthetic induced apoptosis at about 14 days post birth.

GABA-A mediated excitation during the neonatal period has also been shown to lead to seizure-like activity on the EEG. Both sevoflurane and propofol manifest seizure-like activity; this can potentially contribute to the cognitive deficits that are apparent later in life. Of interest are recent observations which indicate that anesthetics increase the concentration of the stress hormones corticosterone and aldosterone14,15. Both these stress hormones, in conjunction with GABA-A mediated excitation, can precipitate seizures. Antagonists of these steroids, as well as the loop diuretic bumetanide (blocks NKCC1) can prevent seizure like activity induced by anesthetics. In fact, butametanide administration during anesthetic exposure in neonatal animals can prevent cognitive dysfunction in adulthood.

3) **NMDAR excitotoxicity.**

This mechanism has been proposed primarily for NMDAR antagonists such as ketamine 16. With prolonged blockade of NMDAR with ketamine, a compensatory increase in NMDAR expression has been demonstrated in primate neurons. Upon withdrawal of ketamine, this increased NMDAR expression makes neurons vulnerable to excitotoxic...
injury. Indeed, prevention of the increase in NMDAR expression makes neurons less susceptible to ketamine induced apoptosis.

4) Aberrant cell cycle entry.

Mature, terminally differentiated cells do not undergo proliferation by mitosis. These cells are in the G1/G0 state. Recent work from the Soriano laboratory has shown that exposure of the neonatal brain to ketamine results in the expression of cell cycle proteins cdk4 and cyclin D17. Movement of cells through mitosis requires proper passage through a number of checkpoints and an elaborate biochemical machinery is involved to ensure fidelity of cell replication. Aberrant expression of cell cycle proteins, especially in a non-coordinated and incomplete manner, rapidly leads to apoptosis. Suppression of ketamine induced increase in cyclin D dramatically reduced the vulnerability of the neurons to ketamine induced apoptosis. This suggests aberrant entry of terminally differentiated cells induced by anesthetics could play a role in neuronal apoptosis.

5) Loss of trophic factor signaling.

A variety of trophic factor signaling pathways in developing neurons are essential for neuronal survival and growth. Loss of these trophic signals can lead to apoptosis. In the neonatal brain that is exposed to anesthetics such as ketamine and propofol, there is a loss of pro-survival signaling (loss of ERK and Akt signaling)18,19. This triggers apoptosis. Enhancement of these pathways with lithium can reduce neurodegeneration.

6) proBDNF-p75NTR signaling.

During synaptogenesis, maturation and stabilization of synapses is critically dependent upon trophic factors. A key trophic factor is BDNF (brain derived neurotrophic factor). BDNF is synthesized and secreted as proBDNF; it undergoes both activity dependent (regulated) and constitutive release. Secreted proBDNF is proteolytically cleaved to mature BDNF (mBDNF) in the synaptic cleft by the action of plasmin, which in turn is formed by the proteolytic cleavage of plasminogen by tPA. tPA release is activity dependent. mBDNF signals via the TrkB receptor to increase neuronal survival and growth20. Under anesthesia, regulated tPA and proBDNF secretion is reduced whereas the constitutive release of proBDNF is not affected. This results in the accumulation of proBDNF in the synaptic cleft. proBDNF preferentially signals through the p75NTR receptor. The downstream consequences of proBDNF-p75NTR signaling are depolymerization of the actin cytoskeleton, loss of dendritic spines and synapses, and apoptosis10,21. Inhibition of p75NTR signaling significantly attenuates anesthetic induced neurodegeneration.

7) Impairment of glial development.

All cells have a functional cytoskeletal architecture that is essential to its form and function. In the developing brain, glia undergo maturation over 7 to 10 days. There is a gradual expansion in cell size that is accompanied by a developing cytoskeleton. In mature glia, the cytoskeleton is well developed. In developing glia, isoflurane leads to actin depolymerization and a substantial loss of the actin cytoskeleton22. These glia, some of which undergo apoptosis, are functionally compromised and may contribute to the total burden of anesthetic neurotoxicity.

8) Modulation of synaptic plasticity.

Much of the research on anesthetic neurotoxicity has been focused on neuronal...
apoptosis. The peak period of vulnerability is at PND 5-7. Although this is within the period of synaptogenesis, much of the brain growth spurt (with a dramatic increase in the number of synapses) occurs from PND10 to PND20, a time when neurons are not vulnerable to apoptosis. More recent data indicate that anesthetic exposure during rapid synaptic development fundamentally alters synaptic plasticity. Specifically, volatile anesthetics and propofol increase the number of synapses when exposure occurs at either PND15 or PND20. Such an effect is not apparent when exposure occurs at PND30 8,9. Moreover, these synapses are active and they persist for several weeks to months. These data suggest that anesthetics fundamentally alter synaptic plasticity and may in fact modulate the development of neuronal networks. The functional consequence of synaptic modulation is not clear at present. However, it is possible that it may contribute to the cognitive dysfunction that has been demonstrated in adult animals that were exposed to anesthetics during the neonatal period.

9) Neurogenesis.
The generation of new neurons, neurogenesis, occurs in two regions within the brain: the subventricular zone and the dentate gyrus. The newly synthesized neurons are integrated into neuronal networks. Suppression of neurogenesis is associated with a substantial cognitive decline. Work from the Stratmann laboratory has shown that isoflurane reduces neurogenesis transiently when exposure occurs at PND5-7 23. Neurogenesis is restored in about 3-4 weeks post exposure. However, Repeated exposure to isoflurane in PND14 mice leads to a dramatic reduction in neurogenesis 24. In addition, the pool of progenitor cells that gives rise to new neurons is permanently reduced by repeated anesthetic exposure. Repeated exposure at PND60 does not affect neurogenesis or cognitive function. These data suggest that isoflurane can impact neurogenesis, that this effect can permanently reduce the progenitor cell population, and that this reduction in neurogenesis may contribute to anesthesia induced cognitive dysfunction.

Summary
A number of investigators have shown that exposure of the developing brain to anesthetics can lead structural changes in the brain. The initial focus of inquiry has been on neuronal apoptosis and the data suggest that the peak period of vulnerability is approximately one week after birth. More recent data also indicate that anesthetics can modulate synaptic plasticity up to about 20 days post birth. The changes in synaptic plasticity induced by anesthetics results in a long lasting change in synapse number up to at least 3 months post exposure. Therefore, the prevailing view that susceptibility to anesthetics is limited to the first two weeks post birth needs revision. Indeed, the brain is vulnerable to anesthetic induced changes in synaptic plasticity for at least 3 weeks post birth. A variety of mechanisms contribute to anesthetic neurotoxicity. What is not clear is whether the aggregate toxicity that has been demonstrated is due to one dominant mechanism or due to a combination of mechanisms. Of considerable interest are the data that show that anesthetic neurotoxicity can be abolished, or at least attenuated, by a number of therapeutic interventions. Several of these directly modulate the mechanisms of neurotoxicity discussed above while others are non-specific in their effect. These therapeutic approaches offer hope for the prevention of anesthetic neurotoxicity in the clinical setting should this toxicity be proven to be relevant to humans.

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Incidental Surgery in a Patient with Epilepsy

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Epilepsy is a clinical disorder of paroxysmal, unprovoked, recurring seizures and is the most common serious neurological disorder, with a prevalence of 0.5–1% of the population; 25–30% of epileptics have seizures more than once per month. Epileptic seizures can be focal or partial seizures arising from one hemisphere (simple, complex, partial onset with generalization) and, generalized seizures arising over both hemispheres which can be inhibitory (absence, atonic) or excitatory (myoclonic, clonic, tonic). Lamotrigine and carbamazepine are drugs of choice in focal epilepsies, while valproate is the most effective drug for primary generalized seizures; combination therapy may be necessary in refractory cases. New generation antiepileptic drugs (AEDs) like, felbamate, vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine, oxcarbazepine, levetiracetam, pregabalin, and zonisamide are available with fewer adverse effects and drug interactions.

Anesthetic concerns in surgical patients with epilepsy

Anesthetists commonly encounter patients with epilepsy in the perioperative setting, either during epilepsy surgery or during other elective and emergency incidental surgeries. They may also be involved in airway management and administration of general anesthesia (GA) for treatment of status epilepticus (SE). The main anesthetic considerations in surgical epilepsy patients relate to the ability of anesthetics to modulate or potentiate seizure activity (proconvulsant/anticonvulsant actions), adverse effects of AEDs and their interactions with anesthetic agents and, the presence of concomitant medical problems occasionally associated with epilepsy. These factors have a significant bearing on anesthesia practice and necessitate a thorough preoperative evaluation of the epileptic patient, appropriate choice of anesthetic drugs, perioperative management of the AED therapy for maintaining seizure control particularly during periods of starvation, management of breakthrough seizures in the perioperative period and prompt treatment of SE in the operating room (OR), or postoperatively in the intensive care unit (ICU); psychogenic non-epileptic attacks can also occur in the perioperative setting while some patients may experience shivering and myoclonus during recovery from anesthesia which needs to be differentiated from epilepsy. Awareness of pharmacological properties of AEDs and potential interactions with drugs used in anesthesia and the effects of anesthetic drugs on epilepsy is thus essential for adequate perioperative management of patients with epilepsy.

Effects of anesthetic agents on epilepsy (proconvulsant and anticonvulsant actions)

Some anesthetics can produce seizures whereas others tend to stop them; most anesthetics however, exhibit both proconvulsant and anticonvulsant properties with different doses or under different physiologic situations; lower anesthetic doses are often associated with proconvulsant tendencies. Among the inhalational anesthetics, nitrous oxide (N2O) can inhibit seizure spikes which though, may manifest again on N2O withdrawal. Sevoflurane-provoked seizure-like activity has been seen in children and when sevoflurane is used in high concentrations in the presence of hypocapnea; enflurane is also reported to induce seizure activity in humans. Desflurane and isoflurane have anticonvulsant
properties and can be used in refractory SE. Opioid anesthetic agents (fentanyl, alfentanil, sufentanil, morphine) in low-to-moderate doses can cause generalized seizures in patients with epilepsy with meperidine having the strongest association with myoclonus and tonic-clonic seizure activity. The barbiturates (thiopental, methohexital, pentobarbital) and propofol are well established agents for the treatment of refractory SE; however, etomidate is reported to increase seizure duration during electroconvulsive therapy (ECT). Ketamine in low doses may facilitate seizures, but at sedative or anesthetic doses, it shows anticonvulsant properties. All benzodiazepines are potent anticonvulsants; diazepam, midazolam and lorazepam are widely used to terminate episodes of SE. Neuromuscular blocking agents do not have any apparent proconvulsant or anticonvulsant effects. A combination of anesthetic drugs with anticonvulsant or no convulsion-provoking actions may thus be chosen for anesthetizing epilepsy patients presenting for incidental surgeries.

Effects of AEDs on anesthesia (drug interactions and adverse effects)

The pharmacokinetic and pharmacodynamics interactions between AEDs and commonly used anesthetic drugs can affect drug efficacy and the risk of intraoperative seizure activity. The induction and inhibition of the cytochrome P450 isoenzymes in hepatic metabolism is the most significant mechanism of drug interactions involving AEDs. Many older-generation AEDs (carbamazepine, phenytoin, phenobarbital, primidone) have an increased potential for interactions with anesthetic agents and adverse effects secondary to potent enzyme-inducing properties, leading to a decreased plasma concentration of many medications including immunosuppressants, antibacterials and cardiovascular drugs, particularly amiodarone, b-blockers (propranolol, metoprolol), and calcium channel antagonists (nifedipine, felodipine, nimodipine, and verapamil). In patients taking warfarin, introduction or withdrawal of enzyme-inducing AEDs requires close monitoring of the international normalized ratio (INR). The newer AEDs have decreased drug interactions and greater safety. Oxcarbazepine and eslicarbazepine are weaker inducers of hepatic microsomal enzymes while topiramate induces the hepatic enzymes in a dose-dependent manner. AEDs which produce sedation or inhibit metabolizing enzymes will decrease the anesthetic drug doses; Valproate is an inhibitor of hepatic microsomal enzyme systems and may reduce the clearance of many concurrently administered medications, including other AEDs. Gabapentin, lamotrigine, levetiracetam, tiagabine and vigabatrin do not induce hepatic enzymes. Macrolide antibiotics, particularly erythromycin, are potent inhibitors of CYP3A4, which is involved in carbamazepine metabolism and can lead to carbamazepine toxicity. Concomitant use of carbapenem antibiotics can lead to a significant decrease in serum valproate concentrations. Patients receiving enzyme-inducing AEDs such as phenytoin, carbamazepine and phenobarbital have resistance to the effects of neuromuscular-blocking agents and also require higher doses of fentanyl to maintain a comparable depth of anesthesia.

The adverse effects reported with the use of AEDs include multi-system derangement, hypersensitivity reactions, anemia, platelet dysfunction, behavior disorders, osteoporosis, weight alterations etc. Patients with impaired liver function may show early signs of toxicity with the use of phenytoin. Phenytoin, valproate, or phenobarbital therapy may contribute to the development of post-halothane hepatitis; drugs with significant hepatic or hematologic toxicity also impact the anesthetic management.

Certain medical problems have been associated with epilepsy which should be evaluated and treated where possible preoperatively. Most common disorders are psychiatric problems like neuroses or psychoses and the less common are tuberous sclerosis and neurofibromatosis.
Perioperative management of AEDs in epilepsy patients

Perioperative disruption of antiepileptic medication should be avoided; regular medications should be taken on the morning of surgery and regular dosing re-established as early as possible after surgery. If multiple doses are likely to be missed, AEDs should be administered by the parenteral route. Intravenous (IV) phenytoin, sodium valproate and levetiracetam are available and carbamazepine is available as a suppository; neurologist advice regarding alternative drugs to cover the perioperative period should be sought. Routine drug level monitoring is not required perioperatively however, a prolonged ICU stay with attendant changes in serum pH and albumin levels and use of drugs and antibiotics that interact with AEDs, the serum concentrations of AEDs may be affected, and hence, daily checking of serum concentrations of phenytoin to guide dosing is advocated in the ICU.

Anesthetic management of status epilepticus

SE is defined as more than 30 min of continuous seizure activity or, two or more sequential seizures without full recovery of consciousness between seizures. A seizure that continues for more than 5 min has a low chance of terminating spontaneously. Uncontrolled SE for 20 min or longer even with neuromuscular blockade is associated with neuronal damage. Hence seizures should be treated with emergency AEDs and, if refractory, induction of anesthesia maybe required. SE can produce many systemic abnormalities directly concerning the anesthesiologists like airway and gas exchange compromise, increased risk of aspiration pneumonitis, neurogenic pulmonary edema, hypoxemia, hypercarbia, initial hypertension followed by hypotension, bradyarrhythmias, tachyarrhythmias, cardiac arrest, hypoglycemia followed by hyperglycemia, renal dysfunction due to rhabdomyolysis, traumatic injuries to the body and, metabolic abnormalities like acidosis, hyperkalemia, hypoglycemia and hyponatremia. Treatment with benzodiazepines (preferably lorazepam 0.1 mg/ kg or 4–8 mg IV bolus, repeated) should be started as soon as it is apparent that the seizure is not self-terminating within 2 min. In the early stage (5-10 min), supportive management is initiated with airway protection and supplemental oxygen. For established seizures (5-30 min), administration of phenytoin (15–18 mg/ kg loading dose given at 50 mg/ min) or phenobarbital (10–15 mg/ kg given at 100 mg/ min) or sodium valproate (25 mg/ kg over 30 min, then 100 mg/ h for 24 h) or levetiracetam (2000–3000 mg/ day) is advocated. If the SE becomes refractory (30-60 min), general anesthesia should be induced and maintained with thiopental (100–250 mg IV bolus, then 50 mg increments until seizures are controlled, then 3–5 mg/ kg/ h; infusion doses titrated to EEG burst suppression), midazolam (0.1–0.3 mg/ kg bolus then 0.05–0.4 mg/ kg/ h infusion), or propofol (2 mg/ kg IV bolus, then 5–10 mg/ kg/ h). Maximal therapy should be maintained until 12–24 h after the last clinical or electrographic seizure, after which the dose should be tapered. If seizures recur, therapy can be re-instituted or altered. Ketamine (0.4- 7.5 mg/ kg/ h) can be effective in cases of SE refractory to other agents however, the risk of ketamine-related neurotoxicity needs to be considered; opioids should be avoided in SE. In patients who do not respond to IV anesthetics, inhalation agents, such as 1.2–5% isoflurane and desflurane have been shown to cause effective EEG burst suppression.

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Anesthetic concern for seizure surgery

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Introduction

Epilepsy surgery is one of the therapeutic options for patients with refractory epilepsy. Initially started as an option in patients with drug resistant epilepsy, the spectrum of epilepsy surgery has expanded and includes other patient groups also. The most important aspect of the epilepsy surgery for the neurologist and neurosurgeons is pre-surgical evaluation to assess the localization of the epileptic focus. However, for the anesthesiologist the focus in a patient with epilepsy for surgery is to understand the effects of anesthetic drugs on the intra-operative monitoring and the drug interactions of anti-epileptics with anesthetic agents.

Indications for epilepsy surgery:

Following are some of the indications for performing epilepsy surgery.

1. Drug resistant epilepsy (defines as poor control of seizures despite full dose of two anti-epileptic drugs or following polytherapy)
2. Frequent seizures (one per month) incapacitating the normal life in an active individual
3. MRI documented lesions as a cause of epilepsy like cavernoma, tumors etc.
4. Video electroencephalogram (VEEG) documented localization of seizures in a particular area of brain
5. Epileptic syndromes like tuberous sclerosis, pediatric epilepsy etc.

Pre-surgical evaluation of epilepsy patients

It is important to identify the patients who are eligible for epilepsy surgery. The purpose is to delineate the epileptogenic zone, defined as "the area of cortex indispensable to the generation of epileptic seizures" and resect the area to achieve seizure freedom. In addition there are few other zones; irritative zone where interictal spikes occur; symptomatic zone, which is the zone where symptomatology falls and a functional zone, where normal functional areas of the brain exists near the epileptogenic zone. It is important to identify each of the zone to achieve maximum resection without affecting the function. Patients are evaluated by a combined team of neurologist, neurosurgeons, radiologist and neuropsychologist. In case of children with epilepsy and uncooperative patients, anesthesiologist is also involved in helping the other team members to conduct various tests to confirm and localize the epileptogenic focus. Though the primary evaluation of the patients is a thorough clinical examination, it is mandatory to locate the epileptic zone by a variety of investigation.

A) Video EEG: Video EEG is helpful in localizing the ictal and inter-ictal zones and helps in correlating with the symptomatic zones. Video EEG consists of recording scalp EEGs with video monitoring of patients for clinical seizures. If the diagnosis cannot be obtained with routine video EEG, additional provocative measures can be used like medication reduction, sleep deprivation, photic stimulation or hyperventilation.

B) Invasive EEG: If the video EEG fails to give adequate information regarding the seizure localization, invasive EEG is used. Invasive electrodes can be a depth electrode or strip electrode or grid electrode. Placement of invasive electrode is done in the
operation theater under general anesthesia and the standard general anesthesia with endotracheal intubation is used in our hospital. Following the electrode placement the patients are monitored in the epilepsy monitoring unit for almost a week. It is important that strict asepsis is maintained during the procedure as infections can be dangerous complications.

C) Magnetic Resonance Imaging: MRI forms the mainstay in the diagnosis of structural abnormality like medial temporal sclerosis, focal cortical dysphasia (FCD), tumors like low grade glioma, cavernous etc. The diagnosis is usually achieved using different MRI sequences using a 1.5 tesla unit. In addition functional MRI is also being done to assess the location of functional areas of brain with respect to epileptogenic zone. If there is no obvious structural abnormality then the planning for epilepsy surgery is based on the video EEG or if the video EEG is inconclusive, invasive EEG monitoring needs to be performed.

D) Functional MRI: If the lesion or the epileptic zones like close to eloquent areas of the brain functional MRI (fMRI) is mainly used to delineate for identifying areas of eloquent cortex, including motor, sensory, language, and memory areas from the lesion. It also helps in planning the type of anesthesia that needs to be administer like awake craniotomy or general anesthesia.

E) Other modalities like positron emission tomography (PET) and single photon emission computed tomography (SPECT) can be used to identify the epileptic zone from normal brain. However the limitation is lack of widespread availability of equipment and the higher cost of the procedure.

A) Neuropsychological tests: Neuropsychological tests are done for language, memory and cognitive functions to identify the degree of peroperative dysfunction and to localize the dominant hemisphere.

WADA test: WADA test once used most frequently in the preoperative evaluation for testing memory and language of epilepsy patients has now been replaced with functional MRI and neuropsychological tests. WADA test was performed using selective injection of amobarbital into the middle cerebral artery. Lack of availability of amobarbital (25 mg/ml) has led to use of propofol (1mg/ml) as a drug of choice for testing. However in children our center still perform WADA test under monitored anesthesia care using propofol or dexmetidomidine. We prefer propofol because of rapid awakening between the test and better patient cooperation.

Pre operative anesthetic evaluation

Pre-operative evaluation of the patient is very important in the evaluation of epilepsy patients. Majority of the patients are young and without comorbidities. Some of them may have associated congenital defects like Down's syndrome where thorough evaluation. However children may suffer from recurrent respiratory infections which need to be evaluated before surgery. It is important to understand the anti-epileptic drugs the patients are on as they can cause bone marrow suppression, coagulation alterations, and altered liver and renal functions. It is important to have complete hemogram, liver, renal function test and coagulation test before surgery. Though airway related problems like difficult intubation are less in epilepsy patients in our experience, occasional patients with Downs or Lennox gastaut syndromes who are generally obese can pose problems.

Anesthetic management

The anesthetic management of the patients depends on the type of intraoperative monitoring, location of the lesion, age and cooperation of the patients. Discussion about the type of anesthesia administered should be made with the neurologist and neurosurgeons. Accordingly the anesthesiologist can choose one of the following methods.
a) **General anesthesia with endotracheal intubation**: General anesthesia is usually administered in patients with temporal lobe epilepsy where the eloquent areas are usually spared, lesions like low grade gliomas, well defined dysplasia or gliosis, when the resection involves positioning in prone position, in uncooperative patients, higher ASA grade patients, extra temporal surgery like callosotomy, hemispherotomy. Anesthetic induction in our institute is usually done with thiopentone or propofol, fentanyl and vecuronium is used as muscle relaxant. In addition to routine monitoring, it is important to monitor the neuromuscular blockade as these patients are on multiple antiepileptic drugs some of them are enzyme inducers and there can be resistance to muscle relaxants. Maintenance of anesthesia is done with 1 MAC of sevoflurane inhalation accompanied with infusion of fentanyl and vecuronium. Patients are ventilated in controlled mode with target PaCO2 of 33-35 mmHg. Administration of osmotic diuretic is not needed unless the surgeon request for it. Bispectral index can also be monitored if intraoperative ECoG is planned. Too deep anesthesia can interfere with ECoG recordings and the level of anesthesia can be adjusted to 55-65 during recordings. At the end of surgery patients are usually administered reversal for neuromuscular agents and once the criteria for extubation is achieved, the endotracheal tube is removed. Postoperatively analgesia can be administered as per institute protocol. Postoperatively the patients should be monitored for seizure, neurological deficit in the intensive care for 24 hours. Routine anti-epileptic medications the patient is taking regularly are given two hours post-surgery. If an uncontrolled seizure occurs in the postoperative period either IV valproate, levitiracetam or benzodiazepine like midazolam or lorazepam can be administered.

b) **Awake craniotomy**: Awake craniotomy is used when the lesion (epileptic foci or tumors) are located close to the eloquent areas of brain. The advantages of awake craniotomy include achieving maximum resection of the lesion with the preservation of brain function. The common anaesthetic techniques used for awake craniotomy are sedation only (monitored anesthesia care-MAC) or general anaesthesia, and awakening the patient for cortical mapping and resection, with the option of re-anaesthetizing for closure (asleep-awake-asleep technique). For both the techniques preoperative psychological preparation of the patient is important. With good counselling many of the patients will agree for undergoing the surgical procedure in awake state. Patient refusal, inability to cooperate are contraindications for awake craniotomy.

**Monitored anesthesia care for Awake Craniotomy**

Patients are given standard fasting protocols. Premedication is usually avoided. In apprehensive patients drugs like tab clonidine can be administered orally as it produces sedation and hemodynamic stability. Benzodiazepines are avoided for premedication. Patients are given anti emetic prophylaxis. In the operation room patients are allowed to position themselves comfortably. Shivering can be problematic and the OT temperature needs to be adjusted along with the warming blankets. Patients are connected to standard monitoring. Intravenous line and arterial cannulation is done under local anesthesia. Some centers avoid urinary catheter; in our center patient’s bladder is routinely catheterized. Sedation consists of infusion of propofol 75 to 100 mic /kg/hr and fentanyl 1 mics /kg/hr. Bispectral index monitoring is used in our center. Oxygen by nasal cannula or by mask with facility for end tidal carbon di oxide monitoring is employed in our institute. Once the patients are adequately sedated, scalp block with 0.25% to 0.5% bupivacaine in adrenaline (1:200000) is administered. Once adequate block is achieved skull pin insertion is done. In addition to the scalp block local
infiltration is done at pin site, incision and over dura if patients feel pain or discomfort during making of burr hole. If the patient complains of pain during procedure additional bolus doses of fentanyl are administered. Intraoperative complications include pain, uncooperative patient, airway obstruction, full brain, seizures especially if motor cortex stimulation is used. General anesthesia may be resorted if patients become uncooperative or airway obstruction is not relieved with corrective measures. Full brain is treated with mannitol or diuretics. Seizures can be terminated with IV phenytoin or propofol and cold instillation of saline over brain by the surgeon. IV paracetamol can be used for intraoperative as well as postoperative supplemental analgesia. At the end of the procedure patients are shifted to intensive care unit and watched for postoperative problems.

Asleep–awake–asleep technique: This technique is more challenging than the above technique. The procedure consists of administration of general anesthesia with either laryngeal mask airway or endotracheal intubation from the beginning till the time of testing of neurological function, marking the eloquent areas and resection of lesion, followed by reintroduction of general anesthesia. Once the dura is opened the anesthesia is stopped, the patients are extubated. Neuromonitoring and resection of the lesion is performed. General anesthesia is induced and LMA or endotracheal tube is reinserted till completion of the procedure. The advantages are patient comfort during painful phase of incision, shortened time interval, prevention of full brain by hyperventilation if needed, and adequate time available for surgeon for resection and achieving hemostasis.

Intraoperative electrocorticogram: (EoCG) Intraoperative ECoG forms a major monitoring during epilepsy surgery. It is important for the anesthesiologist to be familiar with the procedure and the effect of different drugs on the intraoperative ECoG. Intraoperative ECoG is performed by the placement of a special electrode array using strips, grid, and/or depth electrodes directly on the surface or within the substance of the brain. The monitoring consists of recording the ictal and inter ictal activity (IEA). The ictal waves are usually sharp waves; however they are difficult to obtain intraoperatively. Interictal waves are spontaneous epileptiform activity which consists of spikes, polyspikes, sharp waves, spikes-and-waves, sharp-and-slow wave complexes, and/or any combination. Inter ictal spikes are used for localization of epileptic zone intraoperatively. Though awake craniotomy is ideal for recording intraoperative ECoG, many times it may not be possible. The anesthetic agents as well as their doses can interfere in the intraoperative monitoring.

Among the inhalational agents sevoflurane and enflurane produces or enhances the epileptogenic activity whereas other agents suppresses the activity. Nitrous oxide more than 50% also suppresses the epileptiform activity. Propofol can activate or suppress IEA, Methohexital and etomidate can produce seizures. Dexmedetomidine has minimal effect on IEA. High doses of opioids like fentanyl, alfentanil, sufentanil can induce IEA whereas morphine does not produce proconvulsant property. The commonly employed methods for getting a good IEA are reducing/ stopping of volatile anesthetic agents, administration of proconvulsants like alfentanil or methohexital.

Fluids and Blood loss in epilepsy surgery; Routine Intraoperative fluid management consists of use of crystalloids. Osmotic agents are not administered in epilepsy surgery unless full brain interferes in surgical resection. Majority can be managed with hyperventilation. Children presenting for epilepsy surgery poses risk of severe blood loss during resection and craniotomy. Adequate amount of cross matched blood must be available in case of severe blood loss.

Postoperative Complications: Majority of the epilepsy surgery is uncomplicated. Minor complications like
nausea, vomiting, pain can be dealt with. Severe complications can occur rarely which includes status epilepticus, intra cranial hematoma, delayed awakening in cases like hemispherotomies.

**Conclusion:**
Management of patients with epilepsy for epilepsy surgery is a team effort with involvement of multiple specialties. However, it should be borne in mind that the anesthesiologist plays a crucial role in achieving a good outcome of the patient by providing optimal condition for a successful surgery.

**Suggested readings:**


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Subarachnoid hemorrhage (SAH) continues to be a major etiology of neurological injury requiring management in the neurocritical care unit, with the majority (greater than 75%) being secondary to aneurysmal rupture. This review will concentrate on that etiology, its complications and its treatment. The prevalence of aneurysms is reportedly low in India. The incidence of SAH within India is difficult to establish clearly, but might be as high as 13% in certain circulations. Recent estimates put the incidence in the USA at 9.7 per 100,000 per year, but some projections estimate as high as 14.5% per 100,000/year. Of relatively new note is the changing ratio of female: male cases. Previously described as 1.6:1, the ratio has shifted more towards an increasing male incidence at 1.24. The morbidity and mortality remain significant with 12-15% of patients dying before hospitalization, and 25% dying within the first 48 hours. The anatomic and perfusion-related consequences of the initial hemorrhage are the primary causes of death, followed by repetition or aggravation due to rebleeding.

Subsequent morbidity and death is attributable to neurologic deficits due to ischemia, but appearing over a slower time course.

Pathophysiology of the disease is still imperfectly understood but appears to involve wall shear stress with consequent endothelial injury and subsequent remodeling, modified by varying degrees of genetic predisposition to oxidative stress and endothelial degeneration, as well as local and systemic hemodynamic forces, which in turn are affected by the local anatomy.

Methods for primary treatment of the aneurysm remain controversial in the context of increasing frequency and sophistication of endovascular occlusion techniques with detachable coils and stents — many US vascular neurosurgeons still advocate surgical clipping of certain aneurysmal types and within certain patient populations, while European practice leans more towards coiling in most cases.

**Initial Acute Management**

After presentation and diagnosis, until such time as the aneurysm is definitively controlled, the risk of rebleeding is frequently managed with pharmacological control of blood pressure (BP) on the basis that unopposed peaks may possibly disrupt the fibrin net patching the rupture site. However, the evidence for BP limitation is limited to observational studies, and is criticized by some who suggest that BP elevation is an epiphenomenon of the rebleed as opposed to a causative factor.

Nonetheless, many clinicians will empirically treat systolic BP values of greater than 160 mm Hg, or mean arterial pressure (MAP) greater than 110 mm Hg, adjusting for age and ischemic risk. It is worthwhile considering that control of pain and/or nausea may often relieve hypertension.

Another approach for control of rebleeding has been to use anti-fibrinolytics. Although these agents were previously associated with an increased incidence of stroke, their use may offer some benefit when used transiently (no longer than 72 hours) prior to clipping or coiling.

**Dysfunction as Sequelae of SAH**

**Neurologic:**

While rebleeding is the greatest initial mortality risk, once the aneurysm is secured, then subsequent poor outcome is largely due to secondary ischemia. Vasospasm of the cerebral circulation has been a long-standing source of pathology, with putative mechanisms including abnormal induction of endothelin along with nitric oxide.
scavenging. This view suggested the induction of hypertension back in the 1950’s\textsuperscript{12}, followed by the classical ‘triple-H’ therapy in the 1980’s\textsuperscript{13}. However, while there exist many anecdotal reports of improvement using the combined package of therapy, this has not been supported in randomized controlled trials or meta-analysis\textsuperscript{14}. In fact, there have been suggestions of an increased complication rate associated with the use of hypervolemia\textsuperscript{14,15}. A consensus conference organized by the Neurocritical Care Society concluded that while hypovolemia is associated with a worse outcome, hypervolemia is not a valid therapeutic target and euvolemia is the preferable goal. Subsequently, augmentation of blood pressure may be accomplished by pressors or inotropes\textsuperscript{5}.

In a similar questioning approach, the role of vasospasm as the arbiter of delayed cerebral ischemia (DCI) has been held up to scrutiny, in the light of recent results from trials of Clazosentan, an endothelin antagonist. The CONSCIOUS-I & CONSCIOUS-2 trials of clazosentan demonstrated effects upon large vessel vasospasm, but did not show any beneficial effect upon morbidity, functional outcome or mortality\textsuperscript{16}. Clearly, the association between vasospasm and outcome (as marked by DCI) is not an exclusive one\textsuperscript{12}, in that a) not all vasospasm has a symptomatic or pathological cerebral consequence b) DCI can occur in the absence of radiologic vasospasm\textsuperscript{18} c) clazosentan decreases the incidence of vasospasm without an appreciable effect upon the incidence of DCI, and d) nimodipine reduces the incidence of DCI but does not have an appreciable effect upon vasospasm\textsuperscript{19}. Consequently, there is increasing interest in other mechanisms of DCI – including spreading cortical depolarization, inflammation, and cerebral thrombosis\textsuperscript{20}.

Nimodipine remains a fundamental part of most clinical strategies, achieving a modest reduction in the incidence of delayed ischemic deficit\textsuperscript{4}. Consequently, its shortage in recent months, is a significant cause of concern for future patient care. While not affecting vasospasm, it is known to possess antifibrinolytic activity\textsuperscript{21}, which may be of benefit in non-vasospasm mediated ischemia, such as inflammation-induced microthrombosis\textsuperscript{22}.

Statins are known to have effects upon endothelial activation, oxidative stress and platelet adhesion, and several early trials displayed encouraging results upon outcome\textsuperscript{23,24}, but the most recent meta-analysis did not demonstrate any effect upon DCI\textsuperscript{25}. Similar to the case of clazosentan, there may be discordance between effects on vasospasm and DCI\textsuperscript{26}. The results of an adequately powered randomized controlled trial are awaited\textsuperscript{27}.

Anemia is another controversial area - The majority of oxygen carriage is accomplished by hemoglobin, and it comes as no surprise therefore that better outcomes are associated with normal admission hemoglobin levels, and worse outcomes with lower levels\textsuperscript{28}. Transfusion however, is itself associated with adverse outcomes in this population\textsuperscript{29}, as well as an increased incidence of lung injury, which in turn worsens outcome\textsuperscript{30}. Whether transfusion from a low to a normal hemoglobin level confers the same benefit as initially having a higher level, is uncertain and there is conflicting evidence to argue either case\textsuperscript{31}. A properly conducted randomized controlled trial is badly needed, as there is significant variability of practice\textsuperscript{32}.

Cardiac:

Hemodynamic instability may present at the time of aneurysmal rupture, manifesting as arrhythmia\textsuperscript{33}, myocardial stunning\textsuperscript{34} or both and subsequently compromise both initial and subsequent therapy\textsuperscript{35}. The patient who exhibits a low/normal blood pressure values on admission, despite having the ‘worst headache of life’ may have occult cardiac stunning and should be investigated\textsuperscript{36}. Up to 32% of patients will have abnormal perfusion scans independent of history or condition\textsuperscript{37}, while up to 18% have abnormal echocardiography\textsuperscript{38} – usually associated with symmetric T wave inversion and QTc prolongation\textsuperscript{37}. Troponins are elevated in up
to 20% of cases suggesting at least some incidence of strain, and may be associated with increased hemorrhage, and worse outcomes. If the peak troponin I value is greater than 1.0 mcg/L, there is a 65% incidence of regional wall motion abnormality. It should also be noted that there is some degree of crossover between the risk factors for SAH and atherosclerotic myocardial infarction (MI) – while rare, the stress of SAH may also induce a MI if the patient has background coronary artery disease.

There is an interesting incidence of adrenoreceptor polymorphism in patients with SAH associated myocardial stunning, leading to increased expression of, and sensitivities to, catecholamines with a consequently elevated risk of injury and dysfunction. Whether that would aid diagnostic clarity or merely document after the fact, remains to be seen.

Consequently patients with suspected stunning may require aggressive investigation, monitoring and support, with echocardiography, cardiac output monitoring and titrated inotropes. Dobutamine titrated to an appropriately targeted cardiac index, with maintenance of pressure by norepinephrine, is the authors recommended choice.

**Pulmonary:**

Acute lung injury and other pulmonary complications are not infrequent after subarachnoid hemorrhage, with an incidence of 20-27%. Impairment of oxygenation has been estimated to occur in 80% of patients. Possible etiologies range through neurogenic edema associated with myocardial stunning, cerebral cytokine production, transfusion associated lung injury, fluid overload associated with Triple H therapy for vasospasm – or any combination thereof.

Care strategies should start with avoidance/limitation of precipitating factors, especially with respect to fluid loading. The goal should be euvolemia. In cases of established pulmonary compromise, positive pressure ventilation (IPPV) and end-expiratory pressure permit re-recruitment of previous atelectatic segments, with improved oxygenation and ventilation, and a reduction in venous return that may mitigate pump failure. However, at the same time, care should be taken to adhere to goals of cerebral perfusion and avoid cerebral ischemia. Consequently, cardiac output monitoring may be required for titration of inotropic support of blood pressure goals and volume status.

**Endocrinological & Metabolic:**

**Electrolyte abnormalities**

Hyponatremia is the commonest electrolyte abnormality in patients after SAH, with a frequency of between 30-40%. While the Syndrome of Inappropriate Secretion of ADH (SIADH) is the commonest cause in the general population, this should be accompanied by fluid retention and no loss of circulating volume. However, in the authors experience and that of others, most hyponatremic patients are fluid depleted, which is more in keeping with Cerebral Salt Wasting Syndrome (CSWS). The etiology is an increased secretion of ‘B’ natriuretic peptide, which may be produced by both brain and left ventricle. The site of production in SAH is uncertain.

The onset of CSWS may prelude vasospasm by around 24 hours. However, there is an even stronger association with patients who go onto experience DCI in the absence of vasospasm –suggesting again an alternative etiology of DCI, while confirming the association between hyponatremia and infarction. Treatment strategies involve maintenance of fluid volumes, while avoiding free water in favor of electrolyte containing fluids. Fludrocortisone has been shown to retain sodium in CSWS and treat hyponatremia. Other than that, there is no evidence to support the use of steroids in SAH. Even if SIADH cannot be ruled out, the safer course is to replace volume with sodium containing fluids as opposed to fluid restriction. The use of vasopressin antagonists to treat hyponatremia in SAH is not advised.
Hyperglycemia is a well-recognized risk factor for poor outcomes in SAH. There are however, worse outcomes associated with aggressive glycemic control in patients with SAH.

**Metabolic Abnormalities**

Nutrition is a frequently overlooked aspect of care that does have significance in subarachnoid hemorrhage. These patients experience a hypermetabolic state similar to that of injury and sepsis, with consequent catabolism. Despite starting enteral nutrition within 48 hours, a recent study demonstrated a negative energy balance of up to \(-117 \pm 53\) kcal/kg in the first week. Given the acute presentation, consequent investigations, possible airway interventions, along with headache, anorexia, nausea and vomiting, catabolism may be compounded by inadequate intake, and a resulting negative nitrogen balance of up to \(-9.2+/-4.1\) g/day has been described. The energy deficit has been significantly associated with an increased frequency of infective complications. Whether aggressive feeding will ameliorate this remains to be proven, but certainly it seems intuitive that ineffective feeding risks hypoalbuminemia, which may increase the risk of hypovolemia.

**Outcomes:**

There have been definite gains in mortality and morbidity over the last few decades as pathophysiological insights and sophistication of therapies have progressed. Nonetheless, patient perceptions may differ from ours. Buchanan investigated patients between 12-30 months after surgery, who were classed by neurosurgeons as displaying a good or moderate recovery, and contrasted those findings with the perceptions of both patients and relatives. 50% of the cohort remained on disability or assistance with less than 15% returning to the same level of work. Of note, ‘26% of the relatives and 28% of the patients reported having thought that death would have been preferable to the quality of outcome experienced at the time of assessment.’

This sobering perspective requires us to continually examine every possible nuance of care that can be improved upon, so as to realize the best possible patient outcomes in what remains a burdensome and morbid disease.

**References**

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Clinical Neuromonitoring

Clinical deterioration is often the first sign of a secondary insult such as a rise in intracranial pressure (ICP) or developing intracerebral hematoma. Therefore repeated standardized neurological assessments are indispensable particularly if the neurological status needs to be compared to earlier assessments. The most widely used score is the Glasgow Coma Scale (GCS). Of the three components the motor component is considered to be the most important in regard to outcome after head injury. Recently, a new coma scale has been introduced: the Full Outline of UnResponsiveness (FOUR-Score) [1]. It addresses some of the shortcomings of the GCS by including brainstem reflexes and respiration, allowing detection of subtle neurological changes and, thus, further classification of deeply comatose patients.

Intracranial pressure and cerebral perfusion pressure monitoring

ICP is an important treatment endpoint and also used to calculate cerebral perfusion pressure (CPP), i.e. the pressure gradient across the cerebral vascular bed defined as the difference between mean arterial pressure (MAP) and ICP (CPP = MAP - ICP).

The gold standard for assessing ICP is an intraventricular drain inserted into one of the lateral ventricles and connected to an external pressure transducer.[2] The foramen of Monro or for clinical purposes the external auditory meatus is the reference point for zeroing the transducer. As patients are nursed in a 20° – 30° head up position the zero for arterial pressure should be set at the same height to calculate CPP correctly. In addition to monitoring pressure, intraventricular catheters allow withdrawal of CSF to treat raised ICP. The main problem of intraventricular catheters is the risk of infection that increases over time and may reach 20%. Alternatively, intraparenchymal probes are used. The infection rate of these probes is very low. Pressure measured in the lumbar CSF space is not a reliable estimator of ICP and such measurements may be dangerous in patients with space occupying lesions. ICP cannot be assumed to be evenly distributed in many pathological states. With a ventricular catheter, uniformly distributed ICP will only be observed when CSF circulates freely between all its natural pools. An intraparenchymal probe measures local pressure that can be compartmentalized and is not necessarily identical with intraventricular pressure. Significant pressure gradients may exist in patients with intracranial hypertension.

The benefit of ICP monitoring has never been documented in a randomized controlled trial. An observational study has suggested that a CPP/ICP oriented therapy will increase treatment intensity and respirator days without an improvement in outcome.[3] Nevertheless, based on the available evidence the guidelines of the Brain Trauma Foundation conclude that ICP data are useful for guiding therapy.[4] ICP monitoring is recommended in salvageable patients with a GCS of 3-8 and an abnormal CT defined as a scan showing hematomas, contusions, swelling, herniation or compressed basal cisterns. ICP monitoring is also recommended in patients with a GCS of 3-8 and a normal CT scan provided at least two of the following criteria are fulfilled at admission: age > 40 years, unilateral or bilateral motor posturing or systolic blood pressure < 90 mm Hg.[4] Some clinicians will choose to adapt these recommendations and e.g. monitor patients with a GCS > 8 if they will undergo major non cranial surgery soon after admission. In other neurocritical care patients the indications for ICP monitoring are less well defined.
Cerebral blood flow monitors

Methods for quantitative determination of CBF at the bedside based on measurements from the internal jugular vein have been developed but are rarely used. An intraparenchymal probe using thermal diffusion providing continuous quantitative real-time data for a volume of approximately 5 cm³ around the tip of the probe has been used in brain injured patients.[2]

Transcranial Doppler (TCD) is the simplest way to non-invasively obtain repeated real-time estimates of CBF. The linear relationship between CBF and (mean) flow velocity which is measured by TCD is only present if neither the diameter of the insonated vessel, nor the angle of insonation changes during the examination. In subarachnoid hemorrhage TCD is frequently used to detect and document the course of vasospasm. The sensitivity and specificity to detect macrovascular spasm is acceptable in the anterior circulation but less so in the posterior and basilar circulation.[8] However, there is no significant correlation between outcome and TCD velocities.[9] Possibly this is due to the fact that after subarachnoid hemorrhage delayed ischemic neurological deficits are caused by macro- and microvascular vasospasm; the latter is not detected by TCD.

There is no convincing evidence that a strategy that attempts to manipulate CBF is superior to an approach using ICP or CPP to guide treatment. CBF monitoring is an option with unclear clinical benefit only.[10]

Cerebral oxygenation monitoring

Due to the difficulties associated with CBF monitoring and treatment thresholds the focus of interest has shifted to monitoring cerebral oxygenation. Ideally, changes in oxygen extraction fraction should be monitored. Such a monitor is not available but surrogate markers can be monitored.

6.1.4.1. Jugular bulb oxymetry

The placement of a catheter in the jugular bulb allows sampling of blood that almost exclusively drains from the intracranial circulation. Jugular bulb saturation (SJO₂) is measured either from blood which is sampled intermittently from such a catheter or continuously by a fiberoptic catheter. The arterio-jugular oxygen content difference (AJDO₂) is calculated as the difference between the arterial and jugular oxygen content in paired blood samples. Normal values for SJO₂ range from 50 – 75%, normal values for AJDO₂ from 4 ml-100ml⁻¹ – 9 ml-100ml⁻¹.[2] Low CBF and ischemia raise oxygen extraction, decrease SJO₂ and increase AJDO₂. Hyperemia will lead to an increase in SJO₂ and a decrease AJDO₂. Jugular oxymetry provides data on global cerebral oxygen extraction or the adequacy of global CBF in relation to metabolic demand. Despite the fact that blood is usually sampled from one jugular bulb only, it is assumed that the values relate to global CBF rather than hemispherical CBF. However, typically only two thirds of the sampled blood is drained from the ipsilateral hemisphere and there is a large interindividual variability of venous drainage of the brain. Therefore, methods relying on blood sampling from one of the jugular bulbs are prone to the influence of asymmetry of cerebral venous drainage. It is impossible to predict which side in a specific patient will give more important data, and there is no consensus on which side should be cannulated. Generally, the right internal jugular vein is preferred because it often is the dominant vessel. Alternatively, the side with the larger jugular foramen on the CT scan can be used or the side on which a compression of the jugular vein causes a greater increase in ICP. The catheter tip should lie at the level of the first or second cervical vertebral body, i.e. above the point at which the jugular vein receives its first extracranial tributary, the facial vein. If samples are withdrawn too quickly (>2 ml·min⁻¹) falsely elevated values may be found because of retrograde aspiration of extracranial blood. [2] Too low and too high SJO₂ are associated with poor outcome. However, the question whether treatment directed at restoring normal SJO₂ improves outcome is unanswered. [4] This may also be due to the fact that sensitivity of SJO₂ to detect regional ischemia is low. [11]
Brain tissue oxygenation ($P_{btO_2}$)

$P_{btO_2}$ is the partial pressure of oxygen in the extra-cellular fluid of the brain and represents the balance between oxygen delivery and consumption.\[12\] Transiently increasing the FiO$_2$ and observing the corresponding $P_{btO_2}$ increase, is advised to exclude the presence of surrounding micro-hemorrhages or sensor damage at insertion. An equilibration time of up to a half hour is required before readings are stable. Most units use a threshold of 15 mmHg below which therapy is initiated. $P_{btO_2}$ sensors are extremely localized, with a sampling zone of only 15 - 22 mm$^2$. Accordingly, the position of the sensor is critical for the interpretation of the measurements. In ‘tissue at risk’ regions near focal pathology, global assumptions cannot be made and the monitor is purely focal, but when positioned in areas of seemingly normal tissue, or in areas of diffuse injury, the $P_{btO_2}$ can be regarded as an indicator of global oxygenation.\[12\] $P_{btO_2}$ measurements may contribute to the prevention of secondary injury after traumatic brain injury and may allow adapting therapy to the specific needs of an individual patient by observing changes due to interventions such as CPP manipulation or hyperventilation.\[4\]

Near Infra Red Spectroscopy (NIRS)

This technique makes use of the fact that biological material, including the skull, is relatively transparent to light in the near-infrared range. The absorption and scatter of such light allows assessment of cerebral changes in oxyhemoglobin, deoxyhemoglobin and cytochrome oxidase. Detection of transmitted light at two or more different distances from the light-emitting optodes, so called spatially resolved spectroscopy, allows monitoring of the ratio of absolute oxyhemoglobin concentration to total hemoglobin concentration i.e. the hemoglobin saturation, called ‘tissue oxygenation index’ (TOI) or ‘regional oxygen saturation’ (rSO$_2$).\[13\] This value is a surrogate marker of cerebral venous saturation and hence oxygen extraction. Newer devices have been shown to have a good specificity and sensitivity for intracranial changes.\[14\] However, the precise location and size of the monitored brain volume remains unclear. Despite the advantage of being non-invasive and recent data suggesting that NIRS may also allow non-invasive monitoring of cerebral blood volume and cerebrovascular autoregulation, this technology has yet to find its place in the management of neurocritical care patients.

Cerebral biochemistry

Microdialysis allows detection of biochemical changes associated with hypoxia and or ischemia. A dialysis catheter (Ø 0.9 mm) is introduced into the brain parenchyma. A commercially available analyzer allows monitoring at the bedside with an acceptable time delay between sampling and analysis. Cerebral extracellular levels of glucose, glutamate, lactate, pyruvate, and glycerol, the latter indicating loss of cellular structural integrity, are measured. The lactate-pyruvate ratio is calculated, yielding information on the brain’s redox state, a marker of mitochondrial function. The lactate-pyruvate ratio is the most widely used microdialysis variable and values $> 20 – 25$ are considered the critical threshold. There is some evidence that microdialysis has the potential to provide early warning of impending hypoxia or ischemia and neurological deterioration and high levels of this ratio have also been linked to chronic frontal atrophy after TRAUMATIC BRAIN INJURY.\[15\] However, microdialysis reflects only local tissue biochemistry and the accurate placement of the catheter is crucial. Interpretation of trend data is more important than individual values. Microdialysis is still considered a research tool. However, because of its unique ability to contribute important information about the process of secondary brain injury, microdialysis has the potential to become a key component of multi-modality monitoring in many forms of brain injury.

Electrical function monitoring: EEG and evoked potentials

The role of EEG monitoring in neurocritical care is not clearly defined. While EEG
monitoring is useful to detect non-convulsive seizures or to titrate barbiturate therapy, interpretation depends on expert knowledge. Ideally, continuous monitoring should be used. This is technically feasible but interpretation and artifacts remain a major challenge.[16] Evoked potentials, particularly SSEP’s may be used for prognostication in patients with coma following traumatic brain injury.[17]

Multi-modality monitoring

The concept of multimodality monitoring implies that combining several monitors for the detection of secondary brain insults will improve our chances of detecting relevant episodes. Despite the advantage of being able to integrate information from several monitors results may be contradictory and expert knowledge will be needed for interpretation (Figure 4). Multimodality monitoring requires specialized software allowing collecting and integrating data from the various monitors. Such software is commercially available [18] and indispensable when derived parameters such as pressure reactivity [19] or oxygen reactivity [20] are to be integrated into clinical algorithms. So far this concept has not been tested prospectively. Nevertheless, it provides a better understanding of pathophysiology after traumatic brain injury and may be a key to optimizing therapeutic targets for individual patients.

Research on usefulness of any monitoring is notoriously difficult, particularly in brain injured patients and many studies are flawed.[21] Most data regarding neuromonitoring in neurocritical care refer to patients with traumatic brain injury and even this group of patients there is no unequivocal evidence that a particular monitor has a decisive impact on outcome. For all other patient groups data are scarce and there is no evidence that monitoring improves outcome. Nevertheless, in many patients neuromonitoring has an impact on treatment strategies and may facilitate management decisions. In an individual patient the choice of the appropriate monitor(s) will depend on the precise diagnosis, the technical possibilities and the clinical experience and judgment of the involved physicians.

References


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Postoperative Pain Management after Craniotomy

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Craniotomy is a common operative procedure in neurosurgical practice. It involves opening a window in the bony cranium to allow surgical access to the intracranial content. It is the most commonly performed surgical procedure for removal of brain tumor, evacuation of blood clot (hematoma) following traumatic brain injury, control of hemorrhage from an aneurysm, repair of arterio-venous malformations, drainage of brain abscess and to perform a biopsy to confirm the diagnosis.

The brain parenchyma is believed to lack pain sensation. This concept of insensate brain has led to a widespread perception that craniotomy patients experience minimum post-operative pain, and therefore their analgesia received little attention in the past. Subsequently, several reports have challenged this belief and suggested that patients experience pain following craniotomy. However, in reality 70-90% patients experience post-craniotomy pain or headache in the immediate post surgical period. In craniotomy, pain sensitive structures involved are skin, extracranial muscle, fascia, periosteum, meningeal covering, venous sinuses, arteries and falx cerebri. The scalp is richly innervated by several nerves such as supra trochlear, supra orbital, auriculo-temporal divisions of trigeminal nerves and posterior auricular branches of the greater auricular nerve, lesser occipital, greater occipital, and third occipital nerves from C2–C3 nerves.

Post-craniotomy pain is somatic rather than visceral in origin, with possible involvement of pericranial muscles and soft tissues and pain appears to be particularly intense when extensive muscle dissection or infra-tentorial approaches are used. The pain experienced is predominantly superficial in nature and more than 60% of patients experience moderate to severe pain in first 48 hours after craniotomy.

Craniotomy can also lead to the development of chronic pain, reported incidence is as high as 34%. Out of various factors responsible for development of chronic pain after craniotomy, intensity of pain during the acute postoperative period is one of the most common factor. Therefore, adequate pain control is an important aspect in the management of craniotomy patients.

The meningeal inflammation or fibrosis, nerve entrapment or compression and fibrosis of cranial muscles contribute to the pathogenesis of the post-operative pain. Though post operative analgesia after craniotomy is a neglected topic, various drugs and techniques have been tried to control post operative headache after craniotomy.

The methods of post-craniotomy pain control include:
1. Medical management by various drugs used through intramuscular or intravenous route.
2. Scalp infiltration with local anaesthetic agents
3. Scalp block with local anaesthetics
4. Adding adjuvants to local anaesthetics in Scalp infiltration/Scalp block

1. MEDICAL MANAGEMENT IN OF POST-CRANIOTOMY PAIN:
Various drugs like paracetamol, tramadol, nalbuphine, non steroidal anti inflammatory drugs (NSAIDS) and opioids have been used to control post-craniotomy pain with inadequate pain control and various side effects. Acetaminophen 30mg/kg at 1hr before surgery and 6 hourly after surgery alone was found not sufficient to provide adequate postoperative pain after supratentorial craniotomy. Non Steroidal Anti Inflammatory Drugs (NSAIDS) is a
commonly used drug for postoperative analgesia but in neurosurgery it was found to be the most common associated factor in development of postoperative hematoma. Intravenous parecoxib has been tried to control post-craniotomy pain and found to be of no clinical benefit.

2. SCALP INFILTRATION WITH LOCAL ANAESTHETIC AGENT-

Scalp infiltration i.e infiltration around craniotomy incision with local anaesthetics has been tried as a way to provide pain relief after craniotomy and reduce the side effects of intravenous medications. In a randomized double-blind study, Bloomfield et al infiltrated the scalp with 0.25% bupivacaine or saline coupled with epinephrine both before incision and after scalp closure. They observed that wound infiltration with local anaesthetics significantly decreases pain scores as compared to control group. Biswas et al conducted a prospective double blind randomized and placebo-controlled trial showed that 0.25% bupivacaine pre-incision scalp infiltration delayed requirement of rescue analgesic diclofenac for 105 minutes (30-720 minutes) compared with 60 minutes (15-720 minutes) in the intravenous fentanyl group. Thus simple infiltration of craniotomy incision site, helps in management of postcraniotomy pain.

3. SCALP BLOCK WITH LOCAL ANAESTHETIC AGENT:

As scalp is richly innervated by several nerves such as supra trochlear, supra orbital, auriculo-temporal divisions of trigeminal nerves and posterior auricular branches of the greater auricular nerve, lesser occipital, greater occipital, and third occipital nerves from C2 –C3 nerves, scalp nerve block provide adequate analgesia. It is an alternative technique and a major step in local anaesthesia of the scalp. In 1986 Grivin et al described scalp block for awake craniotomy for the first time, but the procedure did not gain popularity. Rubial et al in 1992 administered scalp block in 34 patients with intracranial tumors undergoing craniotomy and gave an idea that blocking of the nerve supplying the scalp may be beneficial in achieving hemodynamic stability during craniotomy. Nguyen et al performed a prospective double-blind randomized study in 30 patients receiving a scalp block with 0.75% ropivacaine or saline. The “scalp block” involved blockade of the supraorbital, supratrochlear, auriculotemporal, great auricular, and greater and lesser occipital nerves as described by Pinosky et al after skin closure and before awakening. Pain was assessed at 4 hours and up to 48 hours postoperatively. They reported that scalp block with ropivacaine decreased the average pain scores and also increased the duration of analgesia till 48 hrs postoperatively.

4. ADDITION OF ADJUVANTS TO LOCAL ANAESTHETIC AGENT USED FOR SCALP BLOCK

Bala et al compared scalp block with bupivacaine and epinephrine with control group getting normal saline. They reported that 60% of patients receiving saline injection experienced moderate to severe pain during the first 12 postoperative hours in comparison to 25% patients who received bupivacaine “scalp block”. In addition, they found that median pain scores were significantly lower in 6 hours postoperatively in patients who had received bupivacaine nerve blockade. The duration of pain relief in this study corresponded with the expected duration of action of bupivacaine with epinephrine.

A recent prospective randomized double-blinded study by Ayoub et al has suggested that the post-operative analgesia offered by scalp blocks and intravenous morphine were equivalent, but the incidence of nausea and vomiting was more frequent in the morphine group. They also observed that the delay before administration of the first dose of codeine was not statistically different between the groups.

There are several adjuvants like opioid agonists, opioid antagonist, neostigmine, dexamethasone, magnesium, hyaluronidase, tramadol and verapamil have been used with local anaesthetic solution to prolong the
peripheral nerve blockade and post operative analgesia.

Perfect anesthetic management after neurosurgery includes not only a fast recovery so that early neurological examination and complications can be detected, but also provide optimal analgesia for adequate postoperative comfort. Ideal analgesic management after neurosurgery should be efficient for controlling both acute and chronic post-craniotomy pain.

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How To Fix The Medical Literature

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Last October I attended a meeting of medical journal editors to discuss the growing body of literature that supports John Ioannidis’ conclusion that “false findings may be the majority or even the vast majority of published research claims” (PubMed ID: 16060722). Every editor at that meeting seemed to accept Ioannidis’s conclusion regarding “most” published research, and most of the editors accepted his extension to “the vast majority of published research claims.”

The underlying cause of this discouraging circumstance is that most research is driven by answers instead of being driven by questions. That is, most investigators devise a logically sound hypothesis ... but instead of testing their hypothesis, they set out to prove it. Unfortunately, they usually appear to succeed regardless of the underlying truth. After a brief description of this problem and its magnitude, we will examine an illustrative example of this phenomenon that has been ongoing for 16 years: investigations of hypothermia after head injury.

Fixing the problem of answer-driven research, and so the medical literature, hinges on the reality that published articles are the currency of both the scientific and the pseudo-scientific realm ... that is, publications are the payoff for both scientists and pseudo-scientists. And the way the process works today, when manuscripts are rejected by journals with high Impact Factors, authors submit revisions of those manuscripts to journals with lower Impact Factors until a suitably revised version is accepted for publication. As you would guess, those suitably revised versions finesse descriptions of unacceptable methodology, present deceptively tailored analyses, and even tailor the data that goes into those analyses. All of that is facilitated by the fact that more than 5,500 medical journals are ‘indexed’ by the National Library of Medicine (i.e., are pronounced to be official journals), while all of the manuscripts that actually warrant publication could be easily accommodated by fewer than 2,000 journals. As such, both the majority of investigators and the majority of journals survive by doing and publishing much research that should not have been published.

As a medical journal editor for the past 27 years (Journal of Neurosurgical Anesthesiology) I will describe a Total Transparency proposal for solving this problem: require that all submissions of all manuscripts to all indexed journals be sent through a central clearinghouse ... a clearinghouse that could be organized by the National Library of Medicine. That clearinghouse would forward each manuscript that purports to be the first submission of a new manuscript to its authors’ intended journal only after running it through modified plagiarism software to detect manuscripts that are, in fact, revisions of papers that have been previously rejected. For manuscripts that are acknowledged to have been previously submitted, the clearinghouse would require each submission to be accompanied by: 1) the manuscript’s complete submission history ... including; a) all prior versions of the manuscript, b) all prior reviews of all prior versions, and, c) all prior editorial correspondence from journals that have asked for revisions of, or have rejected, earlier versions of the manuscript; 2) for clinical trials, require a pdf copy of the trial’s registration at clinicaltrials.gov; 3) for animal experiments, require a pdf of the protocol that was approved by the authors’ Institutional Animal Care and Use Committee; and 4) as suggested 30 years ago for all investigations that present a statistical...
analysis (PMID: 6829975, cf. PMID: 23169872), require a link to all raw data, and 5) require a link in published manuscripts that would give readers access to all of the above.

If editors and reviewers could see all of the above, they could distinguish between a manuscript that should be rejected for the same reasons that it was rejected before, as distinct from a manuscript that should be considered, either because it was not competently reviewed previously, or because a boilerplate rejection letter from a journal with a higher Impact Factor suggests that the submission was rejected because it would not attract enough attention to get enough citations to maintain that journal’s high Impact Factor. This proposed clearinghouse procedure would not have been feasible twenty years ago, but now it is completely doable. My guess is that it would so improve the return on investment of research funding, and so the quality of the medical literature, that its cost would be covered many times over in short order. As such, major funding agencies would be in favor of requiring authors to submit all reports of all funded research through the clearinghouse. Soon enough, journals would want to distinguish themselves by requiring that all submissions be sent to them through the clearinghouse, and they would send all reviews and correspondence back to authors via the clearinghouse. Eventually, the library of unpublished manuscripts submitted through the clearinghouse would be sufficient to enable detection of almost all papers falsely submitted as first submissions of new manuscripts.

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Medical ethics refers to a system of moral principles that can be used to guide some aspects of medical practice. These include the identification, analysis, and resolution of moral problems that arise in patient care. There are four core principles that encompass ethical dilemmas in medical practice:

1) Autonomy: the right of a person who is of sound mind to make decisions about what happens to his/her body.
2) Beneficence: physicians should promote the health of their patients and act in a manner that is in the best interest of the patient.
3) Nonmaleficence: first, do no harm; physicians are responsible for protecting their patients from harm.
4) Justice: the distribution of medical resources should be fair.

It is important to note that these four principles serve as guidelines and are not absolute. Specifically, various ethical dilemmas occur when one or more of these guidelines are at odds with one another, forcing the physician to consider sacrificing one guideline for another in order to serve the best interest of the patient.

In addition to these four guidelines, there are two standards of conduct that may play a role in ethical dilemmas: honesty and patient dignity. These latter standards of conduct are held in higher regard than the four core principals of medical ethics, causing the physician further need to consider one principal over another.

In this lecture, I will focus on ethical issues relevant to the perioperative care of patients with neurologic disorders. The major issues addressed will be consent, futility of care, and withdrawal of care.

Informed consent, or a patient agreement to treatment based upon a clear understanding of risks, benefits, and alternatives, is a core concept in the doctor-patient relationship. The ethical dilemma generally involved with issues of consent pertains to a balance between autonomy and beneficence whereby the patient has the right to make decisions about their healthcare, but they might not always choose the course of action that the doctor thinks is best. This may cause the physician to consider whether he/she should pursue further efforts to persuade the patient to choose the physician's ideal treatment or to respect the patient's autonomy. In neurologically-compromised patients, those with a critical illness or impairment of cognitive function, or in patients with the need for emergent treatments, the recipient of care may not participate in making decisions regarding their care. This may further complicate health care decisions as these choices may need to be made by relatives or caretakers who may or may not have a clear understanding of the patient's ultimate wishes. This may be especially true in cases of accidents or unforeseen emergencies where advanced preparation had not been made. Ultimately, a physician seeking to practice these ethical tenants should carefully consider all circumstances surrounding each patient's care decision.

Physicians can face issues whereby extensive resources may be needed to maintain the care of a severely compromised patient. The prognosis for patients with severe neurologic conditions, such as severe traumatic brain injury or Hunt-Hess Grade 4 or 5 subarachnoid hemorrhage, may be poor. These patients often cannot participate in making decisions regarding their care. The physician often tries to act in a manner to
minimize further injury, improve overall outcome, and minimize risk of mortality. However, these patients generally consume a great deal of medical resources despite a high risk for mortality. Further, patients who survive often have a poor quality of life and continue to utilize health care resources. As such, issues of justice must be balanced with beneficence and autonomy. However, despite prognostic indicators, there are patients who eventually do have a good outcome and are able to return to their normal lives. Therefore, physicians are faced with the dilemma of deciding on which patients to offer treatments despite a high risk of a poor outcome.

Physician involvement in issues pertaining to end-of-life care are at odds with what physicians do – heal. The core principle of nonmaleficence comes into play when dealing with many end of life issues and is generally at odds with patient autonomy where the patient or next-of-kin decide to withhold sustaining therapy to allow the patient to die with dignity.

Although three major ethical dilemmas were addressed in this lecture, physicians caring for critically-ill neurosurgical patients are also faced with other ethical issues. Further, as the anesthesiologist’s role now extends beyond the operating room, other ethical issues may also become apparent. These may include issues pertaining to full disclosure, the physician’s role in palliative care, and ethics involving research studies. When dealing with very difficult ethical issues, one should consider seeking the assistance of an ethics committee.

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...Anesthesiology is an example of a complex, high-risk, dynamic patient care system in which there has been notably reduced error... anesthesiologists confronted the safety issues presented by the need for continuing vigilance during long operations but punctuated by the need for rapid problem evaluation and action... By a combination of technological advances ... standardization of equipment, and changes in training, they were able to bring about major, sustained, widespread reduction in morbidity and mortality attributable to the administration of anesthesia...

These flattering words about our specialty's achievement in reducing the incidence of adverse events in the perioperative period comes from the landmark report that triggered the patient safety revolution: the Institute of Medicine's "To Err is Human" (1999). Indeed, anesthesiology's safety record has gone from the 1:1500 mortality rate reported in the Beecher & Todd study in 1954 to 1:250,000 for a healthy ASA 1 patient undergoing anesthesia reported by Lienhart in 2006.

The original focus of anesthesia safety efforts was on improving the safety of anesthesia delivery: designing safer anesthesia machines and prevention of oxygen pipeline misconnection (pin index system). In the late 1980's pulse oximetry and capnography became the cornerstones of anesthesia monitoring, which has resulted in the near abolishment of hypoxic brain injury due to unrecognized esophageal intubation and the rapid detection of any problems with ventilation and oxygenation. Ironically, these monitors became widely accepted despite lack of high level evidence that they indeed reduce the incidence of death and major morbidity. Subsequently airway management improved dramatically in the 1990's with the development of new devices to secure the airway such as the laryngeal mask, fiberoptic endoscopy and the first publication of the ASA difficult airway algorithm in 1993. These developments in airway management are now well integrated in most anesthesia curricula and have clearly contributed to a decrease of death and brain injury due to failed intubation.

The last decade has seen substantial growth in full-scale simulation to teach anesthesia residents. It is no longer considered ethically acceptable to teach a young resident an invasive procedure (be it central venous cannulation, or fiberoptic intubation) for which a validated simulation model is available. Full scale simulation using physiological ‘model driven’ patient mannequins and life actors playing the various members of the surgical team can prepare residents for the management of rare and potentially catastrophic events. Moreover, it can simultaneously teach important non-technical skills, such as leadership in crisis, teamwork and communication. These skills are collectively known as Crew Resource Management (CRM).

As impressive and encouraging these achievements during the last 4 decades are, we should carefully consider safety risks that have not been adequately controlled and the specific challenges for perioperative safety today. For example, we know in detail how patients died from anesthesia in the 1960's and 70's, but what about today? In France Lienhart et al investigated 4200 death certificates from patients who died in the perioperative period and found that 0.69 deaths in 100,000 were totally related to anesthesia while 4.7 in 100,000 were
partially related to anesthesia. As expected, age and ASA physical status were strong predictors of mortality. The death rate increased from 1 in 250,000 for a healthy ASA I patient to 1 in 1800 for sick ASA IV patients, respectively. Intraoperative hypotension and anemia associated with postoperative ischemic complications were strong predictors of mortality. Also, deviations from standard practice and teamwork factors contributed to anesthetic mortality. In the Netherlands, Arbous et al. performed a case-control study of more than 800,000 patients undergoing anesthesia between 1995 and 1997.6 Cases were patients who died or remained comatose within 24 h of the procedure (n=807), while controls survived without postoperative coma. In a multivariate analysis, documented equipment check with protocol and checklist, direct availability of the anesthesiologist, no change of anesthesiologist during the case, presence of a full-time anesthetic nurse in the room, presence of two persons at emergence, reversal of anesthesia and postoperative pain medication - as opposed to no pain medication all - decreased the risk for the outcome.

Serious adverse events as a result of drug swaps and ‘wrong route’ continue to occur. This has resulted in pressure from regulatory bodies in many countries to adhere to double check procedures when drawing up medication and when administering the drug. Table 1 shows a series of procedures suggested by Orser and Byrick to reduce the risk of medication error in anesthesia. 7 In addition, many accrediting bodies now require that high-risk medication is drawn up and checked independently by two people.

Table: Preventing medication error in anesthesia (from: Orser & Byrick) 7

1. Anesthesiologists should be aware of the risks of drug errors and ensure that checking procedures are in place. Errors often occur in situations of haste, distraction or fatigue.
2. Lighting of the operating room environment is critical for safety. In situations of reduced lighting, specific arrangements should be made for checking anesthetic drugs.
3. Drug storage arrangements should be consistent in all anesthetic care delivery units.
4. Ampoules should be read and re-read before drugs are drawn up into a syringe. Errors are unlikely to be detected once the syringe is prepared.
5. Ideally, drugs are prepared by the person who will administer them, immediately before use.
6. Syringes should be labeled with the name and concentration.
7. Syringes intended for an emergency should be stored away from the immediate work area.
8. The international color-coded syringe labeling system should be used.
9. Consider using pre-filling syringes for emergency drugs that are prepared by the pharmacy unit to assure quality of contents and accurate labeling.
10. Pharmacists should regularly visit the operating rooms to ensure safe drug use.
11. When drug manufactures, packaging and formulation changes, anesthesiologists should be alerted to the change before the drugs are provided in the operating rooms.

Imaging – Anesthesia has recently embraced imaging, in particular the use of ultrasound to identify neural and vascular structures and to evaluate perioperative cardiac function. At least for central venous access this practice has been shown to result in a reduced rate of complications. 8,9

Role of non-technical factors in anesthesia safety

It is increasingly clear that non-technical factors are as important as technical innovations to improve patient safety. For example, the Joint Commission reported that problems with communication were a leading root cause in more than 60% of sentinel events. 10
Figure 1. Communication is the leading root cause of all sentinel events. Source: Joint Commission on Accreditation of Healthcare Organizations.

Handover – Each time a patient is transferred between hospital locations (emergency room, ward, operating room, recovery room, intensive care unit) and when doctors and nurses change shifts, critical patient information needs to be handed over. Patient harm can result from inadequate handovers and there is widespread consensus that robust, structured handover processes are critical for safe patient care. Current handover processes have been described as unstructured, informal and error prone. Moreover, the number of handovers in hospitals has increased dramatically as a result of recent limitations in the maximum number of resident duty hours. This policy is intended to increase patient safety by reducing the impact of fatigue and sleep deprivation on quality of care. However, an increase in the number of handovers is the unavoidable consequence. There has been tremendous activity in studying ways to improve handovers during the last 2 years. Checklists may improve the reliability of handovers. In hospitals that have electronic patient records (EPRs), a promising approach is to support the various verbal handover processes with software tools that can combine specific handover items such as to-do lists, daily goals, and concerns, with automatically extracted data from the EPRs. Such systems may relieve the stress on residents of handing over their patients to the incoming resident. However, there is no ‘one size fits all’ solution to the problems of handover. The process entails more than just information transfer. Redesign of handover can benefit from frontline staff input to ensure that new techniques fit into existing practices and settings. With the “video-reflexive” technique developed by Iedema et al., handover encounters are videotaped and played back to the practitioners involved for analysis and discussion. This ‘bottom-up’ reflection on one’s daily practice by watching the recorded handovers with medical and nursing staff uncovered previously unrecognized clinical and operational problems. The resulting improvement strategies had a high level of practitioner ownership (‘invented here’) and improved coordination of care and strengthened junior–senior communication.

Checklists

Checklists have been used in high-risk industries for decades. They take away the reliance on memory for routine safety checks and allow one to focus on the specifics of the case. After initial professional reluctance, checklists are now an integral part of perioperative care throughout the world. The Harvard surgeon Atul Gawande, popularized the use of checklists in healthcare with his book ‘the Checklist Manifesto’. Two recent studies suggest that using perioperative checklists reduces perioperative mortality. The Haynes study was an uncontrolled ‘before-after’ observational design. In eight hospitals around the world (Toronto, Canada; New Delhi, India; Amman, Jordan; Auckland, New Zealand; Manila, Philippines; Ifakara, Tanzania; London, England; and Seattle, WA) they observed a reduction of mortality from 1.5% before the checklist was introduced to 0.8% afterward. This unusually large effect size has been attributed to a powerful Hawthorne effect. de Vries et al. compared a comprehensive surgical safety system that
uses checklists throughout the entire perioperative process (Surgical Patient Safety System, SURPASS) in 6 Dutch hospitals in a controlled before-after design. Five hospitals not using SURPASS served as controls. Complication rate decreased significantly from 27.3 to 16.7% and in-hospital mortality decreased from 1.5% to 0.8% for an absolute risk reduction of 0.7 percentage points (95% CI, 0.2 to 1.2). In the control hospitals there were no changes in these outcomes.\(^{18}\) van Klei et al. investigated the effect of implementing the WHO checklist on surgical mortality in a university hospital and found a small effect on mortality, that was proportional to the level of checklist adherence.\(^{19}\)

**Multi-component safety interventions.**

*Prevention of central line infections* - Pronovost et al. implemented an evidence-based protocol to decrease the rate of catheter-related infections in ICU's in Michigan (hand washing, using full-barrier precautions during the insertion of central venous catheters, cleaning the skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters). A before after analysis of 1981 ICU-months of data from 103 ICU’s (a total of 375,757 catheter-days) showed a decrease in the median rate of catheter-related bloodstream infection per 1000 catheter-days from 2.7 infections at baseline to zero 3 months after the intervention (P≤0.002). The mean rate per 1000 catheter-days decreased from 7.7 at baseline to 1.4 at 16 to 18 months of follow-up (P<0.002).

*Culture* - One of the less tangible, but important aspects of safety is that of organizational culture. There is evidence from several high-risk industries that a negative safety culture results in a higher rate of adverse incidents. A too strong hierarchy may be an impediment for junior doctors and nurses to ‘speak up’ when they witness unsafe acts by their seniors. There are now several validated instruments to measure culture via self-assessment, such as the SAQ.\(^{20}\) Certain behaviors that are not captured by self-assessment questionnaires, may only be discovered by close ‘ethnographic’ observation of daily clinical practice. A patient safety program designed to improve teamwork and culture improved safety climate scores in a large cohort of 71 intensive care units.\(^{21}\) Definitive proof that such interventions will result in improved patient outcomes is currently not available. In 74 veterans Administration hospitals participation in the Medical Team Training program was associated with an 18% reduction in annual compared with a 7% decrease among the 34 facilities that had not yet undergone training.

*Standardization* - Clinicians are known to highly value their professional autonomy. If this results in excess practice variability, it may result in suboptimal care. Standardization has been proposed as a solution to increase ‘value’ by improving outcomes and reduce costs. The key may be to standardize whenever possible, but at the same time to allow clinicians enough discretion to be able to depart from the standard whenever that is in the patient’s interest. Such deviations need to be documented in the patient chart.

**Specific patient safety considerations for neurosurgery**

Perioperative patient safety in neurosurgery follows the same principles as for other surgical procedures, but neurosurgery poses specific challenges. The risk of ‘wrong side, wrong patient’ errors is higher in neurologically compromised patients and one should always cross-check laterality with the patient chart, imaging data and the patient’s own verbal information. In patients with cerebral aneurysms absolute control over blood pressure is necessary to prevent complications: both hypertensive spikes (risk of rupture) and hypotension during temporary clipping) should be avoided at all cost.

The benefits of having a central line should be carefully weighted against the risks. For routine tumor craniotomies there will seldom be a need for a central line.
Conclusions - Anesthesiology has obtained remarkable safety, at least for healthy patients undergoing surgery of minor to moderate complexity. There is, however, still considerable room to reduce adverse events and improve perioperative outcomes in sicker and more complex patients. Many of the proposed changes are not ‘rocket science’ and have been implemented in other high-risk industries decades ago. They are mostly non-technical in nature and focus on improving communication and teamwork, combined with more acceptance of - and adherence to - standardization including the use of checklists for repetitive tasks where forgetting to check an item can have dramatic consequences for the patient.

References


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To maintain dignity and humanity during the course of the disease is an ethical challenge in medicine. Despite great advancement in therapeutic interventions our ability to predict which patient’s will respond favourably is limited. Therefore uncertainty regarding prognosis makes it further difficult to define an appropriate care plan.

A global accepted body of ethical and legal aspects whether to implement or withdraw therapy in critically ill Neurological patient vary widely. To circumvent some of the variable factors we have to identify the ideal patients who will be best served by NICU.

The patient best served by such specialized unit is the one who would benefit from the unique combination of skills in monitoring and management of patients with acute deterioration due to CNS failure.

Identification of appropriate patients in some cases prior to their arrival in the hospital is an important component e.g. TIA attacks prior to basilar artery occlusion or respiratory compromise in myasthenia gravis or G.B. syndrome require rapid identification for admission to the NICU.

For appropriate use of ICU resources admission criteria for patient selection has to be defined in order of preference. The following priority categories are useful to make the selection.

**Category A:** Patients who are unstable due to acute deterioration of CNS function: Peripheral and central.

1. Acute dysfunction with respiratory depression an e.g. in G.B. syndrome, Myasthenia gravis.
2. Tetanus, status epileptics, cervical cord or medullary compression.
3. Post operative intracranial or spinal procedures who develop complications.
4. Patients who have developed acute CNS infections like encephalitis, meningitis or ventriculities.

**Category B:** Patients who are not critically ill at the time of admission but require sophisticated neurologic monitoring where the treatment is based on the monitoring variables. Priority should be given to those requiring multiple physiologic monitoring like ICP, EEG, Evoked potentials, cardiac rhythm, CVP etc.

**Category C:** Includes patients with acute deterioration of cardiac or pulmonary function unrelated to CNS or PNS diseases like septicemia and aspiration. Patients who require monitoring which is performed in other ICUs should be shifted there like pacemaker implantation, balloon pump, cardiac surgery or general surgery.

**Category D:** Critically ill patients whose previous state of health, underlying disease or acute illness either alone or in combination, severely reduces the benefits of treatment in the NICU.

Patients in Category A,B and C should be always aggressively treated initially with no limitation on therapy. As the clinical situation evolves like lack of response to therapy or progression of the underlying disease or unavoidable complications may suggest that the level of care should be reduced Category D patients may also receive limited care.

**When to Reduce Maximum Care:**

Medicine and Society now consider under certain circumstances acceptable to withdraw life sustaining interventions when they are considered futile. One broad definition considers a futile life sustaining intervention which serves only to preserve life without reversing the underlying medical condition.
Another definition considers intervention futile if they merely sustain permanent state of unconsciousness, vegetative state or permanent dependence on intensive care.

On the other hand some persons argue that even mere preservation of life regardless of quality or expected duration of life is worthy goal and therefore no therapy is futile. So the final determination of what is considered futile for an individual patient now rests with the patient. It usually reflects their feeling about what constitutes a meaningful existence. If a patient loses decision making capacity the authority to take these decisions is shifted to the surrogate.

Ideally one would determine whether a patient will survive an illness and with what quality of life. This determination is based on clinical judgement with limited support from the literature or data banks. There have been attempts to determine outcome on the basis of Electrophysiological or radiologic and metabolic criteria. Examples of such patient is persistent coma 24 hours after cardiac arrest with absent corneal and peapillary reflexes or patients after head injury with absent cortical responses to somato sensory evoked potentials bilaterally and absent brainstem reflexes.

Even when prognosis can be established decisions regarding reduction in therapy are not easily made. Until recently medicine has considered the preservation of life to be paramount. Improvements in technology have created a situation in which the goal needs to be reassessed. Redefinition of the goal of medicine involves both ethical and legal considerations.

ETHICAL PRINCIPLES:
Several fundamental ethical principles are important in making decisions about withdrawing treatment. They include BENEFICENCE, NONMELEFISCENCE, PATIENT AUTONOMY AND SOCIAL JUSTICE.

The principles of beneficence and non meleficence require physicians to act to benefit the patients and to do no harm. This have been the driving force behind medical practice for centuries and justification for continuing medical treatment under any circumstances. However on the other hand aggressive medical care can also put financial burden on the patient and the society. Defining whether the care provides benefit is difficult and is based on patients or surrogates definition of quality of life. The patients capability to adapt to the presumed final outcome should be explored carefully and repeatedly. Conflict arises when the healthcare teams definition differs from that of patients or surrogate. In general patients / surrogate definition should be respected.

Patients autonomy. The right of patients to determine their medical care should be respected by the treating physician.

The principle of social justice requires the allocation of medical resources fairly and according to medical need.

As resources become limited this principle will impact on clinical decision making.

LEGAL CONSIDERATIONS:
Several legal cases have addressed the principle of patient autonomy. They deal with questions of which therapy a patient may refuse and the request of the family to withdraw treatment in the absence of wishes of the patient like withdrawal of ventilator in a persistent vegetative state.

Withdrawal of feeding and nutrition is again controversial in different court cases. In Germany relatives are not allowed to make decision for unconscious patients unless they have been appointed legal guardiance by the court.

ADVANCE DIRECTIONS:
To avoid these conflicts the concept of a “Living Will” has evolved in USA. In this document the patient clearly states his or her wishes regarding withdrawal of therapy in the event of terminal illness. USA enacted federal law called the “Patient Self Determination Act” which requires health care providers to discuss advance directives with all patients.

PRACTICAL PRINCIPLE:
When no advance directions are available the following course of action can facilitate decision making regarding the withdrawal of therapies.

1. Principle of patients autonomy must be respected. A detailed communication between the patient / family to be undertaken by the healthcare provider with sometimes the help of social worker / religious man.

2. There must be unanimity among the members of the health care team to avoid in consistent communication with the family.

3. (a) When there is disagreement with in the family, decision making should not be rushed, ample time should be allowed for discussion with the family

(b) Utilize institutional support such as ethics committee of the hospital.

(c) Transfer the patient to another physician who can accept the patients / surrogate desires.

(d) Utilize the courts only as a last resort.

THE “DO NOT RESUSCITATE” PATIENT

1. With holding CPR in the event of cardiopulmonary arrest in terminally ill patients.

2. Second options is to continue the level of care that the patient is receiving but not increase the level of care if the patient deteriorates.

3. Third option is to provide therapy for patients comfort and not to treat the terminal condition.

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Cerebral protection during Coronary artery bypass grafting

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With the graying of the world population and the increasing population as such, the number of coronary surgeries being performed is increasing.

The results of coronary surgeries are being marred by the complications in other systems of the body. The worst complications of coronary artery bypass graft surgery (CABG) the are those related to the neurological system. **Mortality difference is 21% with neurological dysfunction vs. 2% without CNS dysfunction.** Neurological injury is common in geriatric population undergoing cardiac surgery. Despite a progressive decrease in cardiac surgical mortality since the 1980s, the incidence of postoperative neurologic complications has remained relatively unchanged. Brain injury from CABG is believed to result from cerebral embolism or hypo-perfusion that is exacerbated by inflammatory processes evoked from CPB or ischemia/reperfusion injury. Progression of underlying disease has a major role in assessing late postoperative complications.

Using preoperative and postoperative neuropsychological testing, researchers from many centers have now convincingly demonstrated that measurable cognitive dysfunction (Intellectual function deterioration, agitation memory deficit) is also a common complication of CABG, with an incidence of up to **80% to 90%** at hospital discharge.

This lead to the development of various neuro-monitoring and neuro-protective strategies over the years.

**Etiology**

The commonest cause of neurological complications is **macro and micro-emboli**, caused by handling of atheromatous aorta during cannulation before CPB, cross clamping before cardioplegia, application of side clamp on aorta. Other causes are equally important like **low perfusion pressure** on CPB or while performing OM and PDA grafts in off pump coronary artery bypass surgery (OPCAB) and **poor acid base and temperature management** in the peri-operative period.

**Hemodynamic instability:** Periods of hemodynamic instability while doing CABG whether on pump or off pump can lead to cerebral infarcts in patient who are prone like Geriatric patients or patients with compromised cerebral circulation. The decreases from baseline mean arterial pressure (MAP) of 10 mmHg or greater during CPB was associated with a threefold higher risk for **Watershed stroke.**

![Fig.1: Hatched areas showing the most frequent locations of boundary area, or watershed zone infarcts in the brain, situated between the territories of major cerebral or cerebellar arteries.](image)

**Diabetes mellitus:** Poorly controlled DM has been associated with more incidence and poorer outcome of such neurological episodes.

**Age:** With increasing age the incidence of neurological episodes is higher and the outcome is poorer; the reason being the
increase in the atheromatous changes in the aorta and reduced cerebral auto regulation.

**Combined/complex procedures**: Again, the incidence of neurological episodes is more in combined procedure like CABG with carotid endarterectomy, Valvular surgeries or aortic surgery.

**Prolonged cardiopulmonary bypass (CPB) time**: Increases neurological complications because of inflammatory response to CPB. Other factors related to institution of CPB like sand blasting effect at the time of cannulation are not related to duration of CPB is used.

**Prior stroke**: Pre-existing cerebrovascular disease/stroke is one the major predisposing factors leading to either exacerbation of the existing cerebrovascular disease or new neurological episode if associated with hypoperfusion. The presence of cerebral vascular disease may predispose affected patients to cerebral O2 imbalance during surgery. Indeed, the use of jugular venous bulb (SJVA) monitoring or near infrared spectroscopy (NIRS) has revealed cerebral O2 desaturation in 27% to 43% of patients during CPB, particularly during rewarming, when cerebral metabolic rate increases.

**Renal dysfunction**: Association is seen with increased neurological complication. Mechanisms is not fully clear.

**Atheromatous Aorta**: Embolization during crucial steps of CPB like cannulation, decannulation, cross clamping and side clamping leads to more incidence of neurological complications (Sand Blasting effect).

**Peripheral vascular disease**: Association with increased neurological complication seen.

**Mechanism leading to neurological complications:**

**Embolization**: It may be from the atheromatous aorta or air.

**Hypoperfusion**: Hemodynamic instability during institution and coming off CPB in on pump CABG. In OPCABG during proximal grafting and during distal grafting of obtuse marginal and posterior descending artery.

**Inflammation**: Inflammatory response to the CPB circuit.

**Altered cerebral autoregulation**: more so in geriatrics. Pre-existing hypertension, cerebral vascular disease, or other causes, and are thus prone to cerebral hypoperfusion and subsequent ischemic injury. Aging-associated vascular changes also may be linked to the rising prevalence of cerebral vascular disease in patients presenting for cardiac surgery.

**Intracardiac debris**: This is more relevant in open procedures combined with CABG like Valvular and aortic surgeries, LV clots associated with severe LV dysfunction or ventricular aneurysms.

**Air embolism**: Improper deairing. Massive air embolism during institution of CPB.

**CPB**: Leads to reduced perfusion pressure to brain. (CPP=MAP-CVP)

**Cardiopulmonary bypass circuit surface**: Leads to inflammatory response to CPB circuit.

**Reduced hematocrit**: On CPB.

**Reinfusion of unprocessed shed blood** from the cardiotomy reservoir leads to more episodes of embolisation.

**Cerebral hyperthermia & Hypoxia**: O2 demand to supply ratio is unfavorable (Cerebral hyperthermia causes increased CMRO2 and O2 supply decreased in hypoxia)
The Data registries:

Despite a progressive decrease in cardiac surgical mortality since the 1980s, the incidence of postoperative neurologic complications has remained relatively unchanged. The age, acuity, and extent of comorbidities in cardiac surgical patients have also increased during this same interval.

There is a progressive increase in risk for stroke for CABG with increasing age ranging from 0.5% for patients younger than 55 years to 2.3% for those older than 75 years.

Neurologic events in cardiac surgical patients are associated with increased postoperative mortality, prolonged intensive care unit (JCV), hospital stay, decreased quality of life, and decreased long-term survival.

Neurologic complications range from coma, stroke, and visual field deficits to impairments of cognitive processes (e.g., delirium, impaired memory and attention, mood alterations).

The Cerebral Markers / Monitoring devices:

Why to monitor?

Neurological Monitoring is important because it guides us about an ongoing unfavorable episode which can be averted/harmful effect reduced by an early intervention.

Ideal neurophysiologic monitor: Non invasive continuous, objective, rapid assessment of cerebral perfusion and function.

Uses:

1. To detect neuronal dysfunction while still reversible.
2. To enable intervention and drive strategies to reduce damage

Near-infrared spectroscopy (NIRS) mechanism: Human skull is transparent to infrared light. Near Infrared light is of 2-4 wavelengths at 700-1000 Hz which have distinct absorption spectrum for oxygenated & deoxygenated Hb. Calculates difference between Hb absorption, divided by mean Mixed venous saturation of cerebral blood.

NIRS: Passes through small volume of cerebral cortex detected by 2-3 detectors away from source. It Measures Regional Cerebral Saturation Index (rSO₂)

Cerebral near-infrared spectroscopy can detect cerebral ischemia and has been associated with improved outcomes after cardiac surgery.

Displayed as rSO₂ 15-95%

NIRS Can be measured during: Pulsatile, non pulsatile flow, circulatory arrest.

Dis-advantage: No absolute value for neurological deficit

Intervention Threshold: rSO₂ < 50% or 20% of baseline

Normal: 10% difference between Right hemisphere rSO₂ & left hemisphere rSO₂
Baseline value normal between 50-80 %
Baseline < 50% represents reduced brain tolerance for hypoxic insult

Low rSO₂ Observed during:

1. Desaturation, hemodynamic instability
2. Inadequate hypnosis, anesthesia
3. Improper Head positioning
4. Cardiac manipulation ↓ venous return
5. Regional malperfusion – Aortic Surgery
6. Cannula malposition
7. CHF, patients – low baseline
   ♦ rSO₂ guides
1. ↑ cerebral perfusion in hypothermia
2. Selective cerebral perfusion (ACP, RGP)
3. Anesthetic depth adequacy
   ♦ Intervention for Falling rSO₂
1. Alterable intraoperative variables
2. ↑ Perfusion pressure/ pump flow
3. ↑ PaCO₂ >35 mmHg
4. Hypothermia, ↓ CMRO₂- Propofol
5. ↑ Hematocrit >20%
6. Repositioning of aortic, caval, cannulas
7. Perfusion of contra lateral carotid artery

Before/ after CPB
  o Increase FiO₂
  o Increase PaCO₂
  o Increase cardiac output
    ▪ Volume infusions
    ▪ Inotropes, vasodilators
  o Decrease temperature
  o Increase hemoglobin

Advantages
1. Simple low cost tool
2. Noninvasive continuous measure of global brain metabolism
3. Works in absence of pulsatile flow
   ♦ Expertise required

Transcranial Doppler Ultrasound (TCD)
Pulsed Wave Ultrasound 2 MHz Frequency is used. Sensitive real time monitor of change in Cerebral Blood Flow Velocity (CBFV), Emboli during cardiac surgery.

The left temporal bone window using a 2.0/2.5 MHz TCD device. The middle cerebral artery was insonated at a depth between 50 and 56 mm. Emboli detection was started 10 min prior cannula insertion and continued until 10 min after cannula removal. Microemboli signals were identified by their typical visual appearance on the spectral display and their characteristic sound.

Intervention Threshold: Mean velocity change of 20% from baseline/Absent diastolic velocity/ reduced CBFV

Embolus Detection: Gas bubbles, particulate matter reflect sound waves better than RBCs. Detected by presence of High Intensity Transient Signal (HITS) with spectral or M mode display.

TCD Detects Both Particulate & Gaseous Emboli.

Intervention guided:
• Partial occlusion clamp elimination for proximal anastomosis
• Discontinuation of cardiotomy suction re-infusion
  • Retransfusion stop
  • Cool head. Reperfuse
  • Revert head malposition – neck extension, axial head rotation
  • Appropriate aortic cannulation site
  • Reposition of perfusion cannulas

Advantages
1. Noninvasive, continuous monitor of cerebral perfusion
2. Detects microemboli
3. Allows recognition of instantaneous changes in CBF in carotid, cardiac surgery, selective cerebral perfusion, aortic arch surgery

Limitations
1. Operator dependent. Expertise required
2. Temporal window difficult to locate in up to 25% patient difficulty in reproducibility during low blood flow, hypothermia
3. Not undergone wide spread evaluation or adoption as cerebral oximetry

Electroencephalography (EEG)
Mechanism: the spontaneous electrical activity of cerebral cortex creates electrical
signal which are amplified, filtered & displayed

**For interpretation different processing methods developed**

a. Periodic analysis  
b. Aperiodic analysis  
c. Power spectral analysis
   i. Fast Fourier Transformation → since waves compressed spectral array (CSA)  
   ii. Color density spectral array  

Change in neuronal perfusion changes EEG recording  

**Normal**  CBF 50ml/100gm/min  

**Hypoperfusion**  
22ml/100gm/min  no change in EEG  
22-15ml/100gm/min  ↓ amplitude, slowing  
7-15ml/100gm/min  flat signal  

**Important Imbalances Identified with EEG Preexistent EEG abnormality**

- Hypnotic effect  
- Head malposition  
- Hypocarbia-induced cerebral ischemia  
- Malperfusion syndrome  
- Need for blood replacement  
- Optimal cooling and rewarming technique  
- Seizures  

**Disadvantage**

- Cumbersome, Expert interpretation  
- EEG sensitive indicator of synaptic depression  

But not specific As cooling and hypnosis suppress EEG  

**Jugular Bulb Venous Oximetry (SjvO2)**

Jugular bulb blood reflects GLOBAL mixed cerebral venous oxygenation  
It Is invasive, Does not Detect Small Areas of Malperfusion or Regional Ischemia  
Used as transfusion trigger, Documents cerebral hyperthermia  
Two fold desaturation in OPCAB vs. CCABG  

**Epiaortic Scanning**: Detects athersclerotic plaque in ascending aorta  
Responsible for change in surgical management in 25% cases  
Use associated with decrease in cerebral embolisation and improved CNS outcome  

**Multimodality Monitoring**

Combined use of monitors gives better results  
Other monitors: Hemodynamic Monitoring: For cerebral perfusion pressure(CPP= MAP-CVP)  
↑ CVP – trendelenberg, lifting/rotation of heart, malposition of venous cannula, Reduced drainage on CPB  
↓ CPP - ↓ microemboli clearance - ↑ embolic insult  
↓ blood flow to pressure dependent collateral circulation  

**Cerebral Autoregulation** MAP: 40-100 mm Hg  

**Temperature monitoring:**  
To reduce detrimental effect of hyperthermia  
Guide rate of rewarming  

Alpha-stat pH management during moderate hypothermic CPB  
Avoidance of arterial inflow temperature greater than 37°C  

**Monitoring areas**

Nasopharyngeal, tympanic, rectal temperatures –may underestimate. Ideal - aortic inflow temperature (feasibility?).  

**Acid base management**

**Glucose management**

**Arterial line micro-emboli detection**: this with the help of arterial line filters help in reducing the embolic load.  

**Biomarkers**: A good biomarker is a test that can be done rapidly at most centers, to determine within hours which patients are injured, would be elevated in proportion to the injury, is capable of predicting longer term outcomes early after the course of an
injury, and is easily obtainable, i.e. serum or urine.

**Importance of biomarkers** is in determining which patients are injured, the extent and etiology of injury, and prognosis. In addition, biomarkers would be necessary to identify patient subsets that would benefit from the therapy, and to serve as surrogate outcomes to evaluate the effects of the neuroprotective therapy. These are more relevant in pediatric cardiac surgery and not coronary surgery.

**Previously studied biomarkers**, e.g. creatine kinase brain band (CK-BB), neuron specific enolase (NSE), and S100β protein are that they have not proved to be specific enough to brain tissue.

**Newer biomarkers of brain injury**

**Glial fibrillary acidic protein (GFAP)** is a cytoskeletal protein found in the astroglia of the CNS, first studied in CNS tumors. It is not constitutively expressed and thought to be released only after cell death. Specificity for white matter may be valuable in patients with congenital heart disease (CHD) because of the known association with white matter injury before and after neonatal cardiac surgery.

**Inflammatory cytokine markers such as interleukins (IL) 1β, 6, 8, and tumor necrosis factor (TNF), taken together with markers more specific for CNS injury**, have promise to help predict adverse outcomes after a brain injury. Inflammation is an important component of brain injury after birth asphyxia, cardiac arrest, cardiac surgery, sepsis, and other critical illness. Elevations in serum and CSF levels of IL-1β, 6, 8 have been shown to correlate with long term adverse neuro-developmental outcomes in some studies of birth asphyxia in full term neonates

**Ubiquitin C-terminal hydrolase 1 (UHCL1) and phosphorylated axonal neurofilament heavy chain (pNF-H)** are two novel biomarkers that show promise for better specificity in brain injury, especially in neonates after HIE from birth asphyxia. These new and novel biomarkers of brain injury give rise to the potential that better, more specific tests could discriminate patients at high risk for long term adverse outcomes, and thus are candidates for early neuro-protective therapies. Also, these tests could potentially discriminate between neuronal and white matter injury.

**Potential markers of acute brain injury in cardiac surgery**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Source</th>
<th>Potential predictive value for long term neuro outcomes</th>
<th>Difficulty factor to obtain data</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIRS; including autoregulation</td>
<td>Patient monitor</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>EEG</td>
<td>10–20 lead or aEEG</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>MRI</td>
<td>Research or clinical data</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Biomarkers—older: CK-BB, NSE, S100β</td>
<td>Blood</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Biomarkers—inflammation: IL-1B,6,8, TNF</td>
<td>Blood</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Biomarkers—newer CNS specific: GFAP, UHCL1, pNF-H</td>
<td>Blood</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Biomarker panels: multiple specific, with inflammatory markers</td>
<td>Blood</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

**Neuroprotective strategies and treatments**

Strategies and treatments used for the protection of brain during cardiac surgery. The aims of brain protection during cardiac surgery are to reduce the sources of injury (eg, embolism and hypoperfusion) and to increase brain tolerance to ischemic insults. Brain injury can happen any time perioperatively. In fact, greater than 20% of
Clinical strokes occur postoperatively. In general, protective measures for the brain can be grouped as pharmacologic and nonpharmacologic.

Also Classified as:

**Preventive:** Preventive strategies are therapies given in advance of an anticipated neurological injury or insult, such as an obligate long period of deep hypothermic circulatory arrest (DHCA). They are designed to prevent neuronal and white matter loss.

**Reactive:** Reactive strategies are therapies given in response to a recent neurological insult or injury, for example diagnosed by peri-operative brain MRI or rise in neuronal biomarkers. They are designed to limit the extent of neuronal or white matter loss.

**Reparative:** Reparative strategies are treatments given after a known neurological injury, for example one which produces late MRI injury and clinical neurological deficits, in order to repair and restore neuronal or white matter loss by growing new neural tissue.

<table>
<thead>
<tr>
<th>Treatment/strategy</th>
<th>Preventive or reactive/reparative</th>
<th>Feasibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB techniques: DHCA vs. ACP</td>
<td>Preventive</td>
<td>+++</td>
</tr>
<tr>
<td>NIRS monitoring and treatment of low rSO₂; autoregulation</td>
<td>Preventive</td>
<td>+++</td>
</tr>
<tr>
<td>Anesthetic regimens: dexmedetomidine vs. GABA/NMDA agents</td>
<td>Preventive</td>
<td>+++</td>
</tr>
<tr>
<td>Therapeutic hypothermia</td>
<td>Preventive/reactive</td>
<td>++++</td>
</tr>
<tr>
<td>Remote ischemic preconditioning</td>
<td>Preventive</td>
<td>++++</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Preventive/reactive/reparative</td>
<td>++</td>
</tr>
<tr>
<td>Neurotrophic factors: BDNF</td>
<td>Preventive/reactive/reparative</td>
<td>++</td>
</tr>
<tr>
<td>Umbilical cord stem cells</td>
<td>Preventive/reactive/reparative</td>
<td>+</td>
</tr>
<tr>
<td>intra aortic filter (Embol X)</td>
<td>Preventive; designed to reduce solid micro emboli</td>
<td>+</td>
</tr>
<tr>
<td>dynamic bubble trap (DBT)</td>
<td>Preventive; designed to reduce gaseous micro emboli</td>
<td>++</td>
</tr>
</tbody>
</table>
Potential strategies for the neuroprotection

Epiaortic Scanning guided decisions:
Epiaortic Routine epi-aortic scanning before instrumentation of the ascending aorta is a sensitive and reasonably specific technique to detect the non-palpable aortic atheromatosis at the time of surgery, and allows physicians to avoid atheroma during surgical aortic manipulations (eg. cannulating for CPB, applying an aortic cross-clamp). Epiaortic guided surgery is reported to reduce cerebral embolic signals detected with TCD and to improve neurologic outcomes.

In patients with significant ascending aorta atheromatosis, avoidance of aortic manipulation (“no-touch technique”) can decrease perioperative stroke.

Surgical approaches for this situation might include: (1) Avoiding CPB by converting to OPCAB surgery, (2) cannulating for CPB via the axillary artery or alternative sites, (3) avoiding partial occlusion clamps for proximal bypass graft anastomosis by using a “single cross-clamp” technique, (4) avoiding aorta cross-clamping by using fibrillatory arrest, (5) using all arterial bypass grafts to avoid proximal anastomosis, and (6) performing circulatory arrest and replacing the ascending aorta.

Avoiding CPB altogether: OPCAB avoids all the complications of CPB (inflammatory response to CPB circuit) but still has all the complications related to aortic handling like at the time of putting side clamp for proximal grafting. Additional effect is that of the hemodynamic derangement during proximal grafting and during distal grafting at obtuse marginal, posterior descending artery and right coronary artery. Data from prospectively randomized trials comparing “on” versus “off” CPB CABG surgery have failed to show a markedly reduced frequency of neurologic complications with OPCAB.

There is a greater incidence of early postoperative cognitive dysfunction in patients exposed to CPB compared with off-pump and noncardiac surgery patients.

The incidence of late cognitive dysfunction appears to be similar between groups whether exposed to cardiopulmonary bypass, percutaneous coronary intervention, or medical management, implying progression of underlying disease as a primary mechanism.(stressing the role of maintain hemodynamics and other variables within normal limits.

Pericardial suction aspirate (through cell saver)
Lipid-laden emboli resulting in small capillary arteriolar dilations (SCADs) are found in the brains of patients at autopsy after cardiac surgery. These SCADs can be reproduced in canines subjected to CPB, and appear to arise from fat returned unfiltered to the CPB with cardiotomy suction aspirate. The usual CPB arterial line filters are inefficient in preventing SCADs compared with processing of the cardiotomy suction aspirate with a cell saver. In a human investigation, processing pericardial suction blood with a cell saver before return to the CPB circuit significantly reduced blood lipid content compared with controls (filtering only)

MAP: Most institutions keep MAP greater than 70 mmHg in high risk patients during CPB. A common clinical dictum invoked by many centers is to keep MAP targets within the same numerical value as the decade of the patient’s age (eg. 70 mmHg for 70-year-olds, 80 mmHg for 80-year-olds). Early and aggressive control of hemodynamic instability is desirable.

Mediastinal CO2 insufflation: more relevant with combined procedures. Most cerebral emboli detected with TCD during CPB are composed of air. Because CO2 is more soluble in blood than air is, replacing air in the pericardium during surgery by simply insufflating the wound with CO2 is a strategy often used to increase the rate of absorption of intravascular emboli. This method reduces the number of arterial emboli, but it has not been extensively studied as a potential means of brain protection in humans. Few risks are associated with this practice, however.
**Hemoglobin/hematocrit targets**

Hemodilution is used during CPB to reduce the viscosity of blood during hypothermia and to reduce the need for allogeneic blood transfusion. The brain compensates for decreased blood oxygen carrying capacity by increasing CBF and tissue O2 extraction. Karkouti and colleagues [56] found that the odds of stroke increased 10% for each 1% decrease in hematocrit during CPB.

**Glycemic control:** The benefits to neurologic outcome of maintaining tight glycemic control during cardiac surgery are currently unproven. It is reasonable to initiate insulin therapy when glucose is greater than 140 to 185 mg/dL (class IIa, level of evidence C).

**Pharmacologic protection:** Agents tested have included those that reduce brain oxygen consumption to increase tolerance to ischemia and those that target established neuro-protective pathways, including the N-methyl-D-aspartate (NMDA) receptor, calcium channels, oxidant stress, the GABA receptor, and others.

**CPB for neuroprotection:**

**pH stat management** of CPB is associated with some early outcome advantages.

**Higher hematocrit on CPB** for cardiac surgery is associated with better psychomotor functions.

The leucocyte-depleting arterial line filters (40-μm arterial line filter) on cerebral microemboli and neuropsychological outcome following CABG are better.

**Use of surface-modified and reduced-area CPB circuitry**

**The role of anesthetic agents:** Recent years there has been a significant concern about increased neuro-apoptosis with the use of inhalational agents like isoflurane, sevoflurane, desflurane; and agents that produce their anesthetic and sedative effects by interacting with γ-aminobutyric acid (GABA) receptors as agonists like benzodiazepines, nitrous oxide, propofol, and barbiturates.

The mechanism is thought to be interference with the actions of the GABA and glutamate receptors as neurotransmitter mediators during the period of rapid synapto-genesis.

But, there have been studies which on the contrary say that the inhalational agents are rather beneficial.

Loepke et al. demonstrated that desflurane given in the sweep gas of the CPB circuit in a model of low flow CPB in neonatal piglets, has profound neuroprotective effects, including a significant reduction in apoptosis and excitatory cell death, as well as an improved neurobehavioral examination in recovered animals.

McAuliffe et al. studied neonatal mice with preconditioning with desflurane, sevoflurane, or isoflurane for a 3 h period, and 24 h later subjected them to 1 h of hypoxia. All 3 anesthetic gases protected against HIE when compared with no preconditioning on a battery of neurobehavioral tests.

Ketamine may also have neuro-protective properties in pediatric cardiac surgery. Ketamine antagonizes the NMDA receptor, which can block the influx of Ca^2+ in response to neuronal ischemia. The influx of Ca^2+ rapidly initiates apoptosis and cellular necrosis; thus ketamine potentially has important effects that would offset any adverse effect of increased apoptosis in the developing brain.

Dexmedetomidine is a centrally acting α2 receptor antagonist that produces sedation and analgesia by reducing flux of the excitatory neurotransmitter norepinephrine in the CNS. This agent does not produce apoptosis, and has profound neuroprotective effects in animal models of focal cerebral ischemia, and even isoflurane neurotoxicity. It reduces isoflurane-induced apoptosis by reversing the reduction in the anti-apoptotic signaling pathways caused by isoflurane. The mechanism for the protection achieved is poorly understood.

Studies randomizing patients to different anesthetic regimens, especially comparing dexmedetomidine against GABA agonists or
NMDA antagonists would be important to clarify the neuroprotective/neurodegenerative impacts of these agents.

**Hypothermia vs. Warm perfusion:**
The temperature used during CPB may be important with regard to these adverse outcomes, where hypothermia is used as a means of neuroprotection. The degree to which metabolism is suppressed (reduced CMRO2) in patients during hypothermia has been difficult to determine.

The temperature coefficient, Q10, is the ratio of metabolic rates at temperatures 10 degrees C apart. The human cerebral Q10 was found to be 2.3.

HYPOTHERMIA during cardiac surgery is a long-accepted technique for end-organ protection during the nonphysiologic period of CPB and, in particular, during periods of ischemia. Hypothermia decreases whole-body oxygen consumption and increases the ischemic tolerance of organ systems. In addition to systemic hypothermia, hypothermic cardioplegic myocardial arrest is a well-established approach to protect the heart during ischemic cross-clamp periods. Despite the benefits of cooling, hypothermia can produce deleterious effects on myocardial performance and systemic organ function during the peri-operative period.

To address these concerns, techniques that use warm perfusion (systemic normothermia) and warm cardioplegia were developed. Together, these 2 elements define the current concept of warm heart surgery. Although warm heart surgery was introduced as early as 1957, it was only in the 1990s that serious interest and routine clinical application occurred. Since then, numerous comparisons between hypothermic and normo-thermic cardiac surgery have taken place, and the current results indicate that the debate will continue regarding the optimal method for cardiac surgery. Current evidence suggests warm heart surgery is safe and effective and, more importantly, may decrease some of the negative effects of hypothermia, thereby having a role in most “routine” cardiac surgical cases.

**Hypoxic–ischemic preconditioning and remote ischemic preconditioning**

Hypoxic–ischemic preconditioning refers to the intriguing finding that a mild, short lived period of ischemia and/or hypoxia, experienced in advance of a major hypoxic ischemic insult, confers neuroprotection by limiting the extent of brain injury. This phenomenon is nearly ubiquitous across all tissues.

The mechanisms of ischemic preconditioning are extremely complex, and involve many changes in transmembrane and intracellular signaling that result in protection from excitotoxic and apoptotic cell death. Molecules and receptors involved include GABA receptors, nitric oxide, protein kinase C, glutamate, brain derived neurotrophic factor (BDNF), nuclear factor kappa B (NFκB), heat shock proteins, hypoxia-inducible factor, erythropoietin, vascular endothelial growth factor (VEGF), and many others.

The classic initial preconditioning effect is short lived, not persisting beyond a few hours; however a second window of protection recurs after 24–48 h and can persist for up to 3–4 days

**Remote ischemic preconditioning**

Within a decade of the elucidation of the phenomenon of ischemic preconditioning, the concept that ischemia in a remote organ can produce protective effects, similar to those observed in classic ischemic preconditioning, was discovered.

Mechanisms are not fully understood, the phenomenon has been applied to pediatric cardiac surgery patients.
Erythropoietin

Erythropoietin (EPO) is a 30.4 kDa glycoprotein. New information about the multiple biological roles of EPO has become available, specifically the neurological and cardio-protective effects of EPO.

Schematic diagram of the beneficial acute and longer term effects of erythropoietin administration for neuroprotection.
Neurotrophic factors
There has been a recent interest about the protein growth factors necessary for normal development of the central nervous system, and also of the factors involved in response to hypoxic ischemic injury and other brain insults, that both protect neurons from injury and go on to promote repair and growth of new neurons.

This is of more relevance in pediatric cardiac surgery rather than coronary artery bypass grafting in adults.

Recommendations for measures to reduce brain injury during cardiac surgery
1. A membrane oxygenator and an arterial line filter (%40 mM) should be used for CPB. Class I (level A)
2. Epiaortic ultrasound for detection of atherosclerosis of the ascending aorta Class I (level B)
3. Hyperthermia should be avoided during and after CPB. Class I (level B)
4. A single aortic cross-clamp technique should be used for patients at risk for atheroembolism. Class IIa (level B)
5. During CPB in adults, a-stat pH management should be considered. Class IIa (level A)
6. Arterial line temperature during CPB rewarming should be limited to 37 degree C. Class IIa (level B)
7. NIRS monitoring should be considered, especially in high-risk patients. Class IIb (level B)
8. Arterial blood pressure should be maintained at 70 mmHg during CPB in high-risk patients. Class IIb (level B)
9. Serum glucose should be kept at 140 mg/dL with an infusion of insulin. Class IIb (level C)
10. Transfusion of packed red blood cells should be considered in high risk patients when hemoglobin is ≤ 7 g/dL or higher, depending on other patient-specific considerations. Class IIb (level C)
11. Processing cardiectomy suction aspirate with a cell-saver device as a means for preventing neurocognitive dysfunction Class indeterminate (level A)
12. There are currently no pharmacologic neuroprotective agents with proven efficacy in humans. Class indeterminate (level B)

Conclusion: The field of neuro-protection in CABG (in general in cardiac surgery) is still clearly in its infancy. These treatments range from the simple, such as therapeutic hypothermia, remote ischemic preconditioning, or administering different anesthetic agents or EPO, to the very complex monitoring devices. For the complex strategies, the studies will require many years, and ideally coordinated multicenter approaches to get sufficient patient numbers for valid conclusions. Trials will have to be planned carefully to account for the multitude of confounding variables affecting neurological injury.

Till then, the simple but proven techniques for neuro-protection will remain.

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* * *
Brain Death

Dr. Sanjith Saseedharan Saroja

Care of a severe brain injury is one of the most daunting tasks in critical care and the importance of golden hour and quick treatment cannot be overemphasized while dealing with such patients.

On many occasions the severity of injury or the unfortunate incident of not getting timely help may see many a patient evolve to the condition of brain death. It is important to understand that brain death for all practical reasons is death and there is futility of medical science in the treatment of this condition which is a prerequisite for organ donation and transplantation.

Certification of brain death and thus facilitation of organ donation results in many patients getting a new lease of life.

The evolution of brain death.
Mollaret and Goulon coined the term “Coma depasse” which means irreversible coma after studying 23 patients who were unconscious, had no brainstem reflexes, no respiratory efforts and no electric activity seen on an Electroencephalogram. An adhoc committee at Harvard medical school in 1968 conceptualized and defined brain death or irreversible coma¹. It was in 1976 that UK Royal Medical Colleges defined brain death as complete irreversible loss of brainstem function and specified clinical criteria to certify brain death. In 1981 USA Presidents Commission recommended confirmatory tests to reduce the required period of observation. However the commission recommended a period of 24 hours observation for patients with anoxic brain damage. The Transplantation of Human Organ Bill was introduced in the Lok Sabha on 20th August 1992 and became the Transplantation of Human Organ Act in 1994 which essentially follows the UK definition of brain stem death. Hence in India it is brain stem death and not brain death as it were in the United States. Hence there is no need for confirmatory tests like eeg, radionuclide scans, transcranial dopplers or angiography. Essentially in India, this makes the diagnosis of brain death clinical and confirmatory tests are used only in the event of disagreement between the doctors certifying brain death.

Diagnosis of brain death in India
The Transplantation of Human Organs Act, 1994 (Central Act 42 of 1994), lays down the definition of death as follows: 'Deceased person' means a person in whom permanent disappearance of all evidence of life occurs, by reason of brain-stem death or in a cardio-pulmonary sense at any time after live birth has taken place. It goes on to state that 'brain-stem death' means the stage at which all functions of the brain stem have permanently and irreversibly ceased.

Clinical examination forms the cornerstone in the diagnosis of brain death. However before embarking on the clinical examination certain prerequisites have to be satisfied:

a) the cause of coma should be clear
b) cause of coma is irreversible
c) absence of following confounding factors should be ascertained
1. alcohol or drug intoxication
2. hypothermia
3. muscle relaxant
4. primary hypothermia
5. depressant medications like benzodiazepines and opioids
6. metabolic causes
7. hypovolemic shock
8. endocrinal disturbances

As per the Transplantation of Human Organ Act of 1994, brain death certification would require 4 doctors i.e. 1) the treating doctor
2) doctor in charge of the hospital
3) independent specialist of unspecified speciality
4) neurologist or neurosurgeon

All the above mentioned doctors would carry out tests documenting the cessation of brain stem activity. However the onus for certification would lie on the neurologist and neurosurgeon with others confirming the findings.

The tests required in the certification of brain death involve:
1) demonstration of a state of extreme coma or unarousable unconsciousness
2) absence of brain stem reflexes
3) apnea even after respiratory challenge

1) Demonstration of a state of extreme coma or unarousable unconsciousness:
   Absence of response to a deep painful stimulus like:
   a) nail bed pressure
   b) supraorbital ridge pressure
   c) sternal rub.

2) Absence of brain stem reflexes.
   a) pupillary reflex (midbrain function; Reflex: afferent nerve II and efferent nerve III) - no response to bright light shone into the eye
   b) facial sensation and motor response corneal reflex (Reflex: afferent nerve V and efferent nerve VII) - no response to wisp of cotton wool/swabstick being touched to the edge of cornea
   jaw reflex - absent
   facial grimace - absence of

   c) pharyngeal reflex and tracheal reflex afferent nerve IX and efferent nerve X - absence of gagging on stimulating the post pharyngeal wall/coughing or “bucking” on suction through the endotracheal tube (bronchial stimulation).

   d) absence of oculo-vestibular reflex (cold caloric test) - No deviation of the eyes with irrigation of the tympanic membrane (clear of cerumen or clotted blood) with head placed at 30 degrees each ear with 50 ml of cold water (allow 1 minute after injection and at least 5 minutes between testing on each side)

   d) absence of oculocephalic reflex (commonly known as dolls eye movement) - The examiner holds the patient’s eyes open and the head is turned suddenly from the neutral position to 90 degrees on both sides. When the reflex is intact the eyes turn opposite to the side of head movement as if lagging behind. The reflex is absent when the eyes move with the head and do not move within the orbit. (performed only when no fracture or instability of the cervical spine is absent).

3) Apnea test.
   Considered as the most essential and integral part of the component of brain death determination which needs to be performed in the right way. The test could be termed as a brain challenge which includes:
   (a) Disconnection from ventilator for till arterial co2 rises to critical level
   (b) Preventing hypoxia during this time
   (c) looking for spontaneous respiratory efforts.

Prerequisites for the test
1) Core temperature 36.5°C or 97°F
2) Systolic blood pressure > 90 mm Hg
3) Euvolemia or positive fluid balance in the previous 6 hours
4) Normal PCO2.
5) Normal PO2

Following normalization to paco2 to 40 mm of hg and preoxygenation for a period of 10 minutes the patient is disconnected from the ventilator with all monitoring devices attached after placing a catheter placed at the carina with oxygen being provided at rate of 6-8 litres/min.

A positive apnea test is said to have occurred in the absence of spontaneous respiratory efforts at the end of 6 minutes and arterial pCO2 more than or equal to 60 mm Hg or the rise is by 10 to 15 mm above the baseline (i.e. 2 mm rise per minute). The test is indeterminate if respiratory movements are absent, and arterial pCO2 is less than 60 mm Hg. In such a scenario if the hemodynamics allow the test could be prolonged till a paco2 of greater than 60 mm of Hg were achieved.

The above mentioned examination should be repeated by the team of doctors separately two times at least 6 hours apart in order to certify brain death in the purview of organ donation and none of the doctors involved in the certification should be involved with any aspect of organ harvesting and transplantation.

In most case scenarios the brain death determination is completely clinical and does not require the help of confirmatory tests however in the event of discrepancy of diagnosis among the certifying doctors or in the event that some test cannot be completely successfully then the following confirmatory tests may be used. In order of sensitivity conventional angiography, eeg, transcranial Doppler ultrasonography, technetium-99m cerebral blood flow scan and somatosensory evoked potentials.

**Management of brain dead organ donor.**

Brain death can provide a new lease of life to a recipient and optimum management of a brain death organ donor will help the cause effectively.

A brain dead organ donor is known to go through many complications like arrhythmia, diabetes insipidus, metabolic acidosis, DIC, infections, pulmonary edema, hypothermia, endocrine disturbances etc.

The following monitoring are considered essential during the management of brain dead organ donor

1) continuous ecg
2) pulse oxymetry
3) end tidal carbon dioxide monitoring
4) arterial blood pressure monitoring
5) central venous pressure monitoring
6) hourly urine output monitoring
7) core body temperature monitoring
8) input/output monitoring

The “100 rule” is a very easy method of remembering the goals to be achieved during maintenance of an organ donor systolic arterial pressure >100 mm Hg, urine output >100 ml h⁻¹, Pao2 >100 mm Hg, haemoglobin concentration >100 g litre⁻¹ and blood sugar 100 % normal (added later).

The most common problems that warrant immediate attention are hypotension, hypothermia and diabetes insipidus.

There are a number of societies who have specific guidelines in the management of a brain dead organ donor. Below mentioned is the summary of the various techniques in the maintenance of a brain dead organ donor which helps in facilitating optimal organ retrieval and transplant success.

**General Care:**

- standard monitoring as mentioned above
- Maintain heart rate between 60-120/min, Cvp- 6-10 mm of hg
- Regular monitoring of electrolytes and appropriate correction
- Treatment of infection with appropriate antibiotics
- Aggressive warming in order to keep core temperature >35 degrees
- Stop unnecessary drugs like opioids, sedatives and analgesics
- Head up position
- Continuation of enteral nutrition as tolerated
Target HB of 9-10 g/dl to optimize cardio pulmonary function in unstable hemodynamics
HB-7 g/dl is acceptable in stable brain dead patients.

Specific management:

Hypotension management -
Hypotension could result due to absolute hypovolemia, neurogenic shock or myocardial dysfunction. Cause based management would be the need of the hour and optimal fluid therapy is the cornerstone of management. Central venous pressure, echocardiography or other minimally invasive monitoring should be used judiciously in the management of fluids. Basing the fluid management purely on the basis of urine output would be erroneous due to the presence of diabetes insipidus in most cases. Vasopressor and inotrope use should be minimized as much as possible and at times a pulmonary artery catheter may be utilised for optimal management. Some transplant services have catecholamines in their donor preservation algorithm to exploit their reported anti-inflammatory and preservation effects. Increased cardiac graft dysfunction however has been noticed with the use of high dose nor-adrenaline infusion. Vasopressin could be effectively used in this cases as vasopressin is known to help to reduce the doses of noradrenaline. In fact some societies like the Canadian societies have recommended vasopressin as the first choice in donor resuscitation. There may be a dilemma in fluid management between generous fluid administration (which tends to benefit kidneys and liver) and fluid restriction (which tends to benefit lungs and heart). However an adequate trade off is not difficult with experience and avoidance of a positive fluid balance is important.

Respiratory system support
Maintain tidal volume of 6-8 ml/kg to achieve etco2 in normal range with avoidance of >30 plateau pressures and assuring spo2>93%. Application of peep to 4-6 cm h20 is advisable in order to prevent microataelectasis. However some guidelines for management of lung donors suggest larger Vt of 10-12 ml/kg. A reasonable compromise seems to be the Canadian recommendation of 8-10ml/kg. If the patient is not going to be a lung donor, possibly Vt should be reduced to 6-8ml/kg so that worsening ALI/ARDS does not affect the function of other organs.

Diabetes Insipidus and hyperglycemia management:
Immediate diagnosis and appropriate treatment is very important when this condition arises. This condition should be suspected in the presence of large urine volume (>4 ml/kg/hr) with rising serum sodium. Time should not be wasted in waiting for investigations like urine specific gravity, serum osmolality. Prompt replacement of intravenous fluids should be commenced with 0.45% normal saline. If it is still difficult to get the sodium down then it would be reasonable to start 5% dextrose. Utilisation of desmopressin is very essential in this scenario. (vasopressin can also be used however it does have undesirable splancnic and renal vasoconstrictive effects. DDAVP is an analog of arginine vasopressin with enhanced anti-diuretic potency, negligible vasopressor activity and a prolonged half-life compared to vasopressin. Dose of DDAVP in adults is 1-2 microgram s.c. or i.v., then 1-2 microgram s.c. or i.v. PRN to achieve urine output < 3ml/kg/hr. Aim to normalise the sodium as hypernatremia is associated with hepatic dysfunction and graft loss. Use of catecholamines and dextrose caused hyperglycemia which needs to be controlled with iv insulin infusion.

Arrhythmia
Atropine is ineffective for bradycardia after brain death has occurred and optimisation of magnesium, potassium, calcium and sodium forms the basis of avoidance of arrhythmias.

Endocrine support
As per a retrospective cohort study triple hormone therapy increased kidney liver and heart utilisation in donors and improved 1yr survival in transplanted kidneys and heart as
per a retrospective cohort study.\textsuperscript{12} The decision to administer these drugs should be on a case by case basis. In patients with hemodynamic instability inspite of volume loading and vasoactive medication the use of combined hormone therapy as mentioned below may be reasonable.

- T3 (tri-iodothyronine); 4 microgram bolus followed by infusion at 3 micrograms/hour.
- Vasopressin, 1 international unit bolus followed by 2.4 units/hr infusion
- Methylprednisolone, 1 Gram i.v. every 24 hours

The use of methylprednisolone is associated with improved oxygenation, reduced increases in extravascular lung water,\textsuperscript{13} and increased lung yield. Inflammation in the liver,\textsuperscript{14} heart,\textsuperscript{15} and kidney\textsuperscript{16} is also reduced.

- Insulin as indicated by blood sugars, minimum 1 unit/hr

Final decisions about transplantability rest with the relevant transplant teams.

The benefits of delay in organ retrieval to improve the condition of organs must be balanced against the risk of increasing distress in the patients family. Brain dead organ donor management, goals etc are subject to considerable variability and it is just time before “care bundles” for brain dead donors will come into place similar to sepsis care bundles. Reputable societies like the I.S.N.A.C.C will probably provide the platform for research in this field as currently evidence based care is currently not optimally delivered to all such donors.

References.


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Palliative care to neurological and neurosurgical patients

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Introduction
Palliative care to neurological and neurosurgical patients presents many challenges. These challenges are age of presentation, the rapidity of symptoms development, type of symptoms, variability of disease progression and associated cognitive change. Such patients present at elderly age, the disease progression is gradual, are functionally more impaired at terminal stages with disability and inability to communicate, presents with less of symptoms like pain, nausea and vomiting but have multiple physical, psychological and spiritual needs.[1]

As per the World Health Organization definition of palliative care as ‘an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual’.[2] There is increasing acceptance of the principles of palliative and supportive care for non cancer patients to provide supportive multidisciplinary symptom management.[3] Hence Palliative care aims to improve the outcome of patients through prevention and relieving of suffering by a holistic approach; considering the physical, psychosocial and spiritual modes of treatment.

Who are in need of palliative care in neurological and neurosurgical patients
Palliative care services are required in progressive neurological diseases with fluctuating natural course. Diseases like motor neuron disease (MND), multiple sclerosis (MS), parkinson’s disease (PD), Alzheimer’s disease (AD) and other associated disorders presents at different stages with gradual to sudden deterioration in physical and cognitive functions. The other most common cause is ischemic stroke (80%) followed by intracerebral hemorrhage (ICH) (10%–15%), and subarachnoid hemorrhage (SAH) or subdural hematoma (SDH) (5%–10%). Of these stroke patients, up to 30% are permanently disabled and another 20% require institutional care at 3 months due to variety of morbidity. Due to limited prospective information on palliative care need of stroke patients, these services are very limited and a lot has to be done for it.

Another major cause is Traumatic brain injury which is a public and medical health problem throughout the world but is becoming an epidemic in Low and Middle Income Countries (LMIC).

How should we approach these patients.
The palliative care needs of neurological patients will vary according to stage of disease and individual needs. But some of the needs and concerns are common to many patients and their families, particularly at the end of life.

As palliative care is developed basically on the need of patients with advanced cancers but neurological diseases represent a different spectrum of diseases with different needs. The main differences are:
1. Delayed diagnosis at advanced stage.
2. Variable rate of progression.
3. Marked cognitive and physical disability.
4. Combination of physical, communication, cognitive and mental health issues.
5. Inherited neurological diseases have different palliative care needs.
6. Difficulty in recognizing end of life.
7. Increased incidence of associated comorbidities such as hypertension, diabetes...
mellitus, coronary artery disease, chronic obstructive pulmonary diseases (COPD).

For some diseases, palliative care is required in the early course of disease whereas in others, it may be needed at the later stage. The progressive nature and the poor prognosis of motor neuron disease will often require palliative care from the time of diagnosis. However, for some conditions like Parkinson’s disease and multiple sclerosis, although a progressive disease, the need for palliative care arises late particularly when the disease is at the final stages. For neurological disease, the palliative care team needs integration of general practitioners, physicians, neurologists and specialist palliative care provider. Apart from management of non specific complaints, a expert opinion by a neurologist is required for management of specific complaints like treatment of spasticity, adjustment of anti parkinsonian drugs and for treatment of autonomic dysfunction. However, palliative care expert is required for more complex issues like psychological issues, spiritual issues, family issues and end of life issues apart from coordinating team member.[4]

Palliative care need in TBI arises when a person has a life-threatening illness and requires specific treatment to symptom control as well as end-of-life issues. However it is imperative to clarify that palliative care is not about bringing death.

Palliative care is a multi-disciplinary approach to support the patient and his or her family physically, socially, emotionally and spiritually. This holistic care should be continued throughout the illness and even after the person’s death in the form of bereavement support.

Rehabilitation

Rehabilitation services in palliative setting is goal directed measure to optimize the functional ability of patient with respect to physical, psychological, social and spiritual needs. It will always be a multidisciplinary team approach which includes rehabilitation medical consultant, physiotherapist, occupational therapist, speech therapist, psychologist, dietitian, rehabilitation nurses, general practitioners and spiritual preachers.[5] All those involved in the rehabilitative care should work together cohesively with a well defined role for better outcome. Rehabilitation services can be hospital based or it can be home based.

End-of-Life Care

In advanced neurological condition, identification of patients approaching the end of life care phase of their illness is important because it enables the appropriate care to be planned and communicated to the patients and family. It is important in those people who have lived with chronic disability to distinguish this from deterioration, due to an inter current illness. There may be specific triggers for a particular disease but it is essential to consider every patient individually, as there will be a great variation in the disease progression and patients need, even within the disease.

The End of Life Care Pathway suggested that end of life care should be considered throughout the disease progression [6] and Some of the common symptoms encountered at the end of life are:

- Swallowing problems
- Recurrent infection – particularly respiratory infection that may be associated with aspiration
- Marked decline in physical status – generalized weakness and reduced mobility and activity
- First episode of aspiration pneumonia
- Cognitive difficulties – confusion or more subtle cognitive change
- Weight loss
- Significant complex symptoms: Pain, Spasticity, Nausea, Psychosocial or spiritual issues

The care of people with neurological disease, particularly at the end of life, is complex and involves many different disciplines and teams. There is the need to recognize the needs of patients and their families throughout the disease progression and identify and recognize the triggers that may
indicate that there is significant deterioration requiring a palliative approach to improve the quality of life at the end of life. Withdrawal of nutrition and hydration is a sensitive issue because of no well defined guidelines. Those in favor of withdrawal argue that it is undignified and an assault, to insert tubes into a permanently unconscious person where survival is uncertain and that it prevents loved ones from grieving. Those against it are of view that every life is precious and have rights to get maximum care at any stage and there may be new scientific developments in the future from which the patient would benefit. Palliative care service would be helpful in making such decisions. It is important that both nutrition and hydration are removed simultaneously: death will be due to the effects of cellular dehydration rather than those of under nutrition. Peaceful death normally occurs in 10–14 days. But it was cautioned that DNR orders should not misunderstood as withdrawing all aggressive therapy. Palliative care team have to play an important role here to make it understand to the treating physician and other supporting staff vis a vis educating the family members.\textsuperscript{(7)}

**Withdrawal of life support measures**

In contrast to medical intensive care unit (MICU) where patients are on multiple life saving measures, the stroke patients are hemodynamically stable and require only ventilatory support. The process of withdrawing life support from an ICH patient can differ greatly from that of a medical ICU (MICU) patient.\textsuperscript{[7,8]} These differences can lead to longer survival and difficulties in decision-making. Only after a consensus is reached between the treating physician and families for withdrawal of ventilatory support, terminal extubation is performed. Palliative care team has to take a proactive role to explain the consequences of terminal extubation to the family and will have to manage the post extubation events which may appear to be a suffering and agony to the patients. There is wide range of survival time after extubation varying between 10 minutes to 11 days.\textsuperscript{[8,9,10]} In a study of life support withdrawal in neurologic ICU patients, 25% of patients died within one hour of extubation and 69% deaths occurred within 24 hours. The median duration of survival was 7.5 hours. One interesting finding is that the GCS score at the time of extubation had no effect on the duration of survival. Most common presentation following terminal extubation is labored breathing in 59% of the patients.\textsuperscript{(11,12)}

After terminal extubation, the common complications are dyspnea, pain, post extubation stridor and death rattle and it is the primary responsibility of the palliative care provider to take measures to ease the process of death for the patient and family members.\textsuperscript{(13)}

Opioids have been used to decrease the work of breathing, control tachypnea, and decrease feelings of air-hunger without causing co\textsubscript{2} retention.\textsuperscript{[14]} Pain, although uncommon in stroke patients, may be present and should be considered if the patient is in distress. Opioids are used liberally to control dyspnea and pain, starting with a bolus of 5 to 10 mg of morphine if signs of distress are present, and repeat doses as often as every 10 minutes if needed. After the symptoms get settled then a continuous infusion of 50% the loading dose per hour can be started and titrated as per the need. But a common barrier in using narcotic is concerns of families and health care providers over hastening death by respiratory depression. Although this misbelieve is disproven by various studies.\textsuperscript{[14]} But the fact is that opioids do not cause respiratory depression, rather it can actually lead to a small prolongation of life. The physiological basis is that opioids decrease the demand for oxygen and attenuate the cardiopulmonary response to increased work of breathing, leading to a higher tolerance to decreased levels of oxygen delivery.\textsuperscript{[15]}

Stridor and “death rattle” are common following terminal extubation and can be quite distressing to family members. Postextubation stridor can be managed with
the bolus dose of steroid (100 mg methylprednisolone IV ) few hours before extubation. The death rattle usually results from excessive bronchopulmonary secretion. It can be managed effectively by reducing the parenteral fluid intake, stopping the enteral feed few hours before extubation, diuretics if cases of fluid overload and antisialogogues agents to reduce the excess secretion.

Palliative sedation is often not required in terminal stroke patients due to the existing neurologic damage but it may be required for relief of intractable symptoms distressing to the patient and family despite opioid administration. Most common drugs used for palliative sedation are Propofol and benzodiazepines (midazolam or lorazepam). But it’s always recommended to make an institutional protocol for terminal sedation.

**Family issues**

Family meeting is a vital intervention to help explain prognosis, to formulate a plan of care as per the wish of the patient, and to get all family members involved in decision making. The other important aspect is to know the responsibilities of the dying patients and how it can be finished in future. The positive aspect of these family sessions is that it expedite the decision making and measures taken to withdraw life supporting interventions that ultimately improves quality of life, overall prognosis, and reduces level of suffering to both patient and family.

**Care of the dying patient**

A common practice among health care professionals is to transfer the dying patient to a side room and separate from family members. This is because they are not trained in handling the end of life issues. Palliative care provider have a greater role in such cases as they are proficient in providing physical, psychological, social, and spiritual care for the patient and the relatives.

**Physical care**

After a combined decision is taken to withdraw the life support, all oral and non essential drugs like antacids, antibiotics should be discontinued. Drugs that need to be continued, such as opioids, anxiolytics, and antiemetic, may be converted to the subcutaneous route if feasible and used with a syringe pump as per hospital protocols. Inappropriate interventions like intubation; central venous cannulation etc. should be discouraged. Unnecessary investigations including blood tests and invasive monitoring should be discontinued.

Primary goal is to achieve good symptom control (pain, nausea, vomiting, agitations etc.) along with development of community and home based palliative care services to avoid unwanted hospital admission.

Adequate mouth care is essential in dying patients and it can be taken care by adequate oral hygiene measures. Family members are encouraged to give sips water and moisten patients mouth to avoid excess drying. If required Foleys catheterization should be considered for urinary retention.

In literature, evidence is limited to support that continuing hydration and nutrition in the dying patient is of much benefit and should in most cases be discontinued. Dying patients should not be subjected to “cardiopulmonary resuscitation,” as this constitutes a futile and inappropriate medical management. Patients advance directive should be honored.

**Psychological care**

Assessment of patient’s insight into their condition should be done and issues relating to dying and death should be done sensitively.

**Social care**

Patient’s condition and clinical expectation that patient is dying and will die should be explained and discussed with family members in a simple and explicit language. Family members and relatives should have given ample opportunity to stay with patient, to discuss his or her will and say good bye.

**Spiritual care**

Patient's cultural background along with religious believes and tradition related to care of the body after death should be taken care in a compassionate manner.

**Respite care and Bereavement care**

**Future Need**
Primary aim for the future needs is to disseminate the principles of palliative care to all healthcare providers. It is high time to create awareness among physicians, nurses, paramedics and in community for palliative care need of terminally ill and dying patients with variety of neurological and neurosurgical diseases and associated disorders.

References
Pathology of the central nervous system (CNS) remains a leading cause of indirect maternal mortality. Although needed infrequently, pregnant women may present with pathology requiring neurosurgical intervention. Services of a neuroanaesthetist may be sought for indications like, intracranial tumor or abscess excision, spinal cord tumors and lesions removal, and for diagnostic and therapeutic interventions. Direct involvement of the neuroanaesthetist may also be required in neuroradiological interventions in subarachnoid hemorrhage (intracranial aneurysms, arteriovenous malformations) and stroke.

A pregnant patient presents with significant physiological alterations that may pose challenges in their management during neurosurgery. Principles of management may be contradictory, and both maternal and fetal well being need to be taken into consideration.

**REQUIREMENT OF NEUROSURGERY DURING PREGNANCY**

**Intracranial Haemorrhage**: Intracerebral hemorrhage (ICH) accounts for a substantial portion of pregnancy-related mortality. In a multicentric study conducted in the United States, the risk of stroke (both cerebral infarction and intracerebral hemorrhage) are increased in the six weeks after delivery but not during pregnancy itself. Intracerebral hemorrhage is most commonly due to subarachnoid hemorrhage (SAH) due to ruptured arterial aneurysms and arteriovenous malformations (AVM). Pregnancy does not confer an increased risk of hemorrhage in patients with AVM; however, the risk of rebleeding is 25% during the same pregnancy, as against a 3%–6% risk during the first year in the general population. The risk of aneurysmal SAH was previously believed to be increased during pregnancy, a phenomena contributed by the pregnancy-induced increase in circulating blood volume and cardiac output, and the hormonal changes to the arterial wall. Recent studies however, do not find an increased association between pregnancy or delivery and the risk of rupture of cerebral aneurysms.

**Primary Central Nervous System Tumours**: The incidence of brain tumors is not known to be increased in pregnant women, with 85% of such tumors consisting of meningiomas, gliomas, pituitary tumors and vestibular schwannomas. Some of these tumours, such as meningiomas, however, may become symptomatic in the pregnant state due to water retention, engorgement of vessels, and the presence of sex hormone receptors on tumor cells, leading to explosive growth of the tumor. Choriocarcinoma is an aggressive gestational tumour that metastasizes to the brain. The clinical diagnosis of intracranial neoplasms may be challenging, as the symptoms of headache upon awakening, nausea, vomiting, or seizures could be easily misdiagnosed as hyperemesis gravidarium during early pregnancy, or as eclampsia during late pregnancy. However, the presence of an abnormal fundoscopic examination, visual impairment, focal seizures, and lateralizing neurological deficits should alert clinicians to the possibility of an intracranial tumor, and prompt further investigations like MRI to confirm the diagnosis. Urgent neurosurgical intervention may be required for the management of (a) malignancies, (b) active hydrocephalus, and (c) benign brain tumors associated with signs of impending herniation or progressive neurological deficit.
Spinal Pathology: Symptomatic disc herniation is reported to have an incidence of around 1:10,000 pregnancies. Severe backache is a common complaint during pregnancy, and is attributable to ligamentous laxity secondary to high serum levels of relaxin, and extra mechanical stress. 85% of patients with symptomatic disc herniation due to nerve root compression improve with conservative management within 6 weeks. In contrast, women presenting with worsening neurological deficit may require surgical intervention and those with a cauda equina syndrome represent a surgical emergency. Patients may also present for surgery for newly symptomatic spinal tumors, and rarely for spontaneous spinal epidural hematoma (SSEH), vertebral canal abscess or spinal AVMs.

Traumatic brain injury: Trauma is the leading non-obstetric cause of maternal death. It complicates 6-7% of pregnancies and may well involve cranial or spinal injury that will necessitate surgery. Optimal management of the pregnant trauma patient requires a multidisciplinary approach. Primary goals are aggressive resuscitation of the mother and maintenance of uteroplacental perfusion and fetal oxygenation by the avoidance of hypoxia, hypotension, hypocapnia, acidosis and hypothermia. What must always be remembered is that resuscitating the mother will resuscitate the fetus!

PHYSIOLOGICAL ALTERATIONS DURING PREGNANCY

RESPIRATORY AND AIRWAY MECHANICS: The oxygen consumption increases about 20-40% at term, and the functional residual capacity (FRC) decreases up to 20%; both contributing to a rapid oxygen desaturation during periods of apnoea, as occurs during induction of anaesthesia. Therefore, at least 2 minutes of preoxygenation and denitrogenation with a tightly fitting face mask is mandatory before the induction of general anesthesia during pregnancy.

Progesterone mediated increases in respiratory rate and minute volume result in a reduced arterial partial pressure of carbon dioxide (PaCO2) of around 30mmHg. Maternal pH, however, remains within normal limits due to compensatory renal excretion of bicarbonate. During anaesthesia PaCO2 levels should be maintained within these norms.

Airway changes during pregnancy include capillary engorgement of the respiratory mucosa and friability of oropharyngeal tissues (due to soft tissue edema caused by accumulation of extracellular fluid), predisposing the upper airway to trauma, bleeding and obstruction. The size of the glottic opening is reduced; gentle laryngoscopy and the use of small endotracheal tubes (6-7 mm ID), therefore, is the dictum. Difficult airway is commonly encountered, and the incidence of failed intubations is eight times higher in the pregnant as compared to the general population.

CARDIOVASCULAR CHANGES: Haemodynamic changes during pregnancy include a 40-50% increase in blood volume and cardiac output and a 20% reduction in haematocrit due to dilution, resulting in dilutional anemia. At term, maternal blood volume reaches 90 ml/kg, an increase of 1000-1500 ml in most women. Aortocaval compression is of concern to the anaesthesiologist during and after the second trimester. The combination of systemic hypotension due to decreased venous return, increased uterine venous pressure, and uterine arterial hypoperfusion severely compromise uterine and placental blood flows. When combined with the hypotensive effects of regional or general anaesthesia, aortocaval compression can readily produce fetal asphyxia. These considerations emphasise the need for left uterine displacement during anaesthesia and surgery, most effectively accomplished by tilting the operating table 30 degrees to the left or placing a roll under the patient’s right hip.

GASTROINTESTINAL SYSTEM: The upward and anterior displacement of the stomach by the gravid uterus, combined with the reduced
gastroesophageal sphincter tone by the elevated progesterone levels, place the parturient at a high risk for regurgitation and pulmonary aspiration. A history of active reflux or obesity poses additional risk. All pregnant patients are therefore, considered full stomach, and adequate aspiration prophylaxis with either a nonparticulate antacid, or a combination of a histamine H2 blocking drug and metoclopramide, is administered prior to induction.

CENTRAL NERVOUS SYSTEM CHANGES: The minimum alveolar concentration (MAC) of inhalational anaesthetics decreases progressively by as much as 40% during pregnancy, due to a surge in endorphin levels and the sedating effects of progesterone. The requirement for inhalational anaesthetics therefore decreases considerably in a pregnant patient for surgery.

The dose requirements for local anaesthetics may be reduced by about 1/3rd in the pregnant population at term. The reduced volume of CSF secondary to epidural venous engorgement may cause a more extensive spread of the local anesthetic, thereby reducing the dose by 30%. Also, the increased pressure in the epidural space facilitates diffusion across the dura and produces higher concentration of local anesthetic in the CSF.

An increase in the epidural venous pressure caused by the increased intra-abdominal pressure and direct vena cava compression, predispose a pre-existing pathology in the valveless epidural veins to rupture in the presence of abrupt pressure changes like sneezing, coughing or a forceful valsalva manoeuvre. The epidural arterial vessels are equally prone to rupture and produce a hematoma, due to the degenerative changes in vessel walls produced by progesterone and estrogen during pregnancy.

Neurosurgical lesions may require radiation exposure, for diagnostic imaging or for radiological intervention such as coiling of aneurysms. The fetus may thus be exposed to recurrent, cumulative radiation doses. A head CT exposes a fetus to 0.01-0.1 mSv, while a CT angiogram and coiling results in a greater radiation dose with estimates ranging up to 10 mSv exposure to the mother. International Commission on Radiological Protection (ICRP) 2007 review has essentially confirmed that at doses under 100 mGy (1 Gy = 1 Sv), lethal effects in the pre-implantation period of embryonic developments will be very infrequent.

TIMING AND METHOD OF DELIVERY

Pregnant women presenting with a neurosurgical emergency, like a ruptured aneurysm, neurological deterioration in a previously diagnosed intracranial tumour, or cauda equina symptoms in a spine pathology, need urgent intervention regardless of the gestational age. At gestational ages < 24 weeks, neurosurgical intervention has to proceed, and all care should be taken to optimise maternal hemodynamics so as to preserve fetal well being. Fetal management following surgery then proceeds around obstetric indications.

At gestational ages > 24 weeks, one of the three decisions have to be made –
1. Caesarean delivery followed by neurosurgery as continuous procedures
2. Caesarean section proceeded by neurosurgical intervention at a later date
3. Neurosurgery with an aim to maintain pregnancy

The use of fetal heart rate (FHR) monitoring to monitor fetal well being perioperatively needs to be individualised. Such monitoring would have clinical utility only if there are expert personnel to interpret acute changes in the FHR and intervention is feasible (in terms of staff and facility) if need arises. It may serve as a guide to search for potential reversible causes of fetal distress, like maternal hypotension and hypoxemia.

ANAESTHETIC CONSIDERATIONS DURING PREGNANCY

Anaesthetic management during pregnancy requires a balanced consideration of both the maternal as well as fetal physiology.
Whenever feasible, a multidisciplinary team approach including the neurosurgeon, neuroanaesthesiologist, neuroradiologist, neurologist, obstetrician, neonatologist and neurointensivist, is desirable for an optimal planning of surgery and anaesthesia.

**PREMEDICATION**

Sedative premedication is largely restricted to highly anxious patients, and that too in the preoperative area where the patient can be adequately monitored, as it may cause hypoventilation, hypercarbia and a concomitant rise in intracranial pressure (ICP).

All pregnant patients must undergo an aspiration prophylaxis as a part of premedication. 30 ml of 0.3M sodium citrate 30 minutes prior to induction of anaesthesia, metoclopramide 10 mg and an H2 receptor blocker like ranitidine 50 mg iv effectively reduce the acidity and volume of gastric secretions in a parturient.

Anticonvulsant therapy may need to be started or continued in the preoperative phase. The plasma concentrations of most antiepileptic drugs declines during pregnancy, owing to an increased renal clearance, impaired drug absorption and decreased protein binding. The therapeutic plasma levels may therefore need to be monitored preoperatively.

**INDUCTION : RAPID SEQUENCE Vs SLOW NEURO INDUCTION**

The anaesthetic goals for induction of anaesthesia in obstetrics and neurosurgery are contradictory (rapid sequence induction to reduce risk of aspiration, vs slow neuro induction to reduce ICP). The attending anaesthesiologist has to therefore, balance the need of the hour and adopt a modified rapid sequence technique to meet these competing goals.

Pregnant patients are placed supine with a wedge under the right hip or a 15° leftwards tilt of the operating table. Anaesthesia induction must begin with adequate pre-oxygenation of the patients for 3-5 minutes. All pregnant females should be assumed to be a difficult airway, and appropriate equipment for management of difficult airway should be kept handy, with a thorough discussion on the alternative airway management plans should intubation fail. Obese, pregnant patients should be placed in the head up ‘ramped’ position, by elevation of the shoulders with a pillow underneath.

Induction of anaesthesia is accomplished with thiopentone 4-6 mg/kg. Propofol may be used alternatively in a single bolus dose of 2 mg/kg iv. Short acting opioids such as fentanyl (2-5 mcg/kg) or remifentanil (1 mcg/kg given over 60 seconds) are administered to blunt pressor responses to laryngoscopy. Lignocaine 1mg/kg may be used concomitantly, but it is less effective as compared to opioids. Magnesium sulphate (30-60mg/kg) is the drug of choice for blunting the response to laryngoscopy in eclamptic and pre-eclamptic patients. Succinylcholine is avoided in neurosurgery as it causes a transient increase in ICP. Rapid sequence induction is therefore modified by administering a non depolarising muscle relaxant like rocuronium (0.9-1.2 mg/kg). Cricoid pressure is applied from the time consciousness is lost, and maintained till intubation is confirmed by capnography and the endotracheal cuff is inflated. The patient may be gently ventilated by a mask in a modified rapid sequence induction technique.

**MAINTAINENCE**

As in any non pregnant patient, anaesthesia is maintained with an inhalational anaesthetic like isoflurane or sevoflurane, an opioid such as fentanyl 1-2 µg/hr, a non depolarising muscle relaxant, and a 1:1 O2-air mixture. The MAC of most volatile anesthetics is reduced by approximately 25% during pregnancy, and so initial end-tidal isoflurane or sevoflurane concentrations of 1.0% and 1.5%, respectively, are appropriate (39). These maintain a suitable depth of anesthesia, a degree of uterine relaxation because of their tocolytic effect and preserve cerebral autoregulation. Both thiopental or propofol infusions (5-6 mg/kg/hr) may be administered to reduce ICP in cases of a tight brain.
HEMODYNAMIC CONSIDERATIONS: Maintenance of a normal blood pressure, close to baseline values, is mandatory during the operative course, for the maintenance of cerebral perfusion pressure (CPP) in the mother on one hand, and avoidance of intrauterine fetal asphyxia, on the other. Invasive blood pressure monitoring is therefore indicated prior to induction, to avoid and treat excessive swings in blood pressure. Large bore intravenous access should be taken for appropriate administration of iv fluids. Central venous access may be considered for administration of concentrated vasoactive drugs, central venous pressure monitoring, or aspiration of air emboli (in cases of sitting craniotomies). Effective maternal positioning also aids in preventing hypotension.

VENTILATION: Hyperventilation to maintain maternal PaCO2 between 25-30 mm Hg should be continued intraoperatively to decrease ICP. The compensated maternal respiratory alkalosis that pre-exists in pregnant females should be taken into consideration.

MANNITOL & IV FLUIDS: In animal studies, maternal administration of mannitol results in significant increases in maternal osmolality, with subsequent fetal dehydration and contraction of blood volume. However, in individual case reports, mannitol in doses of 0.25–0.5 mg/kg has been used and appears safe. Furosemide is an alternative but should also be used cautiously. Intravenous fluid replacement should be limited to glucose free isotonic crystalloid or colloid solutions, to prevent brain edema and increased ICP.

STEROIDS: Continued use of steroids during pregnancy, especially during the third trimester, results in fetal adrenal suppression and neonatal hypoadrenalism. Short term use of dexamethasone (4 mg iv 6 hrly), however, is indicated to reduce peritumor edema. It also acts to accelerate fetal lung maturity by increasing surfactant production, although betamethasone is preferred for this purpose, as it has a better neonatal outcome.

TEMPERATURE REGULATION: Induced hypothermia is no longer recommended in neurosurgery as a means of neuronal preservation. Normothermia should therefore be maintained in pregnant females undergoing neurosurgery with the use of forced warm air blankets, and body temperature monitored with a temperature probe (nasopharyngeal/oesophageal/axillary).

EMERGENCE

The pregnant patient is at a high risk of aspiration following extubation and therefore, should be extubated only after the patient is fully awake and the airway reflexes are intact. Airway stimulation and bucking on the endotracheal tube can be prevented by administering lidocaine, fentanyl or sedative doses of propofol. Early extubation is favoured to facilitate early neurological evaluation. However, the patient may be ventilated postoperatively if the preoperative neurologic status was poor, or the intraoperative course has been significant in terms of bleeding, cerebral edema or ischemia.

POSTOPERATIVE MANAGEMENT

PAIN MANAGEMENT: Good postoperative analgesia should be provided for maternal comfort and mobility and to reduce undesirable hemodynamic disturbances. Multimodal analgesia using local infiltration of the incision site/scalp blocks, iv paracetamol, and opioids such as fentanyl & morphine in controlled doses should be given. Tramadol is discouraged in neurosurgical patients as it lowers the seizure threshold. The nonsteroidal antiinflammatory drugs (NSAIDs) are avoided because of their antiplatelet effect and the tendency to cause potential bleeding after intracranial surgery, or because of their potential fetal complications (renal failure, necrotizing enterocolitis, and persistent fetal circulation after birth) when used in the last trimester.
DEEP VEIN THROMBOSIS PROPHYLAXIS: Pregnant women have a 4-5 fold increased risk of thromboembolism as compared to the non-pregnant population, owing to their hypercoagulable state. Intermittent pneumatic leg compression devices or elastic stockings should be used peri- and post-operatively in all patients. Starting pharmacological prophylaxis with heparin as early as feasible in the post operative period should be discussed with the neurosurgeon.

CEREBRAL VASOSPASM: The parturient is somewhat protected from cerebral artery vasospasm in their relatively haemodiluted and hypervolaemic state. Magnesium sulphate, the drug of choice for preventing and treating eclampsia, has been shown to reduce the severity of vasospasm after SAH. The evidence base for the use of nimodipine in pregnancy is limited. However, the known benefits of nimodipine in preventing spasm are likely to outweigh any potential risk to the fetus and should be administered as clinically indicated.

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Anesthesia for Minimally Invasive Neuro Surgery

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Minimally invasive neurosurgery is coming into vogue because of certain perceived benefits such as enhanced patient safety, shorter hospital stays, reduced invasiveness and lower postoperative morbidity. Procedures include endoscopic third ventriculostomy, transphenoidal hypophysectomy, deep brain stimulation, video assisted thoracic surgery, vertebroplasty and kyphoplasty amongst others. As in other types of neurosurgery, the goals of anesthesia remain the same viz. ensure patient immobility, ensure safe rapid emergence, control ICP, facilitate intraoperative neurophysiological monitoring techniques and minimize postoperative complications.

1. NEUROENDOSCOPY- Indicated for the treatment of noncommunicating hydrocephalus. It has an operative mortality of 0.1% and a complication rate of 5-30%. It involves placement of a frontal burrhole and the introduction of a rigid or flexible scope into the ventricle through it. The ventricles are irrigated with warmed saline or RL with simultaneous drainage of CSF and irrigation fluid. Though the procedure can be done under monitored anesthesia care, general anesthesia is preferred. Sedative premedication should be avoided. Intraoperative immobility needs to be ensured. Cardiovascular stability needs to be maintained. The use of nitrous oxide should be avoided. Though the procedure is normally minimally invasive, there is a possibility that conversion to a formal craniotomy may be required and a backup plan should be in place. Postoperative pain is minimal and short acting opioids are sufficient. Neuroendoscopy is associated with certain peculiar problems – continuous irrigation produces pressure inside the system which can result in cerebrovascular circulatory insufficiency. Pressure on the hypothalamic nuclei can produce autonomic disturbances resulting in cardiovascular instability. Intraoperative bradycardia is a common occurrence. Significant intraoperative bleeding can result from injury to the basilar artery. Tension pneumocephalus and venous air embolism can occur in patients with a VA shunt. Delayed emergence is also common in these patients.

ENDOSCOPIC TRANSPHENOIDAL HYPOPHYSECTOMY

Endoscopic transphenoidal pituitary surgery has gained popularity as it is associated with lower morbidity, wider and clearer surgical view and decreased length of stay while being more acceptable cosmetically. Preoperative evaluation should identify the presence of panhypopituitarism, acromegaly, cushings disease, hypo or hyperthyroidism in addition to the presence of comorbidities, intubation problems and electrolyte imbalance. Intraoperative blood pressure control needs to be meticulous as hypertensive surges at the time of nasal packing or dissection can lead to a bloody field. The use of epinephrine at the time of packing can lead to arrhythmias. Blood loss is generally minimal unless there is carotid artery or cavernous sinus injury. Emergence should be clear headed and rapid with minimal coughing in order to avoid bleeding. Aspiration of blood pooled in the pharynx with laryngospasm is also a danger with this type of surgery. If the patient needs to be re-explored due to the presence of a hematoma then the risk of pneumocephalus at the time of ventilating the patient prior to intubation needs to be kept in mind.

DEEP BRAIN STIMULATION

Deep brain stimulation is used as a treatment modality for the treatment of Parkinsons disease, dystonia and essential tremors. It
INVASIVE NEUROSTIMULATION

Involves placement of image guided neurostimulators in the thalamus, globus pallidus and subthalamic nuclei. The stimulator leads are connected to an external pulse generator. During placement of the stimulator, changes in the motor symptoms in response to stimulation are used to guide lead placement. These inputs are lost if the procedure is done under general anesthesia and hence most procedures are done under minimal sedation. Medications used for the treatment of motor symptoms as well as sedation are withheld so as to prevent any interference with the interpretation of the results. Propofol even in low doses can cause reduction of tremors and confound results. Hypertension, venous air embolism, pneumocephalus and seizures can complicate the procedure.

ENDOSCOPIC STRIP CRANIECTOMY

Endoscopic cranial vault remodeling is a wide sutural excision combined with lateral osteotomies which are combined with helmet molding therapy postoperatively. The advantage of this procedure over conventional surgery is that it is associated with decreased operative time and blood loss as well as decreased hospital stay. The main preoperative concern is the fact that it is a surgery which needs to be done in younger patients (below 6 months) who may be having other cardiac, respiratory problems as well as C-spine problems. The main intraoperative concerns are those of blood loss and venous air embolism though the incidence of these are less than in conventional surgery. Appropriate venous access therefore needs to be secured prior to surgery, pressure points padded and the ET tube secured appropriately.

MINIMALLY INVASIVE SPINE SURGERY

Spinal endoscopic technique is a good alternative to open reconstructive surgery and decompression of the thoracolumbar spine. The fact that the amount of muscle dissected is less decreases postoperative pain and recovery time. Video assisted thoracoscopic surgery is now being used for anterior thoracic spine release and fusion. Thoracoscopically and laparoscopically assisted scoliosis correction, multilevel spinal fusions and thoracic corpectomies often require the placement of double lumen tubes which are difficult to place in these patients and moreover may require conversion to a single lumen tube in combined anteroposterior fusions. Restrictions in the use of anesthetics and muscle relaxants in patients undergoing somatosensory and evoked potentials further complicate management. Unintended entry into large vessels or viscera may occur and should be managed appropriately. Postoperatively meticulous attention to chest toileting is necessary to minimize postoperative lung complications.

Kyphoplasty and vertebroplasty are minimally invasive procedures developed to treat osteoporotic and osteolytic lesions of the thoracic and lumbar vertebra. Though the procedure is a low surgical risk procedure most patients chosen for the procedure are offered the treatment because they are unfit for extensive procedures. The anesthetic plan needs to include a plan for perioperative pain control.

Endoscopic cervical discectomy and foraminectomy can be used for cervical root decompression with the advantage of lesser blood loss and postoperative pain. The potential complications include the risk of dural puncture, nerve root injury and vertebral artery injury.

Minimally invasive neurosurgery is an evolving speciality which has its own set of inherent problems. Therefore the attending anesthesiologist needs to be aware of the potential problems and their remedy.

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**Introduction**: Wertheimer a disciple of Rene Leriche first compiled a book on movement disorders while Otfrid Foerster has been recognized as the pioneer of movement disorder surgery. The movement disorder program is a multidisciplinary program staffed by a neurosurgeon, neurologist, neuropsychologist, neuroanesthesiologist, nurse and physical therapist with specialization in the care and rehabilitation of patients with movement disorders. Surgery is considered only after all attempts at conservative management have failed or have provided suboptimal results. The type of surgery varies depending upon the particular movement disorder. Currently, Deep Brain Stimulation (DBS) is also used for essential or familial tremor. Pallidotomy for the most part has been replaced by (STN) DBS in Parkinson’s disease. The FDA has approved pallidal DBS for treatment of certain dystonias. Thalamotomy is rarely used since the introduction of DBS.

Deep brain stimulation is a safe, effective, reversible, therapy without permanent damage. Currently, DBS is most commonly performed on drug-resistant Parkinson’s disease. It must be performed stereotactically. Precise placement of the electrodes is the most important criteria. The exact technique depends on the skill, experience, technical expertise, habits of the team that produces satisfactory results. It is effective in alleviating the rigidity, slowness of movement, on stage dyskinesias, and tremor in about 80% of cases. It has also been effective in improving gait and gait freezing, but this usually requires bilateral (i.e., right and left) implants. It is more effective in younger and less disabled patients. It is not effective in cases that have not shown a good response to L-DOPA. In general, it improves signs and symptoms most that are present when a patient is in the "off-state" (the wearing off state of L-DOPA, nearing the time when the next dose is due). The exception to this is the "on-stage" dyskinesias which also improve after STN DBS. DBS patients reduce their dose of L-DOPA an average of 50%.

It involves three surgical procedures and two MRI sessions.

**Step1:** Frame fixation / ventricular implantation: of titanium skull screws for repositioning. After sedation, a scalp infiltration at the pin sites is performed and a
Stereotaxic base-ring together with a localizer is fixed to the patient’s head.

**Step 2**: Targeting MRI:. High resolution images of the target area are obtained and transferred via ethernet to the computer workstation, which is used to derive the target coordinates and pathway or trajectory for the recording and stimulating electrodes and DBS electrode.

**Step 3**: Implantation of electrodes in target: After the scalp nerve block, a transverse frontal incision is made and right and left frontal bur holes (about 1/2 inch diameter) are made. The aiming arc is then placed on the basering and the microelectrode guide is attached to it. An array of four microelectrodes is advanced to the right (and subsequently the left) targets with continuous recording of electrical activity. Typically, high frequency and amplitude electrical activity is recorded at the target point and this activity is further amplified with passive movement of the opposite arm. During the recording the patient is usually awake so that recordings from the target site are optimized. After completion of the recordings, the DBS electrode is introduced to the target area. Proper positioning is confirmed with intraoperative fluoroscopy. Stimulation is performed after the implant to assure that no unwanted motor or speech responses are obtained. None of this is felt by the patient since the brain is not pain-sensitive. The DBS electrode is then locked in place with a silastic ring, and fluoroscopy is repeated to assure proper electrode position.

**Step 4**: Post-implant control MRI: to confirm the position of the electrodes

**Step 5**: Implantation of programmable stimulator: after the test stimulation has been found to be satisfactory, the permanent stimulator is inserted in the subclavicular region in a subcutaneous pouch.

**Anesthetic Considerations**: The essential components of success outlined are establishing rapport with the patient, careful patient positioning and coordinated teamwork. Attention should be directed toward maintenance of peri-operative drug therapy, associated physiological disturbances and potential adverse drug interactions. Emotional stress, which is unavoidable and difficult to address can exacerbate the disease. Parkinson related disturbances of systemic physiology include respiratory dysfunction, dysphagia, autonomic dysfunction, and sleep related ventilatory abnormalities.

**Respiratory dysfunction**: is particularly a prominent feature. Parkinson’s disease can produce restrictive lung disease secondary to chest wall rigidity but pulmonary function tests often reveal an obstructive pattern with a “saw tooth” pattern on flow volume loops. Upper airway abnormalities may occur. Involuntary movements of the glottis and supra glottic structures cause intermittent airway obstruction a condition that can be exacerbated by levodopa withdrawal. Upper airway obstruction, laryngospasm, and respiratory arrest are documented complications of Parkinson’s disease and may occur outside the setting of anesthesia and surgery. Laryngospasm has been reported in awake patients hours after surgery. Direct visualization of the larynx during such episodes reveals complete apposition of the vocal cords requiring succinyl choline administration to provide relief. Although some cases occur despite maintenance of anti-parkinsonism drugs, most followed withdrawal of drug therapy of Parkinsonism medication. Not only should interruption in drug therapy be avoided but the dosage may need to be increased if airway problems persist despite otherwise adequate therapy.

**Aspiration**: Parkinsonism patients have a propensity to aspiration because they often have severe though asymptomatic, dysphagia and dysmotility that combined with upper airway abnormalities present an especially troublesome situation. In fact pulmonary aspiration is a common cause of death in
patients with Parkinson's disease. Administration of antacids and prokinetic drugs should be considered, but whether anesthesia increases the risk of aspiration in these patients is unknown. Metoclopramide should be avoided, however, because it is a dopamine receptor antagonist and could exacerbate the disease. In contrast prokinetic drugs like cisapride or domperidone have no effect on dopaminergic balance and are reasonable alternatives.

**Autonomic dysfunction:** can be an issue as it affects the ability of Parkinsonism patients to respond to hypovolemia and vasodilatation sometimes associated with anesthesia and surgery. Orthostatic hypotension or thermoregulatory or genitourinary dysfunction suggests preexisting autonomic insufficiency and should heighten the awareness of the potential for peri-operative hemodynamic stability and altered responses to vasopressors.

**Anesthetic agents:** and a number of other agents used in the peri-operative period may affect the disease process. Volatile anesthetic agents may alter the dopaminergic balance in the brain, but whether they exacerbate Parkinson’s disease is unknown. Propofol produces both dyskinesias and ablation of resting tremor, suggesting that it may have both excitatory as well as inhibitory effects in this patient population. Propofol is known to decrease neuronal firing rates in the locus coeruleus and neocortical areas confounding the assessments of neuronal firing rates in the dystonic pallidium.

Dexmedetomidine a selective α2 agonist, is a unique sedative medication as it can provide patient comfort with respiratory and hemodynamic stability. It does not impair the intensity of the movement disorder or interfere with micro electrode recordings which are significant favourable features of dexmedetomidine use in DBS surgery.

Ketamine should be used avoided because of interactions with levodopa and its sympathomimetic properties. However in one single case report ketamine stopped temporarily the motor symptoms of the disease.

Butyrophenones and phenothiazines, which block dopamine receptors, exacerbate Parkinson's disease. In one case droperidol actually induced parkinsonism is a normal patient.

Ondansetron, a serotonin antagonist, appears to be a safe alternative for the prevention and treatment of emesis in these patients.

Opioids are considerably more likely to produce muscular rigidity in Parkinsonism patients but acute dystonia has been observed in only a single patient of untreated disease. Meperidine should be avoided in patients taking Mono Amine Oxidase inhibitors because of the potential for developing stupor, rigidity agitation and hyperthermia.

Muscle relaxants: responses to depolarizing and non depolarizing muscle relaxants are normal in Parkinson's disease though a single case of succinyl choline induced hyperkalemia has been reported.

Confusion is seen more commonly in such patients that in the rest of the population.

**Anesthetic technique:** General anesthesia is administered in the pediatric population as well as some uncooperative adults; while local anesthesia as a scalp nerve block with conscious sedation is an option in some adults.

**Pre-anesthetic preparation:** a detailed anesthetic assessment is performed with a special emphasis on the basic pathology, maintenance of peri-operative drug therapy, establishing a rapport with the patient, explaining the risks involved and formulating the anesthetic plan. The importance of pre-procedure fasting is explained. Any contraindications to MRI are also determined at this stage. In adults, patients on antiplatelet medication care should be taken to stop antiplatelet medication 72 hours prior to surgery and the coagulation profile should be tested. Surgery may be delayed if the INR >1.5 since frame fixation and implantation of the electrodes may be complicated by intra and post operative bleeding.
**Monitoring**: in the operation theatre involves the continuous electrocardiogram (ECG), pulse oximetry (SPO2), End-tidal carbon dioxide (ETCO2) and the Noninvasive blood pressure (NIBP). This monitoring also is required while the patient is transported to the MRI suite and back to the operating room. Monitoring in the MRI suite is a challenge, since the equipment has to be MR safe as well as MR compatible. MR safe indicates that when the device is used in the suite it presents no additional risk to the patient; while MR compatible indicates that the device is MR safe as well as has been demonstrated to neither affect the diagnostic quality of the imaging procedure. The availability of commercial systems for safe monitoring makes “practical” MRI incompatible/ unsafe solutions unacceptable. In addition to the ECG, End-tidal carbon dioxide (ETCO2) Noninvasive / Invasive blood pressures, pulse oximetry, respiratory rate and a slave monitor in the console room along with closed circuit television monitoring which can zoom in on the patient in the gantry. The anesthesiologist must be familiar with the MR installation, particularly the extent of the fringe fields and the location of the resuscitation equipment. The use of ear plugs or other auditory protection can reduce the stimulation associated with imaging and permit the use of lower doses of sedatives or anesthetic agents. Anesthetic equipment may be within the MRI suite or outside it. The former will ensure that the anesthesiologist will be able to leave the room without interrupting the scan the latter will limit access to the patient to inter-scan intervals, except in an emergency.

**Local anesthesia**: is a practical and effective technique with a low complication rate and provides an excellent alternative to general anesthesia because it allows the opportunity for neurological testing during surgery. The preliminary portions of the operation, which do not require patient cooperation like frame fixation and the scalp nerve block, are performed with patient receiving a rapid-acting intravenous sedative (Midazolam 0.03mg/kg) and a narcotic (Fentanyl citrate1µg/kg) in order to maximize comfort. A technique consisting of a regional field nerve block of the scalp with 0.5% bupivacaine with epinephrine as well as a judicious titration of drugs providing conscious sedation (Propofol 1-2mg/kg/hr) in an atmosphere of monitored anesthesia care.

**Local scalp nerve block**: The scalp is innervated by the supraorbital, supratrochlear, auriculotemporal, posterior auricular, greater and lesser occipital nerves. A solution of 0.25% bupivacaine through a 23 gauge needle under aseptic conditions for the scalp nerve block is used. The supraorbital and the supratrochlear nerves are anesthetized as they exit from the orbit above the eyebrow by injecting 2 ml of bupivacaine at each site. The auriculotemporal nerve is anesthetized with 5 ml of bupivacaine 2 cm anterior to the tragus, the postauricular nerve with 2 ml of the local anesthetic solution 2 cm posterior to the pinna at the level of the tragus. The greater and lesser occipital nerves are injected using 5 ml in a fan shaped injection commencing midway between the inion and the mastoid process crossing over to the opposite side at the level of the inion. The block is similarly replicated on the contra lateral side.

**Conscious sedation**: Intravenous Midazolam (0.005 mg/kg) may be administered as soon as monitoring is established. This followed by Intravenous Fentanyl (1µg/kg) just prior to the scalp nerve block. After 15-20 minutes the frame is applied by the surgeon preceded by a bolus of Propofol (0.5-1mg/kg) this dose is titrated to effect ensuring the patient is comfortable, pain free, breathing spontaneously and maintained the airway independently. For the rest of the procedure the dose of Propofol is titrated (1mg/kg to 2 mg/kg) varying the dose depending on the comfort of the patient as well as ensuring the patient cooperation and participation in the neurological assessment and monitoring during the procedure. However since Propofol is known to decrease neuronal firing rates in the locus coeruleus and neocortical areas confounding the assessments of...
neuronal firing rates in the dystonic palladium intravenous Propofol may be avoided in favor of a technique involving Opioids (Fentanyl) boluses besides the scalp nerve block, or the dose of Propofol should be titrated to the bare minimum. During the procedure, intravenous fluids are kept at minimum (50ml/hr). Anticipation of the phases of the surgery when the plane of anesthesia has to be carefully altered and patient required to be sedated, anesthetized or awake titrating the appropriate dose of Propofol necessitates for team work between the surgeon and the anesthesiologist. The initial hour of the surgery starting from the infiltration, skin incision, infiltration of the skin and the drilling of the burr holes necessitates deeper planes of anesthesia, later the surgery on the brain parenchyma are painless and the plane of anesthesia may be lightened maintaining patient comfort. Skin infiltration and dural infiltration with 1% lignocaine by the surgeon is performed to ensure an absolutely pain free procedure. The risk of patient losing consciousness and becoming apnoic is a paramount concern. Full preparation for immediate control of the patient’s airway must be available during the procedure, in the event that the operation does not go as planned. Oxygen is supplemented throughout the intraoperative period with an oxygen mask ensuring oxygen delivery throughout the procedure thus avoiding the feeling of claustrophobia under the drapes. The patient is made as comfortable as possible on the operation table. Careful attention is paid to the protection of all the pressure points, which are padded an extra thick foam mattress ensuring patient comfort. The back of the patient is provided with a firm support, and a pillow below the legs. The ambient temperature of the operation theatre is kept at comfortable level and the patient is provided with a warming mattress and forced warming air blanket. A definite attempt is made to permit maximum exposure of the face and head to allow access to the patient and communication. The position of the drapes is such as to avoid a feeling of suffocation. Freedom of some movements of hands and legs is permitted to ensure the patient comfort. Constant reassurance and verbal contact helps in allaying anxiety. Human traffic is restricted in the theatre and a calm operating environment without disquieting conversation is provided. The other pharmacological interventions include antiemesis. Intraoperative vomiting, regurgitation and aspiration are extremely hazardous since access to the airway can be compromised. Ondansetron in the dose of 0.08 mg - 0.15 mg / kg administered prophylactically. Propofol is also well known for its antiemetic action. The advantages of Propofol include short elimination half life leading to rapid recovery profile thus permitting, intraoperative and immediate postoperative neurological assessment, minimal PONV, no psychomotor impairment, minimal inhibition of cortisol production and no hallucinations as compared to other intravenous non narcotic sedatives drug to achieve the desired end point. Conversion to general anesthesia may be required in case of inadequate analgesia, a restless, uncooperative patient or excessive sedation leading to loss of airway. Hence preparations for general anesthesia with airway control is mandatory for every case, as controlling the airway with the frame on is challenging right from mask holding to securing the airway with an endotracheal tube. Removal of apart of the frame directly across the mandible may be necessitated in an emergency at the risk of losing the alignment of the coordinates however the airway must be given priority. Dexmedetomidine a selective α2 agonist, is a unique sedative medication as it can provide patient comfort with respiratory and hemodynamic stability. It has been used in cases of DBS and the number of interventions to prevent hypertension during the procedure were found to be reduced as compared to patients where no procedural sedation was used. The fact that it does not impair the intensity of the movement disorder or interfere with micro electrode recordings are significant favourable features
of Dexmedetomidine use in DBS surgery. Dexmedetomidine is used as a bolus of 0.5-1µg/kg followed by an titrated infusion of 0.1-0.4µg/kg/minute during the stage of insertion of the electrodes, bradyarrhythmias are prevented by intravenous Glycopyrrolate. The infusion of Dexmedetomidine is tapered down to ensure complete emergence. We have commenced using Dexmedetomidine in our institution and have found it a safe, effective method of conscious sedation in this patient population with the benefit of hemodynamic and respiratory stability besides no effect on the microelectrode recordings. However due to lack of large randomized controlled trials involving its use during DBS at present it is early to recommend it as the standard of care.

Conscious sedation combined with a scalp block is an extremely effective, safe anesthetic technique with a low complication rate, uniform patient tolerance and it facilitates awake neurological testing. It carries low morbidity and mortality rates and minimizes ICU and total hospital stay.

**General anesthesia:** The patient is pre-oxygenated, prior to induction intravenous Fentanyl citrate (1µg/kg) followed by Thiopentone Sodium (3-5 mg/kg) and Atracurium besylate (0.5mg/kg) the airway is secured with a cuffed endotracheal tube that is taped securely after confirming its position. Anesthesia is maintained with the patient either ventilated using a mixture of nitrous oxide: oxygen and volatile anesthetic agents like Sevoflurane or Isoflurane or a mixture of oxygen: air with total intravenous anesthesia using Propofol and muscle relaxation maintained with an infusion of Atracurium besylate (0.5mg/kg/hr) monitored by (TOF) Train of Four Neuromuscular Monitoring. Anesthesia is prolonged since this involves all the stages of the procedure following frame fixation, the patient is transported, monitored to the MRI suite for the targeting MRI.

**MRI Challenges:** besides the monitoring issues described above there are also safety issues in the MRI suite.

**Implanted electrically magnetically and mechanically activated devices:** MRI may interfere with the function of such devices or result in image distortion or burns. Cardiac pacemakers are the most common electrically activated devices found in patients referred for MRI the acceptable safe level for exposure to magnetic fringe fields for cardiac patients with pacemakers is set at 5G. Above this the pacemaker will go into the fixed rate mode and may trigger ventricular fibrillation. MRI is contraindicated in any person with any implantable devise unless it is known that it will function with certainty.

**Potential biological effects:** Higher fields and rapidly switched gradient fields can cause altered taste, dizziness and nausea. Exposure to gradient or radiofrequency fields can reach biologically relevant levels and produce local heating effects. While available human data generally supports the safety of exposure to low magnetic fields in clinical staff, there is currently an impetus to measure occupational exposure to static, gradient and radio frequency fields and define safety limits for exposure.

**Others:** The contrast agent, gadopentate dimeglumine (Gd-DTPA Magnevist) can improve image quality and has an excellent

**Projectile risks from ferromagnetic objects:** Identification badges, scissors, coins, hair pins, paging devices, mobile phones, credit cards, watches, oxygen cylinders constitute missile risks to patients and all individuals should be screened for such object which should be left outside the suite. Ideally patients and staff should be provided with lockers to keep such valuables safe and secure. Ferromagnetic objects that are essential can be kept outside the 50Gauss line. Many implanted clinical devices are non-ferromagnetic, movement of implanted ferromagnetic implants under the influence of the magnet can be catastrophic. While product information supplied with some implants make statements regarding MR compatibility or otherwise, repeated sterilization and handling could induce ferromagnetism in some previously non-magnetic alloys.
safety record in comparison to other contrast agents. Cryogenic magnets with superconducting coils operate in liquid helium that boils (quenches) rapidly if the cryostat temperature rises. The released helium dilutes room oxygen and the cold vapor caused cryogenic burns and frostbite. Following the MRI the patient is transported monitored back to the operation theatre for the insertion of the electrodes into the target areas. This is later followed by yet another post implant control MRI. The patient is then transferred back again to the operating room for the implantation of programmable stimulator.

Reversal of the neuromuscular blockade is performed with Neostigmine (0.05mg/kg) and Glycopyrrolate after the return of the train of four (TOF).

Complications: surgical complications described in a larger series are related to hemorrhage supraventricular hematoma, microhematoma with transient minor permanent symptoms, asymptomatic microhematoma, subdural hematoma, MRI hyper signals along electrode tracks, asymptomatic presence of blood in the ventricles (trans ventricular approach), local late infections, local hematoma in subcutaneous pocket, ruptures of external extension needing replacement. Hence preoperative normal coagulation profile must be ensured as these patients are on antiplatelet medication for their co morbidities. Other complications reported are thrombophlebitis with thromboembolism, pulmonary embolism, and post operative confusion related to the general condition of the patient, apraxia of the eyelid, transient psychological complications mania, paranoia, and depression leading to suicide /suicide attempts. However no mortality has been reported.

Post operative care: After surgery, patients spend the first postoperative night in the ICU (intensive care unit) for precautionary purposes. They then transfer to a regular room, and usually are discharged home on the third postoperative day. This later followed by the programming of the stimulators. Safe anesthesia depends on team work, well designed protocols and systems not just individual competence and care.
Translational research aims to bridge the gap between basic and clinical research with the ultimate goal of advancing healthcare. Given the profound impact that the specialty has got on the management of patients, anaesthesiology researchers have as much stake on the research funds meant for this purpose as the researchers from the other specialities (1). A good translational work prevents ill-conceived clinical trials without a strong and unequivocal basic science background. Successful translational research requires channelization of all the involved teams – laboratory scientists, clinical researchers, healthcare and health-economics planners – into a translational path (2). Translational research accelerates the rational transfer of new insights and knowledge into clinical practice for improving patient outcomes and public health [3]. Put in simple terms, translational research provides a framework through which investigators or laboratories can maximize the likelihood that their research product gets adopted into medical practice.

The two common courses of translational research are: investigator driven and industry enabled. Investigator-driven research has a wider scope because it does not take into account the profit margin of research, but it is a slow process. The industry-enabled model accelerates the translational research through its power for funding the process. But industry would be interested primarily in products with potential for profit (4).

**Historical perspectives of translational research in neuroanaesthesia**

Anaesthesia, by itself is a great innovation of translational nature in the history of medicine. The anaesthetic techniques have become refined and safer over time through translational work. Anaesthetics being drugs with a potential to impact every aspect of systemic physiology, anaesthesiologists got involved in research that encompassed several areas of medicine (physiology, pharmacology, clinical medicine and patient care delivery etc.). The resultant exploration of science by anaesthesiologists has greatly transformed patient care in several areas outside anaesthesia. The following are examples of a few major successes and failures of translational work in neuroanaesthesia in the past:

**Brain and anaesthetics**

The contributions made Dr. J.D. Michenfelder and colleagues on the effects of anaesthetics on brain have had a profound impact on clinical practices in the neurosurgical operating rooms and intensive care units. Extensive experimental research followed by clinical investigation provided concepts that could be incorporated into neuroanaesthetic practice. These studies provided insights into the effects of anaesthetics on cerebral blood flow, metabolism, flow-metabolism coupling, autoregulation, response to CO2 changes, intracranial pressure, and brain electrical activity, the knowledge that has been extremely relevant to plan a safe anaesthetic for a patient with cerebral pathology (5-13).

**Cerebral ischemia and protection**

Cerebral ischemia and cerebral protection has been a thrust area of research in neurosciences. Models of global and focal ischemia (14), used in studies of cerebral protection through anaesthetics, have remained the standard models in subsequent research too. Over years, research involving cerebral protection has followed two major
streams of interventions: anaesthetic drugs and hypothermia.

Anaesthetics: That anaesthetics cause a considerable decrease in brain metabolism provided an attractive hypothesis to use them to protect against cerebral ischemia. A 50-60% reduction in CMRO2 at a clinically-relevant anaesthetic concentration appeared to be a great solution to salvage the ischemic neurons. Experimental studies in smaller animals and primate models of global and focal ischemia supported the concept (15-16). Several other potential mechanisms for protection have been unraveled in these studies. Encouraged by these results, large-scale clinical trials have been undertaken. Barbiturates have been used in clinical trials of cardiac arrest (17), stroke (18), traumatic brain injury (19) and cardiopulmonary bypass (20-21). All these studies met with either disappointing results or false promises that could not be replicated. The end result was a colossal loss of time and resources and a failure of translation of laboratory studies into clinical practices. The introspection that followed offered several lessons on translational research (22). The fundamental lesson learnt was that animal studies conducted under experimental conditions cannot be directly translated into clinical practice. Also, consistency in results of basic research should be established before undertaking large clinical trials. Clearly-defined and realistic outcome targets should be set before embarking on clinical trials to reduce the costs of translational research, avoid frustration, and to hasten the translational process.

The story of moderate hypothermia in cerebral injury is no different. Profound hypothermia has a long-established beneficial effect in complex cardiac surgery. Experimental studies on mild and moderate hypothermia have documented benefit in both focal and global ischemia. However, large-scale clinical trials have failed both in traumatic brain injury (23) and subarachnoid haemorrhage (24). Benefit has been limited to only studies in cardiac arrest (25-26). Hypothermia has found its place in guidelines for post-resuscitation care of survivors of paediatric cardiac arrest (27).

Several molecules, tried for cerebral protection in various forms of brain injury, have yielded uniformly disappointing results, superoxide dismutase (28), selfotel (29), and tirilazad (30), just to name a few.

**Mechanical ventilation in neurological diseases**

Work done during the European polio epidemics in 1950’s (31-32) may be considered a pioneering effort at translational science that paved the way for mechanical ventilation to save lives of patients with reversible neuromuscular diseases. Credit for successful mechanical ventilation of patients with Guillain Barre syndrome, myasthenia gravis etc. in the current day neurological practice, goes to the translational work of those early years.

**Cardiopulmonary Resuscitation**

Pioneering work carried out by Peter Safar and colleagues in 1960’s transformed the chances of survival of patients of cardiac arrest (33-37). Their innovative work enhanced the probability of successful restoration of circulation. Provided the ischemic-hypoxic time is kept short, the odds of good functional survival are very high. However, very little has been done to alleviate the cerebral outcomes of those who have sustained more severe hypoxic injury.

**Contemporary Translational Research**

Necessity and opportunities are driving the present day anaesthesiologists to perform research in areas, which a few decades ago would have been considered well outside the scope of the anaesthesiology. A few examples are given below:

**Neurotoxicity of anaesthetics**

Neurodevelopmental concerns in neonates exposed to anaesthetics have necessitated anaesthesiologists to enter the area of research on development of nervous system (38-39). A systematic clinical review using Bayesian technique, concluded that there is a modestly elevated risk of adverse behavioral or developmental outcomes in 60,485
children who were exposed to anaesthesia/surgery during early childhood. The evidence, however, is considerably uncertain (40). Major clinical trials are underway to explore the effect. PANDA (Pediatric Anesthesia and NeuroDevelopment Assessment) is a cohort study that will enroll 500 sibling matched pairs (1000 children) who underwent hernia surgery under general anaesthesia (ASA I–II) before 36 months of age. The children will undergo a series of neuropsychological tests between 8 and 15 years of age (41). The results of this study could prove interesting from a clinical standpoint.

**Neuroprotection**

Need for neuroprotection in several acute neurological situations has opened a vast scope for work into pathophysiological mechanisms and therapy of brain injury. The mechanisms, currently being targeted by several researchers in anaesthesia, include inflammation, necrosis, apoptosis, and neuronal preconditioning (42-48). This work, when translated into clinical tools, is expected to protect the brain during perioperative ischemic events.

**Mechanisms of anaesthesia**

The mechanisms of anaesthetic action remain an enigma even today. Research, in this area implies not just exploring the mechanisms of anaesthetic action, but understanding the very basis of consciousness (49), which neuroscientists from various disciplines have been trying to unravel. Some recent approaches in this area involve study of the neural networks using functional magnetic resonance imaging (fMRI) (50-52), and positron transmission tomography (53-54). This is also a fertile domain for collaborative research across the disciplines in neurosciences (55-56), of which anaesthesia could play a major role.

**Cognition and anaesthesia**

Post-operative cognitive dysfunction remains an under-explored area. Here again, a great scope exists for research in cognitive neurosciences. This line of research may have fallouts that may answer questions in cognitive neurosciences and help understanding phenomena like ageing, dementia, and Alzheimer’s disease (57-58).

**Traumatic brain injury**

Hardly any definitive therapy exists for restoration of neuronal integrity after traumatic brain injury, excepting timely removal of mass lesions and prevention of secondary insults. This calls for translational research in two areas: Limiting the early secondary injury through better care-delivery processes (transportation, resuscitation) and simpler, effective and affordable systems for monitoring cerebral physiology – blood flow, oxygenation and metabolism – with the aim of limiting secondary injury.

**Cerebral function monitoring**

The need to preserve the neuronal viability during surgery in the operating room and in the intensive care units demands research into innovative technologies that have better sensitivity and specificity and would preferably be noninvasive and inexpensive. Very little scope exists at this time to monitor the cerebral function and the available monitors are cumbersome, expensive and labor-intensive with limited sensitivity and specificity.

**Monitors of the depth of anaesthesia**

After decades of reflection on defining the state of anaesthesia, in recent years there has been an attempt at quantification of the depth of anaesthesia, but several questions are raised about these gadgets (59). Bringing in objectivity into prevention of intraoperative awareness requires a lot more of translational research. This research also assumes importance on the background of several reports linking intraoperative depth of anaesthesia with adverse postoperative outcomes (60-62).

**Sleep-related research**

Modulation of respiration during anaesthesia with its implications for perioperative respiratory complications, is an interesting field for research (63). Sleep apnea and sleep-related disordered respiration have attracted
anaesthesiologists for a long time. Naturally occurring NREM sleep and anesthesia have been found to have neurophysiological similarities. EEG-based depth-of-anesthesia monitors are being used in this area of research (64).

**Pain management**

Preclinical and clinical research has led to significant progress in clinical pain management. Translational pain research is a definite need as many important questions do not have definitive answers. The gap between pain research and clinical pain management is wide. Objective pain-assessment tools are far too few. The relevance of the current theories of pain mechanisms to clinical pain is not well-understood. Reliable tools for both preclinical and clinical pain research should be developed. Coordinated research is required among basic scientists, clinical investigators, and pain-medicine practitioners (65).

**Anaesthetics and tumor-cell invasion/proliferation**

Recent studies have shown that anaesthetics have an influence on the migration and invasion of cancer cells in the lung and colonic carcinomas (66-67). The exact clinical relevance of these findings is not clear at this time. But when understood, this information may have a bearing on the choice of anaesthetic during surgery for cancer. The mechanisms involved may pave the way for a new line of research into anti-malignant therapy.

**Complementary systems of medicine**

Some alternative systems of medicine have claimed ability to decrease the perioperative pain/need for pain medications. Acupuncture and acupressure deserve systematic studies for their efficacy in providing analgesia and postoperative antiemetic effect (68-70).

**Pharmacogenetics**

There is growing evidence, in the recent years, that the susceptibility of an individual to anaesthetic actions and their side effects is dependent on the genetic polymorphism. Genetic factors seem to contribute to a majority of the severe adverse drug reactions (71). A day may come in future when anaesthetic management is likely to be assisted by genetic factors with a view to reduce the risk of side effects and undesirable actions (72). A similar strategy is likely in the management of acute pain relief over a shorter period of time, and prevention of acute pain becoming chronic (73).

**Making translational research more effective**

Failure to translate potential basic sciences research into clinical practices is very conspicuous in recent years. Considering the heavy resource implications of medical research, a systematic approach is required to translational research.

When potential clinical applications of basic research findings are identified, they should be first tested in a collaborative multicenter basic research project, rather than jumping into a multicenter clinical trial. Using different animal models would be preferable. The research groups are required to disclose all their data. A collective analysis of the results is to be done to decide whether a collaborative multicenter clinical trial is justified (74).

Journals often tend to accept studies with positive data more than those with negative data, and this trend has to change where the negative results have as much clinical relevance as the positive data. Identification of the priority areas for future research, as has been done by the national Institute of Academic Anaesthesia in UK recently, should be the responsibility of the scientific bodies in neuroanaesthesia (75).

To conclude, translational research in anaesthesia provided great solutions to medicine well beyond its scope in the past. Despite all the technical developments, progress in translational sciences has been rather slow in the recent decades. Reorientation of the research programmes to a translational format with the involvement of all the stakeholders is likely to conserve on the resources and provide rapid solutions to the healthcare.
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How I do it? Extracranial surgery in head injured patients

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Though the prevalence of Traumatic brain injury (TBI) is not well documented, the incidence accounts for around 1% of overall injuries as per National Health Interview Survey. TBI is associated with other injuries like cervical spine injuries, lower limb injuries, abdominal injuries, thoracic injuries, etc. This may be associated rarely with some non-emergent conditions like splenomegaly, etc. which may flare up after the insult or presents as an incidental finding like cerebral aneurysm, aortic aneurysm, etc. Extracranial cerebrovascular injury is believed to be another important cause of neurological injury in patients who have suffered blunt trauma.\[1\]

On one hand, the type of extracranial surgery is either elective or emergency. If elective, then the outcome depends on the type of brain insult, major or minor extracranial surgery, type of anaesthesia planned, intraoperative haemodynamic perturbations, manipulations and interventions interfering with the cerebral perfusion pressure, etc. Emergent type of extracranial surgery depends again on the severity of head trauma, blood loss, anaesthesia per se, etc. On the other hand, the site, severity and size of brain insult, neurological deterioration pre and post surgery, avoidance of secondary insults, the natural progress of the insult, the timing of surgery i.e., days after injury are other factors which can predict the outcome following any extracranial surgery.\[2\]

Primary management of head injury

Resuscitation of the head injured patient associated with other injuries depends on the severity of the injury presenting either as hypoxia or hypotension, neurological deterioration, etc. Glasgow coma scale (GCS) is the gold standard still followed worldwide for initial assessment and management. Airway manipulation is mandatory as increased chances of aspiration and impaired gas exchange leading to hypoxia is increased in patients with GCS ≤ 8. Manual in line stabilization should be maintained to prevent further neurological deterioration during airway interventions as cervical spine injuries are commonly associated. Avoid nasal intubation as the chance of endotracheal tube entry into the brain is a possibility in patients with skull base fractures. An Italian survey of anaesthetists by Latronico et al has shown that increased awareness regarding the management of polytrauma patients with head injury is required for a better outcome.\[3\]

Patients with head injury have delayed gastric emptying time. Rapid sequence intubation is required to prevent aspiration. This can be accomplished with titrated doses of anaesthetic drugs like midazolam, thiopental, propofol, ketamine, succinyl choline and rocuronium depending on the GCS and haemodynamic status of the patient. Maintenance of adequate oxygenation, haemodynamics, normocapnia to mild hypocapnia, normoglycaemia and avoiding or treating acidosis is required to maintain perfusion pressure and thus prevents further aggravation of neurological deterioration. The patient is sedated and paralysed to maintain oxygenation and even to avoid hypercapnia. Patients with head injury unless and until diagnosed and monitored deemed to be associated with an increase in intracranial pressure (ICP). Transcranial Doppler (TCD) can be a useful tool to monitor ICP at bed side. Monitoring blood pressure along with ICP gives a rough estimate of cerebral perfusion pressure (CPP) and guides the physician for further interventions if required.

Approximately 60-70% of cases with severe TBI is associated with extracranial injuries.
Usually, they present with hypotension and shock. The choice of fluid for resuscitation depends on the severity of head injury and other associated injuries. It does not matter if the amount is given judiciously and at the same time hyperglycaemia and lactic acidosis should be avoided as far as possible in emergent situations. The different fluids available for resuscitation include normal saline, 3% hypertonic saline, colloids, albumin, etc. Use of hypotonic and isotonic fluids is discouraged due to their negative effects on glucose balance and metabolism leading to lactic and metabolic acidosis. Evidence has shown the beneficial effects of hypertonic fluids in treating hypotension with better cerebral haemodynamic stability, decreased inflammatory mediators and positively influencing outcome.\(^{[4,5]}\) In view of the cerebral and other systemic adverse effects, both colloids and albumin does not seem to be fluids of choice for resuscitation in patients with TBI. However current literature highlights the emerging role of the osmolality of an infusion solution rather than the colloid osmotic pressure _per se_ as a key determinant in the pathogenesis of cerebral edema formation. Finally, the aim of fluid resuscitation should be targeted at preventing secondary insults like hypotension and shock and maintaining CPP. Mild hypothermia instituted within 24 hours of injury has shown beneficial effects in improving the neurological outcome in patients with severe TBI. Severe TBI with polytrauma may be associated with massive blood loss and coagulation derangements.\(^{[6]}\) The coagulopathy identified reflects the severity of injury rather than its localization. These need to be monitored and treated accordingly. Transfusion of blood and blood products with continuous surveillance and vigilant monitoring is essential in patients with ongoing blood loss. Recent evidence has shown good outcome with administration of red cell concentrate: plasma: platelet concentrate in a ratio of 1:1:1 in patients with major trauma.

**Specific management for head injury**

1. Adequate resuscitation should be followed by complete re-examination and appropriate investigations to achieve proper diagnosis and accordingly management. Computed tomography of the suspected areas of insult should be screened properly and supplemented with other mandatory investigations. Further investigations can be done to rule out any vascular injury, unstable cervical spine injury, major lower limb injury, abdominal injuries like splenic and liver injury, etc. Critical, in addition to establishing the nature of head trauma and associated injuries, is timely diagnosis and treatment of blood loss and shock. Once stabilized and near diagnosis is achieved, the patient can be shifted to an intensive care unit for specialized service based management of both TBI and other major extracranial insult.

2. The severity and type of injury dictates the type of monitoring apart from basic standard monitoring. Beat to beat measurement of heart rate and blood pressure would give us a rough indication either for an impending increase in ICP or for continuing hypotension. Central venous pressure or continuous cardiac output monitoring with systolic pressure variation may be useful in monitoring resuscitation in severe cases of polytrauma.

ICP monitoring is mandatory in patients with GCS ≤ 8. TCD is an essential alternative noninvasive tool for monitoring ICP at bedside. Monitoring and interpretation of ICP will guide the physician in diagnosing, to see the effectiveness of response to ICP management and in prognosticating the outcome.

3. The guideline management for ICP should be followed to prevent further neurological deterioration with some alterations to prevent secondary insults of hypoxia, hypotension, acidosis, etc. Slight head up positioning is essential in patients with TBI. This may be compromised in sick patients with shock and severe hypotension.
4. Hyperventilation causes cerebral vasoconstriction and reduces CBF significantly. This may have deleterious ischaemic effects in patients with head injury where CBF is already compromised. Mild hyperventilation can be used as a temporary measure in patients with impending brain herniation until definitive treatment is available and instituted like barbiturate therapy, decompressive craniectomy, etc.

5. Diuretics like mannitol and hypertonic saline are useful in reducing ICP. Brain trauma foundation (BTF) guidelines recommend the use of mannitol for raised ICP in a dosage of 0.25-1 gm/kg. Mannitol has the disadvantage of causing hypovolaemia and hypotension thus aggravating secondary brain ischaemia. Hypertonic saline is beneficial in patients with polytrauma as it preserves and restores the haemodynamic parameters with better survival.

6. Hyperglycaemia and metabolic acidosis are detrimental to nerve cells and are associated with poor outcome; hence these metabolic parameters should be optimized to avoid further insult. If required, insulin should be supplemented to regulate normoglycaemia.

7. Analgesics and sedatives are drugs commonly used to supplement other measures for controlling ICP. Barbiturates are used effectively for control of ICP when all other measures fail. This is limited to critical care setup and stable haemodynamics should be maintained during this therapy.

8. Mild to moderate hypothermia is effective in patients with head injury and improves the Glasgow Outcome Scale. This is level III recommendation of updated recent Brain Trauma Foundation (BTF) guidelines. Hyperthermia aggravates brain ischaemia and should be treated effectively to improve the outcome.

9. Tourniquets are used effectively to control extremity bleeding. The effect of tourniquet application on haemodynamics depends upon the duration, the pressure applied, and the release. Acute release of tourniquets may lead to release of inflammatory mediators and hypotension.

10. Head injury patients may present with seizures which may aggravate the secondary ischaemic injury. Anti-epileptic drugs are useful to prevent and treat seizures.

**Acute management of critical extracranial injury patients with head injury.**

Patients with head injury may be accompanied with acute emergent conditions like blunt trauma abdomen, chest injury, long bone injury, etc. These patients usually present with persistent hypotension and shock and should be evaluated for the same. Life threatening insults like ruptured spleen, liver laceration and other major vessel injury should be sought immediately for emergency surgery. The actual site of abdominal bleeding is difficult to diagnose, especially in a paralysed and ventilated patient. Shifting such unstable patients to radiology suites for confirmatory diagnosis is very challenging and sometimes deferred. CT scan of head and neck should be done in stable patients with ongoing resuscitation. This is important for taking up a decision for emergency craniotomy. Similarly a bedside ultrasound abdomen or even a needle aspiration is useful for diagnosis of bleeding abdomen.

The morbidity and mortality following delay in emergency surgery either for laparotomy or craniotomy needs to be considered. Delay or difficulty in resuscitation and management of hypotension may aggravate secondary insult and result in further neurological deterioration. Even delayed craniotomy also results in poor outcome in cases such as subdural haematoma (SDH). Balanced approach and timely decision for operative interventions is essential for a better outcome. Usually polytrauma patients with abdominal trauma are young adults. Though they may present with head injury, the incidence is less and rarely require a craniotomy. Old age patients, fall from...
heights, etc, usually sustain head injury and require intervention.

Proper planning and preparation for haemodynamic restoration for any life threatening emergency laparotomy should be done in the form of large bore canulas, continuous monitoring of invasive blood pressure and central venous pressure, arrangement for massive transfusion, availability of inotropes and vasopressors, personnel, etc. Patients with lateralizing symptoms of head injury may require a simultaneous craniotomy in the same sitting. Occasionally, patients attain hemodynamic stability after resuscitation. These patients are then investigated with CT head and abdomen and then managed accordingly. Conservative management is again based on maintenance of optimal CPP without endangering the risk of re-bleeding.

**Head injury patients with less critical extracranial insults like chest injury and long bone and pelvic fractures.**

These fractures are sometimes concealed and may present with persistent hypotension. Radiography of the chest, neck, long bones and pelvis may reveal the injury and cause of bleeding. Patients with thoracic injuries like pneumothorax, lung contusion, are prone to hypoxaemia and needs optimization of the same. Early operative intervention for long bone and pelvic fractures has shown to have significant benefits like reduced bleeding, infection, length of stay, days of mechanical ventilation, respiratory complications, deep vein thrombosis (DVT) etc. This may be difficult in cases with chest injuries, other associated injuries and also if associated with other secondary insults like hypotension, hypoxia, coagulation derangements, hypothermia, acidosis, etc. This is mandatory to treat these insults as they aggravate brain ischaemia if not treated. Early intervention for head injury is given importance compared to other injuries, if otherwise the patient is stable.

 Already decompressed patients with head injury or patients under conservative management for head injury may later present with surgery for the orthopaedic fractures. Consensus has reported debatable use of regional anaesthesia for such interventions. This carries the disadvantage of severe hypotension in some cases with devastating effect on the CPP. Titrated general anaesthesia may be preferred with supplementation of nerve blocks for maintaining optimal cerebral perfusion pressure. Successful intervention under regional anaesthesia is also reported. The risk benefit for general or regional anaesthesia and other co-morbidities like elderly, stroke patients, type of surgery should be considered for the type of anaesthesia to be administered. The haemodynamics should be maintained, wide fluctuations in heart rate and blood pressure are to be avoided, alongwith monitoring of all vital parameters, ICP with overall vigilant clinical monitoring of the neurological status.

Resuscitation with fluid and blood products acts like a double edge sword in patients with associated head injury. On one hand, resuscitation is essential for maintaining cerebral perfusion pressure and on the other hand, overzealous resuscitation may precipitate cerebral oedema. Meticulous attention to resuscitation with continuous monitoring of haemodynamics is required to avoid any secondary insult to the brain.

**Head injury with other extracranial injuries whose intervention can be delayed beyond 72 hours: Maxillofacial injuries are common.** Though immediate intervention is not required, early fixation (after 72 hours) is essential to get aesthetic benefits. The perioperative management of maxillofacial injuries will consider the same rational points like any long bone fracture taken after 72 hours. Patients may present with a delayed intracranial haematoma even with a negative initial CT scan later in the setting of extracranial surgery. The duration of extracranial surgery in the acute period should be as short as possible in patients with suspected head injury. If these patients fail to wake up as expected following anaesthesia or new neurologic deficits develop, an urgent follow up CT scan should
be performed. Some patients with acute SDH managed conservatively may later deteriorate. These patients should be reinvestigated in case of any neurologic deterioration.

Some patients may present with minor head injury and other non-significant extracranial injury which requires intervention like that of an elective surgery. Evidence has shown improvement in neurological outcome in patients hospitalized rather than those who were discharged and managed at home. Patients with extracranial cerebrovascular injury may later present with ischaemic stroke due to emboli and this is usually seen in patients with other positive confounding factors.[1]

Overall the timing of surgical intervention depends on the severity of head injury, the severity of extra cranial injury like splenic rupture, response to initial resuscitation and stabilization, and risk-benefit ratio of delaying other interventions, and prevention and treatment of secondary insults. Major extracranial injury is an important prognostic factor for mortality in TBI patients. The strength of this effect is smaller in patients with more severe brain injury.[1,1] Management of TBI is mandatory and should be the first priority and not to be bypassed. This needs to be done along with other life threatening emergency surgeries if called for. Surgical traction can be used during the transitory period to improve the functional results before any specific fixation procedure is carried out. Mechanical prophylaxis in the form of compression stockings is useful in patients with TBI to prevent venous thromboembolism.

In pregnant patients: Those with severe head, abdominal, thoracic, or lower extremity injuries are at high risk for pregnancy loss. Reduction of secondary insults and early recognition of fetal distress may improve outcomes for both the mother and fetus in this high-risk group.[1,2]

In paediatric patients: Pediatric head injury is associated with a high incidence of intracranial hypertension. Patients coupled with other injuries carries grave outcome. Early surgical treatment and intensive care may achieve favorable outcome.[1,3]

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Awake Craniotomy (AC) was introduced at the turn of the 20th century, primarily for treatment of patients with epilepsy. AC is performed when tissue resection requires mapping of eloquent cortical tissue located in close proximity to the area to be resected. Performing the procedure with an awake patient allows for brain mapping and the continuous assessment of neuropsychological parameters that ordinarily would not be accessible until after the surgery is complete. Thus, because the surgeon may identify and avoid functional tissues, AC may offer a better alternative for tumors located in critical areas. Although traditionally reserved for lesions in eloquent cortex, AC has had recent success when applied to the resection of various supratentorial tumors, regardless of location and histology. The effectiveness of this “routine” use of AC surgery may stem from avoiding the side effects and complications of general anesthesia (GA). The challenge for the anaesthetist is to find a technique which provides adequate sedation, analgesia, and respiratory and haemodynamic control, but also an awake and cooperative patient for neurological testing.

**Preoperative assessment**

Patients presenting for awake craniotomy are often highly motivated and naturally eager to maximize the chance of cure and minimize the possibility of a postoperative neurological deficit. Preoperative evaluation must consider the following aspects.

1. Upper airways:
   — prediction of difficult tracheal intubation (physical conformation and past intubation);
   — obstructive apnea risk (obesity, sleep apnea, retrognathia).
2. Epilepsy:
   — pharmacotherapy;
   — antiepileptic drug serum concentration;
   — type and frequency of seizures.
3. Nausea and vomiting:
   — past anesthesia;
   — kinetosis.
4. Intracranial pressure estimation:
   — type of lesion;
   — radiological and clinical signs.
5. Hemorrhagic risk:
   — type and localization of lesion;
   — therapy (antiplatelet drugs);
   — medical history.
6. Patient cooperation:
   — anxiety;
   — pain tolerance;
   — neurological deficits.

Occasionally, a patient may be considered to be unsuitable due to emotional, psychological reasons; or simply being afraid of an awake surgery. But patient counselling by the anaesthesiologist and surgeon can overcome all the fears and is the most important preoperative preparation of the patient.

**Technical Principles**

A variety of anesthetic techniques have been successfully implemented for AC surgery, but an experienced anesthesia team is essential for each. One of the major goals for providing anesthesia for an AC includes patient cooperation. Regardless of the anesthesia technique or agents used, the patient’s airway must be protected. In some cases, only local anesthesia is used for the scalp and dural incisions. More commonly, additional sedation and analgesia is achieved with compounds such as propofol, dexmedetomidine, fentanyl and remifentanil.

Excellent scalp block block is required for patient comfort.
Scalp Block

Six nerves need to be blocked bilaterally to completely anaesthetise the scalp: the supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, the lesser and greater occipital nerves.

A brief description is included for each nerve:

1. The supraorbital nerve is blocked just above the supraorbital notch and local anaesthetic is deposited just superficial to the periosteum.

2. The temporal branch of the auriculotemporal nerve is blocked immediately posterior to the superficial temporal artery at the level of the auditory meatus. Injection is superficial and subcutaneous. Too deep an injection will produce facial nerve block.

3. The main branch of the zygomaticotemporal nerve emerges from the temporalis fascia near the lateral border of the orbit, although many smaller deep branches ramify within the temporalis muscle. These small branches are especially important to block so as to cover temporally based flap incisions. Field infiltration above the zygoma through the temporalis muscle and almost down to the periosteum of the temporal bone will give a good result, without causing a facial nerve block. Up to 5 ml can be used on the operative side.

4. The lesser occipital nerve can be blocked either deep or superficial to the fascia at the upper, posterior border of sternocleidomastoid.

5. The greater occipital nerve is blocked subcutaneously by injecting along the middle third of a line between the mastoid process and the external occipital protuberance along the superior nuchal ridge. This injection will also reinforce the lesser occipital nerve block as it becomes subcutaneous.

Additional infiltration is usually performed at the three head holder pin sites and along the skin incision line. A 40 to 60 mL anesthetic volume is used for infiltration. High local anesthetic volume and well-vascularized areas may predispose to anesthetic toxicity. The use of adrenaline (5 mcg/mL, 1:200 000 dilution) both minimizes acute rises in plasma anesthetic concentration and maximizes the duration of the block. With regards to toxicity, ropivacaine appear to be safer than bupivacaine. Despite this difference, bupivacaine is the most commonly used local anesthetic in the literature.

Monitored anesthesia care

According to the ASA, MAC is a specific anesthetic protocol that includes careful monitoring and support of vital functions. The anesthetist administers sedatives, analgesics, and hypnotics, addresses any clinical problems, and provides the patient with psychological support during diagnostic and therapeutic procedures. The ASA recommends that the provider of MAC must be prepared and qualified to convert to general anesthesia if necessary. With regards to awake craniotomy, this type of anesthetic care has developed from the logic evolution of pioneering experiences using neurollep analgesia. The introduction of clinical propofol use has favored this evolution by allowing for better patient management. After Silbergeld’s publication, Gignac in 1993 compared droperidol administration with fentanyl, alfentanil, or sufentanil in 30 patients. The conclusion of this study was that there was no difference between fentanyl and newer opioids in awake craniotomy. Four years later, Herrick proposed patient-controlled sedation (PCS) with propofol as a valid alternative to
neuroleptoanalgesia. Since that time, the neurolept analgesia era could be considered finished in the field of awake craniotomy. The diffusion of new short acting drugs such as propofol and remifentanil has simplified sedation and allows for rapid awakening in 5-20 minutes. Despite rapid and complete diffusion of propofol, Danks has determined that propofol use is less safe when compared to midazolam combined with opioids in two different studies. Since this study, all awake craniotomy published protocols have included propofol administration except Manninen’s study in 2002 (optional propofol infusion) and some dexmedetomidine regimens. Today, propofol is widely employed for neurosurgical anesthesia (and awake craniotomy) because of its easily titratable sedative effect and rapid recovery with clear-headedness. Propofol may be administered using a TCI technique which allows for good drug titration, allowing the anesthetist to predict arousal after long-term infusions and avoid oversedation. Furthermore, the use of propofol sedation does not appear to interfere with ECoG if infusion is stopped 15 minutes before recording according to Herrick, and 20 minutes in pediatric settings according to Soriano. Some authors employ propofol sedation only in combination with local anesthesia and without opioids infusion and are able to achieve good pain control. In recent years, most anesthetists have replaced fentanyl with low dose remifentanil (0.05-0.1 mcg/kg/min if a TCI protocol is used). Remifentanil is a clinically versatile opioid and is useful for intravenous analgesia and sedation in spontaneously breathing patients. Right now it is not available in India. In the MAC protocol, the first aim is to ensure adequate spontaneous ventilation. During this anesthetic technique, airway management is minimal and non-invasive, as indicated by prior definition. In most centers, patients receive supplemental oxygen via nasal prongs or facial mask. Nasopharynx cannula may be a good alternative choice. This airway device is rarely used because of the risk of nose bleeding, however, once positioned correctly it is well-tolerated. Adequate clinical vigilance concerning respiratory function is necessary throughout the procedure.

**Dexmedetomidine: the new alternative**

Dexmedetomidine is a highly selective alpha2-agonist with dose-dependent sedative, anxyolitic, and analgesic effects without ventilation suppression. The primary action of alpha2-agonists is the inhibition of norepinephrine release, causing excitation inhibition in the central nervous system. Compared to clonidine, dexmedetomidine has eight times greater affinity for alpha2-receptors and a shorter half-life. Hall demonstrated that low dose infusion of this drug in healthy volunteers provides sedation that can be easily reversed with verbal stimulation. At clinical doses, patients remain somnolent without signs of paradoxical agitation or confusion. The analgesic effect of dexmedetomidine consistently reduces opioid administration even if it does not have the same efficacy. In 2001, Bekker et al. reported the first application of dexmedetomidine combined with LMA (spontaneous breathing), fentanyl, sevoflurane (0.3-0.7%), nitrous oxide (70%), and BIS monitoring in an awake craniotomy. In 2004, Fogarty Mack’s group evaluated dexmedetomidine administration in five patients managed by MAC and five patients under an AAA approach. In this study, the AAA anesthetic approach was judged to result in more intraoperative discomfort. Recently, this drug has been used to treat intractable discomfort in patients sedated with a propofol and remifentanil combination. Generally, a dexmedetomidine load of 0.5 to 1 mcg/kg/h over 20 minutes is followed by infusion at rates of 0.1 to 0.7 mcg/kg/h to 20 minutes prior to testing. During cortical mapping the infusion rate is usually set to 0.1 to 0.2 mcg/kg/h. **We in our institute use dexmedetomidine along with scalp block for awake craniotomy.**

**Asleep-awake-asleep technique**

This anesthetic approach consists of general anesthesia before and after brain mapping. In 1998, Huncke et al. gave great force to the
AAA technique for epilepsy surgery. They described their experience with 10 patients who, after local anesthesia, were awake intubated with a fiberoptic laryngoscope at the beginning of the procedure and again after cortical mapping (two orotracheal intubations and eight nasotracheal intubations). The tracheal tube was modified by attaching a fine catheter with multiple holes for topic delivery of local anesthetic. The described technique, although complex, was considered to be safe with respect to airway and CO2 control. The described technique, although complex, was considered to be safe with respect to airway and CO2 control. Over the following years, this article became a landmark publication for many authors who proposed similar anesthetic approaches which described use of a laryngeal mask instead of a tracheal tube. In recent years, LMA has been widely used for awake craniotomy with patients under spontaneous breathing protocols. These patients are supported with mechanical ventilation only if necessary. Other anesthetists have preferred mechanical ventilation with LMA with or without myoresolution. Even if LMA cannot ensure the same airway protection as a tracheal tube, it has renewed great interest in this type of surgery. Different techniques of LMA positioning have been widely described in awake patients and in both lateral and semi-sitting positions.

LMA approaches offer significant advantages over tracheal tube approaches, including avoidance of the laryngoscope and the need for head extension, easier placement in difficult patient position, and reduced incidence of coughing and gagging during emergence. ProSeal LMA may be a better choice than classic LMA because it incorporates a second tube that permits blind insertion of a gastric tube, thus reducing risks of gastric insufflations and pulmonary aspiration. The AAA technique is mostly commonly performed by administering propofol and remifentanil in combination. In conclusion, the AAA technique offers, undoubtedly, the advantages of good airway control and adequate deep sedation, and the patient does not suffer from pain or discomfort. Nevertheless, this anesthetic approach is more complex than MAC, particularly when repositioning of an airway device is necessary for closure (while the patient is often in the lateral position with his/her head fixed to the Mayfield head holder).

Intraoperative monitoring

Intraoperative monitoring typically includes electrocardiogram, invasive and non-invasive blood pressure measurements, pulse oximetry (SpO2), respiratory rate, capnography (EtCO2), and body temperature. Normally, a urinary catheter is also inserted. If large blood losses are expected, a central venous catheter is positioned. Different methods ensure variable measurements of exhaled CO2, and this value is important in order to observe the trend of EtCO2 and evaluate the patient’s hypo- or hyperventilation tendencies. Today, monitoring of the level of consciousness during anesthesia or sedation is possible using electroencephalographic analysis by Bispectral Index (BIS). This instrument may be useful during the sedation/anesthesia period and also to evaluate the level of responsiveness during awake cortical mapping. Most authors use clinical sedation scales such as the Ramsay Sedation Score. Ghisi suggests adopting the OAA/S scale when performing MAC. Finally, Tijero et al. have proposed a possible intraoperative use for brain tissue oxygen pressure (PtiO2) as a precocious local damage indicator in proximity of the surgical resection area.

In conclusion, we believe that with:

- A sound knowledge of the anatomy of the nerves innervating the scalp,
- A good command of airway and
- An appreciation of the likely intraoperative events and possible interventions required, awake craniotomy can be added to the repertoire of all neuroanaesthetists. It is equally likely that, if modern worldwide trends in neurosurgery are followed, more
surgeons will be requesting this technique in the future.

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Intravenous versus Inhalational Induction in Children

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Introduction:
Induction of anaesthesia in infants and children always pose multiple challenges to an anaesthesiologist. When the patient is undergoing a neurosurgical procedure, additional concerns of increased intracranial pressure, compromised cerebral perfusion, pre-existing neurological damage, risk of secondary brain injury and associated medical problems and their sequelae also play significant roles.

In the recent times, increasingly complex neurosurgical procedures in sicker patients are being performed where appropriate anaesthetic techniques with advanced monitoring are vital for favourable outcome.

The anaesthetic management of neurosurgical patients is, by necessity, based upon our understanding of the physiology and pathophysiology of the central nervous system (CNS) and the effect of anaesthetic agents on the CNS. The desirable properties in an ideal anaesthetic agent for neurosurgery include-

- Rapid onset and rapid offset
- Maintains haemodynamic stability.
- Decreases cerebral blood volume (CBV).
- Does not alter CSF production or reabsorption.
- Decreases intracranial pressure.
- Maintains CO₂ reactivity.
- Maintains cerebral autoregulation.
- Allows EEG/EP monitoring for ischaemia and seizures
- Does not increase cerebral metabolic rate
- Anticonvulsant.
- Decrease cerebral oedema.
- Protect the brain from ischaemia.

Although all the objectives of neurosurgical anaesthesia cannot be met by one single anaesthetic agent or technique, the agent or combination of agents which fulfills these criteria most should logically be the choice of agent in neuroanaesthesia practice. All known anaesthetic agents have some effect on intracranial dynamics and must be considered in developing anaesthesia plan.

Inhalational Agents and Cerebral Physiology:
All inhalational agents except halothane cause no change or an increase in cerebral blood flow (CBF) and decrease in cerebral metabolic rate for oxygen (CMRO₂).

At doses 1.5-2 MAC the commonly used agents Isoflurane, Sevoflurane and Desflurane all cause burst suppression on electroencephalogram (EEG) which is usually associated with reduction in CMRO₂ to 50-60%.

They are also vasodilators. Despite the disassociation of CBF and CMRO₂, changes in the magnitude of cerebral vasodilation appear to be related to the level of tissue metabolism. At doses of about 0.5 MAC, the reduction in CMRO₂ due to metabolic coupling balances the vasodilatory effects and the CBF does not change significantly. In doses greater than 1 MAC, vasodilatory effects predominate and CBF increases. Halothane on the other hand causes significantly higher increase in CBF. When N₂O is added, the agents will increase CBF and CMRO₂. When administered alone, N₂O causes cerebral vasodilatation and increases CBF. It causes insignificant increase in CMRO₂. The increases in CBF may not be reflected as increases in intracranial pressure (ICP). The effects on cerebral blood volume (CBV) are parallel to CBF but are of significantly lesser magnitude. Effects of
Inhalational agents on brain are summarized in Table 1.

**Table 1: Effects of Inhalational agents on Brain**

<table>
<thead>
<tr>
<th>Drug</th>
<th>CBF</th>
<th>CMRO₂</th>
<th>ICP</th>
</tr>
</thead>
<tbody>
<tr>
<td>N₂O</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Halothane</td>
<td>↑↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Enflurane</td>
<td>↑</td>
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<td>↑</td>
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<tr>
<td>Sevoflurane</td>
<td>↑</td>
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<td>↑</td>
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<tr>
<td>Desflurane</td>
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</tbody>
</table>

**Intravenous Agents and Cerebral Physiology:**

All intravenous (IV) agents with the exception of ketamine decrease CMRO₂ and CBF substantially.¹ Thiopentone produces a dose-dependent reduction in CBF and CMRO₂. With the onset of anaesthesia, CBF and CMRO₂ are reduced by about 30 percent. Large doses of thiopentone cause complete EEG suppression and CBF and CMRO₂ are reduced by about 50 percent. Further increases in the dose of barbiturate have no additional effect on CMRO₂.

The effects of propofol on CBF and CMRO₂ appear to be quite similar to those of the thiopentone. Both CO₂ responsiveness and autoregulation appear to be preserved during the administration of propofol.

Etomidate produces parallel reductions in CBF and CMRO₂ which are accompanied by progressive suppression of the EEG. Etomidate has been shown to be effective in reducing ICP without causing reduction of cerebral perfusion pressure (CPP) in patients with intracranial tumours. Reactivity to CO₂ is preserved in humans during etomidate administration.

Effect of ketamine on CBF and CMRO₂ are regionally specific; in limbic system CBF and CMRO₂ increase whereas in cerebral cortex reduction in both occur.² Effects of intravenous agents on brain are summarized in Table 2.

**Table 2: Effects of Intravenous agents on Brain**

<table>
<thead>
<tr>
<th>Drug</th>
<th>CBF</th>
<th>CMRO₂</th>
<th>ICP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbiturates</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Propofol</td>
<td>↓</td>
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<tr>
<td>Etomidate</td>
<td>↓</td>
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<td>↓</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Opioids</td>
<td>=</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Ketamine</td>
<td>↑</td>
<td>=</td>
<td>↑</td>
</tr>
</tbody>
</table>

When N₂O is combined with an intravenous anaesthetic agent like thiopentone or propofol, benzodiazepine and opioids, the increase in CBF and CMRO₂ produced by N₂O is significantly reduced.²

**Anaesthetic Agents and Intracranial Pressure:**

Patients with intracranial hypertension have limited capacity accommodate additional CBV and even a slight increase in volume can dramatically increase the ICP. Agents that cause vasodilatation have potential to cause increase in ICP. Minor increases in ICP can be countered by modest hyperventilation and use of diuretics. Hence for majority of the patients, it is unlikely that anaesthetic agents induced increase in ICP should compromise the brain. However in patients with reduced intracranial compliance, N₂O can contribute to increased intracranial pressure and hence should be eliminated.

It is observed that in patients with intracranial space occupying lesion, there is no difference in outcome whether intravenous or inhalational agents are used. However higher dural tension have been found when isoflurane or sevoflurane with fentanyl were used as compared to propofol-fentanyl.³

Thus, it is apparent that intravenous anaesthetic agents like thiopentone and propofol affect cerebral dynamics favourably in patients with low intracranial compliance. Though selection of anaesthetic agent is a complex task based upon several factors including presumed intracranial status, fasting status and underlying medical conditions, intravenous agents should be
preferred for induction of anaesthesia in such patients. This is also the commonest practice in adult neuroanaesthesia.

There are still several questions and doubts which remain in mind to consider this as universal practice in children.

1. It should be noted that most studies done to find effects of various agents on brain have been conducted in laboratory animals and the applicability of the findings to the developing child is still questionable.

2. Currently inhalational agent induced neuroprotection and neurotoxicity both are hot research topics. There is relatively weak data to support neuroprotection and no data to prove its neurotoxicity at present.\textsuperscript{4,5}

3. A lot of stress has been placed on the minor differences in anaesthetic-induced changes in cerebral blood flow (CBF), cerebral metabolic rate (CMR) and intracranial pressure (ICP). Are these differences clinically relevant? Controlled studies demonstrating the superiority of one technique over another in children are lacking.

4. All neurosurgical patients are not same. So, are these minor differences in CNS physiology induced by anaesthetics are important to all neurosurgical patients? It is necessary to identify clinical situations in which effects of anaesthetic agent might be significant.\textsuperscript{2}

5. Besides, anaesthetic drugs, cerebral dynamics are affected by several other factors like preoperative stress, anxiety and fear of needles etc. in children. Struggle during intravenous access can probably take away the benefit of intravenous agent in a conscious crying baby and may lead to postoperative anxiety and psychological problems.

6. Many children coming for neurosurgical procedures have difficult intravenous access due to diuretic therapy, associated medical problems, multiple previous venepunctures or dehydration. Multiple attempts of venous access in a conscious child are undesirable.\textsuperscript{6} Is it safe to proceed with induction without an IV in such situations?

7. Often a difficult airway is anticipated in children. An intravenous induction may not be suitable in some cases when ‘can’t intubate, can’t ventilate’ situations may arise.

8. In hypovolaemic patients, a bolus intravenous agent may produce exaggerated haemodynamic response. The resultant hypotension can be more detrimental to cerebral perfusion.

9. Many neurosurgical patients have pre-existing or tendency towards bradycardia. Using supplemental drugs like midazolam, fentanyl, vecuronium can further lower heart rate. In such patients, giving thiopentone is preferred over propofol. Besides, propofol causes pain on injection.

10. Halothane can produce significant increase in intracranial pressure. Sevoflurane confers benefits over other inhalational agents, in that its odour is well tolerated, has rapid onset, haemodynamic safety and the likelihood of airway irritation, laryngospasm, and breath holding is reduced. Sudden increase in inhaled anaesthetic concentration may induce bronchospasm or coughing.

With such several factors in consideration, it is important to have a suitable approach to answer each of the anticipated problems. Mainly, the patient's neurological status and coexisting abnormalities will dictate the appropriate anaesthesia technique besides the individual drug choice. Some of the following points would be useful for smooth induction of anaesthesia in a paediatric neurosurgical patient.

- Developing rapport with a conscious patient will allay anxiety and reduce fear for injections. This step should not be overlooked. Preoperative amnesia should be provided.\textsuperscript{7}
- Having a secured intravenous access prior to induction of anaesthesia is needed in most neurosurgical patients and lack of it should not be a reason for choosing inhalational induction technique.
• If needed, distraction of patient, explanation of procedure, local application of EMLA cream etc. should be done to ease intravenous access.
• These patients are not for practicing venepuncture by trainee residents.
• Other measures to reduce ICP like control of CO₂ and administration of fentanyl should be used during induction to attenuate the hypertensive responses to laryngoscopy, intubation and surgery especially while using inhalational agents.
• Nitrous oxide is not a good choice in patients with increased intracranial pressure. When an anaesthesia technique avoiding N₂O is used, the depth of anaesthesia should not be compromised.
• Nitrous oxide should be avoided in patients with pneumoencephalus.
• Appropriate haemodynamic monitoring along with pulse oximetry and capnography with size specific probes and adapters should be used during induction.

Thus, both intravenous and inhalational anaesthesia are suitable in paediatric neuroanaesthesia practice with preference for intravenous agents in most patients with normal ICP. In children with raised ICP an intravenous induction with thiopentone 4-8 mg/kg or propofol 2-4 mg/kg and neuromuscular block to facilitate endotracheal intubation is preferred over sevoflurane induction. Alternatively, in children without IV access or with difficult IV access, inhalational induction by facemask with low dose sevoflurane may be done if they are not full stomach till intravenous access is secured. After that thiopentone or propofol may be used along with other intravenous agents and neuromuscular blocking agents prior to intubation.

Children at risk for aspiration should undergo rapid-sequence anaesthetic induction with thiopentone or propofol followed by rapid-acting neuromuscular blocking agents such as succinylcholine or rocuronium. In children with anticipated difficult airway inhalational induction with sevoflurane along with mild hyperventilation to control intracranial pressure may be done to assess ease of ventilation or to perform check laryngoscopy and such assessment procedures. Etomidate may be an appropriate choice for haemodynamically unstable patient. However, concerns regarding the risk of adrenocortical suppression and renal injury prevent routine use of this drug.

It is more important how the induction is done and not only what is given.

References new:

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Transcranial Doppler monitoring: Applications in neuroanaesthesia and critical care

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Transcranial Doppler sonography (TCD) is used to assess cerebral blood flow velocity in basal cerebral arteries and is a common noninvasive tool for the diagnosis and follow-up of cerebrovascular disease. Transcranial Doppler ultrasonography, however, allows an on-line and continuous monitoring of cerebrovascular dynamics with a time resolution within seconds. This technique, therefore, enables us to obtain improved insight into fast-acting components of homeostatic cerebrovascular mechanisms such as autoregulation and CO2 reactivity, something that could never be done using traditional methods.

Technique:
With TCD, three ‘windows’ (temporal, orbital and foramen magnum) can be used to insonate different cerebral arteries. The different cerebral arteries can be identified at different depth. The middle cerebral artery (MCA) is most commonly insonated because of the ease of access through the temporal window and the quality of the signal. Also the MCA carries 50–60% of the ipsilateral carotid artery blood flow and thus can be taken to represent blood flow to the hemisphere. Acoustic gel is applied to the area to be examined and the probe is applied with consistent gentle force to the skin. The temporal window is defined as an area delineated by a line drawn from the tragus to the lateral canthus of the eye, and the area 2 cm above this. Moving the probe slowly and systematically over the whole area, the examiner searches for a signal, initially starting at a depth of 50 mm. Initially, the area is scanned with the probe perpendicular to the skull. If a faint signal is found, then slight adjustments of the angle between the probe and skull may allow an optimal signal to be obtained. Some practitioners find the audio signal useful in initial identification of the vessel. If no signal is found then the process is repeated using depths from 45 to 70 mm. The examiner should attempt to follow the vessel toward the bifurcation of the internal carotid artery (ICA) into the MCA and anterior cerebral artery at greater depth. The bifurcation of the ICA is usually identified at a depth of 60–65 mm; the typical Doppler signal at this point has FV pulse wave images above and below the zero line of reference, representing the flow directions towards (MCA) and away (anterior cerebral artery), respectively. The first part of the ACA (the A1 segment) is recognized by a direction of flow...
that is away from the probe. The transorbital (orbital) window gives access to insonate the ophthalmic artery (OA) as well as the internal carotid artery at the siphon level. The power of the TCD should be reduced to 50% before insonating through Transorbital window. The transforaminal (occipital) window allows insonation of the distal vertebral arteries (VA) and the basilar artery (BA). Finally, the submandibular window allows insonation of the more distal portions of the extracranial internal carotid artery.

The normal values of the cerebral blood flow velocity may be affected by the following factors:

1. Age
2. Gender
3. Pregnancy
4. Asleep / arousal state
5. PCO₂ levels in blood
6. PO₂ levels in blood
7. Blood viscosity
8. Cerebral perfusion pressure

TCD is a useful tool for determining the cerebral autoregulation. The cerebral blood flow velocities change in response to the changes in cerebral perfusion pressure. Following important methods have been used to determine the autoregulatory testing:

1. Static autoregulation: MCA flow velocity is measured after achieving steady state following induction of 20 – 30 mmHg rise in MAP using phenylephrine infusion. The Autoregulatory index (ARI) is defined as percentage change in cerebrovascular resistance per percentage change in mean arterial pressure. ARI < 0.4 indicates impaired autoregulation.

2. Dynamic autoregulation: MCA flow velocity is measured while the mean arterial pressure is lowered transiently by rapid deflation of bilateral thigh cuffs. In normal course, there is initial fall in the MCA velocity which rises to normal even though MAP takes longer time to recover. It is considered impaired autoregulation if the flow velocity recovers passively following recovery of mean arterial pressure.

3. Transient Hyperemic Response: Here the change in flow velocity following release of brief compression (3 – 10 seconds) of ipsilateral common carotid artery is measured. There occurs transient hyperemia due to vasodilation, secondary to reduction in cerebral perfusion pressure due to compressed carotid artery, which is suggestive of intact autoregulation.

**Subarachnoid Hemorrhage: Detection of Vasospasm**

Cerebral vasospasm is a delayed narrowing or vasoconstriction of the cerebral vessels that is induced by blood products that remain in contact with the cerebral vessel wall after SAH. Vasospasm usually begins about day 3 after SAH onset and is maximal by day 6 to day 8. It is often responsible for the delayed ischemic neurologic defects and significantly higher mortality. The most common cause of SAH is the spontaneous rupture of a cerebral aneurysm. Other causes include head injury and neurosurgical procedures.

The degree of vasospasm in the basal vessels is correlated with the amount of acceleration of blood flow velocities through the vessels as they become narrowed. The best work on correlation between TCD means flow velocities (MFVs) and with vessel narrowing using cerebral angiography was performed in the MCA. Lindegaard et al. showed in their work that vasospastic MCAs usually demonstrate velocities of >120 cm/sec on TCD, with the velocities being inversely related to arterial diameter. In addition, velocities of >200 cm/sec are predictive of a residual MCA lumen diameter of <1 mm (normal MCA diameter is approximately 3 mm).

Higher MCA FV (>200 cm/sec) is associated with poorer computed tomography (CT) grade of SAH and worse outcome. Repeated testing of all accessible vessels improves sensitivity and allows earlier detection of possible vasospasm. A rapid increase in FV (>65 cm/sec over 24 h) is associated with a poorer outcome, and has been suggested as
an indication for initiation of treatment with haemodilution, hypertension, and hyperventilation (‘triple H’ therapy).

The Lindegaard index (MCA FV/ICA FV) has been used to predict the presence of vasospasm. A ratio of less than 3 is rarely found in patients with vasospasm, and ratios of greater than 6 may distinguish moderate from severe MCA vasospasm.

**Arterial Stenosis and Occlusion**

TCD measurements that correlate with stenosis would be increase FV at the stenotic site.

1. Decrease FV downstream from a stenotic site.
2. Decrease FV proximal and increase PI proximal to the stenotic site.
3. Increase FV and/or reverse flow in collateral vessels (like the finding of increased FV of the first segment of contralateral ACA shunting blood through the anterior communicating artery to the contralateral hemisphere in the same scenario).

In a case of total occlusion, there should be no flow signal from the occluded site. Increased velocity and/or reversed flow in the collateral vessels may also be seen. Sensitivity, specificity, positive predictive value, and negative predictive value of TCD are generally higher in the anterior circulation than in the vertebro-basilar circulation owing to more variable anatomy and technical difficulties in insonation of the vertebrobasilar circulation.

Since TCD is a noninvasive and inexpensive technique with no known risks or side effects, it can be an excellent tool for frequent follow-up of vascular lesions to assess effectiveness of a therapy without the concern of subjecting the patient to frequent radiation and the increasing costs of diagnostic testing like MRI. TCD can also be used to observe the effectiveness of thrombolytic treatment in stroke patients.

**Cardiac surgery**

TCD has been used as an embolic monitor that appears as high intensity transient signals (HITS) on the TCD spectrum. TCD can detect the presence of right-to-left shunts such as patent foramen ovale in patients with contraindications to transequaphageal echo (TEE) with similar sensitivity and specificity (Type A, Class II evidence). This clinic use requires the administration of agitated saline after which the patient performs a valsava maneuver. The test is positive for right to left shunt if a shower of high signal material (air) is detected in the MCA by TCD 5 to 10 seconds after the intravenous injection of 10 mL of agitated saline. If this shower of air emboli is detected after a minute of injection, it might indicate the presence of a pulmonary shunt; a diagnosis that cannot be obtained by TEE.

**Sickle Cell Disease**

Sickle cell disease is associated with progressive occlusion of large intracranial arteries (most frequently the intracranial ICA and MCA). According to the TCD criteria for sickle cell disease, a MFV of up to 170 cm/s is considered normal and a MFV of 171 to 199 cm/s is called “conditional.” MFV of equal or greater than 200 cm/s is considered abnormal and require transfusion. A mean FV (MFV) of 200 cm/s or greater is accompanied by a stroke risk of 40% within the next 3 years. Transfusion, with reduction of hemoglobin S to less than 30% of total hemoglobin, will lower this risk by 70% compared with standard care alone.

Recent guidelines regard the use of TCD4 as a type A level of evidence (established as useful predictive for suspected condition), and class I (evidence provided by prospective studies in broad spectrum of persons with suspected condition) screening tool to assess stroke risk in children aged 2 to 16 years with sickle cell disease. An optimal timing to re-screen children with sickle cell disease and normal TCD is not set, but a repeat TCD examination every 6 months seems to be a reasonable objective.

**Brain stem death**

Transcranial Doppler is not a formal part of brain stem death testing in the UK, nor in the USA. However, when performed, it shows
100% specificity and 96% sensitivity. Typical flow patterns are: reduced or absent diastolic flow, reverberant flow and short systolic spikes. PI is high with markedly reduced systolic flows. It may be useful in demonstrating cerebral circulatory arrest when sedative drugs preclude formal testing. Even if ‘typical’ patterns are seen with TCD, the diagnosis of brain stem death remains a clinical one based on clear inclusion and exclusion criteria.

**Carotid endarterectomy**

Monitoring for carotid endarterectomy is directed mainly towards detection of cerebral ischaemia during cross clamping, indicating when a shunt is needed, and detection of microemboli. Transcranial Doppler provides information about ipsilateral reduction in flow. Transcranial Doppler appears to be about as sensitive and specific at detecting flow ischaemia as EEG or near infra-red spectroscopy. Severe reductions in FV (>90%) at the onset of clamping and an increase in PI (>100%) at the release are associated with intra- and postoperative stroke.

McCarthy and colleagues concluded that using MCA FV less than 30 cm/s, a clamp/pre-clamp ratio less than 0.6 or reduction of MCA FV more than 50% were not reliable methods for detecting cerebral ischaemia, despite sensitivities of 83–92% and specificities of 49–77%.

Transcranial Doppler guided use of shunts appears not to influence morbidity. This may be because the determinant of morbidity is not the use of intraoperative shunts, but the ability of the cerebral circulation to autoregulate when flow is restored. Using TCD to assess autoregulation rather than just FV may be the next step forward, but this is as yet unproven. Some work has been done with CO2 reactivity (CRCO2) as a predictive variable. Patients with normal CRCO2 are less likely to need a shunt intraoperatively, but this was not related to changes in outcome. Impaired CRCO2 before operation does not correlate with intraoperative ischemia assessed by sensory evoked potentials. CRCO2 and cerebrovascular reserve in response to acetazolamide are both shown to improve after carotid endarterectomy. Transcranial Doppler may be a useful tool for the assessment of neurological deterioration after surgery. The main differential diagnoses of stroke post-endarterectomy are carotid occlusion or haemorrhage secondary to hyperperfusion. TCD may be of value in distinguishing between them.

Microemboli may be detected both by visual/audio inspection of the signal and using automated analysis. Various studies have found an association between embolic rates and the risk of clinical neurological events and or changes on CT/ MRI. The presence of emboli during initial dissection and wound closure appears to be more important in predicting adverse events than emboli during clamping or shunting, probably because of the different pathophysiology. Emboli occurring during dissection may also be a marker of a prognostically poor group rather than a preventable event, although it is also associated with excessive handling of the carotid artery, which may be amenable to changes in surgical technique. Emboli during closure may be amenable to changes in surgical technique as this may be a result of residual atheroma and early platelet aggregation.

**Head injury**

The measurement and management of ICP, in conjunction with CPP, is recommended in patients after severe traumatic brain injury. Conventionally, ICP measurement has required placement of an invasive monitor. There is always the risk of infection, hemorrhage, malfunction, obstruction, or malposition with these invasive devices. Consequently, TCD has been suggested as a potential noninvasive assessment of ICP and CPP.

Martin and colleagues found a, three distinct pulsatility phases occurring during the first 2 weeks after injury were described.
1. Phase 1: occurred on the day of injury and was associated with a low CBF, normal MCA FV and normal AVDO2.
2. In phase 2 (1–2 days post-injury), the hyperaemic phase, CBF was increased, MCA FV increased and AVDO2 decreased.
3. In phase 3 (days 4–15), the vasospastic phase, CBF decreased further and MCA FV further increased. The time-courses noted in this study are broadly in keeping with other reports. Together these indicate that the peak MCA FV occurs at around 9–11 days.

More recent work by Schmidt et al. using a prototype bilateral TCD machine with a built-in algorithm to assess CPP and externally measured values for arterial blood pressure has improved agreement. They used the formula: CPP = mean arterial blood pressure x diastolic flow velocity / MFV +14 mm Hg. They found that the absolute difference between measured CPP and estimated CPP was < 10 mm Hg in 89% of measurements and <13 mm Hg in 92% of measurements. The 95% confidence range for predictors was +12 mm Hg for the CPP, varying from 70 to 95 mm Hg. Attempts at estimation of ICP have demonstrated similar confidence intervals.

These studies have significant implications for the interpretation of changes in MCA FV after head injuries. They highlight the continuously changing nature of cerebral haemodynamics in these subjects, and reinforce the need to use TCD in combination with other monitoring modalities to gain an overall understanding of changes in perfusion and oxygenation, and how these can be optimized with different interventions.

Summary and conclusions:

1. **Clinical utility of TCD is established.**
   a. Screening of children with sickle cell disease for assessing stroke risk (Type A, Class I).
   b. Detection and monitoring of angiographic VSP sSAH (Type A, Class I-II).

2. **Clinical utility of TCD, compared with other diagnostic tools, remains to be determined.**
   a. Intracranial steno-occlusive disease. TCD is probably useful (Type B, Class II to III) for the evaluation of occlusive lesions of intracranial arteries in the basal cisterns (especially the ICA siphon and MCA).
   b. Cerebral circulatory arrest (adjunctive test in the determination of brain death). If needed, TCD can be used as a confirmatory test, in support of a clinical diagnosis of brain death (Type A, Class II).

3. **Clinical utility of TCD remains to be determined.**
   a. Cerebral thrombolysis. TCD is probably useful for monitoring thrombolysis of acute MCA occlusions (Type B, Class II to III).
   b. Cerebral microembolism detection. TCD monitoring is probably useful for the detection of cerebral microembolic signals in a variety of cardiovascular/cerebrovascular disorders/procedures (Type B, Class II to IV).
   c. CEA. TCD monitoring is probably useful to detect hemodynamic and embolic events that may result in perioperative stroke during and after CEA in settings where monitoring is felt to be necessary (Type B, Class II to III).
   d. CABG surgery. TCD monitoring is probably useful (Type B, Class II to III) during CABG for detection of cerebral microemboli. TCD is possibly useful to document changes in flow velocities and CO2 reactivity during CABG surgery (Type C, Class III).
   e. VMR testing. TCD is probably useful (Type B, Class II to III) for the detection of impaired cerebral hemodynamics in patients with severe (>70%) asymptomatic extracranial ICA stenosis, symptomatic or asymptomatic extracranial ICA occlusion, and cerebral small-artery disease.
f. VSP after tSAH. TCD is probably useful for the detection of VSP following tSAH (Type B, Class III).

g. TCCS. TCCS is possibly useful (Type C, Class III) for the evaluation and monitoring of space-occupying ischemic MCA infarctions.

4. **Settings in which other diagnostic tests are typically preferable compared to TCD.**
   a. Right-to-left cardiac shunts.
   b. Extracranial ICA stenosis.
   c. Contrast-enhanced TCCS. (Contrast-enhanced) TCCS may provide information in patients with ischemic cerebrovascular disease and aneurysmal SAH (Type B, Class II to IV).

Reference:


PROBLEM BASED LEARNING DISCUSSIONS (PBLD)

Meningomyelocele (MMC)

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Case:
A 2 month old child, referred from another hospital with a h/o swelling since birth in the back with probable diagnosis of MMC. Child was noted to have B/L inguinal hernia, umbilical hernia and rectal prolapse. Child was not moving both the lower limbs. On examination, child was weighing 4 kg, head circumference was 36 cm. child was opening eyes spontaneously, crying normally, moving both upper limbs spontaneously. A swelling of 4 * 6 cm in size extending from L2-S1, with a bony defect in the upper margin was seen. On MRI brain scan hydrocephalus, tonsilar herniation, MMC with tethered cord was seen. Echocardiography showed a small ASD with left to right shunt with good systolic function of ventricles. Routine haemogram and biochemistry was normal. Surgical plan was right sided ventriculo-peritoneal shunt followed by excision of MMC and repair.

Key questions:
1. What other congenital anomalies are associated?
2. Specific issues in the preoperative evaluation of MMC child.
3. When do you operate these children?
4. How do intubate these children?
5. Any specific anaesthetic technique? (TIVA or inhalational)
6. What type of fluids?
7. Any special monitoring? Other than routine
8. What postoperative problems are expected?
9. Is foetal surgery beneficial in MMC?
10. What are the preoperative and intraoperative issues in foetal surgery?
11. What postoperative complications can occur?

MMC is a congenital neural tubal defect with an incidence of 0.3-1.0 per 1000 live births. It is characterized by protrusion of meninges through a midline bony defect of the spine, forming a sac containing cerebrospinal fluid (CSF) and dysplastic neural tissue. Embryologically, neural tube fusion defect occurs between 18 and 21 days of gestation. Meningomyeloceles have been reported at all spinal levels: lumbosacral (30%) and lumbar (26%) being the commonest. The incidence is decreasing with good antenatal care and folic acid supplementation. In India, vitamin B12 supplementation is also important. The cause of MMC is not known but various mechanisms have been postulated including the nutritional deficiencies, teratogens, environmental and genetic factors. It is usually associated with many other congenital anomalies. The central nervous system abnormalities include hydrocephalus (80-90%), Arnold chiari malformation (ACM) type II, corpus calloso agenesis, microgyria, porencephalic cyst and arachnoid cyst. The ACM involves smaller posterior fossa and downward shift of
inferior cerebellar structures and medulla oblongata into the upper cervical region. The symptoms can be headache, hypoventilation, apnoeic episodes, stridor from vocal cord paralysis, bradycardia, upper limb weakness and spasticity. These patients require decompression of the posterior fossa. Congenital heart disease has been seen in 37% of neonates with MMC (Ritter et al) and ASD is the commonest. Other anomalies include VSD, anomalous pulmonary venous return, tetralogy of Fallot, bicuspid aortic valve, coarctation, and hypoplastic left heart syndrome. Genitourinary system problems include hydronephrosis, solitary kidney, horseshoe kidney, bladder extrophy, neurogenic bladder dysfunction, urinary incontinence/obstruction and recurrent UTIs. Scoliosis, high arched foot, upper respiratory tract infections, short trachea, electrolyte imbalance are also seen. The surgery is usually done at the earliest in the first week to prevent any rupture and infection. In India it is common to operate later.

Intubation in these children can be a challenging task. Careful positioning is required to prevent any sort of pressure on the MMC and thus, prevent the possible rupture. Most of the patients can be safely intubated in the lateral position. During the extension of the neck, there can be bradycardia due to compression of the brain stem. The anaesthetic technique can be the one which the anaesthetist is comfortable with as there is no superiority of one technique over other. The fluids with low sodium needs to avoided. It is also better not to give fluids with 5% dextrose to prevent the hyperglycemia. Sudden loss of CSF from the sac can cause hypotension. However, this is rarely documented/ investigated. However, few anaesthesiologists recommend giving additional fluids to replace that third space loss from the sac. Blood transfusion may be required even though the blood loss in these surgeries is less. Careful prone positioning and temperature management is important. There is a high incidence of latex allergy in this group of patients, the cause of which is not known. Most probably it is due to multiple exposures to latex as these patients come for multiple surgeries in the course of their management. Appropriate precautions to prevent the sensitisation and high index of suspicion to identify early and management are needed.

Intraoperative complications include bradycardia (8%), tachycardia (4%), hypotension (4%), cardiac arrest (1.5%), arrhythmia, hypoxaemia (4%), bronchospasm (4%), full intubation (2%), hypothermia and hyperthermia. The children should be extubated when they are awake and breathing well. Be prepared for emergency reintubation. The incidence of respiratory complications are high in the postoperative period. They include hypoventilation, apnoeic episodes, bronchospasm, irregular rhythm, stridor and respiratory arrest. Postoperatively, the children should be monitored continuously for 24-48 hrs preferably in the intensive care unit. Postoperative surgical complications include wound infection (20.7%), pneumonia (3%), meningitis (7.5%), urinary tract infection (15.7%), hematoma (1.5%), cerebrospinal fluid leak (18%), pseudomeningocele (13%) and seizures (2.2%).

Foetal surgery (from Ferschl M et al, 2013):
A two-hit theory of nerve damage has been postulated: the first damage being the failure of the neural tube to form and the second one being nerve damage caused by exposure of the neural tube to the uterine environment. The in utero repair has the potential to decrease neurologic deficits and associated co-morbidities by reducing intrauterine exposure and therefore improving the function and quality of life in these children. The intrauterine surgery is usually done during 18-28 weeks of gestation. Multidisciplinary approach, good understanding of the maternal and foetal physiology helps to improve the outcomes in these surgeries.

The perioperative considerations are Preoperative:
Complete maternal history and physical examination
Complete foetal work-up to exclude other anomalies
Imaging studies to determine foetal lesion and placental location
Maternal counselling by multidisciplinary team and pre-surgical team meeting
Lumbar epidural placed and test dosed
Prophylactic premedication: non-particulate antacid (aspiration), rectal indomethacin (tocolysis)
Blood products typed and crossmatched for potential maternal and foetal transfusion; foetal blood should be type O-negative, leukocyte depleted, irradiated, CMV-negative, and crossmatched against the mother
Obtain estimate of foetal weight to aid in medication preparation for the foetus
Sequential compression devices on lower extremities for thrombosis prophylaxis

Intraoperative:
Left-uterine displacement and standard monitors
Preoxygenation for 3 min prior to induction
Rapid sequence induction and intubation
Maintain maternal Fio2 >50% and end-tidal CO2 28–30 mmHg
Ultrasound to determine foetal and placental positioning
Urinary catheter placed; additional large-bore IV access placed +/- arterial line
Prophylactic antibiotics administered
Foetal resuscitation drugs and fluid transferred to scrub nurse in sterile fashion
Following skin incision, high concentrations of volatile anesthetic (2–3 MAC) started
Blood pressure maintained with IV phenylephrine, ephedrine, and/or glycopyrrolate; typical goal is to maintain mean arterial pressure within 10% of preinduction baseline
Consider IV nitroglycerine if uterine tone remains increased
IM administration of foetal opioid and neuromuscular blocking agent by surgical team following hysterotomy
Crystalloid restriction to <2 litres to reduce risk for maternal pulmonary edema, consider colloid administration
IV loading dose of magnesium once uterine closure begins
Discontinue volatile agents once magnesium load is complete
Administer propofol, opioids, and nitrous oxide as needed
Activate epidural for postoperative analgesia
Monitor neuromuscular blockade carefully due to magnesium
Extubate trachea when patient is fully awake

Early postoperative:
Continue tocolytic therapy
Patient-controlled epidural analgesia
Monitor uterine activity and foetal heart rate
Ongoing foetal evaluation
The maternal complications include spontaneous membrane rupture (46%), uterine rupture (36%), placental abruption (6%), spontaneous labour (38%), oligohydramnios (28%), postop bowel obstruction. The foetal complications include foetal bradycardia, preterm delivery, low birth weight, respiratory distress syndrome.

Suggested References:
OBJECTIVES:
After the PBLD, the participants will be able to:
1. Enumerate concerns which are pertinent to anaesthesia for posterior fossa surgery.
2. Describe the precautions that should be taken while placing the patient in the sitting position.
3. Discuss the complications related to the sitting position.
4. Discuss procedure related complications in patients undergoing posterior fossa surgeries.
5. Describe a safe anaesthetic and emergence plan for patients undergoing post fossa surgery and modifications in technique, so as to facilitate intra-operative electrophysiological monitoring.
6. Discuss differential diagnosis and management of delayed recovery following posterior fossa surgeries.
7. Discuss the postoperative complications in patients undergoing posterior fossa surgery.

STEM CASE
A 44 year old female patient presents with complaints of gradually progressive hearing loss for the past five months, difficulty in walking with a tendency to sway on the left side and numbness on left side of the face, for the past two months. She does not have any other co morbidity or allergies. She is alert and oriented; cardio-respiratory and airway evaluation reveals no abnormality. Neurological examination reveals decreased power in both the limbs (4/5), hypoesthesia in distribution of V1, V2 N, sensorineural hearing loss, Romberg’s test and positive finger- nose test. Routine laboratory investigations are within normal limits. MRI scan of the brain reveals a cerebello-pontine tumour with obstructive hydrocephalus. She undergoes a ventriculoperitoneal shunt procedure and is scheduled for a suboccipital craniectomy in the sitting position.

KEY QUESTIONS
1. What would you specifically like to assess during the pre-anesthetic evaluation of this patient?
2. What monitoring techniques would you like to use for this case?
3. Does intra-operative electrophysiological monitoring have any role in this case? How would you modify your anaesthetic technique accordingly?
4. Would you like to use N₂O as a part of your anaesthetic regimen?
5. What precautions will you take while transferring the patient from the supine to the sitting position?
6. When the surgeon is making the craniectomy, there is a sudden fall in the EtCO₂ from 30 mm.hg to 19mm.hg, along with a drop in oxygen saturation from 99% to 74%, and a decrease in blood pressure from 110/60 to 75/40mm/Hg. How will you respond to this situation?
7. Why is the sitting position contraindicated in patients with right to left intracardiac shunts?
8. While the surgeon is dissecting the tumor, there is a sudden rise in blood pressure from 112/76 to 180/104 along with a fall in heart rate from 82/min to 44 /min. How will you respond to this situation?
9. What will be your considerations regarding tracheal extubation of this patient?
10. The surgeon has successfully removed the tumour and wants you to give a trial of tracheal extubation at the end of the surgery. However the patient does not show signs of emergence till the next 45
minutes. What is your differential diagnosis and how will you manage this situation?

11. What complications should you anticipate in the postoperative period?

**MODEL DISCUSSION**

The posterior fossa is a small, intracranial compartment which contains the cerebellum, pons, medulla oblongata and fourth ventricle. Neurosurgical procedures in this region are often challenging, for both the surgical and anesthetic teams, for the following reasons:

* There is a risk of injury to vital brainstem (neural) structures, such as the cardiorespiratory centre (medulla), reticular activating system and lower cranial nerve nuclei, which control, critical functions such as cardiorespiratory mechanics, cortical activation and protection of the airway, respectively. Damage to these structures results in potentially life threatening sequelae like coma, respiratory arrest, severe hemodynamic instability and aspiration.

* Because of the narrow cerebrospinal fluid outflow tracts, (CSF) (4th ventricle and cerebral aqueduct), even small lesions can produce acute and significant obstructive hydrocephalus with severe intracranial hypertension.

* Because of narrow confines of this fossa with limited compensatory latitude, even relatively little swelling causes significant intracranial hypertension, resulting in impaired consciousness, and cardiorespiratory dysfunction.

* Positioning related complications: Venous air embolism (VAE), haemodynamic instability, quadriplegia, post-operative tension pneumoencephalus, and paradoxical air embolism (PAE). This position should not be used in patients with documented right-to-left intracardiac or pulmonary shunts which can facilitate systemic embolization of air, and should preferably be avoided in extremes of age and in patients with hemodynamic instability.

This position is more of a modified recumbent position, somewhere between semi-recumbent and full sitting, with the head placed in a three point head-holder, and feet at the level of the heart. Care should be taken to avoid over-flexion of the neck and kinking of the endotracheal tube; usually, at least two fingerbreadth’s space is maintained between the chin and sternum. The legs are kept as high as possible (usually with pillows under the knees) to promote venous return; over flexion of the hips can cause traction on the sciatic nerve, and should be avoided. Arms are folded so that the hands rest on the lap; pressure points at the elbows, lateral and medial aspects of the knees and heels are carefully padded, to prevent pressure/ compression related injury. Positioning the head above the heart results in a local reduction in arterial pressure of 0.77 mmHg per centimeter of elevation; to assess cerebral perfusion pressure (CPP) accurately, the arterial considerations are access to the patient, security of the airway and adequate protection of the eyes, skin and peripheral nerves. The potential hazards of each position can be minimized through appropriate patient selection, careful positioning and vigilance throughout the procedure.

**Sitting position**

The sitting position has several advantages, including excellent surgical exposure of posterior fossa structures, better access to the airway and improved ventilatory mechanics. However, it is also associated with several, potentially life threatening complications such as venous air embolism (VAE), haemodynamic instability, quadriplegia, post-operative tension pneumoencephalus, and paradoxical air embolism (PAE). This position should not be used in patients with documented right-to-left intracardiac or pulmonary shunts which can facilitate systemic embolization of air, and should preferably be avoided in extremes of age and in patients with hemodynamic instability.

**POSITIONING FOR POSTERIOR FOSSA SURGERY**

Posterior fossa surgery can be performed in the sitting, prone, three quarter prone, lateral and park-bench positions. Important
pressure transducer should be placed at the level of the skull base.

**Complications of sitting position**

Haemodynamic instability:

Hemodynamic instability may complicate surgery in the sitting position. In addition to the usual vasodilating and myocardial depressant effects of anesthetics, pooling of venous blood in the lower extremities due to sitting position, further exacerbates the intraoperative hypotension. The decrease in cerebral perfusion caused by placing the head above the heart may make this hypotension more detrimental. This hemodynamic instability can be attenuated by pre-positioning volume loading, wrapping the legs and thighs with elastic bandages to counteract gravitational shifts of blood, slow incremental transition from supine to sitting position, and if required, use of vasopressors (ephe drine, phenylephrine) and inotropes.

**Venous air embolism (VAE)**

The incidence of venous air embolism in sitting post fossa craniotomies has been reported to be as high as 76%, though majority of these events do not result in hemodynamic compromise. The entrainment of air from the operative site into the venous circulation occurs due to a combination of factors: sub atmospheric pressure in the opened vein, presence of non collapsible venous channels such as the diploid veins, bridging veins, emissary veins, Dural sinuses and, last but not the least the extent of elevation of the surgical site, compared the heart.

Patho physiology of VAE: The entrained air enters the right atrium, passes through the right ventricle, reaches the pulmonary circulation and causes mechanical obstruction, local hypoxia and endothelial activation in the pulmonary vascular bed. As a result, alveolar dead-space and the Ventilation perfusion mismatch increase; end-tidal carbon dioxide (etCO₂) and systemic oxygen partial pressure (PaO₂) decrease; partial pressure of arterial carbon dioxide (PaCO₂) increases and N₂ appears in the exhaled gas. Reflex sympathetic pulmonary vasoconstriction occurs, resulting in increased pulmonary vascular resistance, right ventricular strain and increase in right atrial and pulmonary artery pressures, decreased venous return and cardiac output. At the endothelial level, an inflammatory response cascade, triggered by the release of endothelial mediators, leads to the production of reactive O₂ molecules which can cause bronchoconstriction, pulmonary hypertension, increased microvascular permeability, and even pulmonary edema. Various mechanisms have been proposed for this injury to the pulmonary vascular bed: platelet aggregation, release of platelet activator inhibitor due to turbulent flow resulting in systemic inflammatory response syndrome; endothelial activation results in cytokine release, complement production, leading to release of reactive O₂ molecules and other toxic free radicals.

A patent foramen ovale is present in approximately 20% of the adult population. In these patients, there is a 5–10% risk of systemic air embolism; air can embolize from the right atrium to the left atrium and subsequently to the systemic circulation, particularly coronary and/ or cerebral vessels. These patients usually have symptoms of coronary or cerebral ischemia.

Clinical manifestations of VAE: VAE can have cardiovascular, pulmonary, and neurologic sequelae; the clinical consequences are determined by the rate and the volume of air entrained. While a small acute volume of air is often well tolerated, a large air embolism (3–5ml/kg), can result in complete right ventricular outflow tract obstruction, right failure and cardiovascular collapse. In more moderate sized embolism, partial outflow tract obstruction can cause decreased cardiac output; hypotension and myocardial ischemia. ECG manifestations include tachyarrythmias, right heart strain pattern, and/or ST–T changes. Pulmonary manifestations have been described above. Cerebral hypoperfusion can occur either due to reduced cardiac output or paradoxical air embolism. In mild form, acute alteration in mental status is observed, but focal deficits
related to cerebral hyperemia and cerebral edema and even frank coma can also occur.

Detection of VAE: The risk of catastrophic air embolism has been reduced dramatically with the availability of monitors that allow prompt detection of VAE. Precordial Doppler is the most sensitive non invasive monitor, which can detect a little as 0.05 ml/ kg of bolused air in the right atrium. Tran esophageal echocardiography (TEE) is more sensitive than Precordial Doppler for VAE detection (detects 0.02 ml /kg of air) and offers the advantage of identifying right-to-left shunting of air. However, it is not specific for air bubbles; moreover detection of air bubbles is qualitative, not quantitative and micro bubbles can generate a dramatic image. Expired CO\(_2\) (ETCO\(_2\)) monitor detects 0.5ml/kg of bloused air; it is convenient and practical, though not as sensitive and specific as Precordial Doppler, for VAE; Other monitors that can be used be used to detect VAE include pulmonary artery catheter (PA) catheter , pulse oximetry and end tidal nitrogen (EtN\(_2\)). It is generally recommended that several monitoring modalities be used in conjunction, to decrease the risk of VAE in sitting craniotomies; a combination of a Precordial Doppler and expired CO\(_2\) monitoring are commonly used for this purpose. A change in the Doppler ultrasound signal and/ or etCO\(_2\) decrease of more than 2 mm usually indicates VAE.

Management of VAE: The main goals of management of VAE are to prevent further air entrainment, decrease the volume of air entrained and provide hemodynamic support. The surgeon should be informed immediately, N\(_2\)O discontinued and the inspired concentration of O\(_2\) should be increased to 1.0. The surgeon should cover the surgical field with saline-soaked dressings to prevent further entrainment of air, and should assess and eliminate any entry site. Lowering the patient’s head can prevent continued entrainment of air; however it may not always be feasible in the surgical setting.

Aspiration of air through a Right atrial catheter (RAC) has established clinical efficacy in reducing the embolic load and decreasing VAE related morbidity. The optimal position of the tip of RAC for this purpose, has been suggested to be 2 cm below the superior vena caval–atrial junction for a multi-orificed catheter, and 3 cm above the superior vena caval–atrial junction for a single-orificed catheter; however, anywhere in the right atrium should suffice for recovery of massive volumes of air in the face of cardiovascular collapse. Temporary jugular venous compression, by causing cerebral venous distension, can help the surgeon to identify and repair a tear in a vein. It may be considered in emergent situations where high volume and rapid entrainment of air occurs, but should be used with caution since it can be associated with inadvertent manipulation of the carotid artery or carotid sinus. Application of PEEP for treatment of VAE is controversial.

Hemodynamic stability is provided by administering intravenous fluids, vasopressors, inotropes, and antidysrhythmics; one should be prepared for cardiopulmonary resuscitation. In the event of a massive air embolism, external cardiac massage can be used to disrupt a large air lock in the right ventricle; it acts by forcing air out of the pulmonary outflow tract into the smaller pulmonary vessels and improves the forward blood flow.

Prevention of VAE: The risk of VAE cannot be completely eliminated in patients undergoing sitting craniotomy, because of the gradient which exists between the operative site and the right atrium. However, its incidence and severity can be decreased by meticulous surgical technique, liberal use of bone wax, maximization of intravascular pressures by adequate intravenous fluid loading and proper wrapping of the lower extremities, positioning so that head elevation is the lowest possible while still providing good surgical exposure, avoidance of drugs that increase venous capacitance and last but not the least, a high degree of suspicion for VAE. Presently, there is no consensus on application of PEEP or routine avoidance of nitrous oxide for prevention of
VAE in the sitting position. For those anesthetists who choose to use N\textsubscript{2}O during neurosurgery, early detection of venous air entrainment is particularly important. Preoperative screening for patent foramen ovale by Precordial echocardiography, contrast enhanced Transcranial Doppler ultrasound (TCD), or prepositioning TEE has been recommended by some centers, however currently this practice has not been universally accepted.

Pneumocephalus

Some amount of pneumoencephalus (presence of intracranial air) is inevitable following posterior fossa surgery and resolves with time. Occurrence of tension pneumocephalus, however, is a cause for concern; it can cause delayed awakening/nonawakening after surgery and if not diagnosed or treated in time, can result in brain herniation and even cardiac arrest.

During a sitting craniotomy, air enters the cranium, when the brain has shrunk due to a combination of hypocapnia, good venous drainage, osmotic diuresis, removal of the mass lesion and CSF loss from the operative field. When the cranium is closed, and the patient is returned to the near-supine position, CSF, venous blood volume, and extracellular fluid return or re-accumulate, and the air pocket becomes an unyielding mass lesion (because of the very slow diffusion of nitrogen). The potential for tension pneumocephalus can be reduced by flushing the subdural space with normal saline, minimizing use of diuretics and hyperventilation, ensuring adequate volume replacement and slowing CSF drainage.

The diagnosis of pneumocephalus is confirmed by a brow-up lateral x-ray or CT scan. The treatment is a twist-drill hole followed by needle puncture of the dura. N\textsubscript{2}O has been incriminated as a causative factor for tension pneumoencephalus; however this condition has been reported to occur even when N\textsubscript{2}O has not been used intraoperatively.

Other significant complications:

Mid-cervical quadriplegia due to cervical cord ischemia, though rare, has been reported in patients undergoing sitting craniotomy. This ischemic damage is attributed to a combination of hypotension and extreme neck flexion (which causes stretching and/or compression of the cord). Monitoring evoked potentials may allow for early detection and intervention with spinal ischemia. Excessive neck flexion in the sitting position can also obstruct venous and lymphatic drainage of the head and neck, resulting in swelling of the face, tongue and oropharynx. Placement of a TEE probe may also contribute to this complication; use of smaller diameter probes may prevent this complication.

Orthopedic, dermatologic, and peripheral nerve injuries can occur in the sitting position, due to pressures exerted on dependent regions of the body. Common peroneal nerve injuries due to nerve compression and/or stretching of the nerve secondary to flexion of the thigh, and recurrent laryngeal nerve palsies, due to compression by the TEE probe and endotracheal tube, have been reported.

ANAESTHETIC MANAGEMENT FOR POSTERIOR FOSSA SURGERY

Intraoperative considerations

1. Sitting position related complications (discussed above)
2. Damage to vital centers (mentioned above)
3. Hemodynamic disturbances during surgery

Irritation of the lower portion of the pons, upper medulla or extra-axial portion of the fifth cranial nerve can result cardiovascular disturbances. The cardiovascular responses may include bradycardia and hypotension, tachycardia and hypertension, bradycardia and hypertension, and ventricular dysrhythmias. The surgeon should be immediately informed of these sudden hemodynamic changes, to prevent iatrogenic damage to the adjacent cranial nerve nuclei and respiratory centers. Pharmacologic treatment of the dysrhythmias is not advised, as it may mask the very warning signs that are being sought.
4. Brainstem monitoring: There is a significant risk of injury to cranial nerves during operations in the cerebello-pontine region, therefore intra-operative stimulation and recording of Cranial nerves (V, VII, VIII, and XI XIII) is often utilized, to help preserve function of these nerves during tumour resection. Monitoring techniques include somatosensory evoked potentials (SSEP), Brainstem auditory evoked potentials (BAEP), and spontaneous and evoked electromyogram (EMG). This monitoring can be a challenge for the anaesthetist because muscle relaxants complicate the interpretation of EMG, and $\text{N}_2\text{O}$ and high dose inhalational anaesthesia can interfere with SSEPs. BAEPs are relatively resistant to the effects of anaesthetic agents.

5. Emergence/ tracheal extubation related concerns (discussed below)

6. Potential for massive intracranial hypertension due the limited compensatory latitudes of this narrow space

**Preoperative assessment**

Pertinent issues in the pre-anaesthetic evaluation of these patients include assessment of the neurological, cardio-respiratory status and ability to protect the airway. Patients can present with altered states of consciousness, respiratory irregularities, and lower cranial nerve deficits such as dysphagia, laryngeal dysfunction, hoarseness of voice, impaired gag reflex, aspiration pneumonitis and signs of raised intracranial pressure. Patients with obstructive hydrocephalus usually have a Venticuloperitoneal shunt procedure, prior to the tumor resection surgery.

**Peri-operative management:**

The goals of intra-operative management are, to maintain hemodynamic and respiratory stability, optimize cerebral perfusion pressure, provide optimal operating conditions to minimize trauma to the nervous tissue, and to avoid positioning related complications. The choice of anaesthetic agents is largely at the discretion of the individual anaesthetist. Induction is usually achieved with administration of an opioid- muscle relaxant- intravenous induction agent combination. Anaesthesia can be maintained by inhalational / intravenous/ combination - muscle relaxant technique; controlled positive-pressure ventilation is used in most patients. Many anaesthetists choose to avoid $\text{N}_2\text{O}$ because of concerns related to tension pneumocephalus and VAE. Some minimize the use of inhalational anaesthetic agents because they facilitate the transpulmonary passage of air and because they interfere with SSEP monitoring. In procedures where EMG monitoring is used, muscle relaxant infusion dose has to be reduced to maintain partial paralysis or avoided altogether; anaesthesia should be supplemented by increasing the rate of the infusion of the intravenous agent eg. Propofol or additional doses of short-acting opioid.

The choice of monitors is based on the operating position along with availability and technical expertise with the equipment. Routine monitoring for sitting position includes electrocardiography (ECG), invasive arterial blood pressure, central venous pressure, end tidal carbon dioxide, pulse oximetry, pre-cordial Doppler ultrasound, (Precordial/esophageal stethoscope if Precordial Doppler is not available), urinary output, temperature and arterial blood gas analysis. Specialized monitoring for sitting position includes end tidal nitrogen, trans-echocardiography and electrophysiological monitoring.

Essentially all patients who undergo sitting posterior fossa procedures should have a right atrial catheter (RAC), to allow immediate evacuation of air from the heart; intravascular ECG guided placement of RAC can help to optimize its position.

The sitting position provides excellent operating conditions to the surgeons: Cerebral venous drainage and cerebrospinal fluid (CSF) drainage is enhanced by the effects of gravity, producing a less “tense” brain, pooling of blood in the surgical field is minimized, potentially improving operating
conditions and reducing blood loss. In most patients, there is usually no need to administer osmotic / loop diuretics during a sitting craniotomy; moreover, they predispose to hemodynamic instability and can also increase the risk of pneumoencephalus. If required, lower doses should be given and intravenous colloid should be given simultaneously, to maintain hemodynamic stability and an optimal cerebral perfusion pressure.

The anesthetic goals during emergence from anesthesia are to prevent abrupt rises in blood pressure, allow rapid awakening, and minimize coughing and straining on the endotracheal tube. Ideally, the surgeon and anesthetist should have a consensus on whether tracheal extubation is appropriate or elective ventilation is advisable. The feasibility of immediate postoperative extubation is usually determined by the patient's preoperative status and the nature and extent of surgery. Generally, a neurologically intact patient who has had an uneventful intra-operative course can be considered for immediate postoperative extubation, if he is conscious, has stable vital parameters, regular respiration with intact airway reflexes and no evidence of facial or airway swelling. On the other hand, extensive brainstem manipulation intra-operatively, increases the likelihood of postoperative brainstem edema or brainstem injury and is an indication for elective ventilation. In patients with significant facial edema (may have associated airway swelling) / macroGLOSSIA, endotracheal intubation should preferably be maintained, till the swelling subsides. Persistent postoperative hypertension in a previously normotensive patient should alert the anesthesiologist to possible brainstem compression, ischemia, or hematoma.

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Anesthetic management for the intra-cerebral aneurysm Clipping

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Objective:
Learner will be able to
1. Describe the physiologic rearrangements that can accompany subarachnoid haemorrhage
2. Define how to conduct a preoperative assessment
3. Identify the physiologic goals when anesthetizing a patient with intracranial aneurysm clipping, and the monitoring and techniques utilizing to reach those goals
4. Define the management of problems that can arise during intracranial aneurysm clipping
5. Describe the challenges encountered when emerging from general anesthesia after clipping of an intracranial aneurysm
6. Discuss appropriate management of these challenges.

Stem question:
55 years old lady presents to the emergency department with “worst headache of her life”, rates as 10/10. ER physician perform a non-contrast CT scan, which reveals subarachnoid haemorrhage and intra-ventricular haemorrhage.

Questions:
1. What is the epidemiology of aneurismal subarachnoid haemorrhage?
Aneurysmal subarachnoid haemorrhage (aSAH), which forms 85% of all cases of non-traumatic SAH, is a neurological emergency [1]. The acute treatment of aSAH requires an understanding and appreciation of both the neurological implications and the multitude of systemic issues. It is a multi-organ system disease. One in eight patients die before reaching the hospital and the case fatality rate ranges between 26 and 50% declining over the past 40 years [2]. Of survivors, nearly half will have long term functional impairment [3]. The incidence of aSAH ranges from 2 to 22 per 100,000 patient-years with the highest incidence seen in Finland and Japan [4, 5]. The incidence is higher among women. Risk factors include hypertension, smoking, family history, and cocaine use.

2. What is the clinical grading of patients with aSAH? Why is this significant?
The severity of clinical presentation is the strongest predictor of prognosis in aSAH [6]. Multiple clinical and radiographic SAH grading scales have been developed. They remain important because of the close relation of clinical presentation and radiographic features to prognosis. The most commonly used include the Hunt and Hess,(Table-1) World Federation of Neurological Surgeons [WFNS](Table-2), and Fisher scales (Table-3). WFNS scale is the preferred scale as it incorporates GCS and presence of focal neurological signs. Major factors associated with poor outcome are patient’s level consciousness, age, amount of blood as shown in initial CT Scan, which are derived from WFNS and Fisher scale.

Cerebral angiogram reveals an 8mm anterior communicating aneurysm. Patient is to arrive to the operating room for the clipping of the ruptured aneurysm.

3. How would you perform a pre-anesthetic assessment of this patient?
Detailed neurological examination is important to understand the pathophysiological changes that occur in patient with aSAH. Important variables that must be included in the preoperative assessment include GCS, presence of focal-neurological deficit, intracranial pressure. In addition,
Patient must be assessed for hemodynamic stability, presence of acute lung injury, electrolyte abnormalities, and presence of invasive monitoring.

4. What laboratory or ancillary data would you like to review prior to anesthetizing this patient?

Electrolyte abnormalities (hyponatremia, hypomagnesaeemia, and hypokalemia) are commonly seen in patients with aSAH. ECG abnormalities include ST elevation, ST depression; QT dispersion, T wave inversion, and presence of U waves are not uncommon. Chest X-ray and arterial blood gases may reveal evidence of acute lung injury. [7]

All cerebral aneurysm-clipping procedure must have blood available in the blood bank. Frequently blood is typed and cross matched, and 2 units available in OR refrigerator, checked by the anesthesia provider.

5. What are the clinical features of aSAH?

The classical description of symptoms of aSAH is the sudden onset of severe headache. The patient may describe this as the “worst headache of my life.” Based on history alone the diagnosis can be difficult because the headache is actually described as developing instantaneously in only 50% of patients. Of those patients prospectively screened for acute severe headache only 6-17% were demonstrated to have SAH. Additional symptoms include seizure at the onset of haemorrhage (6%), transient loss of consciousness (26%) and vomiting preceding the onset of the headache (69%) [8].

The most common findings on neurological exam are depressed level of consciousness or a confusional state, a pupillary involving cranial nerve III palsy. Cranial nerve VI palsy may be a sign of elevated intracranial pressure. Findings on fundoscopic exam can include subhyaloid haemorrhage or papilledema.

6. Describe the anaesthetic induction of patients undergoing cerebral aneurysm clipping.

Anesthetic induction is performed with careful attention to ability to perform the mask ventilation and intubation. There are probability of clinical significant aspiration (0.05%) and rupture of aneurysm during intubation attempt (1-2%). Rupture of IC-aneurysm during induction carries at 75% mortality [9]

For most Hunt and Hess Grade I and II patients, preanesthetic use of divided doses of Midazolam or a calming pre-operative visit from the anaesthesiologist is often enough to alley anxiety. Most Grade III-V patients do not need pre-medication.

Smooth anesthetic induction with maintenance of stable transmural pressure [MAP-ICP], with avoidance of hypoxemia and hypercarbia, and use of adequate depth of anesthesia and paralysis is desired. Avoiding overzealous hyperventilation resulting in a precipitously drop of intracranial pressure, and avoidance of sympathetic (adequate analgesia, anesthesia, and use of iv Lidocaine; 1.5mg/kg, 90 seconds prior to laryngoscopy) may assist anesthesia providers to achieve this goal. Care must be taken to avoid decrease in MAP and thus cerebral perfusion pressure [10]

Care must be taken to prepare patient for a potential difficult intubation. Arterial catheter is often placed prior to anesthesia induction. Central venous assess catheters (to assess for need for intravascular volume, use of vasopressors, use of hypertonic / hyperosmolar agents) are placed after anesthetic induction [10-14]

7. Neurosurgeon requests EEG, MEP and SSEP monitoring. Describe the anesthetic implications of such neuro-monitoring.

Neurological monitoring to avoid significant post-operative neurodeficits requires careful planning, vigilance and execution from an anesthetic provider: While large doses of inhalational agents will abolish most evoked potentials, often a regimen of Isoflurane (mixture of 50% Oxygen + 0.5 MAC),coupled with either remifentanil or fentanyl and neuromuscular blocker infusion, is practiced. Common physiologic derangements that would impact neurological monitoring.
include hypoxia, hypotension, hypothermia and anemia.

8. During the dissection phase the neurosurgeon requests controlled hypotension, burst suppression, and use of transient cardiac standstill. Describe the anesthetic implications.

Controlled hypotension and induction of transient cardiac standstill is used to help neurosurgeons in cases of inadvertent rupture of an aneurysm during dissection. Burst suppression (2MAC Isoflurane / 4 MAC Sevoflurane or Propofol/ Thiopentone Sodium) is aimed to reduce the CMRO2 during temporary clip placement. Induced hypothermia may also be used to aid in reduction of CMRO2 [10].

Adenosine (0.29-0.44mg/kg IBW) can be used to attain transient cardiac standstill, and has been recently studied in patients with complex aneurysms, in whom temporary occlusion is impractical or difficult [15]. This dose results in a reduction of SBP less than 60 mm of Hg for a median of 57 seconds.

9. Describe the extubation technique.

The primary goals during emergence are to avoid coughing, straining, hypercarbia and wide fluctuations in blood pressure. Patient should be kept well oxygenated and residual neuromuscular blockade reversed. Intravenous Lidocaine{1.5 mg/kg} few minutes prior to extubation may minimize coughing. Sustained elevation of blood pressure is reduced pharmacologically e.g.; Beta blockers. In patient with multiple or unclippable aneurysms blood pressure should be kept within 20 % {120-160 mm of Hg} of normal.

10. Discuss the pathophysiology and management of cerebral vasospasm.

Cerebral vasospasm is one of the most commonest neurological complications resulting in significant mortality and morbidity after aSAH. Pathophysiology is complex[16, 17], and interplay between free oxygen radicals, nitric oxide, endothelins and eicosanoids, along with injury to peri-vascular nerves and detrimental effects of the inflammatory reaction induced by aSAH are suspected pathophysiologies. Vasospasm is prevented by use of nimodipine and transcranial Doppler ultrasound is commonly use to screen patients for evidence of elevated mean velocities, and Lindegaard ratios. Commonly used strategies in management of cerebral vasospasm include hypertension, hemodilution and hypervolemia. Cerebral angiography is used to confirmation and treatment using arterial vasodilators like verapamil and nicardipine.

11. What are the commonest medical complications of the aSAH?

Respiratory complications like hypoxemia, pneumonia (both aspiration and ventilator associated), pulmonary or neurogenic oedema, Cardiac complications including hemodynamic instability, myocardial injury and cardiac arrhythmias are also frequently encountered in patients following SAH. Hypotension or hypertension can be seen acutely. Elevation of the myocardial injury marker Troponin I is seen in 20-34% of patients on admission with SAH [18].

Systemic Inflammatory response, hyperglycaemia, hypomagnesaemia, hypokalemia and sodium disturbances both hyper or hyponatremia may present. Fever is commonly encountered in SAH patients and nearly doubles the risk of poor outcome [19]. Fever should be aggressively controlled in the setting of acute SAH utilizing anti-Pyretic agents or by surface or intravascular cooling if necessary.

Table 1. Hunt & Hess Grading Scale

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Unruptured aneurysm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Asymptomatic or minimal headache and slight nuchal rigidity</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Drowsy, confusion, or mild neurological deficit</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Stupor, moderate to severe hemiparesis</td>
</tr>
<tr>
<td>Grade 5</td>
<td>Coma, decerebrate posturing, moribund appearance</td>
</tr>
</tbody>
</table>
Table 2. World Federation of Neurological Surgeons Grading Scale

Grade 1 GCS 15, no motor deficit
Grade 2 GCS 13-14, no motor deficit
Grade 3 GCS 13-14, with motor deficit
Grade 4 GCS 7-12, with or without motor deficit
Grade 5 GCS 3-6, with or without motor deficit

Table 3. Fisher Grading Scale (Based on admission CT scan)

Grade 1 No blood visualized
Grade 2 Diffuse deposition or thin layer of blood with all vertical layers being less than 1mm thick
Grade 3 Localized clots and or vertical layers of blood greater than or equal to 1 mm thick
Grade 4 Diffuse or no subarachnoid

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Anaesthetic Management - Cervical Spine Injury

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Udupi

Objectives:
After preparing and participating in this PBLD, the participants will be able to:
1. Evaluate the patients with cervical spine injury
2. Describe the initial resuscitation of the patient with cervical spine injury
3. Describe radiological investigations and findings in patients with cervical spine injury
4. Evaluation and management of airway in cervical spine injuries
5. Describe anesthetic considerations in cervical spine surgery
6. Enlist spinal cord protection strategies
7. Post-operative management of patients with cervical spine injury

Model case:
A 25 year male, under the influence of alcohol, suffers a road traffic accident and is brought to the emergency department by bystanders. There is no history of loss of consciousness.

In emergency:
Patient is conscious, confused but responding to verbal commands. He complains of severe neck pain and difficulty in moving upper limb and lower limb. He is able to feel bladder sensation. He also complains of numbness of both upper and lower limbs. There is no history of difficulty in breathing.

Past history: no significant medical illness in the past
Personal history: occasional alcoholic
On examination: patient is conscious, confused GCS E4V4M6
Pupils – normal, bilaterally equal and reactive to light
Pulse rate 60/min, regular, BP 80/60 mmHg

RR 16/min
CNS examination: upper limbs shoulder 4/5, elbow flexion 3/5, extension 3/5, wrist 2/5
Lower limb all flexion/extension 4/5. DTR - Mild sensory loss in upper and lower limbs.

Emergency Room management
A 16G intravenous cannula secured in right upper limb and resuscitation with ringer lactate started. After 1L RL infusion patients vital signs stable. A hard collar was placed around the neck and patient was shifted to radiology suite for imaging.

CT scan findings: spiral CT revealed fracture of C-5 vertebral body with prolapsed intervertebral disc at C4-5 and C5-6 levels with severe compromise of spinal canal.

MRI: C5 vertebral body fracture with prolapsed disc at C4-5 and C5-6 levels with severe cord compression.

Laboratory parameters: Hb 11gm%. Other investigations normal.

Planned surgery:
Now the patient is planned for C5 corpectomy, C4-5 and C5-6 discectomy with spacer implantation and fixation of C4-C6 vertebral body by ANTERIOR CERVICAL APPROACH.

Key questions
1. How to evaluate a patient with suspected cervical spine injury?
2. How do you differentiate between complete vs. incomplete spine injury and how do you grade them?
3. How do you determine spinal cord stability?
4. What is primary and secondary injury?
5. What is neurogenic shock? Explain the components of neurogenic shock?
6. What are the radiological investigations carried out in patients with cervical spine injury? Mention the advantages of each.
7. What are the systems involved with cervical spine injury and how?
8. Explain the respiratory system involvement with each level of cervical spine injury.
9. What are the airway management options in patients with high cervical spine injury?
10. What is MILS? How do you perform it and what is the degree of movement of cervical spine with each airway maneuver?
11. What is the role of SUXA in airway management?
12. How do you prepare the airway for awake fiberoptic intubation?
13. What are the intraoperative considerations in cervical spine injury?
14. How do you provide neuroprotection intraoperatively?
15. Explain NASCIS 1, 2 and 3 trails and significance in clinical practice.
16. Do these patients are prone for hypothermia? Why? And how do you maintain the temperature?
17. How do you monitor spinal cord function intra-operatively? what is the influence of anesthesia on intraoperative neurophysiological monitoring?
18. What is “WAKE UP” test? How do you do it and what are the limitations?
19. What is the plan for postoperative analgesia? What are the options?
20. Explain management of post-op mechanical ventilation of cervical spine injury patients?
21. DVT prophylaxis of the patients with spine injury?

Considerations in cervical spine injury – Brief discussion

Introduction
Anesthesiologists are often involved in the initial resuscitation and management of trauma victims. The cervical spine injuries occur in 1.5-3% of all major trauma cases. The type of accidents include motor vehicle accidents (50-60%) and falls (6-10%). The incidence of cervical spine injuries is 1-3% in adults and 0.5% in children. At least 20% patients will have more than one cervical spine fractures. In traumatized patients 3-25% of spinal cord injuries occur during field stabilization, transit to hospital, or early course of therapy. Therefore it is extremely important to stabilize the spine in all trauma victims till cervical spine injury is ruled out.

Mechanism and classification of injury
Injuries of the cervical spine are generally caused by following mechanism:
1. Flexion
2. Flexion-rotation
3. Vertical compression
4. Extension
5. Extension rotation and
The three column concept of the structure of the vertebral body helps to clarify the mechanism of injury. The posterior column is formed by posterior neural tract, spinous process, facet joints and corresponding ligamentous complex. The middle column consists of posterior 1/3rd of the vertebral body, annulus fibrosus and posterior longitudinal ligament. The anterior column comprises of anterior 2/3rd of the vertebral body, and anterior longitudinal ligament.

Flexion injury causes disruption of posterior column whereas extension injury causes disruption of anterior column. The spine is said to be unstable if two or more columns are involved.

Pathophysiology of spinal cord injury
The spinal cord injury can be classified into primary and secondary injury. The primary injury is the result of initial impact leading to direct mechanical damage to the spinal cord, or hematoma formation and edema. The secondary damage can be manipulated and is due to preventable causes like hypoxia, increasing edema, and ischemia and due to release of excitotoxic amino acids. The details of pathophysiology are out of scope of this review and can be found elsewhere in literature.

Considerations in patients with spinal cord injury

1. **Immobilization of cervical spine**: All the patients with Polytrauma or severe traumatic brain injury should be suspected to have a spinal cord injury, until and unless proved otherwise. In a conscious patient, if he is able to lift his arm and keep it on chest, then generally cervical spine injury can be ruled out. Immediate immobilization should be done for the prevention of exacerbation of neurological injury in patients with unstable spine. A variety of devices are available for immobilization of the cervical spine, but none are considered to be gold standard. The most commonly used devices in the prehospital as well as hospital setting are hard and soft collars. Even these devices do not ensure complete immobilization of spine. Hard collars allow up to 72-73% of neck flexion and extension, whereas almost complete range of movements are possible with soft collars. Nevertheless a combination of a Philadelphia collar in combination with sand bags kept on either side of the neck with patient lying on a hard surface is the most effective way of patient transport in the prehospital setting. Manual in line stabilization (MILS) is the commonly used method to prevent cervical spine motion.
during laryngoscopy and endotracheal intubation in these patients.

2. **Airway management** in patients with spinal cord injury:

The potential for increased spinal cord injury due to increased movement during laryngoscopy makes the airway management in patients with suspected cervical spine injury more challenging one. Airway management in these patients depends on the condition of the patient. Patients with respiratory distress, apnea, GCS <9, high risk of aspiration should be intubated without any delay. In these patients endotracheal intubation can be done using direct laryngoscope, maintaining MILS. A variety of devices are available in the market, claiming lesser degree of cervical spine movement during endotracheal intubation. Few examples being air trach, bullard laryngoscope, true view, and videolaryngoscopes. Cost is a limiting factor for these devices and a considerable degree of expertise is required, before attempting intubation with these devices in emergency situations. In failed intubation scenarios, airway can be secured using percutaneous Cricothyroidotomy or a emergency tracheostomy can be performed.

In patients with an elective airway, where no emergency intubation is required, awake fiber-optic intubation can be performed under local anesthesia. It has shown to be effective in patients with cervical spine injuries.

3. **Neurogenic shock**: neurogenic shock is seen in nearly 50-90% of high cervical spinal cord injuries. The loss of sympathetic tone to the heart and blood vessels leads to profound vasodilatation, leading to hypotension. Bradycardia can happen due to unopposed parasympathetic (vagal) activity of the heart. Thus the patients with cervical spine injuries are more prone for bradycardia during endotracheal suctioning and positioning. The hypotension that results from neurogenic shock places patients at increased risk of secondary spinal cord ischemia due to impairment of autoregulation. Though the terms are sometimes used interchangeably, neurogenic shock describes the hemodynamic changes following SCI, whereas spinal shock is characterized by a reversible reduction of sensory, motor, or reflex function of the spinal cord below the level of injury.

Neurogenic shock is a diagnosis of exclusion, but is generally characterized by hypotension
and relative bradycardia. The skin is warm and flushed initially due to profound vasodilatation and patients are at high risk of developing hypothermia. Immediately following injury, patients may develop hypertension due to increased sympathetic discharge. The hypotension may follow later.

**Management:** Decreased systemic vascular resistance (SVR) results in a relative Hypovolemia, thus increased venous capacity, and isotonic fluid administration is often necessary. However hypotension due to decreased SVR is often refractory to intravenous fluid infusion. In Polytrauma patients, all hypotension should not be labeled as neurogenic shock, as associated organ injury may lead to hematoma and hypotension. If hypotensive patients have normal chronotropy and inotropy, then an alpha-1 agonist acting as a peripheral vasoconstrictor such as phenylephrine is indicated. Norepinephrine may also be considered, as it has alpha-1 and beta-1 agonistic activity. College of neurological surgeon recommend the mean arterial pressure to be kept >85 mmHg for 7 days following spinal cord injury. Neurogenic shock often persists for 1-6 weeks following spinal cord injury. In chronic phase the patients develops autonomic hyperreflexia and orthostatic hypotension.

4. **Pharmacological spinal cord protection:** Methyl prednisolone (MP) is the commonly used agent in the protection of spinal cord. It is commonly used in a dose of 30 mg/kg over 15-30 minutes, followed by an infusion of 5.4 mg/kg/hr for the next 23 hours. Though the evidence for the use of MP is conflicting, still it is the commonly used agent for spinal cord protection.

<table>
<thead>
<tr>
<th>Trial</th>
<th>NASCIS 1</th>
<th>NASCIS 2</th>
<th>NASCIS 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Multicenter, randomized, double blind</td>
<td>Multicenter, randomized, placebo controlled, double blind</td>
<td>Multicenter, randomized, double-blind study</td>
</tr>
<tr>
<td>No. of patients</td>
<td>330</td>
<td>487</td>
<td>499</td>
</tr>
<tr>
<td>MP dose</td>
<td>100 mg/d <em>10 days or 1000 mg/d</em> 10 days</td>
<td>MP vs. naloxone 5.4 mg/kg bolus plus 4 mg/kg/hr infusion</td>
<td>MP 24 VS. 48 hours with Tirilazad mesylate with MP</td>
</tr>
<tr>
<td>Results</td>
<td>No difference in neurological recovery</td>
<td>Slight but significant improvement in neurological function</td>
<td>MP 48 hours better neurological recovery</td>
</tr>
<tr>
<td>Side effects</td>
<td>Risk of infection is significantly higher in high dose MP group</td>
<td>Increased risk of infection in MP patients</td>
<td>High risk of pneumonia in MP 48 hours</td>
</tr>
<tr>
<td>Drawbacks</td>
<td>No placebo group in the study</td>
<td>Flawed data Subgroup analysis lacked demographic data</td>
<td>Disparity in the motor function in the groups</td>
</tr>
</tbody>
</table>

Based on the above data it is difficult to advocate routine use of MP for spinal cord injury patients. American association of neurological surgeons, at a consensus conference recommended MP for 24-48 hours, as a treatment option in acute spinal cord injury with a note of caution about the high risk of side effects.
Other drugs for spinal cord protection

- Atorvastatin
- Omega-3 Polyunsaturated fatty acid
- Fenretinide
- Erythropoietin
- Progestron
- Inosine
- Rho Inhibitors – Cethrin
- Rolipram
- Calpain inhibitors
- Folic acid
- Pioglitazone

5. **Autonomic hyperreflexia**: autonomic hyperreflexia is a medical emergency, usually seen in spinal cord injuries above the level of T5 (85% of patients). The phenomenon occurs with recovery from neurogenic shock. Autonomic Dysreflexia results from widespread reflex activity of the sympathetic nervous system below the level of injury, triggered by an ascending sensory (usually noxious) stimulus. Following stimulation, overactivity of sympathetic ganglia remains uncontrolled due to isolation of the spinal cord below the injury from normal regulation by vasomotor centers in the brainstem. Release of substances such as noradrenaline and dopamine cause severe vasoconstriction with skin pallor, piloerection and a sudden rise in blood pressure which is usually accompanied by a pounding headache. Parasympathetic activity above the level of SCI occurs when the rise in blood pressure is sensed by baroreceptors in the aortic arch and carotid bodies, resulting in compensatory bradycardia (via the vagus nerve).

### Symptoms and signs of autonomic hyperreflexia

- Sudden Hypertension
- Pounding Headache
- Bradycardia
- Flushing / blotching of skin above spinal injury level
- Profuse sweating above spinal injury level
- Skin pallor and piloerection below spinal injury level
- Chills without fever
- Nasal congestion
- Blurred vision (dilatation of pupils)
- Shortness of breath, sense of apprehension or anxiety
- Irritability or combative behaviour (in people with limited cognitive and communication skills)

**Treatment**: If symptoms persist or blood pressure remains elevated following the above efforts or a cause cannot be readily identified, pharmacological treatment with a short acting anti-hypertensive medication should be commenced concurrently with the search for and treatment of the noxious stimulus. The inciting stimulus should be stopped. If a bladder catheter block is suspected, it can be gently flushed with saline.
6. Systemic changes following cervical spine injury

a. Respiratory system: The severity of respiratory changes following cervical spine injury depends on the level of injury.

<table>
<thead>
<tr>
<th>Level of injury</th>
<th>Diaphragm function</th>
<th>Coughing ability</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above C3 level</td>
<td>--</td>
<td>--</td>
<td>With no diaphragm function and inability to cough patient will be dependent on ventilator</td>
</tr>
<tr>
<td>C3-5 level</td>
<td>+/-</td>
<td>+/-</td>
<td>The severity of the symptoms depends on the residual function of diaphragm. Patient may be able to breathe and weak cough may be present. Any infection may decompensate respiratory function</td>
</tr>
<tr>
<td>Below C5 level</td>
<td>++</td>
<td>++</td>
<td>Generally below C5 level of injury respiratory functions are well preserved. Intercostal muscles are still paralyzed, affecting the coughing ability particularly in presence of infection.</td>
</tr>
</tbody>
</table>

In addition pulmonary edema and pulmonary embolism may also affect the respiratory function. Pulmonary edema may be because of overenthusiastic fluid administration for correction of hypovolemia in presence of neurogenic shock. Neurogenic pulmonary edema is also possible because of surge of catecholamines following cervical spine injury. Patients with maximal expiratory force <20 cmH2O, negative inspiratory force <20 cmH2O and, vital capacity <15 ml/kg, generally require endotracheal intubation and mechanical ventilation.

b. Cardiovascular system: The common cardiovascular system abnormalities following spinal cord injury are neurogenic shock and autonomic hyperreflexia (discussed above). The degree of bradycardia and hypotension depends on the level of injury. During acute phases of sympathetic surge immediately following the trauma, myocardial injury can occur leading to myocardial infarction. Autonomic hyperreflexia is an acute medical emergency and should be treated as early as possible.

c. Deep vein thrombosis (DVT): The risk of deep vein thrombosis is very high in patients with cervical spine injury. Majority of the patients require prophylactic anticoagulants for the prevention of DVT. The anticoagulation should be initiated as early as possible, but the associated injuries which can increase the risk of bleeding should be carefully ruled out before starting the patients on anticoagulants. In patients where anticoagulation is contraindicated, intermittent pneumatic compression devices may be used to prevent DVT.

d. Temperature control: Vasodilatation due to sympathetic paralyses leads to increased heat loss below the level of lesion. Hence temperature should be monitored in the peri-
operative period to prevent risk of hypothermia.

e. **changes in skeletal muscles:** quadriplegia following spinal cord injury leads to gross wasting of the muscle mass. Proliferation of atypical acetyl cholinesterase receptors occurs over the entire muscle membrane. Use of depolarizing muscle relaxants like succinyl choline may lead to massive efflux of potassium. Hence succinyl choline should not be used in these patients after 24-48 hours after injury. Spasticity of the muscle develops after the phase of spinal shock and generally lasts about for 3-4 months. Spasms can be provoked by minor stimuli and can be violent and painful. Baclofen and dantrolene can be used to relieve spasticity.

f. **other changes:** blood volume is often reduced in spinal injury patients. normocytic hypochromic anemia is common in these patients. basal metabolic rate is reduced in patients with cervical spine injury. The low metabolic rate reduces the production of CO2, hence lower minute ventilation will be required to maintain eucapnia. Infections are the most common cause of mortality in these patients. Due to prolonged ventilation and urinary catheterization, these patients are prone for pneumonia and urosepsis.

**References**

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